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Aims and Scope

Neurospine provides spine clinicians and researchers with peer-reviewed articles on basic and clinical investigation of spine and spinal cord to enhance patient management, education, clinical or experimental research, and professionalism. The journal will consider submissions in areas on craniocervical to lumbosacral spine including the followings: neuroscience and pain research, bone and mineral research, disc and joint research, bio and industrial technology, pathophysiology, risk factors, symptomatology, imaging, treatment, rehabilitation of spine, spinal cord and peripheral nerve diseases. Specifically, basic and technology researches include the most influential research papers from all fields of science and technology, revolutionizing what physicians and researchers practicing the art of spinal neurosurgery worldwide know. Thus, we welcome valuable basic and translational technology research articles to introduce cutting-edge research of fundamental sciences and technology in clinical spinal neurosurgery. Clinical or basic research articles, review articles, case reports, technical notes, and letters to the editor written in English will be accepted.

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Essay

Brief History of Neurosurgical Spine Societies in the United States: Part 2

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In a previous essay,[1] we examined the intertwined history of United States (US) spine surgery pioneers and achievements, and the emergence of domestic spine societies. In this follow-up article, we look towards the future and highlight the critical role of US spine societies in *education*, *research*, and *advocacy*.

Advancing spine care through *education* is a priority of larger US spine societies. The American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) Section on Disorders of the Spine and Peripheral Nerves (DSPN) was the first neurosurgical spine society in the US. The leadership for the annual spine section meeting from 2010–2021 is listed in Fig. 1. The first meeting of the DSPN chaired by Barth Green and George Sypert in 1985 included lectures and hands-on courses in spinal instrumentation to address the educational needs of a growing subspecialty of neurosurgery focused primarily on spine surgery. The DSPN annual meeting has since evolved from a small intimate group to a larger meeting of > 500 domestic and international spine surgeons presenting innovative research, case-based debates, subspecialty symposia, intersociety panel discussions, and surgical technique cadaver labs. Since 2016, the DSPN bestows the Journalistic and Academic Neurosurgical Excellence Award to the senior neurosurgical resident or fellow in an American neurosurgical program that has been academically productive in the previous 12 months and has achieved the top manuscript submitted to the annual DSPN Spine Section meeting (Table 1). Similarly, the Charles Kuntz Scholar awards the top neurosurgical residents or fellows who author outstanding abstracts (Table 2). The rapidly growing number of residents and fellow trainees attending this meeting signifies the critical role of spine societies in not only educating current members, but mentorship and professional development of the next generation of spine surgeons.

Looking to the future, advancing technology may change the way in which education is delivered by societies. Neurosurgery and spine societies in the US have developed robust online educational opportunities. Examples include CNS NEXUS (a repository of neurosurgical operative techniques and approaches), The Neurosurgical Atlas, NASS video library, AO spine webinars, videos, and podcasts. Content is created and/or curated online by experts in their respective fields. *The Neurosurgery Podcast* by Michael Wang and John Kolcun is an example of a popular weekly audio program with guest neurosurgeons sharing expertise in the field of neurosurgery and spine. The clear benefit of digital media is the ability to provide education that is not limited by conventional constraints of geography and travel costs. Further, online education can often be accessed easily via mobile technology

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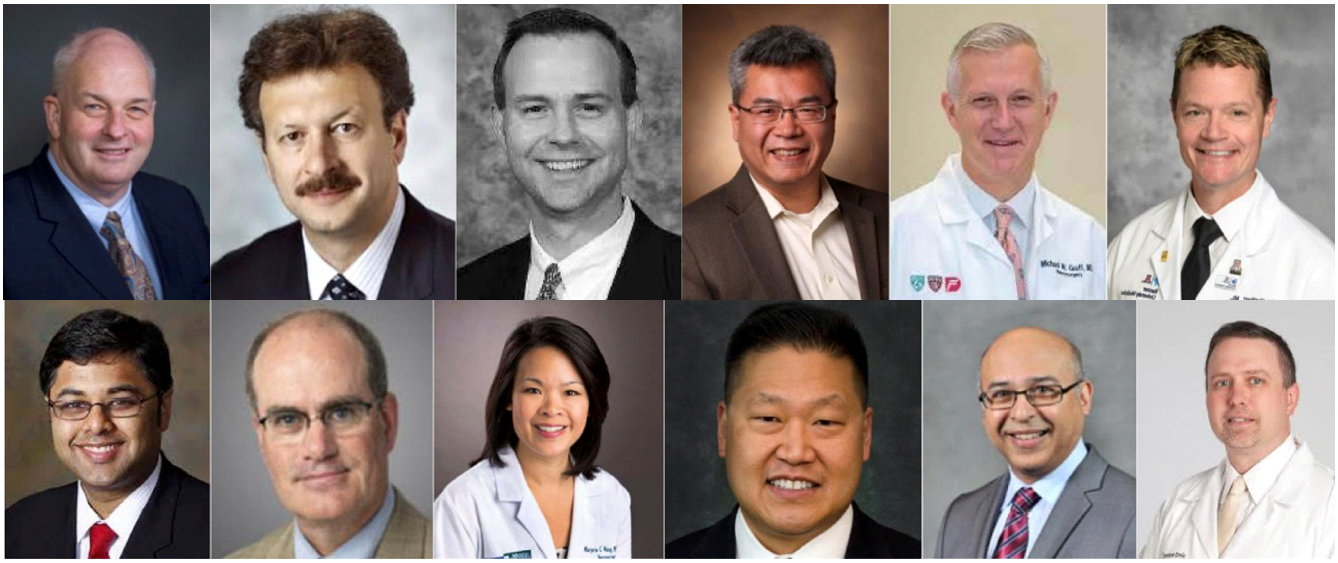

Fig. 1. Disorders of the Spine and Peripheral Nerves (DSPN) Chairperson 2010–2021. Top row from left to right 2010–2015 DSPN Chairpersons: Christopher Shaffrey, Ziya Gokaslan, Christopher Wolfa, Joseph Chang, Michael Groff, R. John Hulbert. Bottom row from left to right 2016–2021 DSPN Chairpersons: Praveen Mummaneni, John Knightly, Marjorie Wang, Micheal Wang, Zoher Ghogawala, Michael Steinmetz.

Table 1. J.A.N.E. Award winners 2016–2020

Year	J.A.N.E. Award winner
2016	Scott L. Parker
2017	Owoicho Adogwa
2018	Nitin Agarwal
2019	Andrew Chan
2020	Jetan H. Badhiwala

J.A.N.E., Journalistic and Academic Neurosurgical Excellence.

and when convenient based on the learner's schedule.

The ongoing coronavirus disease 2019 pandemic has accelerated recent adoption of teleconferencing by spine societies and members. The absence of in-person meetings in 2020 and the potential for lingering travel restrictions for the foreseeable future may further establish digital media as a viable educational outlet. Despite these advantages of online education, a notable loss is the important camaraderie of shared experiences that occurs with live, in-person meetings and events. This social aspect of in-person meetings was clearly a cherished quality dating back to the first DSPN meeting in 1985 and should be preserved moving forward.

In addition to education, *research* is an integral mission of spine societies. Societies have established funds through charitable donations, and annual meeting and corporate sponsorship revenue to support researchers with grants and fellowships. A clear priority of spine society supported research is advancing clinical spine care through clinical trials, comparative effectiveness research, and evidence-based guidelines. As healthcare costs in the US continue to rise, comparative effectiveness and patient-centered outcomes research have increasing importance in informing surgeon practice. Six of the 100 national priorities identified by the Institute of Medicine relate directly to spine surgery.[2-4]

As a result, spine societies have partnered to create surgical registries to objectively measure and demonstrate quality of care. These nation-wide registries collect longitudinal patient reported outcome measures to identify clinical efficacy for various surgical interventions and indications. A pioneering example in neurosurgery was the National Neurosurgical Quality Outcomes Database (originally N2QOD, now QOD). The spine registry component of QOD has accumulated over 25,000 patients across >50 sites and has accounted for numerous research presentations and publications.[5] More recently, the AANS and the American Academy of Orthopaedic Surgeons have partnered to create the American Spine Registry, which will incorporate QOD into a broader platform involving neurosurgery and orthopedics.[6] Neurosurgeons and orthopedic spine surgeons have a shared interest in advancing spine clinical care, and joint collaborative registries are an opportunity to increase study populations across a spectrum of practice patterns. An important directive in the near future is to increase our knowledge base

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Table 2. Charles Kuntz Award winners 2016–2020

Year	Charles Kuntz IV Scholars	
2016	Nitin Agarwal	Michael Mcdowell
	Andrew Chan	Catherine Miller
	Ekamjeet Dhillon	Nelson Moussazadeh
	Doniel Drazin	Rory Murphy
	Benjamin Elder	Tianyi Niu
	Gurpreet Gandhoke	Aria Nouri
	Ezequiel Goldschmidt	Alp Ozpinar
	Randall Graham	Brenton Pennicooke
	Kiyoshi Ito	Kavelin Rumalla
	Ricky Kalra	David Salcetti
	Darryl Lau	Hesham Soliman
	Rory Mayer	Zachary Tempel
	Marcus Mazur	Alexandar Tuchman
	Todd Vogel	Anand Veeravagu
2017	Vincent Alentado	Michael Karsy
	Michael Cloney	Evan Lytle
	Doniel Drazin	Allan Martin
	Benjamin Elder	Meghan Murphy
	Rory Goodwin	Aria Nouri
	Peter Grunert	Vijay Ravindra
	Daipayan Guha	Ahilan Sivaganesan
	Ibrahim Hussain	Vijay Yanamadala
	Christian Iorio-Morin	Michael Yang
		Scott Zuckerman
2018	Mark Attiah	Darryl Lau
	Yi-Ren Chen	Jay Nathan
	Lee Chieng	Tianyi Niu
	Michael Cloney	Imran Noorani
	Shashank Gandhi	Eric Sankey
	Jakub Godzik	Ganesh Shankar
	Jian Guan	Corey Walker
	Allen Ho	Vijay Yanamadala
	Ibrahim Hussain	Juneyoung Yi
	Katie Krause	Hesham Zakaria
2019	Owoicho Adogwa	Anthony Mikula
	Mohammed Alvi	Aria Nouri
	Oliver Ayling	Zachary Sanford
	Andrew Chan	Allison Teles
	Islam Fayed	Zoe Teton
	Shashank Gandhi	Jamie Wilson
	Jack Haglin	Michael Yang
	Allen Ho	Hesham Zakaria
	Sertac Kirnaz	Scott Zuckerman
	Mohamed Macki	
2020	Oliver Ayling	Anshit Goyal
	John Burke	Michael Karsy
	Andrew Chan	Mena Kerolus
	Ken Chang	Darryl Lau
	Lee Chieng	Allan Martin
	Samuel Farber	Anthony Mikula
	Nida Fatima	Harry Mushlin
	Yaroslav Gelfand	Roberto Perez Roman
	Jakub Godzik	Checai Wang
	Jacob Hoffman	Michael Yang

from information garnered via these registries that ultimately translates to improved patient care.

Last, *advocacy* has emerged as a critical mission of spine organizations to ensure patient access to spine surgical care. Spine societies advocate for patients and surgeons through guidelines taskforce committees, payor response committees, and the AANS/CNS Washington Committee. The undue pressures of the current healthcare climate often render individual spine surgeons unable to adequately express their concerns. The AANS/CNS Washington Committee serves as an important voice representing neurosurgeons and spine surgeons before the government and policymakers on issues related to accessibility of care, reimbursement, and health policy. Current initiatives include addressing unnecessary prior authorization practices by insurance companies, serving as surgeon representatives on common procedural terminology coding committees, confronting medical liability reform, and the creating of guidelines to standardize practice. With the increasing healthcare economic burden in the US, it is imperative for spine societies to serve as advocates protecting spine surgeons and their ability to continue to deliver quality care.

In his 2010 CNS presidential address, Gerald "Rusty" Rodts[7] emphasized that if we "do not improve the medical evidence for our treatments, and if we do not improve our training process to better standardize the rates and indications for spinal surgery, the federal government and private insurers will certainly redefine how we care for patients." Led by spine surgeons, spine societies are at the forefront of education, research, and advocacy. With the uncertain healthcare landscape, spine societies will continue to have a central role in supporting US spine surgeons and advancing spine surgical care.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Review Article

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Novel Methods of Necroptosis Inhibition for Spinal Cord Injury Using Translational Research to Limit Secondary Injury and Enhance Endogenous Repair and Regeneration

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Spinal cord injuries (SCIs) pose an immense challenge from a clinical perspective as current treatments and interventions have been found to provide marginal improvements in clinical outcome (with varying degrees of success) particularly in areas of motor and autonomic function. In this review, the pathogenesis of SCI will be described, particularly as it relates to the necroptotic pathway which has been implicated in limiting recovery of SCI via its roles in neuronal cell death, glial scarring, inflammation, and axonal demyelination and degeneration. Major mediators of the necroptotic pathway including receptor-interacting protein kinase 1, receptor-interacting protein kinase 3, and mixed-lineage kinase domain-like will be described in detail regarding their role in facilitating necroptosis. Additionally, due to the rapid accumulation of reactive oxygen species and inflammatory markers, the onset of necroptosis can begin within hours following SCI, thus developing therapeutics that readily cross the blood-brain barrier and inhibit necroptosis during these critical periods of inflammation are imperative in preventing irreversible damage. As such, current therapeutic interventions regarding SCI and targeting of the necroptotic pathway will be explored as will discussion of potential future therapeutics that show promise in minimizing long-term or permanent damage to the spinal cord following severe injury.

Keywords: Necroptosis, Spinal cord injury, Regenerative medicine, Endogenous repair, Neuronal cell death

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INTRODUCTION

Spinal cord injuries (SCIs) present with a litany of sequelae and long-term complications including loss of motor function, loss of organ and autonomic function, increased risk of pressure ulcers and pain, and even death.[1,2] Over the last several decades, advancements in approach and treatment of spinal cord injury (SCI) has led to recovery of the aforementioned functions in some cases (though to varying degrees of success).[3-5] Initially, treatment was designed to attenuate secondary tissue damage as a result of the cascade of pathophysiological processes following the primary damage to neural tissue, which will be described in more detail below.[6] This included pharmacotherapeutic interventions such as corticosteroids which were utilized due to their anti-inflammatory properties and perceived reduction in spinal cord edema, minimizing secondary damage.[7,8] The National Acute Spinal Cord Injury Studies were then conducted to evaluate the efficacy of various doses of methylprednisolone (and later testing the efficacy of the lazaroid tirilazad mesylate as well) in treating SCI.[9,10] Although

these studies standardized the use of these pharmacotherapies in the clinical practice of SCI, later criticism of these interpretations included the level of recovery of previously lost motor and sensory functions and potential for further damage as a result of methylprednisolone administration.[11-14]

Systemic ganglioside administration of monosialotetrahexosylganglioside (Sygen, Fidia Pharmaceutical Corp., Washington, D.C., USA) has also been proposed as a potential treatment of SCI due to its neuroprotective effects including inhibition of apoptosis and excitotoxicity and increases in neuroplasticity and neurite outgrowth.[15-17] Primary efficacy results could not associate GM1 with marked recovery compared to placebo, however, improvements in motor, sensory, and autonomic function were noted in patients with incomplete paraplegia.[18] Beyond GM1 administration, opioid antagonists have been implicated as a potential therapeutic in SCI to antagonize the rise of endogenous opioids following injury as shown in the literature.[19,20] However, a 5.4-mg/kg intravenous bolus of naloxone followed by a 4-mg/kg 23-hour infusion of naloxone was not found to confer any therapeutic benefit.[21] Additional studies examined the benefit of ion channel antagonists. Calcium channel blockers have been theorized to reduce the pathologic influx of calcium into cells following SCI, while also enhancing blood flow to the spinal cord and reversing hypoperfusion, presenting 3 potential mechanisms of action in the pathophysiology of SCI.[22,23] A therapeutic benefit in a patient population could not be established and risks of systemic hypotension were noted.[24] Finally, cyclooxygenase inhibitors have been investigated as the role of inflammatory prostaglandins mediating secondary injury in SCI can serve as a potential therapeutic target.[25] Studies in animals showed maintenance of blood flow to the spinal following cyclooxygenase-2 inhibition via ibuprofen and meclofenamate, however there is a lack of literature conferring on these findings in humans.[26]

Beyond the aforementioned approaches to treating SCI, there are cell therapeutics and nanotechnologies currently being tested with an emphasis on nerve regeneration, including remyelination, axon regeneration, and ultimately the recovery of previously lost nerve function.[4,27,28] One of these approaches involves the use of bone marrow mesenchymal stem cells (BMSCs). Although still in the experimental phase, studies have shown implantation of BMSCs can promote axonal regeneration while limiting immunomodulation, glial scarring, and apoptosis.[4,5] Additional studies are needed regarding long-term complications and efficacy in utilizing these treatments.[29-32] The results of these studies further emphasize the need to investigate alternative molecular pathways and therapeutics to effectively treat, and ultimately cure SCI.

The objective of this study is to analyze novel methods presented in the current literature that is utilized in the inhibition of necroptosis. Further, we wish to investigate the efficacy of these methods in limiting secondary injury.

SPINAL CORD INJURY

1. Mechanism of Action

The most common primary causes of SCI involves the load of a mechanical impact on the spine in which the force of this impact causes disruption and damage to the spinal cord, referred to as impact with either transient or persistent compression (Fig. 1).[6,33-35] Another primary mechanism of SCI is referred to as distraction which involves stretching and shearing of the spinal column in the axial plane, potentially leading to hemorrhage of the spinal cord vascular supply.[35] Laceration and transection are similar to distraction injuries as they too can lead to hemorrhage of the vascular supply, however in these particular cases, damage typically occurs as a result of sharp fragmentation or severe distraction leading to more significant pathology.[35] This is because laceration and distraction are found to occur with significant trauma and a greater disruption to the vascular supply.[35]

Regardless of the mechanism of primary insult incurred, secondary changes readily follow without immediate intervention which includes axonal degeneration and demyelination that can propagate both in an anterograde (Wallerian) and retrograde manner, affecting both the grey and white matter.[33,36,37] Further, acute hemorrhage can rapidly progress to necrosis of the affected regions, with proinflammatory markers and cytokines including interleukin (IL)-1 beta, tumor necrosis factor-alpha (TNF-α), and IL-6 released at the site of injury via the activation of microglia.[34,38] This is followed by production of reactive oxygen species (ROS), including lipid peroxidation leading to axonal disruption and neuronal/glial death via cell lysis and organelle dysfunction of the aforementioned cells[39,40] and ischemia associated with ROS production.[34] This necrosis and cell death is exacerbated by dysregulation of ionic homeostasis (particularly calcium) and excitotoxicity from excess activation of glutamate receptors at the site of injury.[41,42] Cytotoxicity of astrocytes peripheral to the lesion site confers hypertrophy and proliferation of these astrocytes, leading to an increase in expression of glial fibrillary acidic proteins that coalesce and interweave to form a glial scar which presents as a significant barri-

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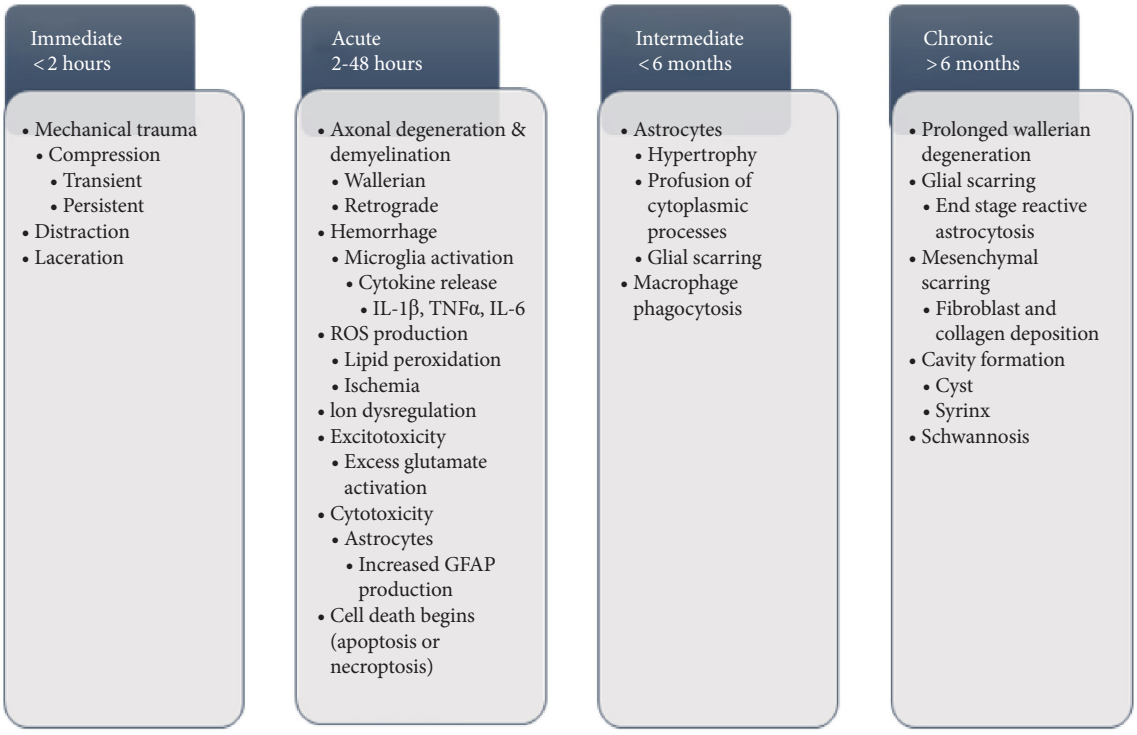

Fig. 1. Progression of spinal cord injury through various critical time points of damage with key molecular and physiological processes noted.[34,46] IL-1β, interleukin-1 beta; TNF-α, tumor necrosis factor-alpha; GFAP, glial fibrillary acidic protein.

er to axonal regeneration and another potential therapeutic target.[43-45]

2. Necroptosis

Necroptosis is a caspase-independent process that is instead dependent on receptor-interacting serine/threonine kinase 3 (RIPK3) (described in detail below) in which cellular contents are not neatly packaged into apoptotic bodies.[46] In the case of SCI, studies show that necroptosis presents—along with apoptosis—as the primary forms of programmed cell death in the spinal cord following traumatic injury.[47,48] However, the relationship between these 2 forms of cell death may be more intertwined than initially presumed. Prior studies have described apoptotic death of oligodendrocytes as a result of microglial activation in cases of SCI, as microglial secretion of TNF-α can trigger the apoptotic pathway.[49] However, if upstream signaling is insufficient to trigger apoptosis, TNF-α can instead activate TNF receptor 1 (TNFR1) thus inducing recruitment of receptor-interacting protein kinase 1 (RIPK1) and triggering the necroptotic pathway.[48] Necroptosis can be initiated by a multitude of other signaling pathways as well including death receptors, protein kinase R, DNA-dependent activator of interferon regulatory factors, pattern recognition receptors (PRRs), in addition to TNF signaling which includes RIPK1/3.[50-52] Cells undergoing necroptosis release their contents into the extracellular space upon death, propagating a proinflammatory state and further cell damage by triggering innate and adaptive immune responses.[53,54] In this proinflammatory state, disruptions in barrier cell integrity allows for microbe invasion leading to recognition of their pathogen-associated molecular patterns (PAMPs) by PRRs that induce the expression of both cytokines and chemokines, including cytokines IL-1α and IL-33, as well as the S100 proteins S100A8, S100A9, and S100A12, which in turn can trigger the death of adjacent cells, propagating a feedback loop that results in non-resolving states of inflammation.[54] *In vivo* studies show in the necroptotic state there is excessive release of damage-associated molecular patterns (DAMPs) from these dying cells which may consist of cellular organelles and components such as mitochondria or F-actin, HMGB1, as well as nucleic acids, ribonucleoproteins, adenosine triphosphate (ATP), or histone proteins as examples.[55] These DAMPs are recognized by PRRs to induce expression of additional cytokines and chemokines, exacerbating the inflammation initially induced by PAMP recognition.[55,56] Inhibiting this necroptotic inflammatory process may be key to attenuating secondary damage and maximizing therapeutic benefit and recovery by

limiting cell death.[47,48]

3. Receptor-Interacting Protein Kinase 1

RIPK1 is an important effector downstream of death receptors and PRRs that govern prosurvival, apoptotic, and especially, inflammatory necroptotic pathways. Thus, much interest has focused on therapeutically targeting RIPK1 in the context of numerous inflammatory diseases. Multiple small molecule inhibitors of RIPK1 have demonstrated protective effects in mouse models of autoimmune or inflammatory disease. These studies were primarily conducted using molecular analogues of necrostatin-1 (Nec-1), which was originally identified in a chemical compound screen. Since then, other chemical families have been identified to inhibit RIPK1, several of which have excellent blood-brain barrier permeability, offering opportunities to address neuroinflammatory central nervous system (CNS) conditions.[47] Several of these inhibitors are currently in phase I and/or II clinical trials by Denali Therapeutics and GlaxoSmithKline, primarily for the treatment of Alzheimer disease (AD) and amyotrophic lateral sclerosis (ALS).[48] Notably, the compound DNL788, a novel brain-penetrant RIPK1 inhibitor, was recently announced by Denali in partnership with the Sanofi biopharmaceutical company to initiate clinical testing in 20201 for neurodegenerative indications.[49] Combination therapy with RIPK1 inhibitors is also feasible and has, in several instances, demonstrated benefit.[50,51] For example, Cougnoux et al.[51] showed that treating mouse models of Niemann-Pick disease type C1 with a combination of the RIPK1 inhibitor GSK547 and the compound HPβCD, which slows neurological decay, resulted in delayed loss of Purkinje neuron density. The neuroprotective value of combination therapies involving RIPK1 inhibitors has not been extensively evaluated in a clinical setting yet represent a promising practical approach toward limiting neurological damage, such as in SCI.

On a molecular level, the activation of RIPK1 has been most studied in the context of TNF signaling via its activation of TNFR1. Binding of TNFR1 to TNF leads to recruitment of RIPK1 via its death domain, which results in the activation of the proapoptotic caspase-8. Typically, caspase-8 inhibits RIPK1-mediated necroptosis, resulting in apoptotic progression; however, when caspase-8 is inhibited, RIPK1 recruits RIPK3 and mixed-lineage kinase domain-like (MLKL), leading to necroptosis.[52] Under *in vitro* conditions, necroptosis is typically elicited artificially by treating cells with a combination of TNF and a pan-caspase inhibitor, which raises the question as to in what *in vivo* contexts necroptosis plays a role. Despite this, studies have demonstrated that abrogation of RIPK1 kinase activity, either pharmacologically or genetically, in mouse models of AD, ALS, and multiple sclerosis (MS) were neuroprotective.[53] In the context of SCI, the role of RIPK1 has not been as comprehensively elucidated. However, given the shared pathophysiological mechanisms between SCI and other neurodegenerative diseases, targeting RIPK1 may prove effective.

Several lines of evidence strongly implicate necroptosis and RIPK1 in the pathogenesis of SCI. First, in the context of MS and ALS, RIPK1 has been shown to contribute to oligodendrocyte dysfunction, causing axonal demyelination.[53] Interestingly, oligodendrocytes are one of the few cell-types that engage necroptosis downstream of TNFR1 signaling without the necessity of caspase inhibition, suggesting these cells may be inherently primed to engage the inflammatory necroptotic pathway.[54] In the context of SCI, oligodendrocyte necroptosis and death impairs axonal function and exacerbates pathology.[55] Therefore, beyond MS and ALS, RIPK1 inhibition may reduce oligodendrocyte dysfunction and improve axonal survival following SCI. Second, apart from inducing cell death, RIPK1 activation also promotes the production of proinflammatory cytokines, notably by myeloid cells such as CNS-resident microglia. In SCI, microglia have been posited to contribute to various aspects of pathogenesis, however, these findings are complicated by (1) the involvement of both microglia and its related myeloid cell-type, monocyte-derived macrophages (MDMs), and (2) the dual capacity for microglia to be neurotoxic and neuroprotective.[56] Despite this, since RIPK1 is critically involved in the inflammatory, neurotoxic activities of both microglia and MDMs in CNS disease, it remains a target with therapeutic promise. Accordingly, Fan et al.[57] in 2015 showed that Nec-1 treatment of mice with SCI reduced the SCI-induced increase in microglia/macrophage cell death. Lastly, RIPK1-mediated necroptosis in astrocytes has also been shown to contribute to SCI. Generally, astrocytes have protective, neurotrophic roles in SCI.[58,59] In a separate publication, Fan et al.[60] also showed that microglia/macrophages in SCI can induce astrocyte necroptosis, diminishing their neuroprotective effects. In SCI mice, depletion of microglia resulted in higher numbers of live astrocytes and treatment with Nec-1 decreases astrocyte necroptosis as well as increases neuronal cell number. Generally, 3 studies have most directly evaluated the potential of RIPK1 inhibition, specifically with Nec-1, as a treatment for SCI.[61-63] The treated SCI mice with Nec-1 and demonstrated a reduction in neuronal death and grey matter lesion area.[61-63] More detailed inspections of post-SCI Nec-1-treated neurons showed reduced apoptosis, necroptosis, and oxidative stress as well as improved mitochondrial function.[61-63]

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From a behavioral standpoint, Nec-1-treated mice also displayed quicker motor recovery and better open-field mobility following recovery.[61-63] Overall, RIPK1 exhibits pleiotropic effects contributing to the exacerbation of SCI and sufficient evidence supports the therapeutic utility of RIPK1 inhibitors.

4. Receptor-Interacting Protein Kinase 3

Receptor-interacting protein kinase 3 (RIPK3) is a member of the RIP family. Similar to RIPK1, RIPK3 can trigger necrosis independently. However, most of its known functions have been studied when its works in conjunction with RIPK1.[64] RIPK1 and RIPK3 interact with each other via the RIP homotypic interaction motif which leads to formation of the necrosome that activates downstream effector proteins to elicit the above-mentioned necroptosis pathway and inflammatory response.[65] In mice, RIPK3 expression is elevated just 24 hours after spinal cord hemisection.[66] An increase in RIPK3 has been shown to contribute to cell loss via its necroptotic pathway. This is the fundamental component leading to neurodegenerative diseases in SCI patients.[67] In addition to its necroptotic properties, RIPK3 can activate caspase-independent cell death through TNF-induced mitochondrial generation of ROS.[68] This increase in ROS is not only correlated with cell death but works in a positive feedback loop to enhance necrosome formation and necroptosis.

The protease caspase-8 and IAP ubiquitin ligases inhibit RIPK1/RIPK3 oligomerization, signaling and thus prevents necroptosis (Fig. 2).[69] Inhibitors of these 2 have been used to study necroptosis for years since they inhibit apoptosis and trigger necroptosis. However, clinically neither of these proteins have been successfully targeted for treatment. Nevertheless, the search for RIPK3 specific inhibitors has been an area of ongoing research. Recent studies suggest that RIPK3 inhibitor, GSK872, improves motor function and spinal cord edema in a SCI mouse model.[70] GSK872 is part of a group of kinase inhibitors. These inhibitors have a type I, II, or III kinase binding mode, with type I binding the ATP-binding site, type II interacting with the hinge region of ATP-binding site, and type III binding the inactive hydrophobic back pocket of the kinase domain.[71] Very few of these inhibitors have been successfully selected for the treatment of disease; having most of their use in cancers. A better understanding of the kinome selectivity and specificity along with an increase in *in vivo* testing of these drugs can help us move towards faster clinical implementation of RIPK3 inhibitors.

Although TNF death receptor, caspase-8, RIP1, and RIP3 are the most studied and important molecules that regulate cell apoptosis and necroptosis, the innate immune system has a set of pathogen-associated receptors that can also lead to cell death. Necroptosis can be triggered by PRRs. These are proteins capable of detecting conserved microbial products and endogenous damaged molecules. There are 4 major subfamilies of PRRs—the Toll-like receptors (TLRs), the nucleotide-binding oligomerization domain–leucin rich repeats-containing receptors,

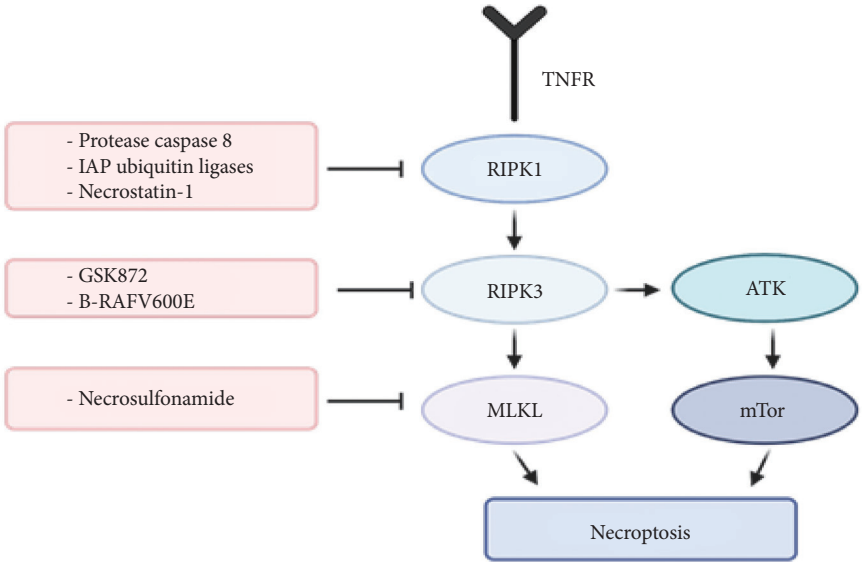

Fig. 2. The action mechanism of RIPK1, RIPK3, MLKL, and combination of necroptosis inhibition with PI3K/AKT/mTOR pathway inhibition. RIPK1, receptor-interacting protein kinase 1; RIPK3, receptor-interacting protein kinase 3; MLKL, mixed-lineage kinase domain-like; PI3K, phosphatidylinositol 3 kinase; AKT, protein kinase B; mTOR, mammalian target of rapamycin; IAP, inhibitor of apoptosis protein; TNFR, tumor necrosis factor receptor.

the retinoic acid-inducible gene 1 (RIG-1)-like receptors, and the C-type lectin receptors. There is evidence that 2 of the 13 TLRs and intracellular sensing proteins, such as RIG can lead to necroptosis. Most endosomal and plasma-membrane associated TLR respond to pathogens and induce necrosis partially through TNF and RIP activation.[72]

MIXED-LINEAGE KINASE DOMAIN-LIKE PROTEIN

As previously alluded to, necroptosis is initiated by TNF and the activity of RIP1 and RIP3. However, another important factor that mediates the activation of necroptosis is MLKL.[73,74] MLKL is another mitochondrial protein that serves as a substrate for RIP3.[75] The RIP1/RIP3 complex initiates and activates programmed necrosis after injury, secondary to phosphorylation of MLKL, thereby causing mitochondrial dysfunction. Given the important role of MLKL, several studies have investigated the effect of manipulation of this factor and the associated pathway. Jiao et al.[76] in a recent study used necrosulfonamide (NSA) to block MLKL, as means to prevent mitochondrial dysfunction. Their results showed that blocking MLKL using NSA prevented a decrease in mitochondrial membrane potential, ATP, glutathione, and superoxide dismutase levels and also prevented an increase in ROS and malondialdehyde levels. In terms of functional effects, the authors showed that among mice treated with NSA to block MLKL, there was a significant improvement in locomotor function.[76] The authors also demonstrated an optimal therapeutic window for treatment with NSA to block MLKL, which was within the first 12 hours of injury. These results show that blocking MLKL may provide an effective way of preventing secondary injury after SCI.

COMBINATION OF NECROPTOSIS INHIBITION WITH PI3K/AKT/mTOR PATHWAY INHIBITION

It has previously been demonstrated that following SCI, RIPK1 and RIPK3 mediate necroptosis, which in addition to several pathways, also involves inhibition of autophagy.[77] Autophagy is a catabolic pathway which has been shown to facilitate degradation of cytoplasmic content in a lysosome-dependent manner.[78] The autophagic flux, consisting of autophagosome formation, maturation, fusion with lysosomes, subsequent breakdown, and the release of macromolecules back into the cytosol, is mediated by several other molecules called the autophagy-related (ATG) protein family. Several studies have suggested a neuroprotective effect of autophagy after traumatic brain injury, including preservation of neurobehavioral function, increased neuronal survival, reduced inflammation and gliosis in the injured brain, and preventing further cell death and apoptosis.[79-81] One of the most significant mediators of autophagy is the phosphatidylinositol 3 kinase (PI3K)/protein kinase B (AKT)/mammalian target of rapamycin (mTOR) pathway.[82] Among these, mTORC1, a component of mTOR has been shown to be a negative mediator of autophagy.[83-85] while PI3K/AKT, in turn, modulates mTORC1.[86] Therefore, combining RIPK1/RIPK3 inhibition with inhibition of mTOR (for e.g., with rapamycin) may help to simultaneously activate autophagy while also inhibit activation of necroptosis pathway, thereby preventing further cell death.

FUTURE PERSPECTIVES

Current therapeutics directed towards specifically inhibiting MLKL are limited. One of the most promising candidates includes the chemical NSA which has shown the ability to attenuate necroptosis in SCI, however additional studies are needed to validate these findings which have only been described in one study thus far.[87]

CONCLUSION

Spinal cord injuries present with a complex series of molecular cascades that ultimately induce cell death of neurons and glia and excitotoxicity of astrocytes, limiting the effect of therapeutic intervention in these damaged regions. In this review, the mechanisms of action underlying SCI were discussed, particularly the roles of RIPK1/RIPK3 signaling pathways and the induction of necroptosis via the activation of death receptor ligands and caspase inhibition. Further emphasis was placed on potential therapeutics to limit the degree of necroptosis, in particular inhibition of RIPK1/3 and mTOR to increase rates of autophagy while inhibiting the necroptotic pathway in order to preserve cell survival and promote recovery via reduced inflammation, gliosis, and cell death.

Additional studies are necessary to investigate and develop therapeutics that successfully inhibit the necroptotic pathway and facilitate recovery following SCI. Studies on the RIPK1 inhibitor Nec-1 implicate this drug as a potential therapeutic as it is highly permeable across the blood-brain barrier with minimal neurotoxicity while ultimately limiting neuronal cell death.

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Currently, there are 6 human clinical trials looking at RIPK1 inhibitors in ALS, AD, psoriasis, ulcerative colitis, rheumatoid arthritis, and pancreatic ductal adenocarcinoma. Further, selective inhibition of RIPK3 via administration of B-RAF^{V600E} inhibitor dabrafenib may be a potential focus of investigation. With the potential of concomitant RIPK1 and RIPK3 inhibition via coadministration of these therapeutics, there holds great promise in sufficient inhibition of the necroptotic pathway following SCI. However, the combined pharmacological effects of these therapeutics have yet to be explored following coadministration. Additionally, these interventions have not been sufficiently studied in human models of SCI either, warranting further investigation in that regard.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Original Article

Comorbidity Influence on Postoperative Outcomes Following Anterior Cervical Discectomy and Fusion

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Objective: This study aims to detail the association between comorbidity burden and achieving minimum clinically important difference (MCID) following anterior cervical discectomy and fusion (ACDF).
Methods: A prospective surgical registry was retrospectively reviewed. Patients with missing preoperative Patient-Reported Outcomes Measurement Information System physical function (PROMIS PF) were excluded. Patients were stratified by Charlson Comorbidity Index (CCI): no comorbidities = 0 point; low CCI = 1–2 points; high CCI = ≥ 3 points. Demographic and perioperative characteristics were collected and evaluated for differences. Visual analogue scale (VAS), 12-item Short Form health survey (SF-12), and PROMIS PF were collected pre- and postoperatively and assessed for differences. Differences in achievement of MCID were compared using established values: VAS neck = 2.6, VAS arm = 4.1, NDI = 8.5, SF-12 physical composite score (SF-12 PCS) = 8.1, PROMIS PF = 4.5.
Results: One hundred twenty-five ACDF patients were included: 37 had no comorbidities, 64 with low CCI, and 24 with high CCI. Higher CCI groups were older, nonsmokers, diabetic, arthritic, hypertensive, and had cancer. Multilevel fusions, operative time, length of stay, and later discharge day were associated with high CCI. VAS neck differed preoperatively by group. SF-12 PCS and PROMIS PF were inversely associated with CCI groups. CCI did not impact achievement of MCID for all outcomes. A lower rate of reaching MCID was demonstrated at 3 months for SF-12 PCS.
Conclusion: Regardless of comorbidity burden, patients undergoing ACDF for cervical pathology demonstrated a similar rate of achieving MCID for VAS neck, VAS arm, NDI, and PROMIS PF. Regardless of CCI score, ACDF can have a significant benefit for patients.

Keywords: Comorbidity, Cervical fusion, Clinically important difference, Outcome measures

INTRODUCTION

The impact of comorbidities on patient quality of life has traditionally been assessed using the Charlson Comorbidity Index (CCI), a validated method for determining risk of mortality.[1] In addition to requiring increased clinical management, individuals with multiple comorbidities are associated with worse surgical outcomes. Among orthopedic spine patients, individuals with higher CCI scores are at an increased risk of readmission, perioperative and postoperative complication rates, and overall increased rate of mortality.[2–7] More specific to the cervical spine, a similar disparity in operative outcomes was also demonstrated in those undergoing anterior cervical discectomy and fusion (ACDF), where investigators reported higher rates of complications for individuals carrying larger comorbidity burdens.[8]

While the negative effects of comorbidities on operative outcomes is well defined, its impact can extend to other areas of a patient's quality of life. Such outcomes associated with ACDF

are commonly assessed with patient-reported outcome measures (PROMs) for neck and arm pain and disability. A more recent use of the minimum clinically important difference (MCID) has provided surgeons with a more clinically relevant measure that offers insight into meaningful perceptions of differences in care from the patients perspective.[9] Past studies have established that multiple comorbidities can negatively impact PROMs such as the visual analogue scale (VAS), EuroQoL 5 Dimensions, Oswestry Disability Index, and 12-item Short Form health survey (SF-12) physical and mental composite scores.[10] Moreover, investigators have reported that higher comorbidity burdens act as negative predictive factors for achieving an MCID for disability and physical function scores among ACDF and lumbar decompressions patients, respectively.[5,11]

While numerous studies report on how multiple comorbidities increase the risk of complications,[12,13] few focus on the cervical spine and even fewer investigate the effects on physical function. Although traditionally more attention has been placed on outcomes in the lumbar spine, cervical spine conditions have distinct etiologies and symptoms, such as myelopathic or radicular arm pain, that can translate into differences in outcomes. Elucidating the effects of comorbidity burden on physical function outcomes will enable surgeons to counsel patients on appropriate expectations and outcomes following cervical procedures such as ACDF. Therefore, this study aims to determine the effect of CCI burden on achievement of a clinically important difference following ACDF procedures. It is hypothesized that a larger comorbidity burden is associated with diminished rates of MCID achievement.

MATERIALS AND METHODS

1. Inclusion and Exclusion Criteria

In accordance with our institution's guidelines, approval by the Institutional Review Board of Rush University Medical Center (ORA 14051301) and written patient informed consent were both granted before any aspect of the study was initiated. Patients included in this study were identified through a retrospective review of a prospective surgical database containing ACDF procedures performed during May 2015 to July 2019. Inclusion criteria was set as primary, single or multilevel ACDF procedures. Exclusion criteria was set as missing preoperative Patient-Reported Outcomes Measurement Information System physical function (PROMIS PF) questionnaire, surgery indicated for infectious, malignant, or traumatic etiologies. All procedures were performed by a single surgeon at either an ambulatory surgical center or inpatient hospital setting.

2. Patient Data Collection

Preoperative CCI scores were collected to determine the comorbidity burden. The CCI is a prognostic scoring system that allows clinicians to assess a patient's 10-year survival probability. Comorbidities are assessed based on the International Classification of Disease and are weighted from 1 up to 6 points. A total score is generated from the sum of all weighted comorbidities with a higher CCI associated with a lower probability of a 10-year survival (Appendix 1). Both demographic and perioperative information was collected at either the preoperative timepoint or the immediate postoperative period. Demographics included age, sex, smoking status, body mass index (BMI), preexisting medical comorbidities, and spinal diagnosis associated with the procedure. Perioperative information included the total number of operative vertebral levels, time from skin incision to skin closure, estimated intraoperative blood loss (EBL), postoperative inpatient length of stay, and day of discharge. A summary of all baseline characteristics can be found in Tables 1 and 2.

3. Patient-Reported Outcome Measures

Outcome measurements were collected for pain, disability, and physical function for all included patients. Neck and arm pain were assessed using the VAS. Disability was evaluated using the Neck Disability Index (NDI), and physical function was evaluated using both SF-12 physical composite score (PCS) and PROMIS PF. All outcome measures were administered and completed at a preoperative timepoint as well as follow-up appointments at 6 weeks, 12 weeks, 6 months, and 1 year.

4. Minimum Clinically Important Difference

Achievement of an MCID was calculated for all patients included in this study. MCID achievement was determined through comparison of the difference in preoperative and postoperative PROM scores to a pre-established value. MCID values from Parker et al.[14] were used for VAS neck (2.6), VAS arm (4.1), NDI (17.3% or 8.5), and SF-12 PCS (8.1); whereas Steinhaus et al.[15] established a PROMIS PF MCID of 4.5.

5. Statistical Analysis

Following data collection, patients were categorized into 1 of 3 groups: no comorbidities (CCI = 0); low comorbidity (CCI = 1–2); or high comorbidity (CCI ≥ 3). Demographic and perioperative characteristics were stratified by CCI group and summary statistics performed. Additionally, univariate analysis was

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Table 1. Baseline characteristics by CCI group

Characteristic	CCI 0 (n = 37)	CCI 1–2 (n = 64)	CCI ≥ 3 (n = 24)	p-value†
Age (yr)	41.60 ± 6.3	51.35 ± 8.06	58.51 ± 10.44	< 0.001*
Sex				0.380
Female	17 (45.9)	28 (43.8)	7 (29.2)	
Male	20 (54.1)	36 (56.3)	17 (70.8)	
Smoking status				0.037*
Nonsmoker	36 (97.3)	54 (84.4)	18 (75.0)	
Smoker	1 (2.7)	10 (15.6)	6 (25.0)	
Body mass index (kg/m^2)				0.863
< 30	21 (56.8)	36 (56.3)	15 (62.5)	
≥ 30	16 (43.2)	28 (43.8)	9 (37.5)	
Preoperative diagnoses				
Myocardial infarction	0 (0)	1 (1.6)	(0) 0	0.619
Diabetes	0 (0)	8 (12.5)	11 (45.8)	0.000*
Arthritis	0 (0)	7 (10.9)	8 (33.3)	0.000*
Hypertension	0 (0)	19 (29.7)	17 (70.8)	0.000*
Malignancy	0 (0)	0 (0)	3 (12.5)	0.002*
Spinal diagnoses				
Herniated nucleus pulposus	36 (97.3)	52 (81.3)	19 (79.2)	0.052
Degenerative disc disease	0 (0)	4 (6.3)	2 (8.3)	0.245
Foraminal stenosis	4 (10.8)	7 (10.9)	3 (12.5)	0.975

Values are presented as mean ± standard deviation or number (%).
CCI, Charlson Comorbidity Index.
*p < 0.05, statistically significant difference. †p-value was calculated for each category using multivariate linear regression (continuous) or chi-square analysis (categorical).

Table 2. Perioperative outcomes by CCI group

Characteristic	CCI 0 (n = 37)	CCI 1–2 (n = 64)	CCI ≥ 3 (n = 24)	p-value†
No. of fusion levels				0.003*
1 Level	28 (75.7)	32 (50.0)	11 (45.8)	
2 Levels	9 (24.3)	27 (42.2)	7 (29.2)	
3 Levels	0 (0)	5 (7.8)	4 (16.7)	
4 Levels	0 (0)	0 (0)	2 (8.3)	
Operative time (min)	51.8 ± 10.3	60.3 ± 15.0	65.8 ± 20.3	0.002*
Estimated blood loss (mL)	26.5 ± 11.4	30.8 ± 13.4	34.4 ± 14.4	0.065
Length of stay (hr)	8.5 ± 6.2	11.0 ± 9.0	24.8 ± 18.2	< 0.001*
Discharge date				< 0.001*
POD 0	33 (89.2)	52 (81.3)	9 (37.5)	
POD 1	4 (10.8)	12 (18.8)	11 (45.8)	
POD 2	0 (0)	0 (0)	3 (12.5)	
POD 3+	0 (0)	0 (0)	1 (4.2)	

Values are presented as number (%) or mean ± standard deviation.
CCI, Charlson Comorbidity Index; POD, postoperative day.
*p < 0.05, statistically significant difference. †p-value was calculated for each category using multivariate linear regression (continuous) or chi-square analysis (categorical).

conducted to determine significant differences in either demographic or perioperative characteristics between groups. Following univariate analysis, intergroup differences in VAS back, VAS neck, NDI, SF-12 PCS, and PROMIS PF at all timepoints was determined using linear regression. Differences in rates of overall MCID achievement at 6 weeks, 12 weeks, 6 months, 1 year were assessed between groups using chi-square analysis. To determine the effect of significant demographic and perioperative characteristics on the achievement of MCID, a multiple logistic regression was performed. In addition to CCI, demographic or perioperative variables with a $p < 0.100$ were selected for inclusion in regression models. Completion rates were also calculated for all PROMs at all timepoints and the effect of demographics and postoperative outcomes on completion rates were evaluated using a simple logistic regression. All statistical analysis was performed using StataMP 16.0 (StataCorp LLC,

Table 3. Patient-reported outcome comparisons by CCI status

Variable	CCI 0	CCI 1–2	CCI ≥ 3	p-value†
VAS neck				
Preoperative	6.78 ± 2.21 (37)	6.01 ± 2.35 (63)	4.81 ± 3.00 (20)	0.016*
6 Weeks	4.01 ± 2.73 (34)	2.93 ± 2.47 (62)	3.20 ± 2.49 (20)	0.140
12 Weeks	2.60 ± 2.47 (33)	2.54 ± 2.41 (55)	3.20 ± 2.37 (17)	0.610
6 Months	3.19 ± 2.43 (26)	2.25 ± 2.64 (49)	2.87 ± 2.46 (14)	0.293
1 Year	2.91 ± 2.60 (14)	2.80 ± 2.89 (23)	2.89 ± 2.73 (12)	0.993
VAS arm				
Preoperative	6.12 ± 2.85 (37)	6.10 ± 2.26 (63)	4.88 ± 2.79 (20)	0.146
6 Weeks	2.42 ± 2.55 (34)	2.57 ± 3.68 (62)	3.43 ± 3.10 (20)	0.533
12 Weeks	2.64 ± 3.20 (33)	2.97 ± 3.20 (55)	3.16 ± 2.61 (17)	0.826
6 Months	2.44 ± 2.84 (24)	3.10 ± 3.34 (49)	2.96 ± 2.25 (14)	0.685
1 Year	3.99 ± 3.19 (14)	3.25 ± 3.82 (23)	2.60 ± 3.27 (12)	0.606
NDI				
Preoperative	41.89 ± 19.22 (37)	35.74 ± 18.36 (62)	31.79 ± 17.76 (19)	0.118
6 Weeks	35.41 ± 21.19 (34)	27.06 ± 20.11 (62)	25.20 ± 14.13 (20)	0.087
12 Weeks	29.97 ± 22.55 (33)	21.81 ± 18.71 (55)	24.43 ± 14.78 (17)	0.168
6 Months	25.35 ± 21.88 (24)	17.35 ± 15.88 (49)	24.35 ± 19.29 (14)	0.158
1 Year	20.43 ± 23.85 (14)	16.09 ± 17.70 (23)	23.07 ± 20.20 (12)	0.559
SF-12 PCS				
Preoperative	36.09 ± 8.99 (34)	36.09 ± 9.25 (56)	34.04 ± 6.39 (22)	0.613
6 Weeks	33.45 ± 7.06 (30)	36.42 ± 8.85 (53)	34.94 ± 9.08 (19)	0.303
12 Weeks	38.93 ± 10.39 (30)	42.04 ± 9.50 (36)	35.55 ± 8.65 (17)	0.073
6 Months	40.82 ± 9.86 (23)	43.05 ± 10.67 (40)	33.42 ± 8.77 (13)	0.015*
1 Year	45.71 ± 13.62 (12)	47.08 ± 9.34 (27)	38.35 ± 7.42 (15)	0.028*
PROMIS PF				
Preoperative	39.19 ± 7.17 (37)	40.73 ± 7.57 (64)	38.66 ± 5.54 (24)	0.376
6 Weeks	39.51 ± 6.65 (24)	41.86 ± 7.11 (50)	40.78 ± 8.07 (14)	0.416
12 Weeks	45.19 ± 9.13 (25)	47.61 ± 9.78 (37)	39.29 ± 9.33 (14)	0.025*
6 Months	47.07 ± 10.98 (16)	49.03 ± 9.12 (38)	41.64 ± 6.32 (12)	0.060
1 Year	50.18 ± 10.68 (13)	50.82 ± 7.63 (26)	43.71 ± 5.52 (14)	0.028*

Values are presented as mean ± standard deviation (number).
CCI, Charlson Comorbidity Index; VAS, visual analogue scale; NDI, Neck Disability Index; SF-12 PCS, 12-item Short Form health survey physical composite score; PROMIS PF, Patient-Reported Outcomes Measurement Information System physical function.
*$p < 0.05$, statistically significant difference. †p-value was calculated using linear regression to compare each timepoint among subgroups.

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College Station, TX, USA). An alpha value was set at 0.05 for significance. To control for a false discovery rate due to repeated statistical tests, the Benjamini-Hochberg procedure was performed with any p-values falling below their respective threshold being labeled as significant.

RESULTS

1. Patient Baseline Characteristics

A total of 125 patients met our inclusion criteria for this study. Among this cohort, 37 were categorized as having no comorbidities, 64 with low comorbidities, and 24 with high comorbidities. Patients with a higher CCI were significantly older (58.51 ± 10.44 years) as compared to low (51.35 ± 8.06 years) and no (41.60 ± 6.3 years) comorbidity groups ($p < 0.001$). Additionally, patients with high comorbidity scores were more likely to be nonsmokers ($p = 0.037$), diabetic, arthritic, hypertensive, and diagnosed with a malignancy (all $p \leq 0.002$) (Table 1). High CCI also was significantly associated with multilevel procedures, longer operative duration (51.8 minutes vs. 60.3 minutes vs. 65.8 minutes, $p = 0.002$), longer postoperative length of inpatient stay (8.5 hours vs. 11.0 hours vs. 24.8 hours, $p \leq 0.001$), and later day of discharge ($p < 0.001$) (Table 2).

Table 4. Achievement of minimum clinically important difference (MCID)

Variable	Preop to 6 wk	Preop to 3 mo	Preop to 6 mo	Preop to 12 mo	Overall met MCID
VAS neck					
CCI 0	19/37 (51.4)	28/37 (75.7)	27/37 (73.0)	30/37 (81.1)	35/37 (94.6)
CCI 1–2	35/64 (54.7)	44/64 (68.8)	49/64 (76.6)	54/64 (84.4)	60/64 (93.8)
CCI ≥ 3	12/24 (50.0)	15/24 (62.5)	15/24 (62.5)	18/24 (75.0)	21/24 (87.5)
p-value	0.906	0.538	0.418	0.597	0.529
VAS arm					
CCI 0	20/37 (54.1)	19/37 (51.4)	24/37 (64.9)	27/37 (73.0)	30/37 (81.1)
CCI 1–2	31/64 (48.4)	32/64 (50.0)	34/64 (53.1)	51/64 (79.7)	56/64 (87.5)
CCI ≥ 3	10/24 (41.7)	12/24 (50.0)	13/24 (54.2)	16/24 (66.7)	18/24 (75.0)
p-value	0.637	0.991	0.496	0.422	0.346
NDI					
CCI 0	15/37 (40.5)	25/37 (67.6)	28/37 (75.7)	33/37 (89.2)	35/37 (94.6)
CCI 1–2	33/64 (51.6)	42/64 (65.6)	53/64 (82.8)	58/64 (90.6)	61/64 (95.3)
CCI ≥ 3	13/24 (54.2)	17/24 (70.8)	17/24 (70.8)	19/24 (79.2)	22/24 (91.7)
p-value	0.477	0.897	0.425	0.326	0.801
SF-12 PCS					
CCI 0	26/37 (70.3)	27/37 (73.0)	20/37 (54.1)	10/37 (27.0)	31/37 (83.8)
CCI 1–2	44/64 (68.8)	29/64 (45.3)	32/64 (50.0)	20/64 (31.3)	52/64 (81.3)
CCI ≥ 3	14/24 (58.3)	13/24 (54.2)	11/24 (45.8)	13/24 (54.2)	19/24 (79.2)
p-value	0.582	0.026*	0.818	0.070	0.897
PROMIS PF					
CCI 0	18/37 (48.7)	23/37 (62.2)	16/37 (43.2)	12/37 (32.4)	30/37 (81.1)
CCI 1–2	38/64 (59.4)	33/64 (51.6)	38/64 (59.4)	26/64 (40.6)	54/64 (84.4)
CCI ≥ 3	13/24 (54.2)	10/24 (41.7)	11/24 (45.8)	14/24 (58.3)	19/24 (79.2)
p-value	0.576	0.282	0.235	0.131	0.823

Values are presented as number (%).
VAS, visual analogue scale; CCI, Charlson Comorbidity Index; NDI, Neck Disability Index; SF-12 PCS, 12-item Short Form health survey physical composite score; PROMIS PF, Patient-Reported Outcomes Measurement Information System physical function.
*$p < 0.05$, statistically significant difference.
The following MCID values derived from Parker et al.[14]; NDI = 17.3% (8.5), VAS neck = 2.6, VAS arm = 4.1, SF-12 PCS = 8.1; PROMIS MCID values derived from Steinhaus et al.[15]: PROMIS PF = 4.5.

2. Primary Outcomes Measures

VAS neck demonstrated a significantly lower preoperative value in patients with a high CCI as compared to patients with no or low comorbidities ($p = 0.016$). No other significant differences were demonstrated for VAS neck between CCI groups from 6-week through the 1-year postoperative timepoint. Arm pain, as measured by VAS arm, did not demonstrate significant differences between comorbidity groups at any preoperative or postoperative timepoint (all $p > 0.100$). Similarly, NDI also did not demonstrate any significant differences between groups for any timepoint (all $p > 0.05$).

Physical function demonstrated significant differences between CCI groups for SF-12 PCS at the 6-month ($p = 0.015$) and 1-year ($p = 0.028$) timepoint but no difference was observed at the preoperative through the 12-week timepoint (all $p > 0.050$). PROMIS PF only demonstrated a significant difference between groups at the 12-week ($p = 0.025$) and 1-year ($p = 0.028$) timepoint. A summary of all PROM results can be found in Table 3.

Completion rates for all PROMs were greatest at the preoperative timepoint (89.6%–100.0%) and the worst completion rates at the 1-year postoperative timepoint (39.2%–43.2%). There were no significant associations with completion rates for all PROMs except for SF-12 PCS at the 1-year postoperative timepoint ($\beta = 0.64$; 95% CI, 1.2–0.08; $p = 0.025$).

3. MCID Achievement Rates

VAS neck and arm did not significantly differ in rates of MCID achievement from the 6-week through the 1-year postoperative timepoint (all $p > 0.400$). Rates of MCID achievement for NDI and PROMIS PF also did not significantly differ between groups for any postoperative timepoints (all $p > 0.300$). SF-12 PCS at the 12-week timepoint ($p = 0.026$) was significantly different in MCID achievement between comorbidity groups, but a similar finding was not demonstrated at 6 weeks, 6 months, or 1 year (all $p > 0.050$) (Table 4). Multiple logistic regression did not demonstrate any significant associations between achievement of MCID and CCI categories or with selected demographic and perioperative characteristics (all $p > 0.050$).

DISCUSSION

Patients having multiple comorbidities has been implicated in contributing to higher complication rates, readmissions, and increased cost to the patient.[4,16-18] With a large proportion of the world population ageing over the next 2 decades, the burden of age related comorbidities has prompted surgeons to further explore the potential impact on patient outcomes. Use of the CCI and similar risk assessment scores can provide insight to the collective effects of multiple medical diagnoses on surgical outcomes. The current study utilized CCI scores to determine the potential negative effects multiple comorbidities may have on patient-reported outcomes following ACDF. We demonstrated that patients with larger CCI scores were still able to achieve clinically meaningful improvements in pain, disability, and physical function at rates on par with patients with lower CCI scores.

ACDF patients with increased comorbidity burden did not drastically differ in their postoperative recovery with regard to disability and arm pain. However, interestingly, our patient cohort reported a significantly different preoperative VAS neck score, with the CCI ≥ 3 group having a lower initial pain level. Although one would not expect patients with greater health concerns to report lower preoperative neck pain, this aligns well with past studies exploring the clinical impact of single level ACDF in diabetic and non-diabetic patients. Arnold et al.[19] focused their attention on clinical outcomes and reported that while VAS arm, SF-36 PCS, and SF-36 MCS did not significantly differ in preoperative scores, VAS neck was reported as lower for diabetic patients ($p = 0.009$). Additionally, a similar finding was also reported in a study by Narain et al.[20] for overweight and obese patients undergoing ACDF; however, it must be noted that while VAS neck was lower than normal weight groups, this difference did not reach statistical significance. Although BMI is not included in the CCI, there are well established associations between rising BMI and higher comorbidities.[21] This presents an interesting finding among ours and other studies, as past neurological studies have concluded that pain thresholds can be reduced with chronic pain resulting from comorbidities.[22,23] Nevertheless, collectively this may suggest that patients with a higher CCI may have decreased potential for improvement of neck pain.

It may be that pain perception for patients carrying a higher number of comorbidities is altered to some extent; however, our study was also able to establish that higher CCI results in poorer improvement of physical function at the long-term follow-up. Though few studies have evaluated the impact of multiple comorbidities on physical function, there are a number of studies that provide contrarian observations. For example, investigators assessing the impact of diabetes on physical function in ACDF patients demonstrated no significant differences through 2 years,[19,24] with a similar result also reported for obese patients.[25] Moreover, patients reported to have lower fusion rates as a consequence of diabetes interestingly were not observed to have

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any significant differences in physical function improvement compared to nondiabetics.[24] Our study's finding that both SF-12 PCS and PROMIS PF demonstrated a lower value among patients with a CCI ≥3 could be attributed to the nature of comorbidities themselves. Such diseases as chronic obstructive pulmonary disease can be included and can negatively impact the ability to perform daily functions as a result of weaker strength in all muscle groups.[26] Moreover, the simple fact that patients with a higher number of comorbidities were associated with a higher proportion of patients diagnosed with arthritis could also contribute to lower postoperative physical function scores.

One of the main strengths of our study is the inclusion of MCID analysis, which few studies, if any, have reported in the ACDF cohort with respect to the impact of comorbidities. Our study established that a higher CCI score did not translate to a lower achievement of MCID for pain, disability, and physical function. This initially appears to be in contrast with our results, which demonstrate significantly lower values for SF-12 PCS and PROMIS PF among patients with a higher CCI; however, the object of MCID calculations is to provide a more clinically relevant depiction of postoperative improvement as opposed to the commonly reported statistical improvements from preoperative baseline values. When comparing our results to others, there appears to be a lack of consensus among the current literature regarding appropriate MCID values, with a wide variety of results being reported. Narain et al.[27] performed a risk factor analysis for failure to achieve an MCID in ACDF patients and demonstrated that an ageless CCI ≥2 was associated with a failure to reach a clinically important difference for NDI; however, they reported a similar noncontributory role of CCI with failure to achieve MCID for both VAS neck and arm. Additionally, Goh et al.[28] established that older age, which also contributes to CCI, was associated with a lower probability of attaining MCID for the Japanese Orthopedic Association score. Other investigators have also reported a lack of effect from obesity on MCID achievement for NDI among ACDF patients.[25] Although our study does not present a statistically similar finding, we were able to observe that achievement rates for NDI, VAS arm and neck, SF-12 PCS, and PROMIS PF were consistently the lowest at all timepoints for patients with a CCI ≥3 as compared to the other comorbid groups.

Several areas of the current study limit our interpretation of the results. Firstly, patients underwent treatment at a single institution with a single surgeon, which will limit our ability to generalize our results. Future studies involving multiple centers and providers would strengthen the study. Secondly, our study was based on a retrospective review of questionnaires which will inherently have some form of bias due to the nature of the data acquisition. Additionally, lower patient completion rates of postoperative outcome measures may also bias patient outcomes towards poorer outcomes and lower satisfaction. However, studies have suggested otherwise,[29] and future studies exploring the relationship between patient satisfaction and questionnaire completion rate may help clarify if a bias exists. Lastly, our study accurately collected CCI scores, but were unable to determine which aspect of the patient's past medical history contributed to the overall score. This would provide invaluable insight as to whether a more serious underlying pathology such as malignancy or vascular disease contributed to a poorer outcome as compared to a relatively benign characteristic as age.

CONCLUSION

Patients with a higher comorbidity classification demonstrated significant associations with older age, nonsmoker status, high number of preoperative medical conditions, longer operative length, and number of operative levels. While arm pain, neck disability, and physical function did not demonstrate differences at the preoperative timepoint across all groups, neck pain was significantly lower for patients with a greater comorbidity burden. These same patients also reported lower physical function scores from intermediate to longitudinal timepoints. MCID achievement for VAS neck and arm, NDI, SF-12 PCS and PROMIS PF largely demonstrated no differences. These results suggest that patients with a greater comorbidity burden are unlikely to experience a vastly different course of postoperative improvement following ACDF and affirm the benefits of the procedure for treatment of differing cervical neck pathologies in a wide variety of patients.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Appendix 1. Charlson Comorbidity Index

Variable	Point
Age (yr)	
< 50	0
50–59	1
60–69	2
70–79	3
≥ 80	4
Myocardial infarction	1
Congestive heart failure	1
Peripheral vascular disease	1
Cerebrovascular accident or transient ischemic attack	1
Dementia	1
Chronic obstructive pulmonary disorder	1
Connective tissue disease	1
Peptic ulcer disease	1
Liver disease	
None	0
Mild	1
Moderate to severe	3
Diabetes mellitus	
None or diet-controlled	0
Uncomplicated	1
Hemiplegia	2
Moderate to severe chronic kidney disease	2
Solid tumor	
None	0
Localized	2
Metastatic	6
Leukemia	2
Lymphoma	2
Acquired immunodeficiency syndrome	6

Score translates into estimated 10-year survival.

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Intraoperative Monitoring for Cauda Equina Tumors: Surgical Outcomes and Neurophysiological Data Accrued Over 10 Years

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Objective: Cauda equina tumors affect the peripheral nervous system, and the validities of triggered electromyogram (tEMG) and intraoperative neurophysiologic monitoring (IOM) are unclear. We sought to evaluate the accuracy and relevance of tEMG combined with IOM during cauda equina tumor resection.
Methods: Between 2008 and 2018, an experienced surgeon performed cauda equina tumor resections using tEMG at a single institution. A cauda equina tumor was defined as an intradural-extramedullary or intradural-extradural tumor at the level of L2 or lower. The clinical presentation, extent of resection, pathology, recurrence, postoperative neurological outcomes, and intraoperative tEMG mapping and IOM data were retrospectively analyzed.
Results: One hundred three patients who underwent intraoperative tEMG were included; 38 underwent only tEMG (tEMG-only group), and 65 underwent a combination of tEMG and multimodal IOM (MIOM group). There were no significant differences between the neurologic outcomes, extents of resection, or recurrence rates of the 2 groups. No significant therapeutic benefit was observed; however, the accuracy of intraoperative predetection improved with the combination of IOM and tEMG (accuracy: tEMG-only group, 86.8%; MIOM group, 92.3%). When the involved rootlet was resected despite the positive tEMG result, motor function worsened in 3 of 8 cases. The sensitivity and specificity of tEMG were 37.5% and 94.7%, respectively.
Conclusion: tEMG is an essential adjunctive surgical tool for deciding on and planning for rootlet resection. If the tEMG finding is negative, complete resection, involving the rootlet, may be safe. The accuracy may be further improved by using a combination of tEMG and IOM.

Keywords: Cauda equina, Electromyogram, Neurological outcome, Neuromonitoring, Spinal cord tumors

INTRODUCTION

It is well-known that multimodal intraoperative monitoring (IOM) during spinal cord surgery is a reliable and valid diagnostic adjunct for assessing spinal cord integrity.[1] IOM is important for preserving neuronal structures and achieving an optimal postoperative functional outcome.[2] Thus, IOM has become the standard for spinal cord tumor surgery.

However, somatosensory evoked potential (SSEP) and motor evoked potential (MEP) monitoring are not routinely used dur-

ing the resection of tumors of the lumbar spine.[3] In addition, the utility of IOM for intradural-extramedullary (IDEM) tumors has not been confirmed.[4,5] Tumors of the cauda equina are rare, and they account for 5% of all primary intraspinal tumors.[6] To the best of our knowledge, the exclusive use of triggered electromyogram (tEMG) and other IOM modalities for cauda equina level tumors have not been the focus of previously published studies. Although root mapping using tEMG is generally performed during cauda equina surgery,[7] no studies have analyzed its accuracy for cauda equina intradural tumor removal. In literature, a limited number of reports describe the intraoperative use of tEMG for tumor removal.[8,9] These reports only describe the usefulness of tEMG for predicting postoperative outcomes of nerve root sacrifice in cervical spinal tumors. Furthermore, since cauda equina tumors affect the peripheral nervous system, the validity of multimodal IOM is also unclear.

We aimed to establish the usefulness of tEMG and IOM for determining surgical strategies and balancing the conflict between the following 2 objectives: (1) the complete resection of pathologic tissue and (2) the preservation of neurologic function. For this purpose, we evaluated the accuracy and relevance of monitoring surgical outcomes with tEMG mapping combined with SSEP, MEP, and bulbocavernosus reflex (BCR) monitoring during the resection of cauda equina IDEM tumors.

MATERIALS AND METHODS

1. Patient Population and Data Selection

Data of 127 consecutive patients who presented with cauda equina tumors treated by a single senior surgeon at a single institution between 2008 and 2018 were prospectively collected in a database and retrospectively analyzed. Cauda equina tumors in this study were defined as IDEM and intradural-extradural (IDED) tumors at the level of L2 or lower. Of these, intramedullary tumors originating from the conus medullaris or metastatic tumors were excluded. No distinction was made between different histopathological diagnoses. The patients who were not monitored using EMG or other modalities were subsequently excluded, leaving 24 patients in the final series. Spontaneous (free-running) EMG (sEMG) data were not analyzed, but tEMG reports with records on the preservation of the adjacent rootlet were analyzed. Baseline characteristics, including sex, age, IOM data, and neurological status on admission, discharge, and at 6-month follow-up, were collected. The pathological diagnosis and recurrence were also investigated. Based on the postoperative magnetic resonance imaging, recurrence was defined as an increase in the residual tumor size or the development of new lesions. This retrospective study was approved by the Institutional Review Board (IRB) of Asan Medical Center (AMC IRB 2019-1308).

2. Intraoperative Neurophysiologic Monitoring

Neurophysiologic monitoring was performed throughout the surgery. The baseline readings were obtained before skin incision and after the exposure of the dura mater. The stimulation alternated between SSEP and MEP. SSEP amplitude reduction of >50% of the baseline value and latency increase by >10% were regarded as significant.[10-12] During the propofol maintenance of anesthesia, an MEP amplitude decrement of >50% of the baseline value was considered indicative of a significant change provided that the levels of neuromuscular blockade and general anesthesia were unchanged.[10,12,13] If the amplitude of the BCR fell below 50% of the baseline value after application of the above criteria, it was considered a positive sign.

In this study, motor root mapping using tEMG was regarded as a modality of IOM. A positive tEMG finding was determined as follows: after the dissection of the rootlets surrounding the tumor, the nerve that was considered as the origin of the tumor was separated with a hook and stimulated with a bipolar nerve stimulator (current: 3–10 mA).[14] To reduce the false positives, a cottonoid was used to insulate the dissected rootlets (Fig. 1). A recording of all the lumbosacral myotomes (sphincter ani exter-

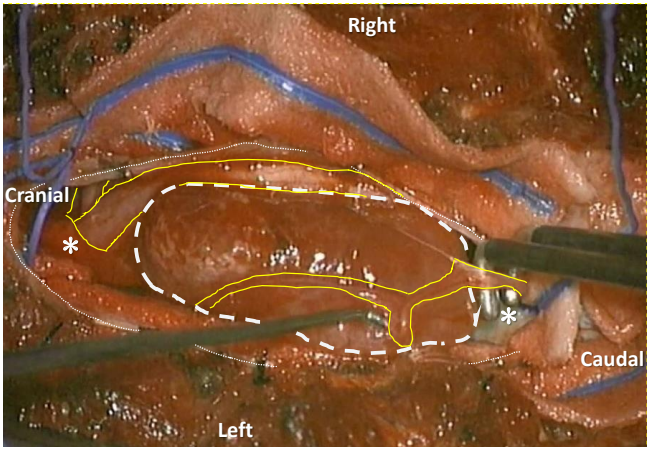

Fig. 1. Triggered electromyogram (tEMG) method: meticulous dissection of the rootlet to preserve nerve function. A right-angle hook was used to pull the rootlet away from the surrounding tissue, including the tumor. After minimizing current interference with a cotton pattie, tEMG was performed using a bipolar stimulator (white dashed line: tumor; white dotted line: dura; yellow full line: rootlet; asterisk: cotton pattie).

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nus, abductor hallucis, gastrocnemius, iliopsoas, tibialis anterior, and vastus lateralis) from all the representative segmental target muscles ensured that all possibly affected motor roots were covered.[7] After stimulating and confirming the compound muscle action potential in the corresponding muscles, a positive finding was characterized by a complete resection of the root, whereas a negative finding was characterized by the preservation of some involved rootlets, even with the tEMG signal.

Table 1. Patient demographics and primary surgical outcomes of both groups

Variable	tEMG-only (n = 38)	MIOM (n = 65)	p-value	Total
Age (yr)	46.0 ± 15.5	45.0 ± 15.4	0.752	45.4 ± 15.3
Sex			0.804	
Male	16 (42.1)	29 (44.6)		45 (43.7)
Female	22 (57.9)	36 (55.4)		58 (56.3)
Follow-up period (mo)				
MR	30.6 ± 31.6	14.8 ± 16.2	0.006	20.6 ± 24.2
Clinical	35.9 ± 27.9	17.4 ± 14.7	0.001	24.2 ± 22.3
Tumor location			0.786	
Intradural-extradural	4 (10.5)	8 (12.3)		12 (11.7)
Intradural only	34 (89.5)	57 (87.7)		91 (88.3)
Lesion level			0.784	
Multilevel lesion	5 (13.2)	10 (15.4)		15 (14.6)
Single level lesion	33 (86.8)	55 (84.6)		88 (85.4)
Pathologic diagnosis				
Schwannoma	32 (84.2)	53 (81.5)	0.794	85 (82.5)
Myxopapillary ependymoma	3 (7.9)	4 (6.2)	0.707	7 (6.8)
Meningioma	2 (5.3)	0 (0)	0.134	2 (1.9)
Others*	1 (2.6)	8 (12.3)	0.094	9 (8.7)
Preoperative neurological deficit				
Overall	3 (7.9)	8 (12.3)	0.488	11 (10.7)
Weakness	2 (5.3); 1 unilateral, 1 bilateral	4 (6.2); 2 unilateral, 2 bilateral	0.852	6 (5.8)
Hypoesthesia (saddle anesthesia)	1 (2.6)	3 (4.6)	0.613	4 (3.9)
Bladder-bowel symptom	1 (2.6)	1 (1.5)	0.695	2 (1.9)
Extent of tumor resection				
Gross total resection	31 (81.6)	49 (75.4)	0.625	80/103 (77.7)
Subtotal (> 50) resection	7 (18.4)	16 (24.6)	0.468	23/103 (22.3)
Recurrence				
Overall	5 (13.2)	11 (16.9)	0.780	16/103 (15.5)
Gross total resection	1/31 (3.2)	2/49 (4.1)	0.893	3/80 (3.8)
Subtotal (> 50) resection	4/7 (57.1)	9/16 (56.2)	0.969	13/23 (56.5)
Postoperative neurological deterioration				
Overall	12 (31.6)	12 (18.5)	0.131	24/103 (23.3)
Motor	4 (10.5)	4 (6.2)	0.463	8/103 (7.8)
Sensory	8 (21.1)	8 (12.3)	0.268	16/103 (15.5)

Values are presented as mean ± standard deviation or number (%).
tEMG, triggered electromyogram; MIOM, multimodal intraoperative monitoring (tEMG + MEP + SSEP + BCR); MEP, motor evoked potential; SSEP, somatosensory evoked potential; BCR, bulbocavernosus reflex.
*Others pathologic diagnoses: 1 mixed germ cell tumor (tEMG-only group); 1 ependymoma; 1 epidermoid cyst; 1 Ewing sarcoma/primitive neuro-ectodermal tumor (MIOM group); 1 hemangioblastoma; 1 lobular capillary hemangioma; 1 mesenchymal chondrosarcoma; 1 neurofibroma; 1 paraganglioma.

3. Postoperative Neurologic Deficits

The neurological state of each patient was evaluated before and immediately after surgery and 6 months later or after a more extended period in the outpatient clinics. Neurological deterioration was defined as new-onset permanent weakness, hypoesthesia, bladder-bowel symptoms after surgery, or worsening of preoperative deficits. Although the last follow-up duration varied from patient to patient, a permanent deficit was defined as a neurologic deficit that persisted after 6 months.

All positive IOM signs were correlated with the findings of neurologic examinations performed by attending surgeons, including neurological spine fellows and residents. A true-positive IOM change was associated with a neurologic deterioration; a false-positive IOM change was not. A true-negative IOM change was associated with a postoperative neurologic deterioration; a false-negative IOM change was not.

4. Statistical Analysis

Sensitivity, specificity, positive predictive value, negative predictive value, prevalence, relative risk, and accuracy, including 95% confidence intervals, were calculated. The data were analyzed for the entire group and subanalyzed based on the monitoring modality. The Student t-test or Mann-Whitney U-test was used to compare continuous variables, and the Pearson chi-square test or Fisher exact test was used to compare discrete variables of the groups. We used IBM SPSS Statistics ver. 21.0 (IBM Co., Armonk, NY, USA) for statistical analyses. A p-value of < 0.05 was considered statistically significant.

RESULTS

1. Patient Demographics and Clinical Presentation

A summary of the demographic data is provided in Table 1. A total of 103 patients who underwent cauda equina tumor resection with IOM were included. Of these, 38 underwent tEMG only (tEMG-only group), and 65 underwent multimodal IOM (MIOM group; tEMG, MEP, SSEP, and BCR combined). The

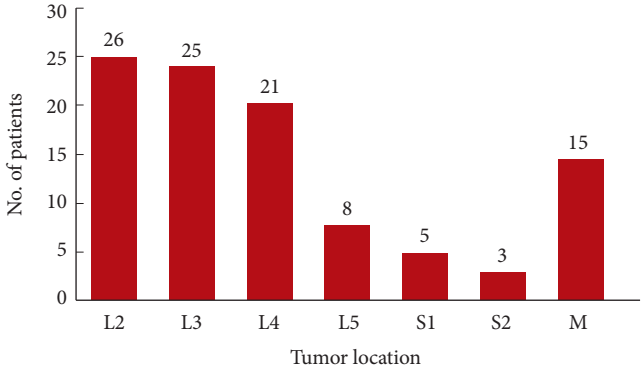

Fig. 2. Distribution of cauda equina tumors in each segment for the 103 cases. M, multilevel lesion.

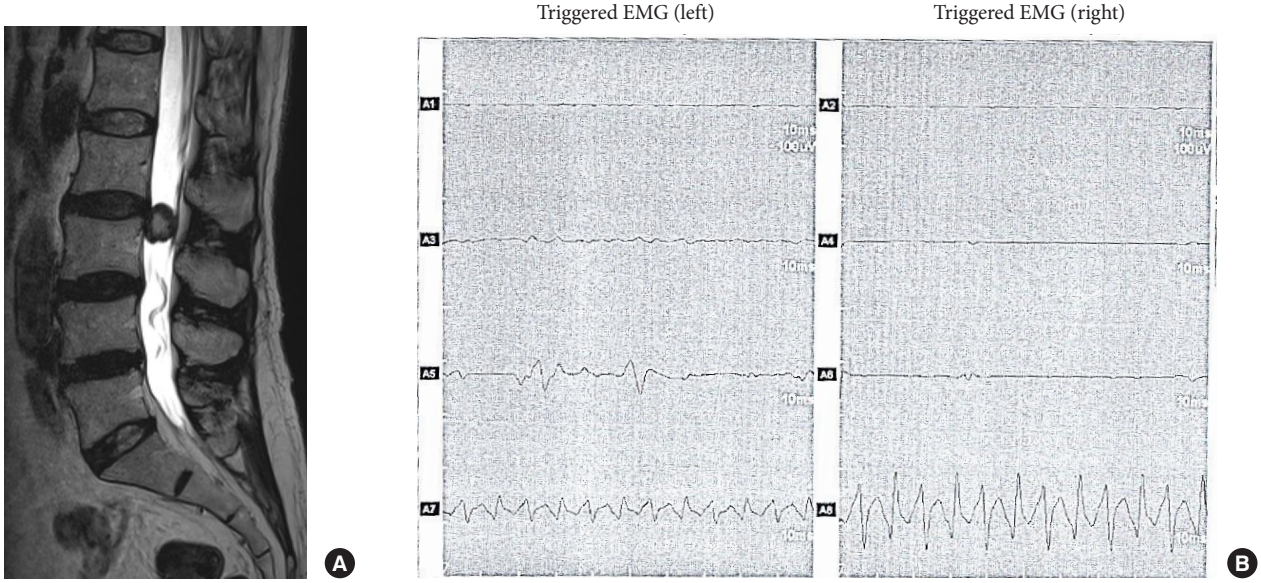

Fig. 3. (A) Preoperative magnetic resonance imaging of a 60-year-old woman who presented with radiating pain in the left leg shows a round intradural-extramedullary mass at the L3 level. (B) On intraoperative triggered electromyogram (EMG), action potentials were identified for the anus bilaterally (A7 & A8) and the left gastrocnemius (A5). A1 & A2, left and right vastus lateralis; A3 & A4, left and right tibialis anterior; A5 & 6, left and right gastrocnemius; A7 & 8, left and right sphincter ani externus.

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mean age of the population was 45.4 ± 15.3 years; 45 (43.7%) were males and 58 (56.3%) were females. All patients underwent surgery with the posterior approach and laminoplasty. IDEM tumors were resected in 91 patients (88.3%), and IDED tumors were resected in 12 patients (11.7%). Tumor size did not exceed one vertebral level in 88 patients, whereas 15 patients had multiple or multilevel lesions (Fig. 2). The most common diagnosis was schwannoma in 85 patients (82.5%), followed by myxopapillary ependymoma in 7 (6.8%), and meningioma in 2 (1.9%). Nine patients were diagnosed with other tumors (1 ependymoma, 1 epidermoid cyst, 1 Ewing sarcoma/primitive neuro-ectodermal tumor, 1 hemangioblastoma, 1 lobular capillary hemangioma, 1 mesenchymal chondrosarcoma, 1 mixed germ cell tumor, 1 neurofibroma, 1 paraganglioma).

The clinical presentations of the patients are as follows: the most common chief complaint was pain in 94 of 103 patients (91.3%). Four of 103 patients (3.9%) had intermittent claudication, 1 (1.0%) had weakness, 1 (1.0%) had urinary symptoms, and 3 (2.0%) had an incidental finding. Preoperative neurologic examination on admission revealed that 6 patients (5.8%) had objective weakness (unilateral lower limb: 3, bilateral lower limb: 3), 4 (3.9%) had hypoesthesia, including saddle anesthesia, and 2 (1.9%) had bladder or bowel symptoms. There was no significant difference between the tEMG-only and MIOM groups, except for the clinical follow-up duration (Table 1).

2. Postoperative Outcome

Regarding the chief complaint, 72 of 94 patients (76.6%) who complained of pain experienced relief. Regarding the neurological outcomes, a permanent postoperative motor deterioration, including bladder and/or bowel symptoms, was observed in 8 of 103 patients (7.8%). Two patients (2 of 103, 1.9%) had bladder and/or bowel symptoms and 6 (6 of 103, 5.8%) had skeletal muscle weakness in a lower limb; the other 16 of 103 patients (15.5%) had sensory deficits. There was no significant difference between the incidences of postoperative neurologic dete-

Table 2. Crosstables of true positives, false positives, true negatives, and false negatives

Overall (tEMG-only group + MIOM group, n = 103)			
tEMG - overall	Neurological deficit (+)	Neurological deficit (-)	Subtotal
EMG (+) & root sacrifice	3	5	8
EMG (-) or (EMG [+] & root preserve)	5	90	95
Subtotal	8	95	103
tEMG-only group (n = 38)			
tEMG single	Neurological deficit (+)	Neurological deficit (-)	Subtotal
EMG (+) & root sacrifice	3	4	7
EMG (-) or (EMG [+] & root preserve)	1	30	31
Subtotal	4	34	38
MIOM group (n = 65)			
tEMG with MEP	Neurological deficit (+)	Neurological deficit (-)	Subtotal
EMG (+) & root sacrifice	0	1	1
EMG (-) or (EMG [+] & root preserve)	4	60	64
Subtotal	4	61	65
MEP	Neurological deficit (+)	Neurological deficit (-)	Subtotal
MEP (+)	3	6	9
MEP (-)	1	55	56
Subtotal	4	61	65
SSEP	Neurological deficit (+)	Neurological deficit (-)	Subtotal
SSEP (+)	3	0	3
SSEP (-)	5	57	62
Subtotal	8	57	65

tEMG, triggered electromyogram; MIOM, multimodal intraoperative monitoring (tEMG + MEP + SSEP + BCR); MEP, motor evoked potential; SSEP, somatosensory evoked potential; BCR, bulbocavernosus reflex; N.Deficit, neurological deficit;

rioration in the 2 groups. Similarly, there were no statistically significant differences between the gross total resection (GTR) or recurrence rates of the 2 groups. Three of the 80 patients (3.8%) who underwent GTR surgery had recurrence; 2 had schwannomas and one had a meningioma. Of the 27 patients who underwent subtotal resections (defined as resection of more than 50% of the tumor but less than complete resection), there was recurrence in 13 (56.5%) (Table 1).

3. tEMG and IOM Data Analysis

Of the 103 patients with tEMG mapping, 8 had a positive tEMG (Fig. 3). Three of these 8 patients developed postoperative motor deficits (true positive) and 5 did not (false positive). The tEMG was negative in 95 patients; 5 developed postoperative motor deficits (false negative) and 90 did not (true negative). The true-positive, false-positive, true-negative, and false-negative tEMG, MEP, and SSEP of the tEMG-only and the MIOM groups were counted. We have summarized the results in Table 2.

The overall tEMG of all the patients showed a sensitivity of 37.5%, a specificity of 94.7%, and an accuracy of 90.3%. When only tEMG was performed, the sensitivity was 75.0%, the specificity was 88.2%, and the accuracy was 86.8%. When combined with MEP, tEMG showed a sensitivity of 0%, a specificity of 98.4%, and an accuracy of 92.3%. The sensitivity and specificity of MEP were 75.0% and 90.2%, and the sensitivity and specificity of SSEP were 37.5% and 100.0%, respectively (Table 3).

One patient in the MIOM group who underwent intraoperative BCR monitoring showed a positive sign (100% amplitude loss) and developed defecation and urination disorders as postoperative complications. Overall, 2 patients had bladder and/or bowel symptoms after surgery; 11 had a positive sign (an amplitude reduction of less than 50%).

4. An Illustrative Case

A 60-year-old woman presented with radiating pain in the left leg. The diagnosis was schwannoma (Fig. 3). On tEMG, action potentials were identified for the anus bilaterally (A7 & A8) and the left gastrocnemius (A5); the action potential was especially definite for the right anus (A8). Before the final assessment of the involved rootlet, the tEMG finding was positive. However, the nerve rootlet was resected as part of GTR. After the surgery, the patient developed urinary incontinence (stimulation settings: rate, 5 Hz; duration, 0.1 msec; intensity, 5.0 mA).

Table 3. Utility of intraoperative monitoring in intradural cauda equina tumor surgery

Variable	tEMG		MEP	SSEP
	Overall (n = 103)	Single (n = 38)	With MEP (n = 65)	
Sensitivity (%) (95% CI)	37.50 (8.52–75.51)	75.00 (19.41–99.37)	0 (0–60.24)	75.00 (19.41–99.37)	37.50 (8.52–75.51)
Specificity (%) (95% CI)	94.74 (88.14–98.27)	88.24 (72.55–96.70)	98.36 (91.20–99.96)	90.16 (79.81–96.30)	100 (93.73–100)
Positive predictive value (%) (95% CI)	37.50 (14.84–67.38)	42.86 (20.29–68.84)	0	33.33 (16.24–56.32)	100
Negative predictive value (%) (95% CI)	94.74 (91.31–96.86)	96.77 (84.55–99.40)	93.75 (93.56–93.94)	98.21 (90.95–99.67)	91.94 (86.95–95.12)
Prevalence (%) (95% CI)	7.77 (3.41–14.73)	10.53 (2.94–24.80)	6.15 (1.70–15.01)	6.15 (1.70–15.01)	12.31 (5.47–22.82)
Odds ratio (%) (95% CI)	10.80 (1.99–58.60)	22.50 (1.86–271.95)	4.48 (0.16 -126.57)	27.50 (2.46–307.72)	73.18 (3.33–1,607.80)
Accuracy (%) (95% CI)	90.29 (82.87–95.25)	86.84 (71.91–95.59)	92.31 (82.95–97.46)	89.23 (79.06–95.56)	92.31 (82.95–97.46)

tEMG, triggered electromyogram; MEP, motor evoked potential; SSEP, somatosensory evoked potential; CI, confidence interval.

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DISCUSSION

We reported the outcomes of the cauda equina tumor resection performed by a single surgeon based on 10-year consecutive data. The most common histological type within the anatomical range was schwannoma (82.5%), followed by myxopapillary ependymoma (6.8%). In a French multicenter retrospective review of 231 cases of adult cauda equina tumors,[15] the most common histologic type was schwannoma (49.3%), followed by ependymoma (34.9%). This is consistent with our findings, although the proportions are different.

IDEM tumors of the cauda equina are rarely associated with postoperative neurological deficits.[6] This has been proposed as a basis for objecting to the need for IOM during cauda equina tumor surgery. The goal of IDEM tumor surgery is to enable the GTR of the tumor while preserving neurological function. However, we often encounter situations in which these 2 goals conflict. A total of 80 patients underwent GTR, and they showed a recurrence rate of 3.8% (3 of 80). Conversely, 23 patients with subtotal resection had a higher recurrence rate of 56.5% (13 of 23). Based on these results, even if cauda equina tumors are mostly benign, the surgeon should make maximal efforts to achieve GTR. Neuromonitoring is important as it increases the rates of total resection while facilitating the preservation of neurological function.[16] In contrast, there was no preventive role for multimodal IOM in cauda equina tumor removal in our study. The surgical outcomes showed no significant differences in neurologic deficits, GTR, or recurrence rate in patients in the tEMG-only and MIOM groups (Table 1). These results are consistent with recent guidelines by Hadley et al.[17] for patients undergoing spinal cord intramedullary tumor resection. There is class I medical evidence supporting the value of IOM as a diagnostic tool for assessing spinal cord integrity in the perioperative setting.[17,18] In lumbosacral spinal procedures, the preservation-related focus of neurological function shifts to the nerve root level, as only the thecal sac and nerve roots are located below the conus medullaris.[19]

Since there was no significant difference between the clinical outcomes of the 2 groups, we focused on the validity of the clinical application of tEMG for cauda equina tumor surgery. tEMG could help determine whether the surgeon will eventually leave residual tumor to preserve the rootlet or resect the rootlet and achieve GTR. In other words, tEMG guides the final decision on sacrificing the nerve, whereas MEP and SSEP are useful for assessing whether the patient will develop neurologic function deficits after the nerve sacrifice. Although MEP and SSEP can be used to diagnose intraoperative neurological injuries, their advantages related to preventing new neurological deficits after spinal surgery are uncertain.[18]

The sensitivity of tEMG was lower (37.5%) than that previously reported,[20] because we included only lesions at the level of the cauda equina. tEMG monitors only a single rootlet, while 2 or 3 nerve segment innervations underlie the final key muscle function based on the results of electrical stimulation studies.[21,22] An additional hypothesis is that a gradual loss of function of the affected root is compensated by concomitant reinnervation of the dependent peripheral structures via the nerve endings of the other roots.[23] When the nerve bundles of the index root are compressed by tumor growth and the lesion of the root develops slowly, functional compensation by innervation from neighboring roots may gradually become predominant.[24] Meanwhile, it is important to perform meticulous dissection of the involved nerve fiber to maximize specificity by gently pulling it away from other surrounding rootlets and tumors. In this procedure, a cotton pattie should be placed under the involved nerve fiber before stimulation to achieve complete isolation, because current interference through other rootlets during stimulation using bipolar forceps leads to false-positive findings (Fig. 1).

Paradiso et al.[20] suggested that SSEP in combination with sEMG is the optimal choice for monitoring in tethered cord release surgery. In that study, the prognostic values of the modalities were similar to those of other lumbosacral procedures owing to the high specificity and relatively low sensitivity of SSEP, which was complemented by a sensitivity of 100% for sEMG/tEMG. Similarly, SSEP showed high specificity (100%) in our study. Although the most common neurological deficit after cauda equina tumor surgery was hypoesthesia, the clinical validity of SSEP was very low because it is very limited in assessing sensory deficits within the global dermatomes of the lower limb; the posterior tibial nerve was the only site being monitored. Nevertheless, SSEP can be used to continuously monitor the sensory pathways of L5 and S1.[7]

Theoretically, BCR examination is effective for functional monitoring of the genitalia, anus, and urethral sphincter. In this study, one of the 65 patients who underwent intraoperative BCR monitoring showed a positive sign (>50% amplitude loss on bilateral BCR monitoring) and developed a severe defecation disorder postoperatively. Because there was only 1 case with serious complications, BCR monitoring showed high specificity, but the finding was not statistically significant. The overall incidence of bladder and/or bowel symptoms after cauda equina IDEM tumor surgery was low (2 of 103, 1.9%). Nevertheless,

the preservation of the S2–4 roots and the pudendal nerve function has the most substantial influence on the quality of life of patients. We believe that changing the criteria to below 50% will be helpful; however, this will require further validation.

This study has several potential limitations. First, there was no histological distinction during the outcome analysis. However, surgeons are usually unsure of the exact histology of the tumor before surgery, and they prepare for perioperative monitoring based on the differential diagnosis of IDEM tumors. Therefore, various histological types were included in the study to evaluate the clinical usefulness of IOM in practice. Second, we did not perform a correlation analysis for sEMG. Third, the MEP, SSEP, and BCR outcome measurement definitions based on the < 50% threshold were not optimum; perhaps those thresholds were not adequate, given that they were reported for intramedullary spinal cord tumors. Fourth, since all the surgeries were performed by a single surgeon, technical progress over 10 years may have affected the results. The surgeries were performed with tEMG alone earlier and multimodal IOM later in this study, and this may have affected the clinical results. Finally, this study was limited by its retrospective design.

CONCLUSION

tEMG is useful for determining whether the involved rootlet needs to be resected. Overall, tEMG showed a low sensitivity (37.5%) and a high specificity (94.7%). Thus, when the tEMG finding is negative, it may be safe to perform the surgery without nerve preservation. Even if the tEMG finding is positive, the probability of actual motor deterioration is less than 50%. The specificity and accuracy can be further improved by using a combination of tEMG and IOM. Nevertheless, to minimize permanent deterioration, maximal efforts should be put into preserving the rootlet through meticulous dissection. All IOM modalities, including tEMG, could not prevent false negatives.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Editorial

Commentary on "Intraoperative Monitoring for Cauda Equina Tumors: Surgical Outcomes and Neurophysiological Data Accrued Over 10 Years"

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See the article "Intraoperative Monitoring for Cauda Equina Tumors: Surgical Outcomes and Neurophysiological Data Accrued Over 10 Years" via https://doi.org/10.14245/ns.2040660.330.

Intra- and perioperative management including radiographic evaluation, fluoroscopic guidance or navigation, and neurological monitoring has facilitated safe and successful spine surgeries. Intraoperative monitoring (IOM) is beneficial to examine whether the nerve is damaged and ultimately to prevent a possible nerve injury. The authors described the utility of triggered electromyogram (tEMG) and multimodal IOM (MIOM) in the resection surgery of cauda equina tumors comparing 38 tEMG-only group and 65 MIOM group.[1] They reported postoperative symptoms with IOM findings and also provided sensitivity and specificity of each modality.

Upon performing resection of cauda equina tumors, surgeons face the decision to sacrifice a nerve root, although it does not always result in a neurological deficit. This may result from the compensation by innervation from neighboring nerve roots while the tumor gradually grows.[2,3] In this study, no significant difference was found in the outcome (neurological deficit, gross total resection, and recurrence rate) between tEMG and MIOM. The authors did not change the surgical strategy depending on the IOM findings, and perhaps do not need to, because total resection of the tumor should be the primary purpose to reduce the recurrence. What we need to discuss carefully is whether the IOM findings could change our intraoperative decision. This study can contribute to balance the conflict between the complete resection of the tumor and the preservation of neurological functions, as the authors suggested that tEMG guided the decision on sacrificing the nerve, and motor evoked potential and somatosensory evoked potential could predict neurological deficits after nerve sacrifice. The authors clarified the reliability of IOM; a low sensitivity and high specificity in tEMG, and improved accuracy with MIOM. This helps us to predict the outcome, however, we need to be aware of false negatives.

The authors should be commended for accumulating the large population of 103 patients treated by a single experienced surgeon, which could make it difficult, on the other hand, to generalize the data for other institutions or surgeons. To demonstrate that tEMG or MIOM eventually reduces the postoperative neurological deficits, a prospective multicenter study would be warranted, which is not so easy to conduct.

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I thank the authors for sharing with us their experience and insight. Although gross total resection of cauda equina tumor should be desirable to reduce the risk of recurrence, it is sometimes hard to achieve depending on tumor size, location, or pathology. The information from IOM to predict the postoperative neurological outcome would help surgeons to decide the nerve root resection and maybe to be less stressed to some extent. I am looking forward to reading another valuable research article from the authors soon.

CONFLICT OF INTEREST

The author has nothing to disclose.

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Title: Still life with cat and lobster
Artist: Pablo Picasso
Year: 1962
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Original Article

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Telemedicine in Neurosurgery: Standardizing the Spinal Physical Examination Using A Modified Delphi Method

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Objective: The use of telemedicine has dramatically increased due to the coronavirus disease 2019 pandemic. Many neurosurgeons are now using telemedicine technologies for preoperative evaluations and routine outpatient visits. Our goal was to standardize the telemedicine motor neurologic examination, summarize the evidence surrounding clinical use of telehealth technologies, and discuss financial and legal considerations.
Methods: We identified a 12-member panel composed of spine surgeons, fellows, and senior residents at a single institution. We created an initial telehealth strength examination protocol based on published data and developed 10 agree/disagree statements summarizing the protocol. A blinded Delphi method was utilized to build consensus for each statement, defined as > 80% agreement and no significant disagreement using a 2-way binomial test (significance threshold of $p < 0.05$). Any statement that did not meet consensus was edited and iteratively resubmitted to the panel until consensus was achieved. In the final round, the panel was unblinded and the protocol was finalized.
Results: After the first round, 4/10 statements failed to meet consensus (< 80% agreement, and $p = 0.031$, $p = 0.031$, $p = 0.003$, and $p = 0.031$ statistical disagreement, respectively). The disagreement pertained to grading of strength of the upper (3/10 statements) and lower extremities (1/10 statement). The amended statements clarified strength grading, achieved consensus (> 80% agreement, $p > 0.05$ disagreement), and were used to create the final telehealth strength examination protocol.
Conclusion: The resulting protocol was used in our clinic to standardize the telehealth strength examination. This protocol, as well as our summary of telehealth clinical practice, should aid neurosurgical clinics in integrating telemedicine modalities into their practice.

Keywords: Telemedicine, Neurosurgery, Telehealth, Neurologic exam, Delphi method

INTRODUCTION

Telemedicine, also known as telehealth, involves the communication of medical information through electronic systems for the delivery of health care, education, and health administration.[1] Potential benefits of telemedicine technologies include providing access to care for patients without a local provider, reducing patient wait and travel times, and decreasing health care costs. Telemedicine has been steadily increasing in use, especially as associated technologies continue to improve.[1,2] In 2016, the Department of Health and Human Services (HHS) estimated that 60% of health care institutions in the United States

used some sort of telemedicine modality, although use remained relatively limited due to lack of patient interest as well as concerns surrounding billing, regulatory and medicolegal matters.[1,3] The coronavirus disease 2019 (COVID-19) pandemic and associated social distancing measures have brought renewed attention to the use of telemedicine in the United States. The HHS has subsequently relaxed regulatory requirements for telemedicine to encourage its use during the pandemic and reduce patient exposure to health care facilities[4]; telemedicine is now an integral part of many health care systems across the country. The use of telemedicine for clinical care will likely remain prevalent throughout the United States given the long-term need for social restrictions.[5]

As a result, neurosurgeons are now faced with the reality of using telemedicine modalities to provide outpatient care, such as in a neurosurgical spine clinic, to minimize the risk of virus transmission. Although new federal policies have increased the accessibility of telemedicine technologies, a number of challenges remain. Primary amongst these is the lack of standardized tele-neurologic examination maneuvers, which is crucial in assessing and following neurosurgical patients. While previous studies have highlighted the reliability of the neurologic exam performed over telehealth technologies, they frequently require the use of an assistant.[6-9] Thus, as patients increasingly attend telehealth visits from their home in order to avoid health care facilities, there is a significant need for a standardized in-home neurologic exam. An additional challenge to the implementation of telehealth technologies in neurosurgical clinics is the lack of familiarity with the clinical evidence surrounding their use as well as unique financial and liability considerations.

To help address these concerns, we (1) describe a standard tele-neurologic examination, based on available evidence in the literature and (2) create a consensus-based tele-strength examination protocol, as this is one of the most challenging parts of a tele-neurologic examination. We then highlight the utility of our protocol through a clinical case of a lumbar disc herniation leading to foot drop that was observed during a telehealth visit using our examination maneuvers. Finally, we discuss the clinical evidence surrounding outpatient neurosurgical telehealth visits, financial and legal considerations, and COVID-19 specific changes.

MATERIALS AND METHODS

1. Literature Review, Quantifying Telehealth Visits

We first performed a literature search to find all spine surgery and neurosurgery articles pertaining to the telehealth neurological examination, as well as billing and coding practices for telemedicine. We found that there were not enough articles to formulate a formal meta-analysis, and therefore used our literature search to create protocol for the Delphi method. Regarding billing, it was not possible to obtain a meta-analysis for 2 reasons: (1) there was an overall lack of published data addressing the billing of the telemedicine in neurosurgery and (2) the COVID-19 pandemic resulted in Centers for Medicare and Medicaid Services (CMS) waiver 1135 (starting March 6, 2020; corona virus waiver) that temporarily reduced restrictions surrounding telehealth care. Thus, the current uncertainty of the permanence of this waiver, combined with the paucity of literature pertaining to neurosurgery clinic visits, precluded a systematic review of telehealth billing. Instead, we summarize current billing practices in the discussion. To better understand the role of telehealth in our patient population, we quantified the number of patients seen in-clinic since the start of the pandemic on a day-by-day basis.

2. Delphi Method

The Delphi Method was used to create a consensus-based tele-strength examination.[10,11] Twelve neurological surgeons (7 spine surgeons, 2 fellows, and 3 senior residents) at our institution were given a 10-item online survey (SurveyMonkey) relating to specific aspects of the tele-strength examination. Surgeons could either "agree" or "disagree" with a given statement. Responses to the initial survey were collected and analyzed. Participants were blinded to each other's responses and to the identity of the other members of the panel. Consensus was defined ahead of time using 2 criteria: (1) $>80\%$ agreement of the panel for a particular question and (2) an exact binomial statistical test against the expected hypothesis of 95% agreement using a 2-tailed p-value threshold of $p<0.05$. All statements failing to meet consensus were analyzed, and direct feedback from disagreeing surgeons was sought. Questions failing to meet consensus were then modified and resubmitted to the expert panel in a second round of the Delphi method. After consensus for all statements was achieved, the final protocol was drafted and sent to the members of the panel. Panel members were unblinded for this portion of the Delphi method. The protocol was then finalized with direct panel member communication to each other.

3. Statistical Methods

All statistical methods were carried out in Matlab (version release 2017b, Mathworks, Inc., Natick, MA, USA) using cus-

tom software to implement the 2-sided exact binomial test, as well as the plotting function.

RESULTS

1. Rate of Telehealth Visits During the COVID-19 Pandemic

Fig. 1 demonstrates the number of patients that were seen using telehealth over an 8-week period at our spine clinic, including before the county's COVID-19 shelter-in-place order (week 1), immediately following the shelter-in-place order (weeks 2–3), and after the shelter-in-place order until the time of writing (weeks 4–8). In order to protect patient identity, exact dates are not shown. As seen, telehealth visits increased in our spine clinic by 10 times following the shelter-in-place order (~0–1 patient

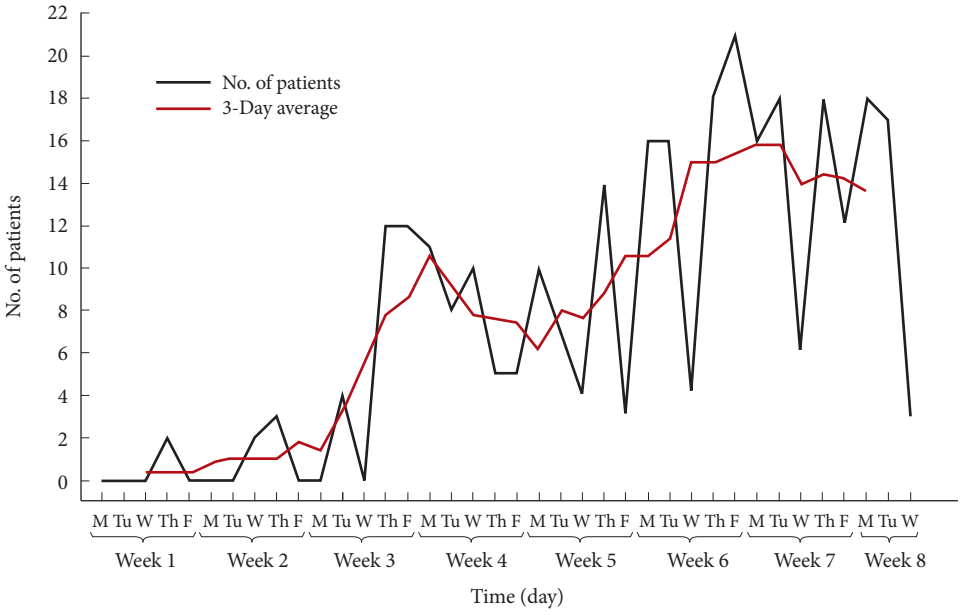

Fig. 1. Line graph of video visits at our spine surgery clinic in the weeks following the city-mandated shelter-in-place order. Daily video visits (thin black line) and the 3-day video visit moving average are shown (thick red line).

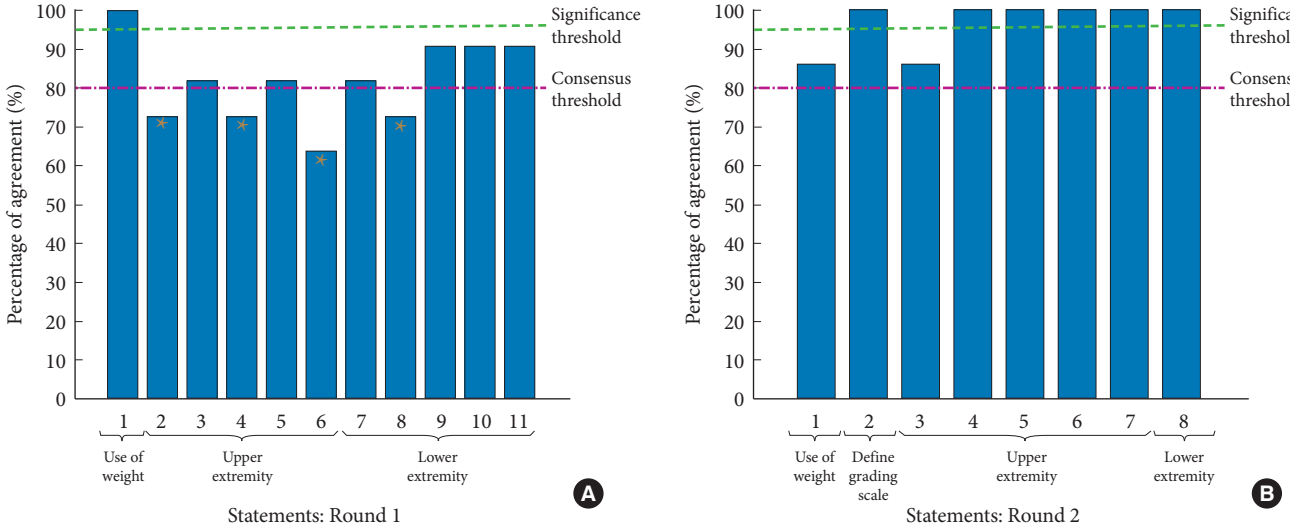

Fig. 2. Percentage of agreement on Delphi consensus statements regarding spine physical exam maneuvers in round 1 (A) and round 2 (B). The consensus threshold was 80% (red dashed line); 95% consensus, used as an expected outcome in 2 tailed binomial testing of significant disagreement, is indicated by the green dashed line. The green asterisk indicates statements that had significant disagreement.

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per day before the pandemic compared to 10–16 patients per day after the pandemic, Fig. 1).

2. Delphi Method

Fig. 2 highlights the results of the first round of the Delphi method. In the first round, 5 statements pertained to the upper

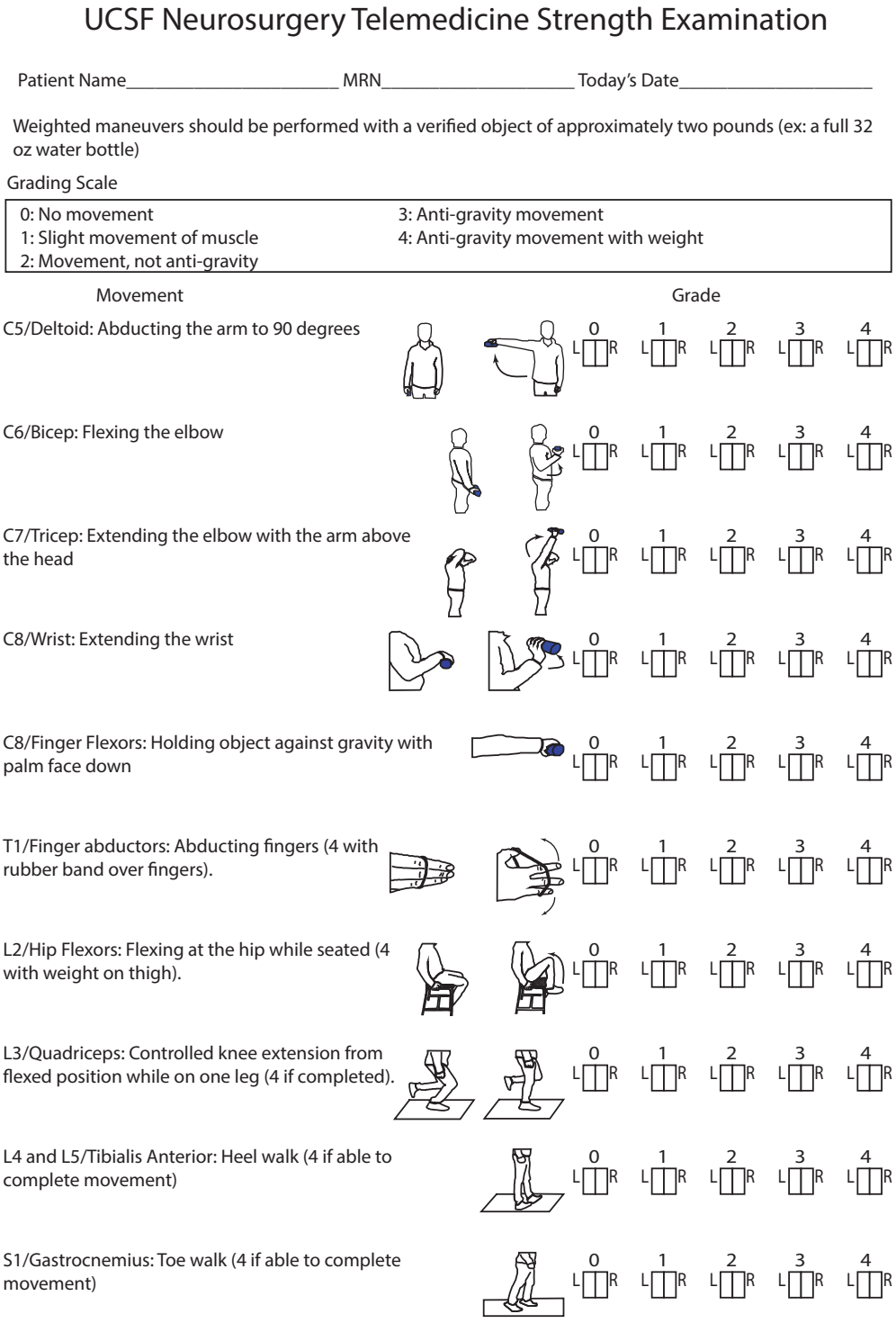

Fig. 3. A consensus-based tele-strength examination as a result of our modified Delphi method. UCSF, University of California, San Francisco.

Table 1. A standard tele-neurologic examination

Exam component	Assessment strategy and comments
Mental status	Can use normal examination methods
Cranial nerves	
II	Visual fields: can be evaluated using a shared screen or with the aid of an assistant. Visual acuity: can be measured with the aid of an assistant and/or the use of a pocket Snellen card. Online tools to measure visual acuity are available, but not yet validated.[49] Fundoscopic exam: currently difficult to accurately performed without an assistant. Can be reported by a trained assistant. New technologies allow assistant to send picture of fundoscopic exam directly to the neurosurgeon.[50] At-home technologies for fundoscopic exams are similarly in development.[51]
III, IV, VI	EOM: can instruct patient which directions to look and observe eyes for deficits or nystagmus. Can also have patient fix eyes on camera and move head from side to site. Pupillary response: can have patient move eye closer to screen and observe response to light. If assistant is present, this can also be performed by assistant with response observed by neurosurgeon. Smart phone based technologies for measurement of pupillary light reflex are accurate, but still under development.[52]
V	Facial sensation: can ask the patient to self-assess, although assistant help is required to accurately perform.
VII	Facial strength: can assess symmetry and gross movements of the face on video.
VIII	Hearing: can grossly assess.
IX and X	Palate: can grossly evaluate palate and phonation of patient.
XI	Shoulder shrug: can assess symmetry of shoulder shrug on video.
XII	Tongue: can assess that tongue is midline on video examination.
Motor	
Upper extremities	Strength: see Fig. 3 for consensus-driven strength exam
Lower extremities	Strength: see Fig. 3 for consensus-driven strength exam Straight leg raise: an assistant can aid by passively raising the leg while observed by the neurosurgeon with moderate accuracy.[53] The patient can also be asked to raise their own leg 20 cm above the table, with any changes in breathing counted as a positive exam. This has demonstrated good reliability.[54]
Tone	Tone can be difficult to assess over telemedicine modalities, although it is possible to grossly assess. An assistant with the patient can also provide some insight into tone, albeit with poor reliability.
Reflexes	Reflexes can be difficult to assess without a trained assistant. The patient or an untrained assistant can be taught how to assess plantar response while observed by neurosurgeon.
Sensation	Frequently requires an assistant with the patient. Often possible to instruct an untrained assistant through a basic sensory examination. The patient can also roughly self-assess how they have been experiencing sensation in day-to-day life.
Cerebellar function	Can ask patient to perform heel to shin test and rapid alternating movements while observed. Can observe patient's gait and ask them to tandem walk if in a safe situation.
Additional spine-specific components	
Assessment of pain/disability	Disability and health-related quality of life: the Oswestry Disability Index and 12-item Short Form health survey can be used to measure disability successfully through telemedicine technologies.[54] Pain: a visual analogue scale and Tampa Scale of Kinesiophobia can both be successfully administered over during a telemedicine visit with good reliability.[54]
Range of motion	Spinal range of motion can be observed by directing the patient through specific maneuvers and asking them bend/twist as far as possible. Studies have shown the assessment of lumbar lateral flexion range of motion to have acceptable reliability when performed in this manner.[54]

extremity, 5 to the lower extremity, and 1 to the use of a weight in the exam. More specifically, statement 1 established that the physical exam should be performed with a known item with a standardized weight. Statements 2–6 described strength testing of the upper extremities, specifically the deltoids, biceps, triceps, wrist extension, grip, and hand intrinsic muscles, respectively. Statements 6–11 then pertained to strength testing of the lower extremities, specifically the iliopsoas, quadriceps, hamstrings, foot dorsiflexion, and foot plantar flexion, respectively. Following completion of the first round, statements 2, 4, 6, and

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Fig. 4. A simulated patient example of the spine telemedicine motor exam performed over an audio/visual communication modality.

8 failed to reach consensus (p = 0.031, p = 0.031, p = 0.003, and p = 0.03, respectively).

We subsequently progressed to the second round of the Delphi method. First, we modified the statements that did not achieve consensus and resubmitted those statements to the panel. We found that the majority of the disagreement in the first round involved how to grade strength using the known object; specifically, that a 5/5 full strength exam is not possible to test over telemedicine. With that feedback, we created new statement that defined strength grading on a 4-point scale (0, no movement; 1, movement not against gravity; 3, movement against gravity; and 4, movement against resistance, and modified the strength testing of muscle groups accordingly (Fig. 2B). After this modification, all statements achieved consensus.

Finally, we used the consensus statements from the Delphi rounds to create the finalized protocol (Fig. 3). This protocol fits on one printed page and can be used by the surgeon or advanced practitioner when completing the muscle strength physical examination over telemedicine.

In addition to the spine-specific motor physical examination, we also list in Table 1 a standard neurological examination. The examination techniques were extracted from both neurosurgery and neurology publications.[6-9,12] We utilized these results and clinical experience to produce a template for a general telemedicine neurologic exam in neurosurgical patients (Table 1). The general neurological examination should be used to supplement the motor examination (Fig. 3) as needed. Fig. 4 depicts a simulated patient example of the spine telemedicine motor examination being performed over an audio/visual communication system.

DISCUSSION

1. Overview of Telemedicine in Surgical and Neurosurgical Clinical Practice

Routine outpatient visits, including preoperative assessment and monitoring of chronic conditions, are key areas in which telemedicine has been shown to be safe, time-saving, and cost effective. One of the leaders of telemedicine in the United States, the Department of Veterans Affairs (VA) has highlighted the applicability of telemedicine technologies for routine outpatient visits beginning in the 1990s, with continued growth since that time.[13] However, there is limited published data from the VA on their telemedicine experience with regard to surgical subspecialties. A 2018 pilot study investigating the use of telemedicine by the Connecticut VA plastic surgery department demonstrated high patient satisfaction among 41 patients who were seen using telemedicine technology.[14] Beyond the VA, preoperative assessment of patients via telemedicine has been shown to be accurate with regards to diagnosis and treatment planning in

both pediatric surgery[15] and oral and maxillofacial surgery[16] with no significant difference in outcomes and reduced cost. Studies within neurology have also demonstrated the feasibility of telemedicine in the evaluation and monitoring of neurologic diseases such as epilepsy,[17] movement disorders,[18,19] and dementia.[20,21]

While literature regarding nonneurosurgical subspecialties and neurology is more plentiful, the application of telemedicine has also been sparsely described in the neurosurgical literature. James[22] describes their experience with the formation of a pediatric neurosurgical telemedicine clinic for routine outpatient visits from 2011–2016. Subsequent analysis of the clinic's socioeconomic impact revealed significant time and cost savings in excess of $233 per family.[23] Similarly, Mendez et al.[24] highlighted the feasibility of using a remote-presence robot for the programming of neuromodulation devices, with comparable outcomes relative to in-person visits. While the described studies are promising, additional investigations evaluating cost and clinical outcomes associated with telemedicine for outpatient care across neurosurgical subspecialties are needed.

Telemedicine technologies have also been described in the routine postoperative care of patients across surgical subspecialties for over a decade.[25] Studies from urology[26] to orthopedic surgery.[27] have demonstrated equivalent or improved efficacy and safety of telemedicine visits when compared to those in the clinic. A systematic review of telemedicine in postsurgical care found a slight increase in complications with telemedicine use (2.8% [7 of 254] vs. 0.4% [1 of 242]); however, there was also no significant difference in postoperative complications in any individual study.[25] Studies performed specifically within neurosurgery have also demonstrated the safety and cost-effectiveness of telemedicine in postoperative care.[28-31] International studies have also demonstrated reduced travel time, cost-effectiveness, and cost-saving associated with the use of Skype teleconferences (Skype Technologies S.A.R.L, Luxembourg City, Luxembourg) in the postoperative management of patients.[28,31] It is also possible that simple postoperative procedures, such as suture removal,[32] may be directed using telemedicine, although further investigation is needed.

Table 2. Traditional telephonic CPT codes

CPT code	Description
99441	5–10 Minutes of medical discussion
99442	11–20 Minutes of medical discussion
99443	21–30 Minutes of medical discussion

CPT, current procedural terminology.

2. Financial and Legal Considerations

Prior to the COVID-19 pandemic, the use of telehealth in the United States was limited by concerns regarding reimbursement as well as federal and state regulations surrounding patient privacy, physician licensure, and liability.[1,3] There was confusion regarding what constituted a "tele-visit" as well, with different definitions, coding requirements and reimbursement rates for provider-patient electronic communication. As an example, Table 2 shows traditional current procedural terminology codes associated with telephonic, patient-initiated interactions. As providers seek to adapt to the pandemic, the HHS has expanded telemedicine coverage and relaxed regulations surrounding telemedicine in an effort to increase patient access to care without the need to travel to a health care facility.[4,33,34] While the regulatory situation remains fluid, there have been key changes that affect the clinical practice of neurosurgery.

A turning point in the use of telemedicine modalities for clinical care was the President's initial declaration of a public health emergency on January 31st, 2020. Subsequently, the federal government, including the HHS and CMS began implementing policies to increase access to telehealth visits for patients. Early changes targeted the coverage of telemedicine, including telehealth visits (defined as using synchronous audio and video technologies to replace visits that usually occur in-person), Virtual Check-Ins (brief communication, including over a telephone, usually patient-initiated but can also be initiated by the provider), and E-Visits (non-face-to-face patient-initiated communications via online patient portal) (Table 3[33]). Historically, Medicare telehealth visits and virtual check-ins were limited to established patients in rural settings, with restrictions on the

Table 3. Telehealth appointment types

CPT code	Description
Face-to-face	
99201-99205	Outpatient new patient encounter
99211-99215	Outpatient established patient encounter
99231-99233	Subsequent hospital care
99354-99357	Prolonged service office/inpatient
Non-face-to-face	
G2012	Brief technology-based assessment 5–10 minutes, "virtual check-in"
99421-99423	Online digital evaluation and management through online portal

CPT, current procedural terminology.

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frequency of visits.[35,36]

Initially, coverage was not extended to telehealth visits with patients in their own homes.[35] On March 6, 2020, however, CMS expanded coverage for telehealth via an 1,135 waiver. The waiver removed geographic and visit frequency restrictions on reimbursement. In addition, coverage was expanded to a variety of office and hospital visits performed via telehealth technologies, including visits with patients at their homes, with equal reimbursement as a regular in-person visit. Also included in this waiver are initial patient evaluations in the hospital and emergency department as well as observation status, which previously were not eligible for telehealth coding and payment. This applies to both new and established patients for the duration of the COVID-19 public health emergency.[33] Although many private insurance payers have follow suit with similar policies, there remains variability in reimbursement guidelines between private insurance plans as well as from state to state Medicaid programs. Nevertheless, the actions taken by CMS with regards to telehealth visit reimbursements have increased the financial viability of using these technologies for patient care. It is unknown how long these waivers will last once the COVID pandemic has resolved but there has been a dramatic surge in their popularity during this crisis.[33]

In an effort to increase telehealth accessibility, the Office for Civil Rights at HHS has determined that essentially any patient-facing audio/visual communication method (e.g., Zoom, Skype, Apple FaceTime) can be used for telehealth visits. While these modalities are not considered Health Insurance Portability and Accountability Act compliant by HHS, the agency has temporarily suspended enforcement of noncompliance with these rules. However, this exemption does not include the use of public facing modalities (e.g., TikTok, Facebook Live).[37] Similarly, Medicare and Medicaid licensure requirements have been relaxed. Thus, physicians can practice, including telehealth visits, outside of the state they are licensed in, although state-specific regulations should be considered as well.[38] The Drug Enforcement Administration has also reduced restrictions, allowing providers to prescribe medications following a telehealth visit.[39] While these policies increase patient and physician access to telehealth visits, their long-term fate and the liability to the physician remain to be determined.

As the use of telemedicine visits grows, so to have concerns regarding associated physician malpractice and liability.[40] Fogel and Kvedar[41] performed a search of legal databases for medical malpractice suits associated with direct-to-consumer telemedicine and found no cases. This is likely due to the relatively low numbers of telemedicine visits.[41,42] Additionally, telehealth visits frequently involve outpatient visits that have relatively low malpractice risk.[41,43] Nevertheless, telehealth-specific malpractice considerations include the need for informed consent of the patient as well as ensuring the security and privacy of communication devices.[43,44] Measures to increase the security of a telemedicine visit vary depending on the service being used, but include the use of a password to access the visit, disallowing participants to join before the host, utilization of a virtual waiting room and preventing additional users from joining the visit once it has started. In addition, physicians should consider that essentially any telecommunication with a patient, regardless of how short, is considered professional advice[45] and establishes the patient-physician relationship, a requisite for professional liability. Thus, while telemedicine does not currently seem to be associated with increased rates of malpractice suits, neurosurgeons should take adequate precautions as we continue to learn more about telehealth practice.

3. Limitations

The most significant limitations of the protocol in Fig. 3 are (1) development at a single-center and (2) lack of prospective validation of this technique. However, given the highly extenuating circumstances involving the COVID-19 pandemic, the use of telemedicine is rapidly rising. It is thus useful to compare institutional protocols during this time, leaving the prospective validation of such protocols to future studies. Similarly, the general tele-neurologic exam in Table 1 requires additional validation, especially as cranial nerve abnormalities can be subtle and difficult to detect over visual/audio communication systems. Rather, Table 1 should serve as a guide to the literature surrounding general tele-neurologic exam maneuvers to supplement our consensus bases tele-strength protocol (Fig. 3) as needed. Despite these limitations, we believe the standardized physical examination maneuvers in our tele-neurologic examination and tele-strength protocols can act as a template for neurosurgical providers in their telehealth clinics, improving the efficacy and reliability of their tele-physical exams. To our knowledge, this is the first study to provide a consensus-based tele-strength examination.

However, there remains paucity of neurosurgical specific data surrounding the clinical applicability of these technologies as well as the performance and reliability of the tele-neurologic exam; additional research is required to determine best practices, including the sensitivity and specificity of telehealth-specific examination maneuvers. As a result, telemedicine examinations

should still be interpreted with caution as their ability to replicate in-person findings has not been fully elucidated. Telemedicine is a newer modality of patient care, especially for spine surgeons, and does not completely replace in-clinic visits at this time. Rather, it should be used in the appropriate clinical scenarios, such as low-risk outpatient visits, and to protect patients from the risk associated with in-person visits to health care facilities. Future studies providing guidelines surrounding which types of patient visits are most amenable to telemedicine are warranted. Patient feedback on telemedicine visits should also be gathered and incorporated into clinical practice. Despite these limitations, telemedicine for neurosurgery will likely continue to play a role in the care of patients even after the COVID-19 pandemic has resolved, particularly as technologies continue to improve. Exciting future applications include telepathology,[46] tele-surgical collaboration,[47] and even the remote performance of surgical procedures.[48]

CONCLUSION

We present a standardized tele-neurological examination and consensus-based tele-strength examination that was created using a formalized Delphi method to build consensus among a panel of spine neurological surgeons. We also provide a brief overview of the clinical evidence surrounding telehealth visits in neurosurgery as well as financial and legal considerations to aid neurosurgeons venturing into telehealth practice.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Original Article

Influence of Frailty on Life Expectancy in Octogenarians After Lumbar Spine Surgery

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Objective: Many studies have reported positive surgical outcomes and decreased mortality after spine surgery in the elderly population, including patients between 85 and 90 years of age. Here, in addition to patient age, we investigated the influence of frailty on short and long-term mortality in octogenarians after lumbar surgery.
Methods: We performed a retrospective analysis of 162 patients over 80 years of age who underwent posterior lumbar fusion or decompressive laminectomy between January 2011 and September 2016. We examined patient survival and modified frailty index (mFI) from medical records.
Results: By October 2019, 29 of 162 patients had expired (follow-up period: 1–105 months). Three-month mortality was 1.9%, and 1-year mortality was 4.9%. Frailty did not affect long-term survival at 1 year but was associated with 3-month mortality ($p = 0.024$).
Conclusion: There was no relationship in long-term survival according to frailty in patients 80 years of age or older, but a difference was identified in short-term mortality. When making a surgical decision for lumbar spine surgery in frail patients over 80 years of age, surgeons should pay attention to the short-term prognosis.

Keywords: Lumbar spine surgery, Octogenarians, Frailty, Mortality, Short-term outcome

INTRODUCTION

The elderly population continues to increase, thereby increasing the need for medical services that support geriatric patients.[1] The degenerative disease spinal stenosis causes radiculopathy or claudication by narrowing the spinal canals. The resulting decrease in activity in lumbar spinal stenosis patients leads to an increase in morbidity of elderly patients. There are reports that surgical treatment of spinal stenosis improves patient quality of life and increases survival by reducing walking disorders and enabling outdoor activities.[2,3] However, the elderly has additional comorbidities, increasing the risk of adverse surgical outcomes. It has been reported that major medical complications and mortality are higher after lumbar spinal surgery in patients 80 years of age or older.[4-6]

Recent reports have indicated that comorbidity is different according to frailty, even within the same age group.[7,8] Frailty, defined as a state of increased vulnerability to poor resolution of homoeostasis after a stressor event, increases the risk of adverse outcomes. A study of United States national database revealed that the frailty index correlated with both mortality and morbidity for all surgical specialties.[9] Using the simplified frailty measurement index, the modified frailty index (mFI), many studies confirmed that frail patients had higher complication and mortality rate in spinal surgery.[10-14] However, no research has investigated short-term or long-term survival in octogenarians compared to the average population and whether it is appropriate to operate a spine surgery on patients with increased frailty. The purpose of our study is to identify long- and short-term (3 months and 1 year after surgery) survival of patients over 80 years of age who received lumbar spine surgery by groups according to frailty and investigate the risk factors such as age,

sex, type of surgery, past history, body mass index (BMI), bone mineral density (BMD), and intraoperative estimated blood loss (EBL).

MATERIALS AND METHODS

We performed a retrospective analysis of 162 patients over 80 years of age who underwent posterior lumbar fusion or decompressive laminectomy for lumbar spinal stenosis between January 2011 and September 2016. Exclusion criteria included (1) history of cancer or other malignancy to influence life expectancy, (2) surgery for infectious lesions (infectious spondylitis or abscess), (3) any history of infection within 3 months of surgery, and (4) quadriplegic or paraplegic patients.

We collected data from hospital records for sex, date of birth, type of surgery, past histories, BMI, BMD, EBL of surgery, and date of death. Date of death was verified by records from the National Health Insurance Corporation. The Institutional Review Board of Gangnam Severance Hospital approved this study (2020-0003-001) with a waiver of informed consents

We calculated the mFI of each patient based on a previously published method.[9] The mFI was simplified from the Canadian Study of Health and Aging Frailty Index, which is based on the theory of accumulating properties that are strongly associated with overall modality of community-dwelling functions. The mFI consists of 11 components: a history of diabetes mellitus, dependent functional status, chronic obstructive pulmonary disease or pneumonia, congestive heart failure, myocardial infarction, percutaneous coronary intervention, stenting, or angina, hypertension requiring medication, peripheral vascular disease or ischemic rest pain, impaired sensorium, transient ischemic attack or cerebrovascular accident, and cerebrovascular accident with neurological deficits (Table 1). The mFI was calculated as the modified frailty score (i.e., the number of deficits present) divided by 11, thus providing an index with a range of 0 to 1. We categorized patients as robust (mFI = 0), prefrail (mFI > 0 and < 0.21), and frail (≥ 0.21) based on previous data defining frailty as an index greater than 0.21.[7]

Data are described as the mean (standard deviation) or median (interquartile range [IQR]). We calculated the survival curve using the Kaplan-Meier survival method and obtained the survival rate for 8 years. We analyzed variation of the survival curve according to structure using log-rank tests. We used linear-by-linear association tests to determine the relationship between 3 months mortality, 1-year modality, and frailty, and the Fisher exact test to identify relationships between sex, age group, and type of surgery. Cox regression analysis was used to compare the survival rate according to sex, type of surgery, and osteoporosis. Hazard ratios and 95% confidence intervals (CIs) were calculated for parameters. All statistical analyses were performed using the IBM SPSS Statistics ver. 25.0 (IBM Co., Armonk, NY, USA).

RESULTS

Of the total 162 patients, mean age was 82.3 ± 2.7 years at surgery (range, 80–92 years). Eighty patients (49.4%) were male (mean age, 83.06 ± 3.31) and 82 patients (50.6%) were female (mean age, 81.62 ± 1.80). The average male age was higher than that of females (p = 0.001). The age distribution was as follows: 80 to 84 years (136 patients; 84%), 85 to 89 years (22 patients; 13.6%), and over 90 years (4 patients; 2.5%). A total of 85 pa-

Table 1. Eleven variables of the modified frailty index

Variable	No. (%)
1. History of diabetes mellitus	47 (29.0)
2. Functional status 2 (not independent)	25 (15.4)
3. History of chronic obstructive pulmonary disease or pneumonia	5 (3.1)
4. History of congestive heart failure	1 (0.6)
5. History of myocardial infarction	1 (0.6)
6. History of percutaneous coronary intervention, stenting, or angina	18 (11.1)
7. History of hypertension requiring medication	113 (69.8)
8. History of peripheral vascular disease or ischemic rest pain	4 (2.5)
9. History of impaired sensorium	5 (3.1)
10. History of transient ischemic attack or cerebrovascular accident	4 (2.5)
11. History of cerebrovascular accident with neurological deficit	5 (3.1)

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tients underwent posterior fusion surgery and 77 patients underwent laminectomy.

The average survival of overall patients was 98.1% at 3-month postsurgery, 95.1% at 1 year, 80.9% at 5 years, and 74% at 8-year postsurgery (48-month median follow-up: 1–105 months). No patient was lost to follow-up. Survival according to sex had no statistical significance (p = 0.051). Three patients expired at 3 months and 8 patients at 1 year postoperatively (Table 2, Fig. 1).

The mean age of patients who underwent posterior lumbar fusion (81.75 ± 2.19 years) was lower than in patients who underwent laminectomy (82.86 ± 3.09 years) (p = 0.01). Except for age, the BMD, BMI, and mFI were not significantly different between the laminectomy group and the posterior lumbar fusion group (Table 3). The mean survival time was higher in patients who underwent fusion surgery (95.86 months [89.8–101.92]) compared to laminectomy (79.17 months [71.82–86.52]) (p = 0.03).

To see an effect on the survival according to the fusion level, we divided fusion surgery patients into who underwent 1- or 2-level fusion (n = 65) and those who underwent more than 3-level fusion surgery (n = 12). There was no significant difference in age, EBL, operation time. mFI scores were lower in more than 3-level fusion surgery than 1- or 2-level fusion surgery (0.15 ± 0.1 vs. 0.08 ± 0.08, p = 0.014). Both in the log-rank test for overall survival time and in the mortality rate at 3 months and 1 year, there was no statistically significant difference.

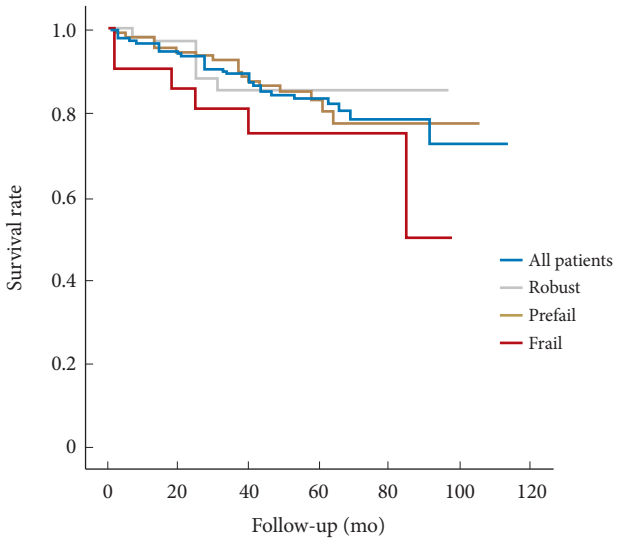

Fig. 1. Kaplan-Meier 8-year survival curves in patients who underwent spine surgery for spinal stenosis according to frailty.

Table 2. Demographic characteristics and cumulative 8-year survival in patients who underwent lumbar spine surgery

Variable	No. (%)	Age (yr), mean ± SD	p-value	3-Month survival (%)	1-Year survival (%)	5-Year survival (%)	8-Year survival (%)	Mean survival time (95% CI)
Total	162 (100)	82.33 ± 2.75		98.1	95.1	80.9	74	88.64 (83.15–94.13)
Sex								
Male	80 (49)	83.06 ± 3.31		98.8	96.3	85	60.4	82.97 (74.96–91.84)
Female	82 (51)	81.62 ± 1.80	< 0.001*	97.6	93.9	90.2	85.1	88.58 (82.51–94.66)
p-value				0.618	0.68			0.051
Type of surgery								
Fusion	77 (48)	81.75 ± 2.19		97.4	96.1	88.5	88.5	95.86 (89.8–101.92)
Nonfusion	85 (53)	82.86 ± 3.09	0.01*	98.8	94.1	74.9	62.9	79.17 (71.82–86.52)
p-value				0.605	1.000			0.032*
Age (yr)								
80–84	136 (84)	-		98.5	95.6	80.5	78.2	86.38 (81.21–91.56)
85–89	22 (14)	-		95.5	90.9	81.8	40.9	82.71 (67.61–97.81)
≥ 90	4 (2.5)	-		100	100	25	No data	39.25 (19.56–58.94)
Frailty								
Robust	34 (21)	82.18 ± 3.42		100	97.1	85.3	85.3	85.06 (76.14–93.98)
Prefail	107 (66)	82.32 ± 2.63		99.1	95.3	80.8	78	90.17 (83.87–96.47)
Frail	21 (13)	82.67 ± 2.13	0.81	90.5	90.5	75.2	50.1	73.96 (58.56–89.36)
p-value				0.043*	0.109			0.381

SD, standard deviation; CI, confidence interval.
*p < 0.05, statistically significant difference.

Table 3. Correlates of patients according to surgery type

Variable	All patients (n = 162)	Posterior lumbar fusion (n = 77)	Laminectomy (n = 85)	p-value
Age (yr)	82.33 ± 2.75	81.75 ± 2.19	82.9 ± 3.09	0.01*
Sex, male:female	80:82	43:42	37:40	0.747
Body mass index (kg/m^2)	23.2 ± 3.5	23.0 ± 3.42	23.39 ± 3.59	0.485
BMD (T-score)	-2.11 ± 1.04	-2.05 ± 1.13	-2.18 ± 0.96	0.464
EBL (mL)	454 ± 398.3	715 ± 374.4	219 ± 242.5	< 0.001*
mFI	0.141 ± 0.108	0.139 ± 0.100	0.142 ± 0.115	0.842
Operation time (min)	152.8 ± 70.6	200 ± 66.0	110 ± 41.6	< 0.001*
ASA PS classification	2.44 ± 0.71	2.53 ± 0.64	2.36 ± 0.77	0.136

Values are presented as mean ± standard deviation or number.
BMD, bone mineral density; EBL, estimated blood loss; mFI, modified frailty index; ASA PS, American Society of Anesthesiologists physical status.
*p < 0.05, statistically significant difference.

Table 4. Patient demographics according to frailty group and components of the modified frailty index

Variable	All patients (n = 162)	Robust (n = 34)	Prefail (n = 107)	Frail (n = 21)	p-value
Age (yr)	82.33 ± 2.75	82.18 ± 3.42	82.32 ± 2.63	82.67 ± 2.13	0.148
Sex, male:female	80:82	22:12	47:60	11:10	0.225
Mean body mass index (kg/m^2)	23.2	22.8	23.4	23.1	0.916
Mean BMD (T-score)	-2.1	-2	-2.2	-1.8	0.399
Type of surgery					
Fusion:laminectomy	77:85	17:17	50:57	10:11	0.892
Mean EBL (mL)	454.8	515.3	432.2	471.9	0.744
Mean operation time (min)	152.8	162	152.5	139.5	0.588
Mean ASA PS classification	2.44	2.29	2.43	2.76	0.660

Values are presented as mean ± standard deviation.
BMD, bone mineral density; EBL, estimated blood loss; ASA PS, American Society of Anesthesiologists physical status.

1. Survival According to Frailty

The mean and median mFI of the study population were 0.18 (standard deviation, 0.09) and 0.09 (IQR, 0.09–0.18), respectively. The maximum mFI was 0.45 (frailty score of 5), which was present in 1 patient. A total of 34 patients (21.0%) were robust, 107 (66.0%) were prefrail, and 21 (13.0%) were frail. The prevalence of individual frailty components is shown in Table 1. Hypertension was the most common individual component of frailty, present in 69.8% of the population. There was no difference in age, sex, BMI, BMD, surgery type, EBL, operation time, and ASA physical status classification among the groups (Table 4). The 8-year survival of robust, prefrail, and frail patient groups was 85.3%, 78%, and 50.1%, respectively, and no difference between each survival curve was identified. However, with linear-by-linear association tests, 3-month survival was related to frailty at 100% in robust, 99.1% in prefrail, and 90.5% in frail patients (p = 0.043) (Table 2, Fig 1).

Table 5. Cox analysis of factors related to patient survival

Risk factor	Hazard ratio	95% CI	p-value
Modified frailty index 0.09 vs. 0	1.232	0.45–3.40	0.69
Modified frailty index > 0.18 vs. 0	1.972	0.56–6.93	0.29
Age	1.125	1.00–1.26	0.04*
Fusion to laminectomy	0.442	0.19–1.02	0.06
Body mass index	1.000	0.90–1.11	0.99
Bone mineral density	1.454	0.99–2.13	0.05
Male to female	1.563	0.67–3.62	0.30

CI, confidence interval.
*p < 0.05, statistically significant difference.

In Cox multivariate analysis, age (hazard ratio [95% CI], 1.125 [1.003–1.262]) was a variable associated with survival. Howev-

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Table 6. Characteristics of mortality cases within 1 year after surgery

Case No.	Age/sex	Underlying Diseases	mFI score	Frailty	Surgery type	Cause of death	Mortality day after surgery
1	80/Female	Hypertension	0.09	Prefrail	1-Level PLIF+PS	Sudden cardiac arrest	5 Days
2	80/Female	Hypertension, asthma, cor pulmonale	0.27	Frail	1-Level laminectomy	Pneumonia	35 Days
3	81/Male	Hypertension, impaired ADL, delirium	0.27	Frail	3-Level PLF+PS	Pneumonia	43 Days
4	86/Female	Hypertension	0.09	Prefrail	1-Level laminectomy	Pancreatic cancer	4 Months
5	82/Male	None	0.00	Robust	3-Level laminectomy	Traffic accident	6 Months
6	80/Male	Hypertension	0.09	Prefrail	1-Level PLIF+PS	Sudden cardiac arrest	10 Months
7	83/Female	Hypertension, diabetes mellitus	0.18	Prefrail	1-Level laminectomy	Stroke	11 Months
8	83/Female	Hypertension, impaired ADL	0.18	Prefrail	1-Level laminectomy	Sudden cardiac arrest	11 Months

mFI, modified frailty index; ADL, activities of daily living; PLIF, posterior lumbar interbody fusion; PLF, posterolateral fusion; PS, pedicle screws fixation.

er, frailty, type of surgery, BMD, BMI, EBL, surgery time, fusion level, and sex did not affect patient survival (Table 5).

Table 6 shows the details of patients who expired within 1 year after surgery. Two frail patients expired of pneumonia within 3 months after surgery and one prefrail patient expired of sudden cardiac arrest 5 days after surgery. One robust patient expired due to a traffic accident 6 months after surgery, and the other 4 were prefrail patients who expired within a year due to medical problems. Patients who expired within 3 months after surgery are described in detail below.

2. Early Mortality Cases

1) Case 1

An 80-year-old prefrail female patient with a history of hypertension, lumbar discectomy, underwent revision laminectomy with 900-mL EBL, and operation time of 160 minutes. On the 5th day after surgery, he expired due to sudden cardiac arrest in the ward.

2) Case 2

An 80-year-old frail female patient with hypertension, asthma, and cor pulmonale underwent revision posterior lumbar interbody fusion surgery on the site where partial hemilaminectomy was performed 12 years ago, and the operation time was slightly longer with 245 minutes, EBL was 700 mL, and incidental durotomy was occurred during the operation. After surgery, she got an acute renal failure and a pneumonia, and on the 35th day after surgery, the patient expired due to multiorgan failure following a pneumonia deterioration.

3) Case 3

An 81-year-old frail male patient with hypertension, dementia, and impaired activities of daily living was presented with quadriparesis after a trauma to the site of stenosis. Before a surgery, a pneumonia was suspected on his chest x-ray, 3-level posterolateral fusion and pedicle screw fixation emergency surgery were performed with 350 mL of EBL and 195 minutes of surgery time. He expired on day 43 due to pneumonia deterioration.

DISCUSSION

People older than 80 years now constitute a rapidly growing portion of the population, and the need for lumbar spinal surgery for elderly patients is increasing.[15] We have seen short- and long-term survival in lumbar spinal surgery in patients over 80 years according to frailty.

It has already been revealed that in the case of 1- or 2-level lumbar fusion surgery, age over 80 years is an important factor in 3-month mortality rate and 1-year mortality rate, which is 3.5-fold and 2.6-fold higher than those of patients aged between 65 and 79, respectively.[4] However, in 10-year survival, it was reported that standardized mortality ratio in patients who received lumbar spinal surgery in the 70- to 85-year age group was 0.45 compared to the general population group.[16] There are debates as to whether surgery has a positive or negative influence on long-term survival, but there is no doubt that surgical treatment has a better outcome for intractable pain or radiculopathy.[17,18] This is because of reducing coronary artery disease by improving ambulation, increasing mobility, and increasing cardiovas-

cular fitness by reducing intractable pain.[19,20]

Fusion surgery has higher rates of postoperative complication in older age groups than decompression surgery, but little is known about the long-term survival after surgery. Posterior lumbar fusion surgery is known to have more complications than decompression surgery due to increased blood loss, longer operation time, and higher infection rate.[21,22] In this study, unexpectedly, patients with fusion surgeries showed higher mean survival compared to patients with laminectomy. We can presume that there would be selection bias because surgeons prefer posterior lumbar fusion for patients who are healthier preoperatively. Kim et al.[16] discussed that in patients over 65 years of age, 10-year survival rate of patients with fusion surgery was greater than the adjusted corresponding portion in general due to these reasons. Thus, we investigated the differences between laminectomy and posterior lumbar fusion groups with regard to age, BMI, BMD, and mFI. Given our results that only age was different between the groups, we presumed that it might be influenced by the higher average age of the decompression surgery group than the fusion surgery group, but there could be many other significant differences that were not evaluated in this study.

Previous reports have shown that higher frailty resulted in increased postsurgical complication rates and higher mortality.[10,23] In these studies, 2.3% to 10% 3-month mortality rates have been reported after spinal surgery in frail patient groups.[24-26] In our study, unlike these studies, survivals were compared using frailty indexes with a group of patients over 80 years of age who underwent posterior lumbar surgery for a single disease. Our result was a 3-month mortality of 9.5% in the frail patient group, both deaths of which were due to septic shock caused by pneumonia after surgery. On the other hand, robust patients within 1 year after surgery showed no death due to medical problems other than a traffic accident. Although our study did not reveal the relationship between longer operation time, longer fusion level, larger EBL, and early mortality, however, when reviewing our early mortality cases, careful attention should be paid to the surgical decision of patients with an unexpected long surgery time and cardiopulmonary problems under general anesthesia in patients over 80 years of age. In addition, when fusion surgery patients were grouped into 1- or 2-level fusion and 3- or more level fusions, only 12 patients with fusion surgery at level 3 or higher were included. It could be a type II error that there was no difference in a short-term mortality and overall survival time in long-level fusion surgery where there are more EBL and longer operation time. A large group study is necessary to reveal this.

Large-scale studies continue to show that high frailty index is a risk factor related to patient long-term survival.[7,27-29] As age increases, frailty index tends to increase, which is associated with the accumulation of adverse events below the subcellular level, indicating that the risk of adverse events may differ even in people of the same chorological age.[30] In the Cox multivariate analysis of our study, we compared survival for 8 years according to frailty, and no statistical significance was found. The maximal mFI of enrolled patients was 0.45, which was present in only 1 patient. Since patients with poor health conditions, as with cancer history excepted from this study, are likely to be excluded before surgery due to surgeon selection bias, the frailty of octogenarians in the general population and the patient group in our study could be different and a bit healthier preoperatively. This exclusion of severe frail patients may have concluded that the survival was associated only with age and not with frailty in multivariate analysis. However, the 3-month mortality rate was significantly higher in patients with an mFI over 0.21 according to our results. We thought that mFIs have a clinical impact on perioperative period. For long-term follow-up, there would be various confounding factors influencing life expectancy. And, this selection bias, one on the main limitation of this study could be teased out by using a propensity score matching.

The major strengths of this study were that we determined the survival rates of patients with long follow-up without a follow-up loss and surveyed patients with obtaining an accurate survival rate and causes of death. Limitations of this study include the lack of a control group, small patient groups, and its retrospective nature. To overcome this limitation, our survival should be compared with an age and sex-matched studies. The number of patients over the age of 90 and frail group was small, so there was a limit to obtaining more powerful statistical results. Surgeon selection bias to rule out unhealthy patients from surgery was inevitable in this study. A randomized controlled trial with larger patient groups would be better to control for this bias.

CONCLUSION

Posterior lumbar surgery in patients over 80 years of age with frailty showed higher mortality in the short-term period, but no difference was found in long-term survival. Therefore, caution is needed regarding short-term postoperative complications when frail patients undergo such a surgery.

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CONFLICT OF INTEREST

The authors have nothing to disclose.

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Original Article

Cervical Lordosis Ratio as a Novel Predictor for the Loss of Cervical Lordosis After Laminoplasty

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Objective: Maintaining cervical lordosis (CL) after laminoplasty is important for indirect decompression of the spinal cord. This study aimed to identify preoperative dynamic radiographic predictors for the loss of CL after laminoplasty.
Methods: We retrospectively analyzed 141 consecutive patients who underwent cervical laminoplasty for cervical myelopathy. The following radiographic parameters were measured before surgery and at 1 year of follow-up: CL, C7 slope, C2–7 sagittal vertical axis (SVA), C2–7 range of motion (ROM), CL in flexion, CL in extension, ROM of flexion (Flex ROM), and ROM of extension. The CL ratio (CLR) was defined as 100 × Flex ROM/C2–7 ROM. ΔCL was defined as postoperative CL minus preoperative CL. Patients were classified into 2 groups: group K (kyphotic change group, ΔCL ≤ -10) and group C (control group, ΔCL > -10).
Results: The patient population comprised 94 men and 47 women (mean age, 70.9 ± 9.4 years), with 24 patients (17.0%) classified into group K. CL, C7 slope, and CLR were significantly higher in group K than in group C. The groups did not significantly differ in age, sex, C2–7 SVA, and C2–7 ROM. On multivariable analysis, the CLR was significantly associated with postoperative kyphotic changes. On receiver-operating characteristic curve analysis (area under the curve = 0.717, $p < 0.001$), the cutoff value for CLR was 68.9%, with sensitivity and specificity of 87.5% and 57.3%, respectively.
Conclusion: The CLR, reflecting the balance between flexion and extension mobility, was identified as a novel predictor for CL loss after laminoplasty, with a cutoff value of 68.9%.

Keywords: Cervical lordosis ratio, T1 slope, Cervical spondylotic myelopathy, Ossification posterior longitudinal ligament, Laminoplasty, Loss of cervical lordosis

INTRODUCTION

Cervical laminoplasty is used to treat cervical myelopathy caused by cervical spondylotic myelopathy (CSM) or ossification of the posterior longitudinal ligament (OPLL). Cervical laminoplasty is an effective posterior surgical method for spinal cord decompression, preserving the motion segments and relatively good long-term results reported.[1-3] The decompression effects of this procedure comprise direct posterior decompression and indirect anterior decompression by a posterior shift of the spinal cord.[4,5] The cervical spine alignment should be lordotic to obtain the indirect decompression effect; thus, maintaining postoperative cervical lordosis (CL) is important. Kyphotic cervical alignment may lead to poor postoperative clinical outcomes.[6] However, cervical laminoplasty, as posterior decompression surgery, can cause injury to the posterior neck muscle-ligament complex; therefore, preoperative CL is not maintained postoperatively in some cases.[7,8]

Several reports have described preoperative predictors of the loss of CL after laminoplasty.[9-17] Recently, the T1 slope has been reported to be an important factor for predicting postoperative kyphosis as the kyphotic alignment change was greater in patients with a high T1 slope.[9,10,12] Other studies have focused on whole-spine alignment parameters for predicting postoperative

kyphotic changes.[16] However, studies evaluating dynamic radiographic parameters are limited.

Therefore, the purpose of this study was to evaluate preoperative dynamic cervical sagittal alignment parameters as potential risk factors for the loss of CL after laminoplasty and determine the cutoff value for the identified risk factor(s). We focused on preoperative radiographic parameters in neutral, extension, and flexion positions.

MATERIALS AND METHODS

1. Patient Enrollment

This study was approved by the Institutional Review Board of Clinical Research Center Kurashiki Central Hospital (No. 3449). We retrospectively reviewed 383 consecutive patients who underwent cervical laminoplasty at our institution between December 2012 and May 2019. Patients diagnosed with CSM or OPLL who underwent cervical laminoplasty from C3 to C6 and completed a 1-year follow-up visit were included. The exclusion criteria were as follows: a history of previous cervical surgery (N = 10), combined with instrumentation (N = 36) and foraminotomy (N = 25), decompression levels including C1 or thoracic spine levels, or use of more selective methods (e.g., C4 to C6) (N = 95), inappropriate radiographic data (N = 33), and follow-up period < 1 year (N = 43). Finally, 141 patients were enrolled in the study. Data regarding demographic variables, including age, sex, body mass index (BMI), and diagnosis (CSM or OPLL), were collected.

2. Surgical Procedures

The muscles attached to the C2 and C7 spinous processes were preserved, while the C3 to C6 laminae were exposed. Double-door laminoplasty[18] was performed from C3 to C6. Hydroxyapatite spacers were placed in the laminar spread from C4 to C6. A spacer could not be placed at C3 because the C2 spinous process was obstructed; however, the C3 lamina was passively maintained spread apart along the C4 lamina. Partial laminectomy was performed at the lower edge of the C2 lamina and the upper edge of the C7 lamina, avoiding damage to the muscle attached to the C2 and C7 spinous processes. Local bone was grafted into the gutter. Postoperatively, patients wore a soft neck collar for several days.

3. Radiographic Parameters

Cervical lateral radiographs were taken in neutral, flexion, and extension positions before surgery and at the 1-year follow-up visit. For radiographs in the neutral position, patients were instructed to stand comfortably and look forward, and CL, C7 slope, and the C2–7 sagittal vertical axis (SVA) were measured (Fig. 1). CL was defined as the angle formed by the inferior end-plates of C2 and C7. The C7 slope was defined as the angle formed by the inferior end-plate of C7 and the horizontal line. C2–7 SVA was defined as the distance between the vertical line from the center of the C2 body and the posterosuperior corner of the C7 body.

For radiographs in the flexion and extension positions, patients either flexed or extended the cervical spine as much as possible, and CL in flexion (Flex CL) and extension (Ext CL)

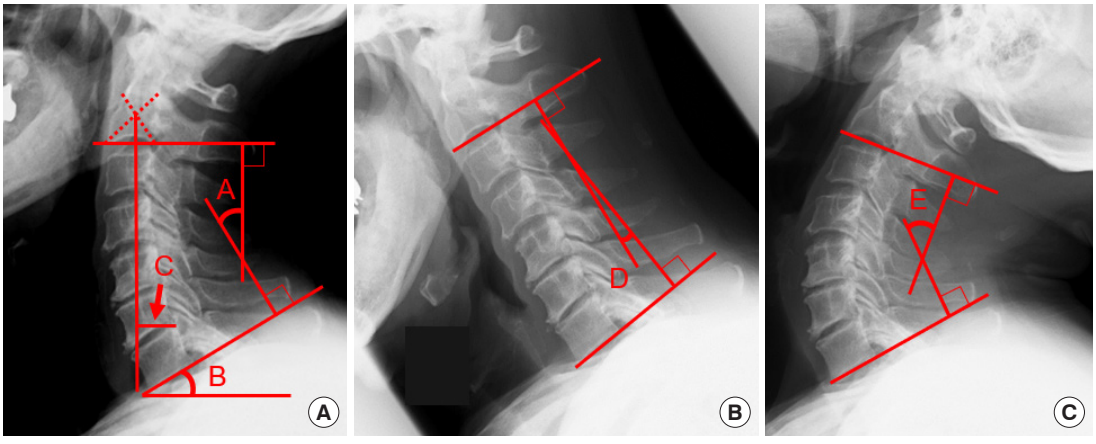

Fig. 1. CL (A), C7 slope (B), and C2–7 SVA (C) were measured in the neutral position. Flex CL (D) and Ext CL (E) were measured with the patients in maximal flexion and extension, respectively. CL, cervical lordosis; SVA, sagittal vertical axis; Flex CL, CL in flexion; Ext CL, CL in extension.

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was measured (Fig. 1). The C2–7 range of motion (ROM) was calculated as Ext CL – Flex CL. ROM of flexion (Flex ROM) was calculated as CL – Flex CL, whereas ROM of extension (Ext ROM) was calculated as Ext CL – CL. The CL ratio (CLR) was defined as 100 × Flex ROM/C2–7 ROM (Fig. 2).

ΔCL was defined as postoperative CL – preoperative CL. Patients were classified into the following 2 groups based on the ΔCL: group K (kyphotic change group, ΔCL ≤ -10) and group C (control group, ΔCL > -10).

4. Clinical Parameters

Clinical outcomes were evaluated using the Japanese Orthopedic Association (JOA) score before surgery and at the 1-year follow-up visit. The recovery rate was calculated based on the Hirabayashi method as follows: JOA recovery rate = 100 × (postoperative JOA – preoperative JOA)/(17 – preoperative JOA).[19]

5. Statistical Analysis

Data are presented as the mean ± standard deviation unless otherwise specified. Spearman rank-order correlation analysis was used to evaluate the relationships between the CLR, ΔCL, and other preoperative parameters. Differences between groups K and C were evaluated using the chi-square test and Mann-Whitney U-test for categorical and continuous variables, respectively. To identify the risk factors for postoperative kyphotic change, a multivariable logistic regression analysis was performed. Receiver-operating characteristic (ROC) curve analysis was used to determine the optimal cutoff value, defined as the point corresponding to the maximum sum of the sensitivity and specificity. Values of $p < 0.05$ were considered statistically significant, and JMP Pro 14 (SAS Institute Inc., Cary, NC, USA) was used for all analyses.

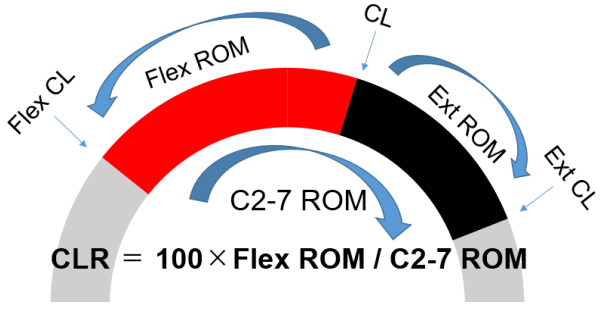

Fig. 2. The CLR was defined as 100 × Flex ROM/C2-7 ROM. CL, cervical lordosis; CLR, CL ratio; Flex CL, CL in flexion; Ext CL, CL in extension; ROM, range of motion; Flex ROM, ROM of flexion; Ext ROM, ROM of extension.

RESULTS

1. Demographic, Radiographic, and Clinical Data

In total, 141 patients (mean age, 70.9 ± 9.4 years; 94 males, 47 females) were enrolled in this study. The overall demographic, radiographic, and clinical data are summarized in Table 1.

2. Correlations Between the CLR, ΔCL, and Other Preoperative Radiographic Parameters

The correlations between the CLR, ΔCL, and other preoperative radiographic parameters are shown in Table 2. ΔCL was correlated with the CLR ($r = -0.499$, $p < 0.001$), CL ($r = -0.282$, $p < 0.001$), Flex ROM ($r = -0.330$, $p < 0.001$), and Ext ROM ($r = 0.390$, $p < 0.001$). In patients with a higher preoperative CL or CLR, greater kyphotic alignment change was observed postoperatively. Similarly, the CLR was correlated with CL ($r = 0.341$, $p < 0.001$), C2-7 SVA ($r = -0.222$, $p = 0.008$), Flex ROM ($r = 0.509$,

Table 1. Demographic, radiographic, and clinical data (n = 141)

Variable	Value
Age (yr)	70.9 ± 9.4
Sex, male:female	94:47
Body mass index (kg/m^2)	23.8 ± 3.7
Diagnosis, CSM:OPLL	118:23
Radiographic data	
Preoperative CL (°)	15.5 ± 12.7
C7 Slope (°)	28.1 ± 9.3
C2–7 SVA (mm)	26.5 ± 13.6
Flex CL (°)	-9.3 ± 13.9
Ext CL (°)	27.2 ± 13.1
C2–7 ROM (°)	36.5 ± 13.6
Flex ROM (°)	24.9 ± 11.4
Ext ROM (°)	11.6 ± 8.0
CLR (%)	67.7 ± 19.3
Postoperative CL (°)	13.1 ± 12.7
ΔCL (°)	-2.5 ± 7.8
Clinical data	
Preoperative JOA score	10.3 ± 2.8
Postoperative JOA score	13.0 ± 2.3
JOA recovery rate (%)	37.1 ± 36.2

Values are presented as mean ± standard deviation or number.
CSM, cervical spondylotic myelopathy; OPLL, ossified posterior longitudinal ligament; CL, cervical lordosis; SVA, sagittal vertical axis; Flex CL, CL in flexion; Ext CL, CL in extension; ROM, range of motion; Flex ROM, ROM of flexion; Ext ROM, ROM of extension; CLR, CL ratio; ΔCL, postoperative CL – preoperative CL; JOA, Japanese Orthopedic Association.

Table 2. Spearman rank-order correlations between CLR, ΔCL, and other preoperative radiographic parameters

Variable	CLR	ΔCL	CL	Flex CL	Ext CL	C7 slope	C2–7 SVA	C2–7 ROM	Flex ROM	Ext ROM
CLR										
r	-	-0.499	0.341	-	-	-	-0.222	-	0.509	-0.807
p-value	-	< 0.001*	< 0.001*	0.215	0.142	0.125	0.008*	0.846	< 0.001*	< 0.001*
ΔCL										
r	-0.499	-	-0.282	-	-	-	-	-	-0.330	0.390
p-value	< 0.001*	-	< 0.001*	0.704	0.538	0.100	0.188	0.368	< 0.001*	< 0.001*

CL, cervical lordosis; CLR, CL ratio; ΔCL, postoperative CL – preoperative CL; Flex CL, CL in flexion; Ext CL, CL in extension; SVA, sagittal vertical axis; ROM, range of motion; Flex ROM, ROM of flexion; Ext ROM, ROM of extension.
*p < 0.05, statistically significant difference.

Table 3. Comparison of each variable according to the postoperative loss of CL

Variable	Group K (n = 24)	Group C (n = 117)	p-value
Age (yr)	72.4 ± 7.8	70.6 ± 9.7	0.651
Sex, male:female	13:11	81:36	0.154
Body mass index (kg/m^2)	23.9 ± 3.3	23.8 ± 3.8	0.958
Diagnosis, CSM:OPLL	22:2	96:21	0.246
Radiographic data			
Preoperative CL (°)	21.5 ± 12.4	14.3 ± 12.5	0.016*
C7 Slope (°)	31.6 ± 9.0	27.4 ± 9.2	0.043*
C2–7 SVA (mm)	25.3 ± 16.8	26.8 ± 12.9	0.777
Flex CL (°)	-9.4 ± 12.8	-9.3 ± 14.2	0.945
Ext CL (°)	30.0 ± 13.0	26.6 ± 13.1	0.163
C2–7 ROM (°)	39.3 ± 14.2	35.9 ± 13.5	0.330
Flex ROM (°)	30.9 ± 13.2	23.6 ± 10.6	0.014*
Ext ROM (°)	8.4 ± 5.2	12.3 ± 8.3	0.037*
CLR (%)	78.1 ± 13.5	65.5 ± 19.7	< 0.001*
Postoperative CL (°)	7.5 ± 11.0	14.2 ± 12.8	0.027*
ΔCL (°)	-14.0 ± 4.1	-0.1 ± 6.2	< 0.001*
Clinical data			
Preoperative JOA score	9.5 ± 2.9	10.4 ± 2.7	0.159
Postoperative JOA score	12.6 ± 2.4	13.1 ± 2.3	0.321
JOA recovery rate (%)	39.6 ± 29.3	36.6 ± 37.6	0.993

Values are presented as mean ± standard deviation or number.
Group K, kyphotic change group (ΔCL ≤ -10); Group C, control group (ΔCL > -10).
CSM, cervical spondylotic myelopathy; OPLL, ossified posterior longitudinal ligament; CL, cervical lordosis; SVA, sagittal vertical axis; Flex CL, CL in flexion; Ext CL, CL in extension; ROM, range of motion; Flex ROM, ROM of flexion; Ext ROM, ROM of extension; CLR, CL ratio; ΔCL, postoperative CL – preoperative CL; JOA, Japanese Orthopedic Association.
*p < 0.05, statistically significant difference.

Table 4. Risk factors for the postoperative loss of CL (ΔCL ≤ -10)

Variable	p-value	OR	95% CI
CL	0.474	-	-
C7 slope	0.275	-	-
CLR	0.012*	42.402	1.906–943.054

CL, cervical lordosis; ΔCL, postoperative CL – preoperative CL; OR, odds ratio; 95% CI, 95% confidence interval; CLR, CL ratio.
*p < 0.05, statistically significant difference.

p < 0.001), and Ext ROM (r = -0.807, p < 0.001). Patients with a higher preoperative CLR had higher CL and lower C2–7 SVA. No significant correlations were observed between the other evaluated parameters.

3. Comparison of Each Variable According to the Postoperative Loss of CL

Postoperative loss of CL (ΔCL ≤ -10) occurred in 24 patients (17.0%; i.e., group K). The differences between groups K and C are summarized in Table 3. The groups did not significantly differ in age, sex, BMI, and diagnosis. The preoperative CL was higher (21.5 ± 12.4 vs. 14.3 ± 12.5, p = 0.016) and the postoperative CL was lower (7.5 ± 11.0 vs. 14.2 ± 12.8, p = 0.027) in group K than in group C. Accordingly, ΔCL was lower in group C than in group K (-14.0 ± 4.1 vs. -0.1 ± 6.2, p < 0.001).

The C7 slope, CLR, Flex ROM, and Ext ROM significantly differed between groups K and C. The C7 slope (31.6 ± 9.0 vs. 27.4 ± 9.2, p = 0.043), CLR (78.1 ± 13.5 vs. 65.5 ± 19.7, p < 0.001), and Flex ROM (30.9 ± 13.2 vs. 23.6 ± 10.6, p = 0.014) were higher and Ext ROM (8.4 ± 5.2 vs. 12.3 ± 8.3, p = 0.037) was lower in group K than in group C. No significant differences were observed in the other radiographic parameters. Preoperative JOA, postoperative JOA, and JOA recovery rates did not significantly differ between groups K and C.

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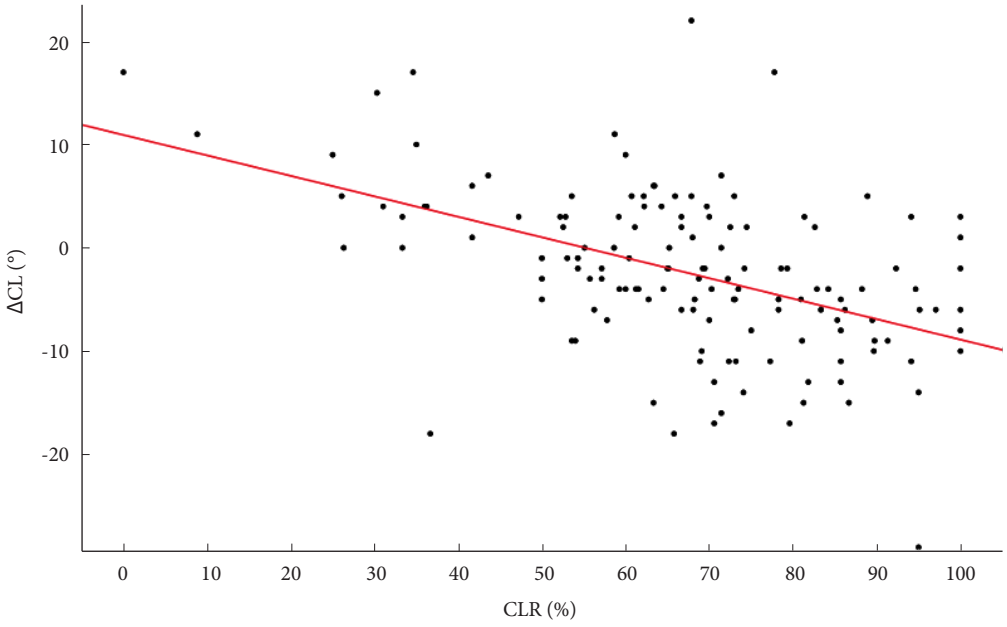

Fig. 3. Scatterplot showing the relationship between ΔCL and CLR. Patients with a higher CLR tended to considerably lose their preoperative CL after surgery (r = -0.499, p < 0.001). CL, cervical lordosis; ΔCL, postoperative CL – preoperative CL; CLR, CL ratio.

4. Risk Factors for Postoperative Kyphotic Change

Multivariable logistic regression analysis was performed to estimate the odds ratio for the postoperative loss of CL (ΔCL ≤ -10) according to 3 preoperative radiographic parameters: CL, C7 slope, and CLR (Table 4). Among the dynamic radiographic factors (CLR, Flex CL, Ext CL, C2–7 ROM, Flex ROM, and Ext ROM), the CLR with the most significant correlation with ΔCL and the smallest p-value on comparison of group K with group C were applied in the multivariable analysis. The CLR was observed to be an independent risk factor for the postoperative loss of CL (p = 0.012; odds ratio, 42.402; 95% confidence interval, 1.906–943.054). The scatterplot in Fig. 3 shows the relationship between ΔCL and CLR. Patients with a higher CLR tended to lose their preoperative CL after surgery considerably. In the ROC curve analysis for the prediction of ΔCL ≤ -10 (area under the curve [AUC] = 0.717, p < 0.001), the cutoff value for CLR was 68.9%, with a sensitivity of 87.5% and a specificity of 57.3% (Fig. 4).

CLR (AUC = 0.717) was more useful as a predictor than CL (AUC = 0.657), C7 slope (AUC = 0.631), Flex ROM (AUC = 0.659), and Ext ROM (AUC = 0.635). CLR was nonnormally distributed, and it did not show significant correlations with age (p = 0.572), sex (p = 0.962), BMI (p = 0.374), and diagnosis (p = 0.744).

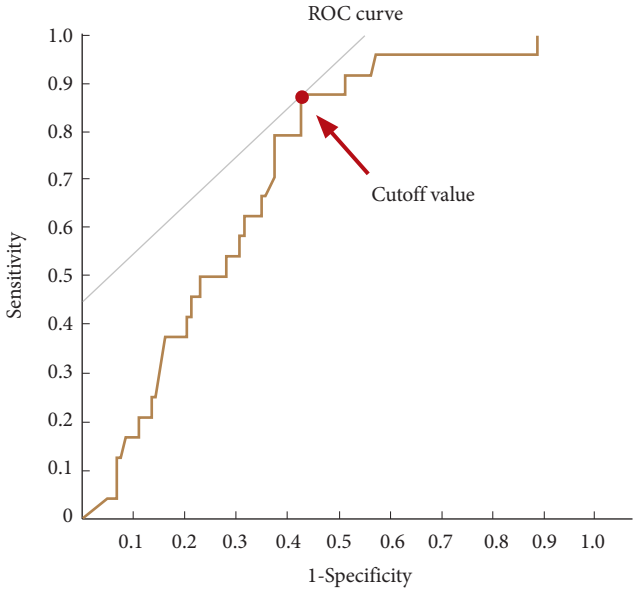

Fig. 4. ROC curve analysis for the prediction of ΔCL ≤ -10 (area under the curve = 0.717, p < 0.001). The cutoff value for the CLR was 68.9%, with a sensitivity of 87.5% and a specificity of 57.3%. CL, cervical lordosis; ΔCL, postoperative CL – preoperative CL; CLR, CL ratio; ROC, receiver-operating characteristic.

DISCUSSION

Cervical laminoplasty is an effective surgical procedure for cervical myelopathy. In this surgical method, posterior com-

pression factors are directly removed and the posterior spinal cord shifts, thus providing indirect decompression effects.[4,5] To obtain this indirect decompression effect, cervical lordotic alignment is important. Therefore, cervical alignment, before and after laminoplasty, is considered to affect clinical outcomes. However, the alignment and ROM of the cervical spine have been reported to change with laminoplasty. For example, Machino et al.[20] reported that the C2–7 Cobb angle became 1.8° more lordotic in the neutral position, 5.9° more lordotic in the flexion position, and 0.6° more kyphotic in the extension position, and the ROM was reduced to 87.9% after surgery. In some cases, the cervical alignment became kyphotic after laminoplasty despite preoperatively maintaining CL. Thus, the preoperative prediction of the loss of CL after surgery would be useful for obtaining good clinical outcomes by laminoplasty.

Various risk factors have been reported for kyphotic alignment change after laminoplasty.[9-17] For example, Machino et al.[15] reported that the cutoff value of the preoperative C2–7 lordosis angle for the prediction of postlaminoplasty kyphosis was 7° in patients with CSM without a preoperative kyphotic angle. Additionally, Sakai et al.[13] reported that a greater center of gravity of the head – C7 SVA (cutoff value, 42 mm) and advanced age (cutoff value, 75 years) were risk factors for kyphotic deformities after laminoplasty in patients without preoperative cervical kyphotic alignment. In contrast, Matsuoka et al.[16] focused on the global spinal alignment and reported that in patients without preoperative cervical and global spinal sagittal imbalance, a small C7 SVA accompanied by lumbar hyperlordosis was the characteristic alignment leading to postoperative cervical kyphosis after laminoplasty. Recently, the T1 slope has been discussed as a predictor of postoperative kyphotic alignment change.[9-12] Kim et al.[9] reported that patients with a high T1 slope had greater kyphotic alignment change after cervical laminoplasty at the 2-year follow-up; the authors hypothesized that kyphotic alignment change by posterior structural injury after laminoplasty was more marked in patients with a high T1 slope. In another study, Kim et al.[10] reported that patients with OPLL and a higher T1 slope had more lordotic curvature before surgery and demonstrated a greater loss of CL at the 2-year follow-up. However, Cho et al.[11] reported that the degree of aggravation did not correlate with the preoperative T1 slope and that most clinical parameters improved regardless of the preoperative T1 slope.

We evaluated both static alignment and dynamic image parameters to identify useful predictors for postoperative kyphotic alignment change. Lee et al.[17] reported extension function (EF, Ext ROM) as a new predictor of the loss of CL; no significant kyphotic changes occurred after laminoplasty when the EF was greater than or equal to 14°. The authors hypothesized that the function of the posterior neck muscle-ligament complex was represented by the EF.[17] Suk et al.[14] reported that one of the preoperative factors affecting postoperative kyphosis is a kyphotic angle during flexion that is larger than the lordotic angle during extension. We proposed a new factor, the CLR, as an index reflecting the location of the neutral cervical position within the range of the extension and flexion motion. This implies that patients with a higher CLR have a large flexion ROM and small extension ROM because the neutral position is closer to the maximum extension. The degree of extension mobility indicates the function of the posterior neck muscle-ligament complex and is considered an inhibiting factor of kyphotic alignment change.[17] Additionally, poor flexion mobility is also considered to indicate that cervical kyphosis is inhibited by structural factors, such as bone, ligament, or muscle. Therefore, both Flex ROM and Ext ROM are important factors. This new factor, the CLR, is a useful and simple index for expressing the balance between flexion and extension mobility.

For cases wherein cervical kyphotic change after laminoplasty is predicted, the indications for laminectomy and fusion or anterior cervical diskectomy and fusion (ACDF) should be considered. However, in this study, no significant differences were observed in clinical outcomes between the kyphotic change and control groups. One reason for this may be that the postoperative CL angle in the kyphotic change group was +7.5° on average, and lordotic alignment was maintained in most cases. Alignment changes were considered insufficient to worsen the clinical outcomes, even in the kyphotic change group. As reflected in the cervical laminoplasty procedures of our institution, we consider that preservation of the posterior neck muscle-ligament complex is important; therefore, the paravertebral muscles attached to the C2 and C7 spinous processes are preserved, even with multilevel stenosis, including C2/3 or C6/7. Supposedly, this minimally invasive surgical procedure contributed to the noninferior clinical outcomes in the kyphotic change group. Takeshita et al.[21] reported that subaxial laminoplasty maintained the cervical alignment; however, if laminoplasty included C2, the alignment worsened. Iizuka et al.[22] reported that preservation of the muscles attached to the C2 spinous process prevented significant changes in cervical alignment after laminoplasty.

This study has several limitations. First, because our study was retrospective, a selection bias may exist. Second, a total of 43 cases were lost to follow-up at 1 year. Third, as the follow-up period was 1 year, the long-term prognosis is unknown. Fourth,

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we could not evaluate the global spinal alignment. Fifth, clinical outcomes were only evaluated by the JOA score. Possibly, the clinical outcomes could be evaluated in a more detailed manner by incorporating other evaluation systems, such as a visual analog scale or the Neck Disability Index. Finally, since this study did not compare surgical techniques (laminoplasty, laminectomy and fusion, ACDF), the optimal surgical procedure could not be indicated based on postoperative kyphotic changes. Hence, this is a theme that should be clarified by future research.

CONCLUSION

We identified a new factor, the CLR, for predicting the loss of CL after laminoplasty. The CLR is a useful and simple index for expressing the balance between flexion and extension mobility. The cutoff value for the CLR was 68.9%.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Original Article

Unilateral Posterior Surgery for Severe Osteoporotic Vertebrae Fractures' Sequelae in Geriatric Population: Minimum 5-Year Results of 109 Patients

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Objective: This study aimed to evaluate the efficacy and safety of modified posterior vertebral column resection (PVCR) combined with anterior column restoration in elderly patients presenting with thoracic or thoracolumbar osteoporotic fractures with spinal cord compression and severe pain.
Methods: One hundred nine patients with one level thoracolumbar osteoporotic fracture and at least 5 years of follow-up were included. They underwent posterior instrumentation performed with polymethymetachrylate augmented pedicle screws. A modified PVCR (unilateral costotransversectomy+hemilaminectomy) combined with the insertion of an expandable titanium cage for anterior column restoration was undertaken. Patients were evaluated clinically and radiographically.
Results: Patients had a mean age of 74.1 and a follow-up duration of 92.3 months. Mean duration of operations, hospital stays, and mean loss of blood were 172.3 minutes, 4.3 days, and 205.4 mL. All of the patients were mobilized immediately after surgery. The mean preoperative local kyphosis angle improved from 39.3° to 4.7° at the last follow-up ($p = 0.003$). Patients preoperative mean visual analogue score, Japanese Orthopaedic Association, and Oswestry Disability Index scores improved from 7.7/8.6/76.3 to 1.6/26.1/17.4 ($p < 0.001$ for all), respectively. The average 36-item Short-Form survey physical component summary/mental component summary scores at the last follow-up were 55.1/56.8. A dural tear was detected intraoperatively in 1 patient and repaired immediately.
Conclusion: Subtotal PVCR combined with the insertion of an expandable titanium cage was detected as a safe and effective method for osteoporotic vertebrae fractures' sequelae in the older population involving spinal cord compression by enabling the decompression of the spinal canal and reconstruction of the resected segment, resulting in significant improvement in clinical and radiographic outcomes.

Keywords: Osteoporotic thoracolumbar vertebrae fractures, Geriatric population, Modified posterior vertebral column resection, Anterior column restoration, Local kyphosis angle, Quality of life

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INTRODUCTION

Osteoporotic vertebrae fractures (OVF) were commonly associated with refractory low back pain and kyphotic deformity. At the same time, all of these clinical features could be complicated with the development of a sagittal imbalance due to progressive kyphosis and with any neurological deterioration as a result of spinal canal compromise.[1-3]

AO (Arbeitsgemeinschaft für Osteosynthesefragen) type A1 and A3[4] simple compression fractures without any neurological involvement can be managed with conservative treatment including pain-medications, brace and bed rest, or with minimal invasive surgery including percutaneous vertebroplasty (PVP) or balloon kyphoplasty.[5,6] However, for severe fractures associated with progressive kyphosis and neurological symptoms, these conservative or minimally invasive methods could neither yield a sufficient spinal cord decompression and clinical amelioration nor could they correct kyphotic deformity together with restoration of sagittal balance and reconstruction of spinal stability.[7-9]

For patients with OVF sequelae, besides the treatment of the underlying cause, open surgery is indicated in the presence of progressive kyphosis (>35°), neurological deficit, and intractable pain, with the aims to eliminate the pain, reconstruct the sagittal balance and mobilize the patients as soon as possible to prevent any immobilization related complication and to provide sufficient quality of life.[9-11]

Dealing with the osteoporotic spine was frequently reported to be extremely challenging because of the poor bone quality, which could jeopardize the pedicle screw holding force leading to increased rates of loosening and pull-out of the screws.[2,3,12] Therefore the ideal treatment of severe OVF requiring open surgery is still under debate. We hypothesized if the modified PVCR was an acceptable treatment alternative for OVF sequela with hyperkyphosis and severe pain requiring open surgery, while presenting the long-term results, our modified posterior vertebral column resection (PVCR) method combined with restoration of anterior column applied that group of patients. We questioned whether this method in the geriatric population was able to provide adequate spinal decompression and successful restoration of the sagittal balance, which could be sustained in the long term.

MATERIALS AND METHODS

Following the approval of the Institutional Review Board of EMSEY Hospital (Nr:1121052), within the framework of a retrospective study, analysis of patients with osteoporotic (T-score <-2.5 standard deviation [SD] measured with dual-energy x-ray absorptiometry performed in the same institution) thoracolumbar vertebral fractures between 2011–2014 was conducted. Four hundred twenty-eight consecutive patients were detected. Among them, 266 patients were noted to have AO type A1 and A3 simple compression fractures, that conservative treatment including brace-pain medication-bed rest (167 patients), PVP (85 patients), and percutaneous balloon kyphoplasty (14 patients) were applied.

The remaining 162 patients with severe OVF have been assessed according to the strict inclusion and exclusion criteria. Table 1.

As a result of the inclusion and exclusion criteria, 53 patients (47 patients had a history of previous thoracolumbar spine surgery; 6 patients had a history of vertebral tuberculosis) were excluded from the study. The remaining 109 patients were enrolled in the study (Fig. 1).

All patients provided informed consent so that their opera-

Table 1. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Diagnosis of osteoporosis (T-score <- 2.5 SD)	No documented diagnosis of osteoporosis
Age >65 years	Age <65 years
Thoracolumbar vertebral fracture requiring open surgery (local kyphosis angle >35°, presenting-deteriorating neurological deficit (any Frankel grade except E and/or nerve compression symptoms), unstable fracture, spinal canal compromise >30%, anterior vertebral body height <30% of the adjacent vertebra)	A thoracolumbar vertebral fracture, that did not require open surgery/managed conservatively or with percutaneous vertebroplasty or percutaneous balloon kyphoplasty
Modified PVCR (as we described) combined with anterior column restoration using a titanium mesh/expandable cage	A history of previous spinal surgery, tumor, infection (including tuberculosis)
A minimum follow-up duration of 60 months (5 years)	A minimum follow-up duration of less than 60 months (5 years)

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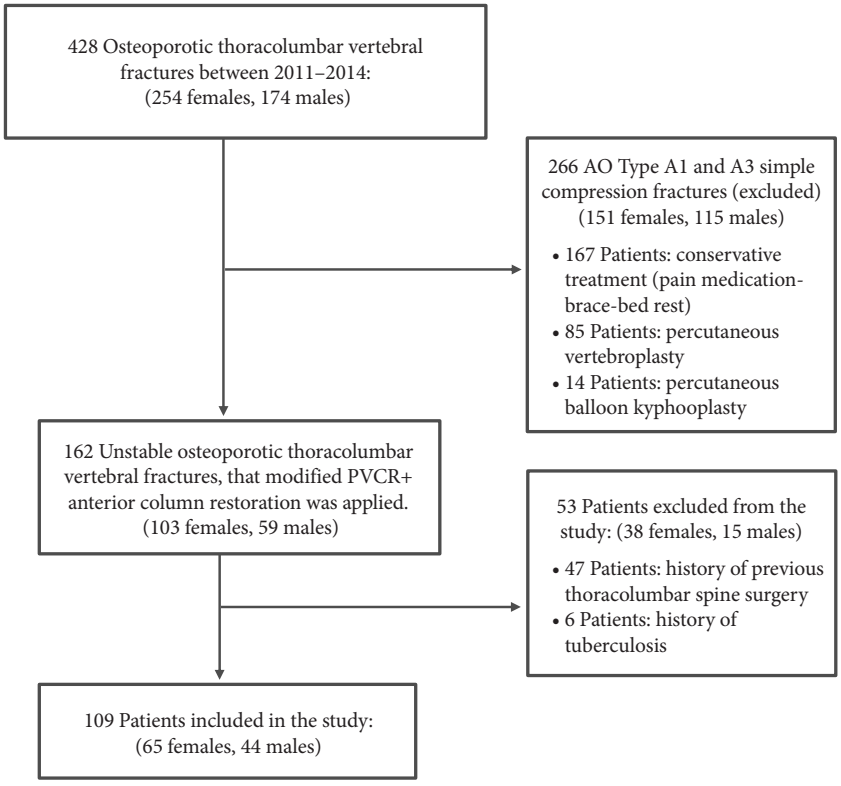

Fig. 1. Flowchart of the study population.

tive, intraoperative, and postoperative data, including the x-rays, computed tomography (CT), and MRI images, could be used for publication by hiding their identity.

1. Surgical Technique

Before the planning of surgeries, patients with poor bone density were placed on bone replacement medication by the endocrinology specialist. However, considering that most of these patients who were needed open surgery were referred to our clinic as a result of failed conservative treatment and worsening of clinical course regarding their neurological status and pain intensity, to prevent any further clinical-neurological deterioration, they were operated on right away after the admission with no additional loss of time. As a result of the consultation with an endocrinology specialist, patients were either started on biphosphonates before the surgery and continued on that medication postoperatively, or they were started with teriparatide postoperatively.

All surgeries were performed with the same technical guidelines under intraoperative neuromonitoring, while the preoperative preparation and postoperative treatment and rehabilitation protocol were also identical in all patients.

Under general anesthesia, patients were placed in a prone position on an operating table. After the confirming the fractured level with the C-arm, a posterior midline skin incision in the length of 2 vertebral levels above and 2 levels below was undertaken. After meticulous soft tissue dissection, pedicle screw entry points were marked. Fenestrated and cannulated pedicle screws were inserted 2/3 levels above and 2/3 levels below the fractured segment under fluoroscopic guidance with the free-hand technique bicortically. Polymethylmethacrylate (PMMA) bone cement was prepared and injected into the pedicle screw channels using PVP catheters with 2 mL/screw in all patients.

After that, modified PVCR was undertaken to the fractured level. A modified PVCR was defined as: (1) unilateral hemilaminectomy combined with costotransversectomy; (2) discectomy of the upper and lower spinal level, together with curettage of the endplates; (3) adequate decompression from one side: At spinal levels above L1 the nerve root was ligated. But at levels below L1, not to cause any neurologic deficit regarding the lower extremity, the posterior ramus of the associated nerve root was ligated, leading to the mobilization of the nerve root. By protecting the nerve root with a root retractor, enough space was freed for the advancement of the expandable cage from

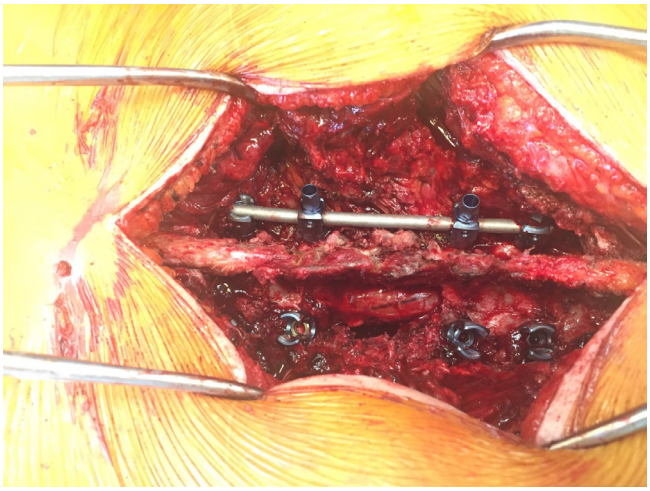

Fig. 2. An intraoperative photo indicating the posterior approach of modified posterior vertebral column resection technique.

posterior; (4) unilateral corpectomy and decancellation of the vertebral body while leaving the anterior cortex and the lateral cortex on the contralateral side intact; (5) insertion of the expandable titanium cage into the vertebral body. During modified PVCR and cage insertion, the posterior construct was secured with one temporary rod placed on the contralateral side. Fig. 2.

After the placement of permanent rods and securing of the entire posterior construct, one-two adjacent uninstrumented level(s) above and below prophylactic vertebroplasty was undertaken in all patients as described formerly.[13]

2. Evaluation of Clinical Outcomes

Clinical outcome parameters were determined using self-assessment questionnaires, including visual analogue score[14] to evaluate the pain level, and Oswestry Disability Index (ODI)[15] completed individually by all patients. Japanese Orthopaedic Association (JOA) scoring system as a validated and reliable method[16] was utilized to evaluate the neurological status and Frankel score.[17] The quality of life of the study population was evaluated by using 36-item Short-Form survey (SF-36) scores.

3. Evaluation of Radiographic Outcomes

Radiographic evaluation was undertaken by 1 senior spine surgeon (TP) pre-, postoperatively and at the follow-up, comprised local kyphosis angle and sagittal vertical axis (SVA).

4. Statistical Analysis

For the statistical analysis IBM SPSS Statistics ver. 22.0 (IBM Co., Armonk, NY, USA) was used. A Wilcoxon signed-rank test was used to evaluate preoperative to postoperative deformity correction. Data were expressed as mean ± SD. Chi-square test and Fisher exact test were used for the analysis of categorical variables where appropriate. One-way analysis of variance was used to determine a significant difference at various time points. A p-value less than 0.05 was considered statistically significant.

Table 2. Demographic data (n = 109)

Variable	Value
Sex, male:femal	44:65
Age (yr)	74.1 (67–84)
Body mass ındex (kg/m^2)	23.4 (21.7–28.2)
Duration of follow-up (mo)	92.3 months (60–106)
Preoperative T-score measured with dual energy x-ray absorptiometry	-3.4 (-2.7 to -4.2)
No. of fractured levels	
T8	2
T9	5
T11	11
T12	47
L1	41
L2	3
Duration from the onset of symptoms to surgery (mo)	4.6 (3–9)
Duration of operation (min)	172.3 (161.4–221.9)
Loss of blood (mL)	205.4 (129.1–467.2)
Duration of hospital stay (day)	4.3 (3–9)

Values are presented as number or mean (range).

RESULTS

1. Demographic Data

A total number of 109 patients (65 females, 44 males) were included. Their demographic data were summarized in Table 2. The average duration of operations was detected as 172.3 minutes (range, 161.4–221.9 minutes), while patients were detected to have an average loss of blood of 205.4 mL (range, 129.1–467.2 mL). The average duration of hospital stay was 4.3 days (range, 3–9 days). All patients were mobilized immediately after surgery.

2. Clinical Outcome Scores

All of the clinical outcome scores, including SF-36 scores in-

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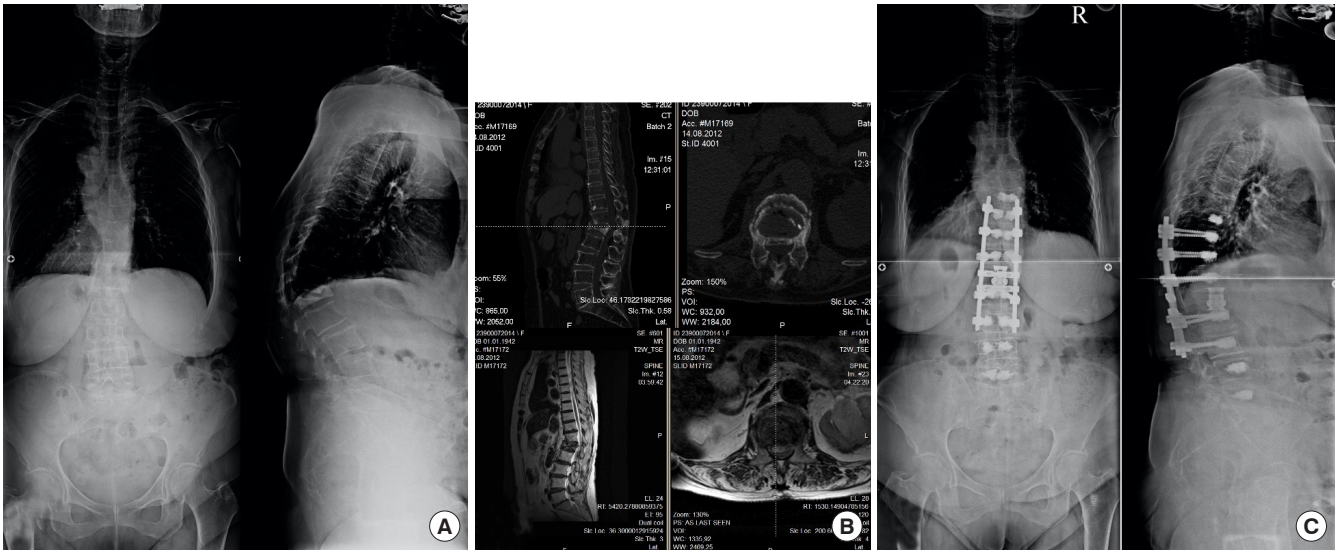

Fig. 3. A 71-year-old female patient with an osteoporotic fracture (A) and canal compromise (B) at the level of L1. Postoperative 6th year (C). The local kyphosis angle of 51.2° improved to 4.1°, sagittal vertical axis improved from 63.4 mm to 9.2 mm.

Table 3. Clinical outcome scores

Variable	Preoperative	Last follow-up	p-value
JOA score	8.6 (8–12)	26.1 (24–27)	<0.001
ODI score	76.3 (73–86)	17.4 (15–21)	<0.001
VAS score	7.7 (5–9)	1.6 (0–3)	<0.001
SF-36 MCS	47.1 (46.4–49.4)	55.1 (53.3–57.6)	<0.001
SF-36 PCS	44.3 (44.2–46.8)	56.8 (54.6–57.7)	<0.001

Values are presented as mean (range).
JOA, Japanese Orthopaedic Association; ODI, Oswestry Disability Index; VAS, visual analogue score; SF-36, 36-item Short-Form survey; MCS, mental component summary; PCS, physical component summary.

dicating quality of life, were detected to be improved with high statistical significance. Patients were Frankel D at the initial presentation, except 3 patients who were Frankel C. All patients were Frankel E postoperatively while those 3 patients improved to Frankel D immediate-postoperatively and were detected to improve to E at the last follow-up appointment. All patients with neurologic symptoms were detected to have complete relief of their nerve compression symptoms at the final follow-up. Table 3.

3. Radiographic Outcome Measurements

The average preoperative local segmental kyphosis angle improved from 39.3° (range, 31.7°–47.4°) to 4.9° (range, 3.9°–10.1°) at the last follow-up ($p < 0.001$). The average preoperative SVA improved from 61.2 mm (range, 43.1–82.4 mm) to 10.2 mm (range 8.7–12.9 mm) at the last follow-up ($p < 0.001$) (Table 4, Fig. 3).

Table 4. Radiographic outcome measurements

Variable	Preoperative	At the last follow-up	p-value
Preoperative local segmental kyphosis (°)	39.3 (31.7–47.4)	4.7 (3.9–10.1)	<0.001
SVA (mm)	61.2 (43.1–82.4)	10.2 (8.7–12.9)	<0.001

Values are presented as mean (range).
SVA, sagittal vertical axis.

4. Complications

Dural tear (1.8%) was detected intraoperatively in 2 patients and repaired immediately. Five patients (4.6%) developed distal junctional level fracture and underwent early vertebroplasty (postoperation 6th-8th month, 1st year). Two patients (1.8%) underwent revision due to cage subsidence (both: postoperation 1st year). Fusion was confirmed on the last follow-up visit using CT, while no pseudoarthrosis or implant failure was evident.

DISCUSSION

Severe OVF in geriatric population accompanied with kyphosis and neurologic deficit are difficult to treat besides causing high-intensity pain, diminished mobility, decreased quality of life, depression, worsening of daily activities of living and

progressive problems regarding pulmonary and gastrointestinal system.[18-21]

As a result of percutaneous kyphoplasty (PKP), a high incidence of recollapse of the treated vertebra in the long-term follow-up was reported,[22,23] while balloon inflation was associated with bone rupture.[24] PMMA augmentation, which was provided as the main goal during PVP and PKP, was reported to be associated with intervertebral cement leakage leading to the collapse of adjacent endplates and intervertebral disks, resulting in intervertebral instability and eventually new compression fractures.[25,26]

In severe, unstable OVFs, which comprise a progressive kyphosis, severe-intractable back pain, and associated neurologic deficits, PVP or PKP can neither provide adequate spinal decompression nor successful fracture reduction, together with anterior column restoration and sagittal balance correction.[2,9,27] Therefore, open surgery is indicated for that particular group of geriatric patients. Meanwhile, open surgery was indicated for patients in the present study, while PVP and PKP were not suited to be applied as standalone treatment options.

Options regarding open surgery comprise anterior, posterior, or combined approaches, while the ideal approach for geriatric patients with severe OVFs' sequela is controversial.[1,28] Geriatric patients with severe OVFs were frequently reported to have an advanced age with a wide spectrum of comorbidities so that they might be unable to tolerate multiple surgical approaches, while a surgery performed in a single seating might be the best option.[2,9] Beside this fact, the anterior or anterior-posterior combined approaches were carried out by opening the thoracic cavity in addition to retroperitoneal space, and was, therefore, associated with higher risks and complications as compared to posterior only approach.[12,29] In the present study, posterior only approaches were applied to geriatric osteoporotic patients to prevent the risks associated with the combined anterior approach, which was in conjunction with the current literature stating that posterior approach could provide shortening of the operative time, reduction of the blood loss and accomplish adequate decompression and anterior column restoration.[30,31]

In terms of posterior approaches, pedicle subtraction osteotomy (PSO) was considered the widely accepted treatment option for vertebral compression pressures with progressive kyphosis and sagittal imbalance.[1,32] However, to perform PSO, the anterior vertebral body was utilized as a hinge, but in OVFs, the anterior portion of the osteoporotic vertebral body might be devoid of adequate bone mass and cannot be used as a hinge, making PSO technically impossible.[1,32] As a result of the aforementioned problems, PSO was preferred not to be applied to osteoporotic patients with severe OVFs.

PVCR was defined as a procedure, which successfully provided adequate spinal cord decompression through the bilateral osteotomy approaches that were capable to completely remove the vertebral body of the fractured segment together with the adjacent cranial and caudal intervertebral discs.[2,9] As combined with the anterior placement of a cage, this procedure was noted to be capable of successfully restoring the anterior column without changing the spinal length and causing any neural damage due to spinal wrinkling.[1,9,12]

There is very limited information regarding the application of PVCR combined with anterior column restoration to patients with OVFs' sequela. The existing literature is mainly based on a small number of patients with relatively short term follow-up (Dreimann et al.[2]: 10 patients, 18.4 ± 8 months, Sehmisch et al.[9]: 10 patients, 14 months, Wei et al.[27]: 24 patients, 32.68 ± 8.72 months, Ma et al.[1]: 26 patients, 28.7 ± 3.2 months). Regarding the application of PVCR in geriatric patients with OVFs, this study has the largest patient number (109) and longest average follow-up duration (92.3 months).

Despite all of the advantages mentioned above, PVCR was considered to be associated with intraoperative risks, including bleeding and long duration of operations as applied to geriatric patients with severe OVFs.[2,9,27] This is why we modified this procedure and reduced it to a unilaterally applicable type of osteotomy, which was shown to shorten the average duration of surgery together with average bleeding. Dreimann et al.,[2] applied PVCR with 2 small titanium mesh cages to 10 patients and reported mean surgical time of 318 ± 62 minutes and an average blood loss of 1,540 ± 745 mL. Wei et al.[27] used a single titanium mesh cage and reported an average surgical duration of 223.08 ± 28.78 minutes and 413.25 ± 84.50 mL of average bleeding. Ma et al.[1] also used a single titanium mesh cage and reported an average surgical duration of 208 ± 49 minutes and an average of 756 ± 244 mL of blood loss. Sehmisch et al.[9] used 2 small titanium mesh cages and reported an average surgical duration of 318 ± 62 minutes and an average blood loss of 1,540 ± 745 mL. The present study reported an average surgical time of 172.3 minutes and an average blood loss of 205.4 mL, which are lower than the reported data in the literature, indicating the less invasiveness of this modification. The limited amount of bleeding might be attributed to the less-invasive nature of the unilateral posterior surgery together with meticulous attempts to coagulate any intraoperative bleeding together with the usage of tranexamic acid.

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While performing the PVCR procedure, correction of the kyphotic deformity and restoration of the anterior column was reported to be of high importance because the correct sagittal balance leading to improvements of the volumes of thoracic and abdominal cavities were highly correlated with patients' quality of life.[33,34] Ma et al.[1] reported an average follow-up SVA of 18.3 ± 3.5 mm, while the other studies did not analyze regarding the SVA and sagittal balance. This study reported an average SVA of 10.2 mm at the latest follow-up showing the efficacy of the modified PVCR procedure in terms of the realignment and correction of sagittal balance.

Correction of kyphosis is considered one of the main goals of surgical treatment in geriatric patients with OVFs. It was reported that the magnitude of kyphosis—sagittal imbalance—was positively correlated with the worsening of quality of life.[33] The average degree of local segmental kyphosis at the last follow-up was 8° ± 7° in the study of Sehmisch et al.,[9] 9.5° ± 3.8° in the study of Ma et al.,[1] 11.65° ± 7.51° in the study of Wei et al.[27] The present study reported an average degree of local segmental kyphosis of 4.7°, underlining the correctional efficacy of this procedure, which would also explain the high scores regarding the quality of life.

Instrumentation of the osteoporotic spine frequently constituted a challenge because patients with low bone mineral density (as the ones in the present study) were noted to be associated with postoperative implant-related complications, including pedicle screw loosening as a result of the fact that screws were subjected to a high force during the correction phase of the PVCR.[2,3] To overcome these problems, larger diameter and longer screws were recommended to increase the surface area and minimize screw toggle within the pedicle.[35] Cement augmented pedicle screw technique was also highly advised in the osteoporotic spine because of enhancing the pull-out strength of the screws, providing a stable screw-bone cement-bone interface to distribute the stresses and assuring a strong fixation resulting in the reduction of the postoperative incidence of screw failure and loosening.[1,36,37] We placed fenestrated pedicle screws 2 levels cranial and caudal of the OVF combined with application of 2-mL PMMA bone cement inside every screw, combined with prophylactic vertebroplasty at the adjacent cranial and caudal levels.

The present study reported excellent clinical results yielded by modified PVCR combined with anterior column restoration. Our results were in conjunction with the previous studies that also reported significant improvements in clinical scores, including VAS, JOA, and ODI.[1,2,9,27] However, this study, for the first time in the literature, by reporting about SF-36 scores, also showed that as a result of modified PVCR combined with anterior column restoration, significant improvements regarding the quality of life could also be achieved.

Application of PVCR to the osteoporotic spine was associated with a wide spectrum of complications. Wei et al.[27] reported 3 of 24 patients with intraoperative dural injury with cerebrospinal fluid leakage, Dreimann et al.[2] reported 3 of 10 rates of complications (1 posterior ligamentous dislocation requiring revision, 1 wound infection requiring debridement, 1 serious clinical deterioration); Ma et al.[1] reported 2 of 26 patients with dural injury and venous thrombosis, 2 of 26 recurrent lumbar backpain. Regarding the relatively short average follow-up duration of the studies mentioned above (18 to 32 months), it is expected that no implant-related complication was reported so far. In contrast, the present study reported 2 cases of cage subsidence resulting in revision and underlining that this system might also fail and should further be optimized. The present study with 5 years of minimal follow-up duration reported that distal junctional level fracture and cage subsidence could be encountered, and surgeons performing PVCR to the osteoporotic spine should be aware of that in the long term.

One of the limitations of the present study is its retrospective nature. Another limitation is the relatively limited number of patients, which is owed to the strict inclusion criteria defined to obtain a homogenous group of patients.

CONCLUSION

Application of modified PVCR together with anterior column restoration by using an expandable titanium cage to geriatric patients with severe OVFs' sequela was detected to yield excellent clinical and functional outcomes, in addition to adequate correction of kyphosis together with successful sagittal balance. This approach was shown to provide significant improvement regarding the quality of life in geriatric patients.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Original Article

The Intersection Between Lateral Mass and Inferomedial Edge of the C1 Posterior Arch: A Reference Point for C1 Lateral Mass Screw Insertion

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Objective: To determine the ideal Atlas (C1) lateral mass screw placement and trajectory using the intersection between the lateral mass and inferomedial edge of the posterior arch as an easily identifiable and reproducible medial reference point. Selection of an ideal entry point and trajectory of C1 lateral mass screw insertion can help to minimize neurovascular injuries. While various techniques for screw insertion have been proposed in the past, they all require extensive dissection of the C1 lateral mass, which can cause profuse bleeding.
Methods: Ninety-three 3-dimensional computed tomography reconstructed images of C1 lateral masses in adult patients were utilized to simulate the placement of C1 lateral mass screws via 4 entry points and 2 trajectory angles referencing off of a medial reference point using Vero's VISI 17 software. The safety during screw insertion simulation, as well as the screw length, were evaluated.
Results: We found that C1 lateral mass screws could be safely placed bilaterally at 3 mm lateral to the reference point in both 0° and 15° medial screw angulation without violation of the cortex. The 15° medial angulation allowed for longer (18 mm) screws than the 0° angulation.
Conclusion: We recommend starting C1 lateral mass screws 3 mm lateral to the intersection between the lateral mass and inferomedial edge of the posterior arch at a 15° medial angulation.

Keywords: Atlantoaxial fixation, C1 lateral mass screw fixation, Isolated medial reference, Inferomedial edge of posterior C1 arch, Mediolateral trajectory, Craniocaudal trajectory

INTRODUCTION

Atlas (C1) lateral mass screw fixation is widely used to stabilize the atlantoaxial (C1–2) joint in posterior C1–2 screw-rod constructs. The C1 lateral mass screw and plate were first described by Goel et al.[1] in 1994 and modified for C1 polyaxial screw-rod systems by Harms and Melcher[2] in 2001. Many clinical reports of this technique have demonstrated biomechanical strength comparable to C1–2 transarticular screw fixation,[3-6] but with a minimization of the risk of vertebral artery injury and occipitocervical (C0–1) joint injury. While techniques for C1 lateral mass screw insertion have been proposed in the past, several require an extensive dissection of the entire posterior C1 lateral mass to identify the entry point.[1,2,7,8] This can increase operative time and cause copious bleeding from a venous sinus injury in the C1–2 complex.[1,2,8-10] A reproducible and easily identified optimal entry point and trajectory for C1 lateral mass screw insertion may help to minimize this complication.

This computed tomography (CT) study aims to identify the ideal starting location from an easily identifiable and reproduc-

ible reference point, the intersection between the lateral mass and the inferomedial edge of the C1 posterior arch. We sought to determine the ideal trajectory and unicortical intraosseous screw length at each entry point.

MATERIALS AND METHODS

1. Study Design

Cervical spine CT images with 1 mm cut from 93 consecutive adult patients from March 2016 to January 2017 were utilized. Approval from the Institutional Ethics Board of Research Ethics Committee, Chiang Mai University (ORT-2559-04158) was obtained before initiation of the study. Exclusion criteria were patients younger than 18 years, as well as anyone with C1 anatomical abnormalities due to conditions such as tumor, infection, rheumatism, trauma, or any other defects. The Digital Imaging and Communications in Medicine format from the CT images was processed to stereolithography (STL) format using Mimics software (Materialise HQ, Leven, Belgium). The actual dimension included the core and thread diameters of the 4.0-mm C1 lateral mass screw was also simulated by Mimic software. The STL 3-dimensional (3D) data from C1 and the screws were virtually placed and analyzed using Vero software (Vero's VISI 17, CAD/CAM/CAE software solutions, Cheltenham, UK).

2. Entry Point and Trajectory Assessment

The C1 vertebrae were standardized using the symmetry of the transverse process and the posterior arch in both the coronal and transverse planes. Virtual placement of 4.0-mm C1 lateral mass screws was performed bilaterally at 4 entry points and 2 trajectory angle parameters. The reference point was set at an intersection between the lateral mass and the inferomedial edge of the C1 posterior arch in the transverse plane (Fig. 1A), and the inferior border of the posterior arch in the sagittal plane (Fig. 1B). The lateral entry points were determined at 3 mm, 5 mm, and 7 mm lateral from the reference point in the axial plane (Fig. 1C). The simulated screw placement was performed parallel to the plane of the posterior arch of C1 in the sagittal plane and both 0° and 15° medial trajectory angles at each entry point (Fig. 1D). The ideal end position was set at the point located 2 mm behind the anterior cortex of the C1 lateral mass.

Violation of the cortex during simulated screw insertion was carefully evaluated in a 3D view. The percentage of screw breach at each entry point and trajectory was recorded. The screw breach distance was measured (Fig. 2A) and graded by the Gertzbein

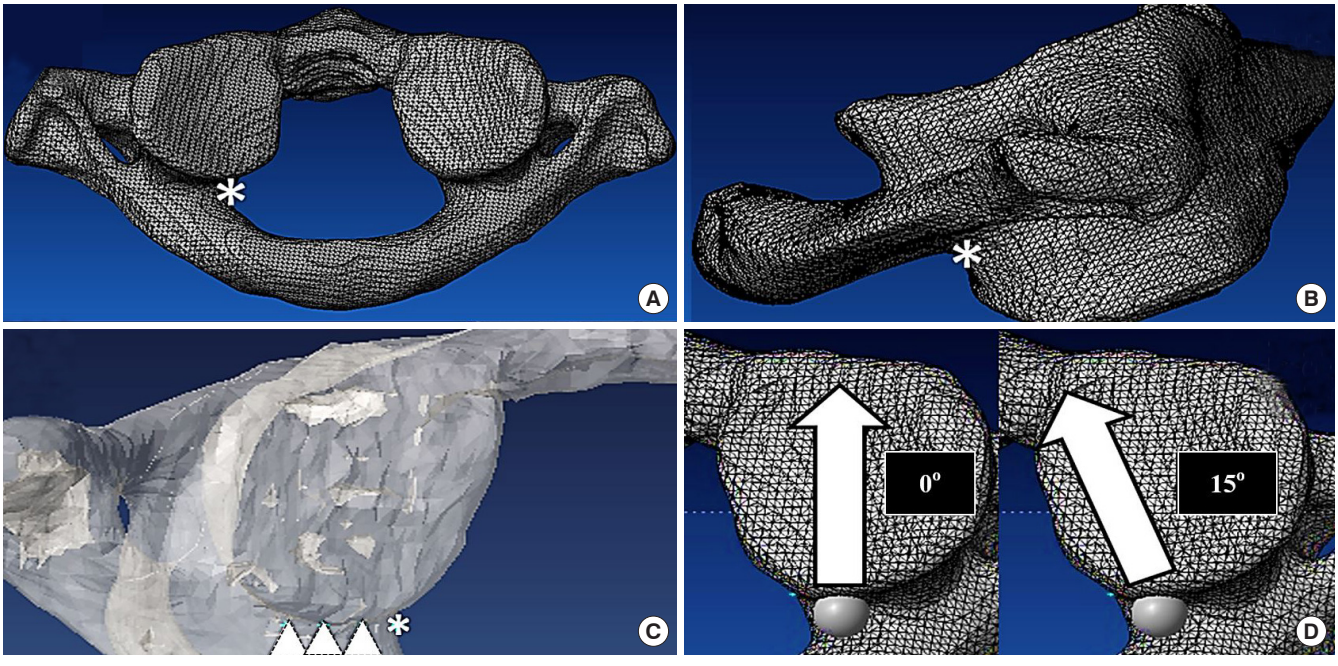

Fig. 1. The reference point was set at the intersection between the lateral mass and the inferomedial edge of the C1 posterior arch (asterisk) in the axial plane (A) and just caudal to where the posterior arch intersects with the lateral mass in the sagittal plane (asterisk) (B). (C) The lateral entry points were determined to be 3 mm, 5 mm, and 7 mm lateral to the reference point (asterisk) in the axial plane (triangles). (D) The axial view demonstrates the screw trajectory in both the 0° and 15° medial trajectory angles.

and Robbins grading system; grade 0: no breach, grade 1: breach distance <2 mm, grade 2: breach distance 2-4 mm, grade 3: breach distance >4 mm.[11] The interosseous screw length at each entry point and trajectory was also measured (Fig. 2B).

3. Statistical Analysis

The intraosseous screw length was calculated by using the mean ± standard deviation. All data were tested for their normality using the Shapiro-Wilk test. A paired t-test was used to analyze the mean intraosseous screw length between 0° and in 15° medial angulation and the Student t-test was used to analyze the mean intraosseous screw length between males and females. Statistical analysis was performed using the IBM SPSS Statistics ver. 20.0 (IBM Co., Armonk, NY, USA). The level of statistical significance was set at 0.05.

RESULTS

There were 55 men and 38 women in the study. A 4.0-mm C1 lateral mass screws could be safely placed bilaterally starting at 3 mm lateral to the reference point in both the 0° and 15° medial angulation. At the entry point located 5 mm lateral to the reference point, the C1 lateral mass screw could also be placed in the 15° medial angulation without any cortical violation (Table 1). However, at other entry points and directions, the screw may breach the lateral mass cortices.

The mean intraosseous unicortical screw lengths at 3 mm lateral to the reference point were approximately 16 mm in 0° medial angulation (16.3 ± 1.57 mm at the right lateral mass and 16.3 ± 1.40 mm at the left lateral mass) and 18 mm in 15° medial angulation (18.3 ± 1.73 mm at the right lateral mass and 18.3 ± 1.69 mm at the left lateral mass), respectively. At 5 mm lateral from the reference point, the optimal screw length was approximately 18 mm in 15° medial angulation (18.0 ± 1.71 mm at the right lateral mass and 17.9 ± 1.54 mm at the left lateral mass) (Table 2). A paired t-test was used to analyze the mean intraosseous screw length between 0° and in 15° medial angulation.

Table 1. Percentage of safe screw placement at each entry point and trajectory

Entry point	Breach	Right C1 lateral mass		Left C1 lateral mass	
		0°	15°	0°	15°
0 mm	Grade 0	92 (98.92)	19 (20.43)	91 (97.85)	23 (24.73)
	Grade 1	1 (1.08)	41 (44.09)	2 (2.15)	34 (36.56)
	Grade 2	0 (0)	33 (35.48)	0 (0)	36 (38.71)
	Grade 3	0 (0)	0 (0)	0 (0)	0 (0)
3 mm	Grade 0	93 (100)	93 (100)	93 (100)	93 (100)
	Grade 1	0 (0)	0 (0)	0 (0)	0 (0)
	Grade 2	0 (0)	0 (0)	0 (0)	0 (0)
	Grade 3	0 (0)	0 (0)	0 (0)	0 (0)
5 mm	Grade 0	91 (97.85)	93 (100)	91 (97.85)	93 (100)
	Grade 1	0 (0)	0 (0)	2 (2.15)	0 (0)
	Grade 2	2 (2.15)	0 (0)	0 (0)	0 (0)
	Grade 3	0 (0)	0 (0)	0 (0)	0 (0)
7 mm	Grade 0	79 (84.95)	89 (95.70)	78 (83.87)	88 (94.62)
	Grade 1	9 (9.68)	4 (4.30)	9 (9.68)	5 (5.38)
	Grade 2	3 (3.23)	0 (0)	4 (4.30)	0 (0)
	Grade 3	2 (2.15)	0 (0)	2 (2.15)	0 (0)

Values are presented as number (%).

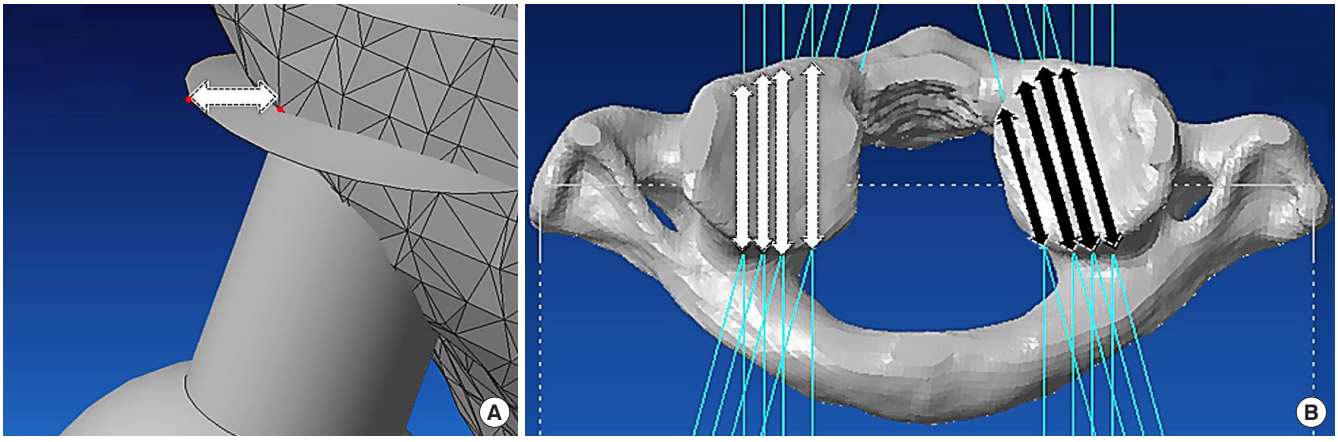

Fig. 2. (A) Measuring and grading the screw breach distance. (B) Measuring the intraosseous screw length with the simulated screw tip 2 mm short of the anterior cortex of the C1 lateral mass in the 0° (white arrows) and 15° (black arrows) medial trajectory angle.

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The mean intraosseous screw length was significantly longer in 15° medial angulation than in 0° medial angulation at every entry point ($p < 0.001$) (Table 3). Student t-test was used to analyze the mean intraosseous screw length between males and females. There was significantly longer in males than in females at almost every entry point and trajectory—except in 15° medial angulation at the reference point ($p < 0.05$) (Table 4). There was no difference in the mean intraosseous screw length in the right and left lateral masses in our study (Table 5). Detailed results and analysis of the data are summarized in Tables 1–5.

DISCUSSION

C1 lateral mass screw placement can be technically demanding and poses risk of injury to major neurovascular structures, including the spinal cord and the vertebral artery.[12] Numerous

Table 2. Mean intraosseous screw length (mm) at each entry point and trajectory

Entry point	Right C1 lateral mass		p-value	Left C1 lateral mass		p-value
	0° Angulation	15° Angulation		0° Angulation	15° Angulation	
0 mm	16.0 ± 1.59	17.4 ± 2.79	< 0.001	16.1 ± 1.5	17.6 ± 2.65	< 0.001
3 mm	16.3 ± 1.57	18.3 ± 1.73	< 0.001	16.3 ± 1.4	18.3 ± 1.69	< 0.001
5 mm	15.7 ± 1.72	18.0 ± 1.71	< 0.001	15.6 ± 1.48	17.9 ± 1.54	< 0.001
7 mm	14.4 ± 2.1	17.1 ± 2.1	< 0.001	14.2 ± 1.91	16.8 ± 1.93	< 0.001

Values are presented as mean ± standard deviation.

Table 3. The difference in mean intraosseous screw lengths between 0° and 15° medial angulation

Side of lateral mass	Entry point	Mean screw length (mm)		p-value
		0° Angulation	15° Angulation	
Right	0 mm	16.0 ± 1.59	17.4 ± 2.79	< 0.001
	3 mm	16.3 ± 1.56	18.3 ± 1.73	< 0.001
	5 mm	15.7 ± 1.73	18.0 ± 1.71	< 0.001
	7 mm	14.4 ± 2.1	17.1 ± 2.1	< 0.001
Left	0 mm	16.1 ± 1.5	17.6 ± 2.65	< 0.001
	3 mm	16.3 ± 1.4	18.3 ± 1.69	< 0.001
	5 mm	15.6 ± 1.48	17.9 ± 1.54	< 0.001
	7 mm	14.2 ± 1.91	16.8 ± 1.93	< 0.001

Values are presented as mean ± standard deviation.

Table 5. The difference in mean intraosseous screw length (mm) between right and left lateral mass

Medial angulation	Entry point	Right C1 lateral mass	Left C1 lateral mass	p-value
0°	0 mm	16.0 ± 1.59	16.1 ± 1.5	0.39
	3 mm	16.3 ± 1.56	16.3 ± 1.4	0.93
	5 mm	15.7 ± 1.73	15.6 ± 1.48	0.40
	7 mm	14.4 ± 2.09	14.2 ± 1.91	0.07
15°	0 mm	17.4 ± 2.79	17.6 ± 2.65	0.26
	3 mm	18.3 ± 1.73	18.3 ± 1.69	0.87
	5 mm	18.0 ± 1.71	17.9 ± 1.54	0.26
	7 mm	17.1 ± 2.1	16.8 ± 1.93	0.08

Table 4. The difference in mean intraosseous screw length (mm) between males and females

Medial angulation	Entry point	Right C1 lateral mass		p-value	Left C1 lateral mass		p-value
		Male	Female		Male	Female	
0°	0 mm	16.4 ± 1.65	15.4 ± 1.31	0.002	16.5 ± 1.62	15.5 ± 1.12	0.002
	3 mm	16.7 ± 1.58	15.8 ± 1.35	0.005	16.7 ± 1.43	15.7 ± 1.14	0.001
	5 mm	16.2 ± 1.73	15.1 ± 1.53	0.002	16.1 ± 1.48	15 ± 1.23	< 0.001
	7 mm	15 ± 2.06	13.7 ± 1.92	0.002	14.8 ± 1.83	13.3 ± 1.71	< 0.001
15°	0 mm	17.8 ± 3.09	16.8 ± 2.19	0.083	18.1 ± 2.87	16.8 ± 2.1	0.018
	3 mm	18.8 ± 1.79	17.6 ± 1.37	0.001	18.7 ± 1.82	17.7 ± 1.28	0.003
	5 mm	18.5 ± 1.75	17.3 ± 1.41	0.001	18.3 ± 1.62	17.3 ± 1.18	0.001
	7 mm	17.6 ± 2.16	16.2 ± 1.75	0.002	17.4 ± 1.89	15.9 ± 1.6	< 0.001

Values are presented as mean ± standard deviation.

complications have been reported, including lethal bleeding from a large venous sinus injury,[1,10,13] vertebral artery injury, violation of the occipitocervical (C0–1) joint, internal carotid injury,[14,15] and hypoglossal nerve injury.[15,16] However, the C1 lateral mass screw can be safely placed with careful attention to the anatomy and using lateral fluoroscopic guidance.[17] One of the most challenging steps of C1 lateral mass screw insertion is avoiding and minimizing the bleeding from the large venous sinus overlying the C1–2 joint during dissection.[1,10]

1. Entry Point

Numerous optimal entry points and the screw trajectories for C1 lateral mass screws have been reported on.[1,2,7,13,18] Goel et al.[1] defined the entry point as being the center of the posterior surface of the lateral mass, 1–2 mm above the articular surface. Harms and Melcher[2] defined the entry point to be the middle of the junction of the C1 posterior arch and the midpoint of the posterior inferior part of the C1 lateral mass. Hong et al.[7] recommended that the entry point should be the intersection of the inferior border of the posterior C1 arch and the midpoint of the posterior aspect of the C1 lateral mass. Simsek et al.[19] stated that the midline of the lateral mass at the intersection of the posterior arch and the C1 lateral mass was the ideal entry point. These recommended entry points for C1 lateral mass screws are at the midpoint of the posterior surface of the lateral mass that is usually covered by a large venous plexus (formed by the anastomosis between the suboccipital cavernous sinus, vertebral plexus, posterior condylar emissary vein, and the sigmoid sinus).[20] Injury to this venous plexus during exposure of the C1 lateral mass borders can cause profuse and even lethal bleeding, extend the operative time and cause the surgeons to alter their plans.[21] A revised technique, starting the screw from the posterior arch[18,22,23] is one simple way to avoid injury to the venous plexus. However, posterior arch screws can put the vertebral artery at risk, result in an arch fracture in small, thin patients, and are not always anatomically feasible in such patients.[24]

In our study, an easily identifiable reference point was set at the intersection between the lateral mass and inferomedial edge of the posterior arch (Fig. 3A). Using this reference point, there is no need to dissect the entire posterior aspect of the C1 lateral mass, which can minimize the risk of venous plexus injury.

2. Trajectory

In the sagittal plane, the craniocaudal screw trajectory was determined to be parallel with the plane of the C1 posterior arch to avoid injury to the occipitocervical joint and the atlantoaxial joint, as mentioned by numerous authors.[1,2,25-27] We can easily obtain this direction intraoperatively using lateral fluoroscopy

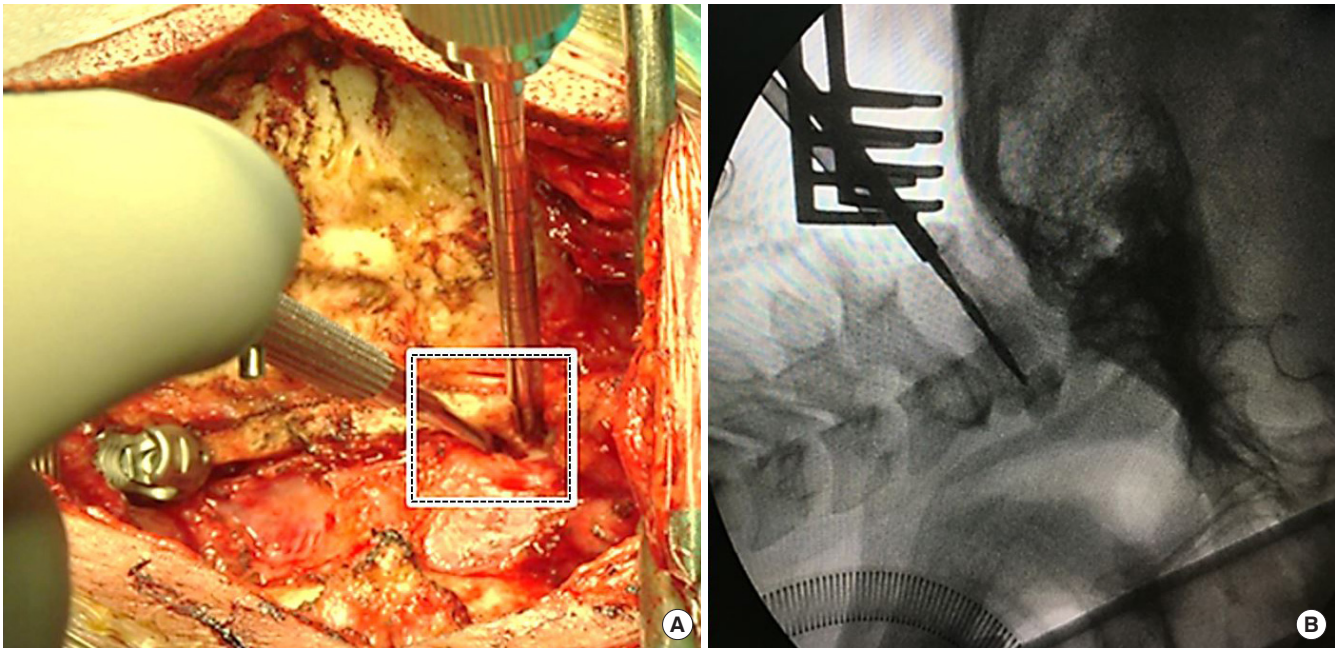

Fig. 3. (A) The reference point from our study (square) is easily visualized and identified using a Penfield dissector intraoperatively. (B) The craniocaudal screw trajectory is parallel with the plane of the C1 posterior arch, which is easily visualized using intraoperative lateral fluoroscopy.

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(Fig. 3B). In the axial plane, the 0° and 15° medial angulation screw trajectories were selected to maximize the margin of safety with the medial angulation trajectory. The unicortical C1 lateral mass screws were used because they can provide an equivalent pullout strength with a much lower risk of injury than the longer bicortical screws placed in a similar orientation.[28]

3. Optimal Entry Point and Medial Trajectory

We found that the ideal entry point of a 4-mm C1 lateral mass screws is 3 mm to the reference point (which is the intersection between the lateral mass and inferomedial edge of the posterior arch). At this entry point, the screw can be safely placed in both the 0° and 15° medial angulation trajectories without any cortical violation. This starting point makes it unnecessary to dissect further laterally, minimizing the bleeding risk.

Hong et al.[7] described the relationship between the reference point in our study and the midpoint of the lateral mass, which is not the midpoint of the posterior surface of the lateral mass. They described the mean distance between the midline of the C1 lamina to the midpoint of the C1 lateral mass as 17.6 ± 1.2 mm; the mean distance between the midline of the C1 lamina to the inner edge of the C1 lateral mass was 14.2 ± 1.2 mm. They found that the center of the C1 lateral mass was, on average, 3.4 mm lateral to the inner edge of the C1 lateral mass. Al-Habib et al.[27] found that the midpoint of the C1 lateral mass was lateral to the medial edge of the C1 posterior arch by a mean of 1.42 ± 0.87 mm. Su et al.[29] stated that the midpoint of the lateral mass, which was the proper screw "start-point," was 1.6 ± 1 mm lateral to the medial wall of the C1 pedicle. We believe that 3 mm lateral to our reference point is the ideal entry point because, according to previous studies, it is at the center, or just lateral to the center of the C1 lateral mass. This is in contradiction to a study by Blagg et al.,[25] who suggested that the C1 lateral mass screw was best placed at the medial border of the posterior arch and its junction with the lateral mass. In our study, at the same point, the proportion of the screw breach is approximately 1%–2% in the 0° medial angulation and 74%–79% in the 15° medial angulation. The results of our study suggest that the medial border of the posterior arch may be too medial to be an appropriate starting point.

4. Intraosseous Screw Length

Several medial trajectory angles have been suggested in a number of published studies. Rocha et al.[20] found that the mean maximum medial angulation was 16.7° ± 1.3° (range, 14.6°–20.7°). Hong et al.[7] stated that the medial screw angulation was approximately 14.7° (left, 14.7° ± 2.9°; right, 14.7° ± 3.1°) and Simsek et al.[19] suggested that the ideal medial angulation was 13.5° ± 1.9° and the maximal medial angulation was 29.4° ± 3.0°. According to our results, a 15° medial angulation is an ideal trajectory because it permits a significantly longer screw, which is associated with a better biomechanical pullout strength.[30] In this direction, the screw can be safely inserted at both 3 mm and 5 mm lateral to the reference point. However, the head of the screws can sometimes impinge on the posterior arch. This might require that part of the posterior arch be notched to utilize this technique. Additionally, it may be necessary to use a longer screw for proper fixation with the rods when using this starting point.

To our knowledge, this is the first study to describe the relationship between C1 screw length and sex. As expected, the intraosseous screw length in males is significantly longer than in females. A study by Al-Habib et al.[27] found that the mean axial diameter of the C1 lateral mass was significantly larger in males than in females but did not comment on the length.

5. Limitations

As with all studies, ours is not without flaws. While we examined a large number of cases, human anatomy is infinitely variable and no recommended surgical starting point and trajectory can be safely utilized in 100% of cases. Rather, our recommended starting points and trajectory should be verified for each surgical patient to ensure that it works in that individual. Second, while it has been our experience that our starting point decreases venous bleeding, it does not eliminate it. The degree to which it decreases the bleeding is not within the scope of this paper and would require a prospective, randomized study. Third, this is a 3D CT simulation study. Therefore, while our paper may help provide some anatomical insights for surgeons, in a clinical situation, it may still be very difficult to find the exact same point intraoperatively.

CONCLUSION

Prior recommended starting points for C1 lateral mass screws are typically covered by a large venous plexus. Using the intersection between the lateral mass and inferomedial edge of the posterior arch, easily identified during surgery, as the starting point, obviates the need for further lateral dissection and thus avoids potentially bleeding. The ideal entry point for C1 lateral mass screws is 3 mm lateral to the reference point (the intersection between the lateral mass and inferomedial edge of the posterior arch). The screw direction should be parallel to the pos-

terior arch of C1 in the sagittal plane. A 15° medial angulation in the axial plane is recommended because it can accommodate longer intraosseous screws.

CONFLICT OF INTEREST

K. Daniel Riew receives royalties from Biomet. He has done consulting work for Medtronic and Nuvasive. He is a stock holder with Amedica, Benvenue, Expanding Orthopedics, Nexgen Spine, Osprey, Paradigm Spine, Spinal Kinetics, Spineology, Vertiflex, PSD and Axiomed. He is a board member on the Global Spine Journal. For the remaining authors, none were declared.

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Factors Predicting the Clinical Outcome After Trans-sacral Epiduroscopic Laser Decompression for Lumbar Disc Herniation

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Objective: Previous literatures have demonstrated widely variable clinical results after trans-sacral epiduroscopic laser decompression (SELD) and the factors predicting outcomes are not yet established. Therefore, we analyzed the clinical outcome and associated predictive factors of SELD in patients with lumbar disc herniation.
Methods: Between 2015 and 2018, 82 patients who underwent single-level SELD and followed up at least 6 months were enrolled. The overall success rate (excellent or good results at final follow-up) was 58.5% according to Odom's criteria. Based on this result, patients were divided to 2 groups: a favorable group (n = 48) and an unfavorable group (n = 34). A retrospective review of the baseline characteristics and clinical outcome were conducted to reveal the predictive factors.
Results: As expected, improvement of pain and patient satisfaction, was more favorable in the favorable group ($p < 0.05$). Moreover, the rate of additional procedure was lower in the favorable group (4.2%, 2 of 48 patients) than in the unfavorable group (35.3%, 12 of 34 patients) ($p = 0.011$). Among the various baseline characteristics, the only significant predictive factor for favorable outcome was the presence of a high-intensity zone (HIZ) on preoperative magnetic resonance imaging (50.0% [24 of 48 patients] in the favorable group vs. 11.8% [4 of 34 patients] in the unfavorable group; odds ratio, 15.67; $p = 0.024$).
Conclusion: Although SELD for lumbar disc herniation resulted in a less favorable clinical outcome than that reported in previous studies, in patients with a HIZ, SELD can be an effective minimally invasive surgery to relieve low back pain and/or leg pain.

Keywords: Disc, High-intensity zone, Low back pain, Lumbar spine, Predictive factor, Trans-sacral epiduroscopic laser decompression

INTRODUCTION

The trans-sacral epiduroscopic laser decompression (SELD) was introduced to resolve a symptomatic epidural lesion of the lumbosacral spine with the development of small-caliber endoscope, flexible video-guided catheters, and less invasive laser technology since 2000s.[1-5] This minimally invasive spinal surgery has been performed as an option among various surgical techniques for treatment of diverse lumbar spinal diseases.[4,6] Many previous literatures have reported the clinical application of SELD in various epidural lesions of the lumbo-sacral spine, such as disc herniation, spinal stenosis, and failed back surgery.[6-15]

In particular, in terms of the principle of lasers to condense hydrated materials, soft disc herniation with mild to moderate degree has been suggested as the appropriate indication of SELD.[16-18] According to previous studies, the clinical results of SELD for lumbar disc herniation was so varied that some reports suggested favorable outcome with a greater than 80% success rate,[16,18-23] while others insisted unfavorable outcome with a lower than 60% success rate.[17,24]

However, to date, no reports have examined the reason of variations and predictive factors affecting clinical results after SELD in lumbar disc herniation. Therefore, we reviewed the patients with lumbar disc herniation after SELD with follow-up data of at least 6 months and analyzed the predictive factors affecting the outcomes.

MATERIALS AND METHODS

1. Indication and Patient Population

This study was approved by the Institutional Review Board of Gil Medical Center (GAIRB2018-214). The ethics committee waived the requirement for informed consent due to its retrospective character and all data were fully anonymized before we accessed them.

As demonstrated in author's previous study about the clinical results of SELD,[17] the indications of SELD were soft disc herniation with mild to moderate features on magnetic resonance imaging (MRI) concordant with low back pain and/or radiating leg pain despite sufficient conservative treatment at least 2 weeks or with severe pain making daily life impossible. The contraindication for SELD included cauda equina syndrome or motor weakness, hard calcified disc herniation, significant spinal stenosis, infection, hemorrhagic diathesis, and anatomical variations including closed sacral hiatus and peridural cyst.[17]

A total of 116 patients who underwent SELD by 1 surgeon in a single institution between November 2015 and November 2018 were analyzed retrospectively. To minimize the selection bias, patients with multilevel procedure, previous history of lumbar spine surgery, and incomplete data of 6-month follow-up were excluded, and eventually, 82 patients were enrolled in final study cohort. Based on patient's satisfaction at 6 months after surgery, final cohort was allocated to 2 groups; favorable group (n = 48) determined as "excellent" or "good" according to Odom's criteria, and unfavorable group (n = 34) determined as "fair" or "poor" according Odom's criteria (Fig. 1).

2. Operative Technique

Under local anesthesia of the sacral hiatus after prone position of the patients, a 5-mm skin incision and insertion of trocar via sacral hiatus were made under fluoroscopic guidance. After the entering of the trocar to the S2–3 level, a 3.2-mm diameter video-guided catheter containing 2 lumens was inserted through the trocar to the ventral epidural space of the target level using bidirectional steering characteristics. Through the video-guided catheter, a 1.0-mm diameter flexible epiduroscope and a 550-μm diameter flexible fiber of the Ho:YAG laser were advanced to the end of the catheter. The Ho:YAG laser with a 0.4-mm penetration depth and a 2,100-nm wavelength leads to effective ablation of the hydrated soft disc herniation without thermal injury to the adjacent neural structures including nerve root or thecal sac.[5,25] Protruded or ruptured discs was shrunk by a high-intensity laser of 8–10 W (0.8–1.0 J, 10 Hz) until the sufficient decompression of the nerve root. Direct visualization of the widening of the epidural space through the epiduroscope and epidurographic images showing flattened disc outlines and free flow beyond the lesion was considered to be the point of sufficient decompression. A 5–10 mL of solution mixture of lidocaine, dexamethasone, and methylprednisolone was injected into the epidural space at the end of the procedure.

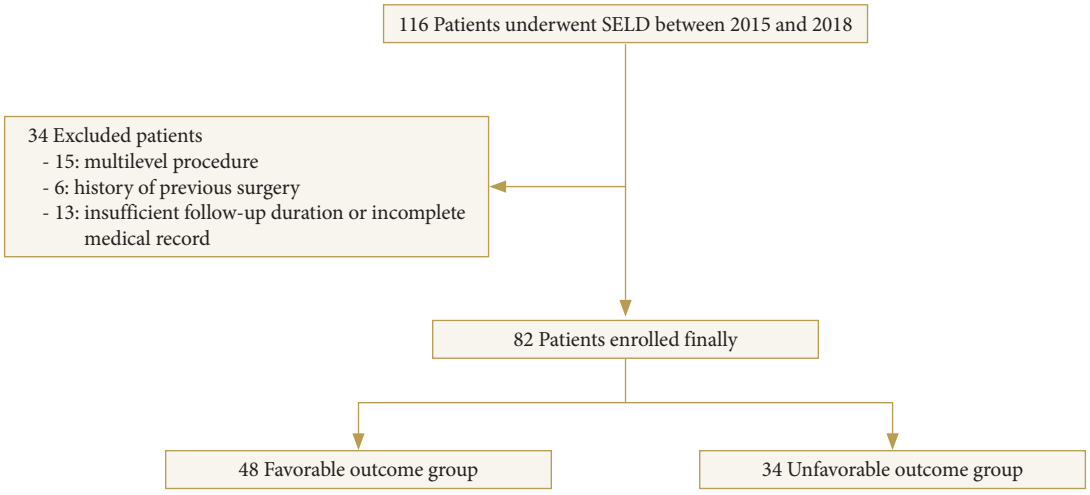

Fig. 1. Selection of the final study cohort. SELD, sacral epiduroscopic laser decompression.

3. Outcome Evaluation

The baseline characteristics such as demographic data including age and sex, body mass index, trauma history, previous history of nerve block, preoperative symptom duration, and surgical level were investigated.

Preoperative lumbar MRI and simple radiographs were performed in all patients. Based on these radiographic findings, disc degeneration based on the Pfirrmann grade,[26] presence of high-intensity zone (HIZ) implying annular tearing, morphology of disc herniation (bulging, protruded, or extruded), location of the pathology (central, right, or left), degree of canal compromise (mild, moderate, or severe), grade of root compression (abutting, displace, near obliteration, or obliteration), degree of combined stenosis (none, mild, moderate, or severe), and volume index of the herniated disc were evaluated. The volume index of disc herniation was calculated as height of disc herniation × depth × transverse diameter × 1/2 of the protruded or ruptured disc fragment on MRI. In addition, degree of adhesion during surgery was subjectively classified according to the operator's experience as mild, moderate, or severe.

The clinical outcomes based on visual analogue scale (VAS) of low back pain, VAS of radiating leg pain, and Odom's criteria for patient's satisfaction were collected preoperatively and at every follow-up visit (at 1 week, 1 month, and 6 months after surgery).

The surgical outcomes were assessed based on operation time, surgical failure, complications, hospital stay, and duration of return-to-work. In addition, the requirement of additional procedures including nerve block or revision surgery during follow-up were surveyed.

Plain and dynamic radiographies were performed at preoperation and at 6 months after surgery to assess the radiographic effect. Disc height was measured as an average of anterior and posterior disc height, and corrected using the ratio of disc height to the anteroposterior diameter of the L5 vertebral body to overcome any variations of x-ray magnification. Segmental angle and range of motion at the index level, and total lumbar lordotic angle were determined using Cobb method to assess the change in lumbar alignment.

4. Statistical Analysis

Data management and statistical analysis were performed using IBM SPSS Statistics ver. 23.0 (IBM Co., Armonk, NY, USA). Pearson chi-square test, independent t-test, and nonparametric Mann-Whitney U-test for comparison according to characteristics of the factors. Also, we performed a dichotomous logistic regression analysis of variables that were assumed to have a p-value less than 0.2 in univariate analysis. Results were expressed as means ± standard deviations, means with 95% confidence interval (CI), median with range, or odds ratio (OR), and statistical significance was accepted for p-values of < 0.05.

Table 1. Difference in the clinical outcomes between the 2 groups

Variable	Favorable group (n = 48)	Unfavorable group (n = 34)	Difference	95% CI	p-value
VAS for back					
Preoperation	5.55 ± 1.80	5.34 ± 1.78	0.21 ± 0.45	-0.790 to 1.419	0.579†
1 Week	2.73 ± 0.79	3.77 ± 1.36	-1.04 ± 0.47	-2.009 to 0.075	0.036†
1 Month	1.73 ± 0.90	4.00 ± 1.22	-2.27 ± 0.45	-3.200 to 1.346	< 0.001†
6 Months	2.36 ± 1.43	3.23 ± 1.36	0.87 ± 0.57	-2.053 to 0.319	0.144†
VAS for leg					
Preoperation	5.72 ± 2.15	6.62 ± 1.04	0.89 ± 0.67	-2.283 to 0.506	0.200†
1 Week	2.82 ± 1.66	4.77 ± 1.53	-1.95 ± 0.65	-3.306 to 0.596	0.007†
1 Month	1.64 ± 1.43	5.69 ± 1.18	-4.056 ± 0.53	-5.162 to 2.649	< 0.001†
6 Months	2.27 ± 1.62	4.69 ± 1.80	-2.42 ± 0.70	-3.879 to 0.960	0.002†
Odom's criteria, excellent:good:fair:poor					
1 Week	10:32:6:0	0:8:24:2	-	-	< 0.001‡
1 Month	20:28:0:0	0:2:28:4	-	-	< 0.001‡
6 Months	16:32:0:0	0:0:30:4	-	-	< 0.001‡

Values are presented as mean ± standard deviation or number.
CI, confidence interval; VAS, visual analogue scale.
†Independent t-test. ‡Pearson chi-square test.

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RESULTS

1. Clinical Outcomes, Surgical Outcomes, and Radiographic Outcomes Between the 2 Groups

A total of 82 patients were comprised of 52 men and 30 women, with a mean age of 40.78 ± 15.24 years.

In terms of the clinical outcome, as expected, low back pain in 1 week and 1 month after surgery; leg pain in 1 week, 1 month, and 6 moths; and Odom's criteria in 1 week, 1 month, and 6 months were significantly better in the favorable group than in the unfavorable group ($p < 0.05$; independent t-test and Pearson chi-square test) (Table 1).

In terms of the surgical outcome, although the complication rate was not significantly different between the groups. Complications included 1 case of dura puncture, 2 cases of transient lower extremity weakness, and 4 cases of transient headaches or nuchal pain. The rate of additional procedure (revision surgery or additional nerve block), implying surgical failure or recurrence, were significantly lower in the favorable group than in the unfavorable group (4.2% [2 of 48 patients] vs. 35.3% [12 of 34 patients], $p = 0.011$; Pearson chi-square test) (Table 2).

There was no difference in radiographic outcome between the 2 groups (Table 3).

Table 2. Difference in the surgical outcomes between the 2 groups

Variable	Favorable group (n = 48)	Unfavorable group (n = 34)	OR or difference	95% CI	p-value
Median operation time (min)	50.00 (95% CI, 43.87–60.00)	52.33 (95% CI, 45.02–59.65)	0.39 ± 4.01	-0.749 to 1.354	0.848†
Hospital stay (day)	3.5 ± 0.9	3.7 ± 1.2	0.2 ± 0.8	-0.847 to 1.247	0.854‡
Return-to-work	15.0 ± 7.1	15.6 ± 4.2	0.6 ± 2.0	-4.178 to 5.378	0.645‡
Complication (n)	3	4	0.727	0.042–12.518	0.826§
Additional procedure	2 (4.2)	12 (35.3)	0.083	0.009–0.781	0.011§
Additional nerve block	2	6	0.212	0.020–2.247	0.166§
Revision surgery	0	6	0.824	0.661–1.026	0.036§

Values are presented as mean ± standard deviation or number (%) unless otherwise indicated.
OR, odds ratio; CI, confidence interval.
†Nonparametric Mann-Whitney U-test, ‡Independent t-test, §Pearson chi-square test.

Table 3. Difference in the radiological outcomes between the 2 groups

Variable	Favorable group (n = 48)	Unfavorable group (n = 34)	Difference	95% CI	p-value
Disc height (mm)					
Preoperation	17.41 ± 3.86	18.46 ± 1.33	1.06 ± 0.98	-3.031 to 0.921	0.377†
6 Months	17.21 ± 1.54	18.35 ± 1.32	1.14 ± 1.45	-3.351 to 1.601	0.260
Segmental angle (°)					
Preoperation	6.56 ± 3.99	9.08 ± 5.30	2.51 ± 1.97	-6.648 to 1.612	0.218†
6 Months	6.78 ± 3.59	9.42 ± 4.61	2.64 ± 1.74	-6.281 to 1.009	0.147†
Range of motion (°)					
Preoperation	5.82 ± 4.06	6.09 ± 5.16	0.27 ± 1.96	-4.372 to 3.825	0.891†
6 Months	10.57 ± 3.05	10.39 ± 3.29	2.65 ± 2.64	-8.152 to 2.843	0.326†
Total lumbar lordosis (°)					
Preoperation	33.88 ± 15.08	34.10 ± 13.90	0.22 ± 6.23	-0.647 to 1.087	0.670†
6 Months	32.21 ± 10.57	40.18 ± 10.39	7.96 ± 4.49	-17.330 to 1.408	0.092†

Values are presented as mean ± standard deviation.
CI, confidence interval.
†Independent t-test.

Table 4. Demographic data and symptom-related characteristics of the 2 groups

Variable	Favorable group (n = 48)	Unfavorable group (n = 34)	OR or difference	95% CI	p-value
Age (yr)	40.38 ± 14.26	41.35 ± 16.97	-0.97 ± 4.89	-10.877 to 8.924	0.256†
Male ratio	30 (62.5)	22 (64.7)	1.18	0.321 to 4.326	0.804‡
Smoking	16 (33.3)	10 (29.4)	1.28	0.332 to 4942	0.720‡
Height (cm)	169.47 ± 10.40	169.44 ± 10.33	0.04 ± 3.29	-6.61 to 6.69	0.991†
Weight (kg)	69.67 ± 13.87	69.24 ± 14.04	0.42 ± 4.42	-8.512 to 9.361	0.924†
Body mass index (kg/m^2)	24.23 ± 4.36	24.02 ± 3.53	0.21 ± 1.28	-2.383 to 2.814	0.869†
Diabetes	2 (4.2)	4 (11.8)	0.34	0.109 to 2.354	0.379‡
Hypertension	8 (16.7)	10 (29.4)	0.50	0.113 to 2.265	0.368‡
Previous block	30 (62.5)	18 (52.9)	1.67	0.463 to 6.006	0.433‡
Trauma history	8 (16.7)	4 (11.8)	1.58	0.254 to 9.817	0.622‡
Median symptom duration (wk)	1.00 (95% CI, 1.04–5.10)	2.00 (95% CI, 1.67–2.60)	0.64 ± 1.06	-0.349 to 2.378	0.132§
Dominant symptom, back pain:leg pain	22:26	4:30	6.346	1.183 to 30.042	0.021‡

Values are presented as mean ± standard deviation or number (%) unless otherwise indicated.
OR, odds ratio; CI, confidence interval.
†Independent t-test. ‡Pearson chi-square test. §Nonparametric Mann-Whitney U-test.

Table 5. Preoperative magnetic resonance imaging and intraoperative findings of the 2 groups

Variable	Favorable group (n = 48)	Unfavorable group (n = 34)	OR or difference	95% CI	p-value
Surgical level, L3–4:L4–5:L5–S1	2:16:30	4:6:24	-	-	0.386†
Pfirrmann grade, I:II:III:IV	0:14:26:8	0:8:24:2	-	-	0.504†
Disc height ratio to vertebral body	0.38 ± 0.10	0.39 ± 0.08	0.01 ± 0.09	-0.102 to 0.111	0.917‡
High intensity zone, n (%)	24 (50.0)	4 (11.8)	7.52	1.401–40.0	0.011†
Morphology of lesion, bulging:protruded:extruded	6:22:20	4:24:6	-	-	0.190†
Location of herniation, central:right:left	14:10:24	12:10:12	-	-	0.517†
Degree of canal compromise, mild:moderate:severe	30:18:0	30:4:0	4.82	0.884–26.300	0.055†
Degree of nerve compression, abutting:displace:near obliteration:obliteration	16:24:6:2	26:4:4:0	-	-	0.048†
Herniated disc volume (mm^3)	33.14 ± 11.52	38.25 ± 8.96	5.11 ± 10.52	-7.56 to 18.59	0.854‡
Degree of stenosis, none:mild:moderate:severe	32:14:2:0	22:12:0:0	-	-	0.667†
Adhesion, mild:moderate:severe	3:13:32	2:9:23	-	-	0.749†

Values are presented as number or mean ± standard deviation unless otherwise indicated.
OR, odds ratio; CI, confidence interval.
†Pearson chi-square test. ‡Independent t-test.

2. Univariate Simple Analysis to Find Predictive Factor

With the exception of low back pain as a dominant symptom, almost none of the baseline characteristics were significantly different between the 2 groups. Low back pain dominance was a significant predictive factor for the favorable group, (45.8% [22 of 48 patients] in the favorable group vs. 11.8% [4 of 34 patients] in the unfavorable group; OR, 6.35; p = 0.021; Pearson chi-square test) (Table 4).

Among the characteristics determined by preoperative MRI and intraoperative findings, the presence of HIZ (50.0% [24 of 48 patients] in the favorable group vs. 11.8% [4 of 34 patients] in the unfavorable group; OR, 7.52; p = 0.011; Pearson chi-square test) and the degree of nerve root compression (p = 0.048; Pearson chi-square test) were significantly different between the 2

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Table 6. Dichotomous logistic regression analysis of various variables between the 2 groups

Variable	Favorable group (n = 48)	Unfavorable group (n = 34)	OR or difference	95% CI	p-value
High intensity zone	24 (50.0)	4 (11.8)	15.67	1.425–172.385	0.024
Dominant symptom, back pain:leg pain	22:26	4:30	16.95	0.570–200.0	0.122
Morphology of lesion, bulging:protruded:extruded	6:22:20	4:24:6	-	-	0.431
Degree of canal compromise, mild:moderate:severe	30:18:0	30:4:0	2.64	0.016–9.009	0.548
Median symptom duration (wk)	1.00 (95% CI, 1.04–5.10)	2.00 (95% CI, 1.67–2.60)	1.10	0.810–1.484	0.553
Degree of nerve compression, abutting:displace:near obliteration:obliteration	16:24:6:2	26:4:4:0	-	-	0.735

Values are presented as number (%) or number unless otherwise indicated.
OR, odds ratio; CI, confidence interval.

groups (Table 5).

3. Dichotomous Logistic Regression Analysis for Finding Predictive Factor

We performed a regression analysis to screen out clear predictive factors among the various baseline characteristic for the favorable group. In the previous univariate simple analysis, symptom duration, low back pain as a dominant symptom, presence of HIZ, morphology of lesion, degree of canal compromise, and degree of root compression showed meaningful values with p-value less than 0.2.

According to regression analysis of these meaningful factors, the HIZ on MRI (OR, 15.67; 95% CI, 1.425–172.385; p = 0.024) was the only significant predictive factor for the favorable group (Table 6). The correlation test showed no correlation between various factors.

DISCUSSION

Some previous literatures reporting the clinical results of SELD for lumbar disc herniation showed that the outcome was favorable, even compared to that of open discectomy or full endoscopic discectomy, in terms of the significant improvement in pain and the high patient's satisfaction rate (more than 80%).[16,20,22,25,27] However, according to the author's previous study, the clinical result was different with that of previous literature as the lower patient's satisfaction rate (58.5%) and the higher symptom recurrence rate (17.1%) during a minimum 6-month follow-up.[17] This result was not favorable compared to other minimally invasive surgical techniques for lumbar disc herniation.

There are a number of possible explanations for this in inconsistency with previous reports. First, the surgical proficiency of surgeons for SELD could affect the clinical result. We speculated that the outcome is not favorable in the early case series compared to the late case series, and this variation of surgical skill could affect the overall outcomes. However, in our previous study, both the surgical outcome and clinical outcome were not different between the early and late surgery groups.[28] Therefore, we speculated that the patient characteristics could affect clinical outcomes after SELD. For example, differences in detailed baseline characteristics such as demographic data, disc level, morphology of pathology could cause varied clinical outcomes. To find out which factors influence the prognosis after SELD, we compared the various factors between the favorable and unfavorable group.

In our study, as expected reasonably, the clinical outcome, including improvement of pain and patient satisfaction, and surgical outcome, including surgical failure or recurrence, were different between the 2 groups; the favorable group showed more favorable outcome than the unfavorable group. Consequently, we analyzed various factors that could influence the clinical result. Among these factors, according to regression analysis, the existence of a HIZ on preoperative MRI was the only significant predictive factor of the clinical outcome. If MRI showed a HIZ at the pathologic disc level, the effect of SELD was maximized, resulting in favorable outcomes after SELD.

A HIZ is defined as focal high signal intensity in the dorsal side of the disc beneath the posterior longitudinal ligament on T2-weighted MRI.[29-31] This bright area surrounded by a low signal intensity of the annulus fibrosus is clearly dissociated from the signal of nucleus pulposus and appreciably brighter than the water signal at the same level on sagittal T2-weighted MRI.[29-31] A HIZ on T2-weighted MRI may represent damage or tearing of the annulus fibrosus and hydrated inflammation of the tear-

ing site.[32-34] Damage or inflammation of the annulus fibrosus can cause low back pain due to irritation of the sinuvertebral nerve or cause radiating leg pain due to irritation or compression of the concordant nerve root, although occasionally there are no related symptoms.[35] Consequently, according to previous studies, a HIZ is known to be correlated with discogenic low back pain.[32,33,36]

With regard to mechanism of laser ablation, SELD could be effective when there are more focal lesions than diffuse lesions and more hydrated lesions than dehydrated lesions. Based on this concept, focal HIZ, i.e., a focal hydrated lesion, could be an optimal target of laser ablation, and the effect of laser ablation can be maximized compared to other soft disc herniation without HIZ. In other words, mild to moderate soft lumbar disc herniation with HIZ can be an optimal indication in performing SELD.

There are several limitations in this study. Because of its retrospective study design, it was difficult to control for all factors related to outcomes. In addition, the number of patients was relatively small and the study was limited in a single institute. However, this single-institute research could keep the quality of data and preclude the diversity of surgeon's skill.

To the best of our knowledge, this is the first study to report on the predictive factor for successful SELD. Further studies with a larger number of patients or prospective studies are required to confirm the correlation between a specific predictive factor and the clinical result of SELD.

CONCLUSION

The only significant baseline predictive factor for the favorable outcome of SELD was the presence of a HIZ in the pathological disc on preoperative T2-weighted MRI. A favorable outcome can be expected when the patient is selected based on this optimal predisposing factor.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Microsurgery Versus Endovascular Treatment - Which Is Adequate for Initial Treatment of Spinal Dural Arteriovenous Fistula: A Case Series

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Objective: Considering the adverse natural history of spinal dural arteriovenous fistula (sDAVF), clinical outcomes may be worsened if the initial occlusive trial does not achieve complete fistula occlusion. We aimed to analyze the initial success rate of microsurgery and embolization and confirm the effects of initial treatment success on the clinical outcomes of sDAVF patients. In addition, we investigated the factors associated with initial treatment failure.

Methods: A total of 38 patients treated for sDAVF at a single institution over a 14-year period were retrospectively reviewed. Clinical outcomes according to the initial treatment modality were quantitatively analyzed. Demographic characteristics and angioarchitecture data were evaluated to identify factors associated with initial treatment failure.

Results: In the study population, 34 patients underwent embolization as the initial treatment, and complete occlusion of the fistula was achieved in 13 patients (38%). However, all patients who underwent microsurgery showed complete fistula occlusion. Among patients with initial treatment success, gait and micturition were improved with statistical significance ($p < 0.001$ each). However, in cases of initial treatment failure, only mild improvements in gait and micturition were observed, which were not statistically significant ($p = 0.097$ and $p = 0.375$, respectively). A narrow feeding artery diameter ($p = 0.007$) and embolization of the artery only ($p = 0.002$) were identified as factors associated with initial treatment failure.

Conclusion: To achieve symptomatic improvement and prevent neurological deterioration due to recurrence, the initial definite occlusion of the fistula is important. Despite advances in endovascular techniques, microsurgical occlusion is still superior in terms of initial complete obliteration.

Keywords: Arteriovenous fistula, Embolization, Microsurgery

INTRODUCTION

Spinal dural arteriovenous fistula (sDAVF) is a rare disease, and diagnosis is difficult as the clinical presentation is nonspecific, the lesion is small and complex, and the angioarchitecture is diverse.[1-3] The appropriate diagnosis and treatment of sDAVF are important because venous hypertension and chronic ischemia due to arterialization of the recipient vein can cause myelopathy or paraplegia. Treatment of sDAVF requires obliteration of the arteriovenous fistula either by microsurgical occlusion or endovascular embolization. The endovascular treatment of sDAVF is preferred because of the technical developments in this procedure and the higher degree of safety attributed to its noninvasive characteristics.[4,5] However, poorer outcomes have been reported using this approach compared with microsurgery.[6-13] Moreover, recent studies have indicated that the pro-

portion of sDAVF patients undergoing microsurgical treatment has been increasing.[14] Some studies suggest that clinical outcomes may improve if additional treatment is performed after an incomplete initial therapy.[15,16] However, treatment failure has been identified as a factor associated with poor prognosis in cases of sDAVF.[16,17] Therefore, initial conclusive treatment is important as this disease can progress with severe deficits and can recur aggressively even after symptoms have been reduced or resolved after an initial therapy.[7]

Several studies have analyzed the clinical outcomes of patients with sDAVF according to the treatment modality.[2,7-9] However, due to its low incidence, studies of the effects of initial treatment success on sDAVF patient outcomes or possible prognostic indicators are limited. Therefore, in our present study, we analyzed and compared not only the outcomes of endovascular treatment and microsurgical treatment in cases of sDAVF but also the effects of initial treatment success on patient outcomes through quantitative analysis. In addition, we investigated the factors associated with initial treatment failure.

MATERIALS AND METHODS

We performed a retrospective analysis of a consecutive series of sDAVF patients treated at our institution from January 2004 to June 2017. The data supporting the findings of this study are available from the corresponding author upon reasonable request. The analyses were approved by the Institutional Review Board of Asan Medical Center (Protocol No. AMC-IRB-2018-0795). This study was a retrospective analysis of the medical records, and there was no risk to the patients. Consent was not obtained due to the retrospective nature of the study.

1. Clinical Data

The clinical variables of the patients including age, sex, and initial neurologic status, duration of symptoms were assessed using the electronic medical record. The classification scale for gait disturbance and micturition used by the Aminoff-Logue scale (ALS) score of disability was applied to analyze the clinical status before and after treatment. Based on the medical records of the patients, the ALS scores were retrospectively calculated by a neurosurgeon not directly involved in the treatments.

2. Radiologic Features

All of the patients underwent a diagnostic workup via magnetic resonance imaging (MRI) of the whole spine and consecutive selective spinal angiography, which confirmed the presence of sDAVF in all cases. The angiographic features of the arteriovenous fistula (AVF) (feeder location, number of feeders, feeder diameter—in the case of multiple feeders, we calculated and analyzed the average value of each feeder diameter, location of the most proximal site of the radiculomedullary vein [RMV], presence of collateral flow to the fistula, venous drainage flow direction) were recorded.

3. Treatments

For all the patients included in this study, the decision to treat was made after diagnosis by angiography. Endovascular treatment was conducted using either N-butyl cyanoacrylate (NBCA; Histoacryl; B. Braun, Tuttlingen, Germany) and/or Lipiodol or Onyx (ev3, Irvine, CA, USA). In most patients, NBCA was administered in a mixture with lipiodol (33 patients). One patient was treated with onyx.

Microsurgery was performed after failed embolization for obliteration of the fistula or if embolization was considered not feasible. Of the 4 patients who underwent microsurgery as the initial treatment, 3 of them showed a relationship between the feeder and anterior spinal artery (ASA) on preoperative spinal angiography, and arterial selection was regarded as difficult during diagnostic angiography for 1 patient. The microsurgery procedure consisted of laminectomy at the level of the fistula and disconnection of the fistula followed by cauterization. Indocyanine green (ICG) angiography was used to identify the fistula before treatment and to confirm fistula obliteration after disconnection.

4. Follow-up

The treatment results were confirmed by angiography and MRI. All patients underwent posttreatment spinal angiography to confirm definite fistula occlusion immediately after treatment. Definite fistula occlusion on postoperative angiography and the absence of or decreased cord swelling and engorged pial vessels on MRI were defined as fistula closure without recurrence. The imaging was repeated when there was a clinical suspicion of recurrent disease. Treatment failure was defined as the presence of a persistent AVF or occurrence of a new fistula at follow-up when compared with the status at posttreatment angiography. However, in the patients receiving embolization treatment, even if the sDAVF was partially occluded at follow-up, we classified it as successful occlusion if the feeder pattern remained unchanged (i.e., no occurrence of a new fistula on angiography, decreased cord swelling and engorged pial vessels on MRI, and the patient's symptoms remained improved). Successful occlusion of the fistula with the initial treatment was de-

fined as initial treatment success. Secondary treatment success was defined as successful occlusion of the fistula after additional treatment for a recurrent or residual lesion.

Successful occlusion of the fistula with the initial treatment was defined as initial treatment success. Secondary treatment success was defined as successful occlusion of the fistula after additional treatment for a recurrent or residual lesion. Patients were classified into the initial treatment success group and initial treatment failure group to analyze factors affecting treatment failure. Microsurgery cases were excluded from factor analysis related to the initial treatment success because this initial treatment was 100% successful. Factor analysis was performed for patients who underwent embolization as the initial treatment. In addition, all events during the operations were recorded, and any complications associated with the microsurgery procedure were documented.

5. Statistical Analysis

Statistical analyses were performed using the commercially available IBM SPSS Statistics ver. 21.0 (IBM Co., Armonk, NY, USA). The chi-square test was performed to assess categorical variables, and the Mann-Whitney test was used to evaluate continuous variables. The clinical outcomes of the groups were compared using the Wilcoxon signed-rank test. Patients who underwent embolization as the initial treatment were divided into 2 groups, and logistic regression was performed to evaluate the odds ratio (OR) and 95% confidence interval (CI) of potential prognostic indicators. The statistical significance level was set at $p < 0.05$.

RESULTS

We initially reviewed the records of 53 cases of spinal AVF evaluated by spinal angiography at our hospital during the study period. Classification according to the angioarchitecture revealed that the study population was composed of 41 patients with sDAVF (78.8%), 5 patients with epidural AVF (9.4%), and 7 patients with perimedullary AVF (13.2%).[1] Of the 41 patients di-

Table 1. Baseline demographics and characteristics of 38 patients with sDAVF

Variable	Initial treatment success (n = 17)	Initial treatment failure (n = 21)	p-value
Demographics and clinical characteristics			
Sex, male:female	12:5	19:2	0.207
Age (yr)	59 ± 12	62 ± 12	0.628
Neurologic status (Aminoff-Logue scale score)			
Gait	2.62 ± 1.49	2.76 ± 1.53	0.791
Micturition	1.5 ± 1.18	1.53 ± 1.50	0.880
Initial treatment modality, microsurgery:embolization	4:13	0:21	0.028*
Follow-up period (mo)	32 ± 26	27 ± 29	0.378
Angiographic characteristics			
Location of the feeding artery			
Cervical	2	3	0.832
Upper thoracic	3 (above T6)	3	
Lower thoracic	7 (below T7)	11	
Lumbar	5	4	
No. of feeders	1.35 ± 0.6	1.40 ± 0.6	0.914
Feeder diameter (mm)	1.1 ± 0.26	0.79 ± 0.23	0.004*
Presence of collateral flow	3 (17.6)	8 (38.1)	0.281
Location of the proximal site of the RMV, dorsal:ventral	14:3	19:2	0.650
Venous drainage flow direction, upward:downward:mixed	4:1:12	1:6:14	0.899
Relationship between the feeder and ASA	3 (17.6)	2 (9.5)	0.647

Values are presented as number, mean ± standard deviation, or number (%).
RMV, radiculomedullary vein; ASA, anterior spinal artery.

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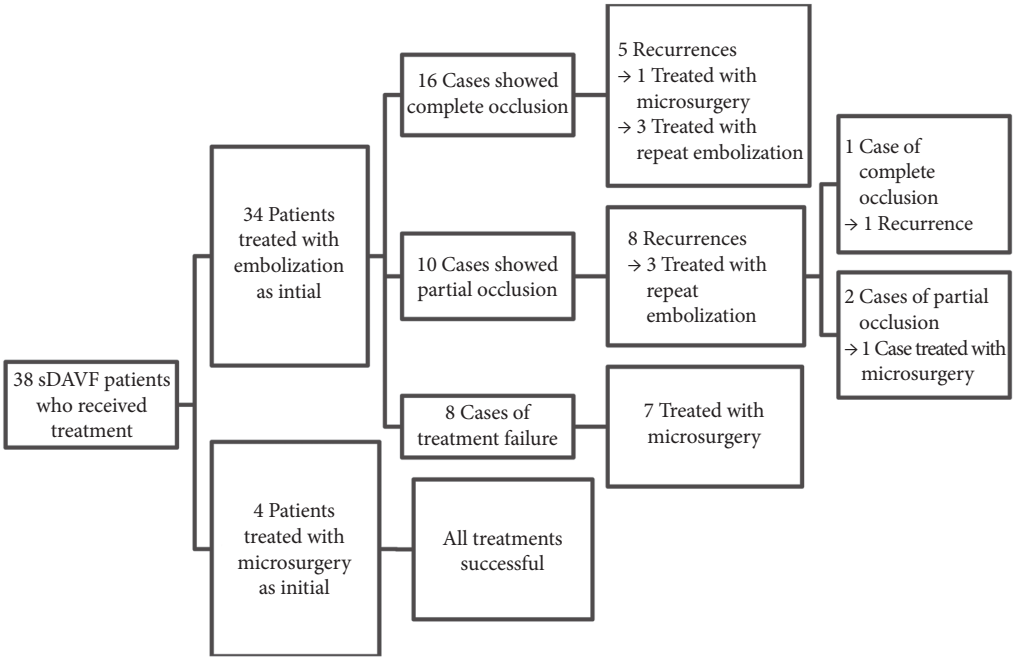
agnosed with sDAVF, 3 patients refused treatment. The remaining 38 patients who underwent treatment were enrolled in the present study. The initial clinical and angiographic data for the 38 patients with sDAVF are shown in Table 1. This cohort was composed of 30 males and 8 females with a median age of 61.2 years. There were 5 cervical lesions and 33 thoracolumbar lesions. All patients with cervical lesions, except one with subarachnoid hemorrhage (SAH) who only had headache and neck pain, and all patients with thoracolumbar lesions had myelopathy.

In the initial neurological evaluation, the values were similar between the 2 groups. There were 4 patients who underwent microsurgery and 13 patients who underwent embolization in the initial treatment success group. However, in the initial treatment failure group, all patients underwent embolization, and there was a statistically significant difference in the initial treatment modality between the 2 groups ($p=0.028$). The lower thoracic region (below T7) was the most common site of the feeding artery. The diameter of the feeding artery was significantly smaller in the initial treatment failure group (0.79 mm) than in the initial treatment success group (1.1 mm) ($p=0.004$). A total of 8 patients (38%) in the initial treatment failure group and 3 patients (17%) in the initial treatment success group exhibited collateral flow.

In present study, the duration from onset to treatment in the initial success group ranged from 0 to 96 months (average, 26 months). If patients were symptomatic for less than 24 months before treatment, gait function improved by 1.7 grades at last follow-up, while in those with longer duration of preoperative symptoms, gait function improved by 1.1 grades at last follow-up ($p=0.48$).

1. Radiologic Outcomes

Among the 38 patients with sDAVF, 34 patients underwent embolization, and 4 patients underwent microsurgical ligation as the initial treatment. Among the patients who underwent initial embolization, treatment failure occurred in 8 patients, and partial occlusion resulting in a residual fistula occurred in 10 patients. The causes of treatment failure in the study population included difficulty in advancing the catheter due to the severe tortuosity of the feeding artery (6 of 8) and the ASA originating with or adjacent to the feeding artery (2 of 8). Complete occlusion was achieved in 16 patients; however, 5 of them sub-



	Embolization	Microsurgery	p-value	OR	95% CI
Initial success rate	38% (13/34)	100% (4/4)	0.018	2.615	1.706–4.009
Secondary success rate	50% (3/6)	100% (9/9)	0.017	2.000	0.899–4.452

Fig. 1. Flow diagram of the treatment modalities and treatment success rates in the current case series. Statistically significant difference. sDAVF, spinal dural arteriovenous fistula; OR, odds ratio; CI, confidence interval. $p<0.05$, chi-square test.

sequently had recurrence in the follow-up period. Among the patients with initial treatment failure including recurrence, 6 patients underwent embolization as the secondary treatment; however, this was only successful in 3 cases. In addition, 9 patients underwent microsurgery as the secondary treatment with subsequent complete occlusion of the fistula. They took a minimum of 7 days, a maximum of 27 days, and an average of 13 days to undergo surgery after embolization failure. One patient who recurred after embolization as the secondary treatment showed complete occlusion after microsurgical treatment as the tertiary treatment. Among the patients treated with embolization, 5 of the 8 patients with partial occlusion were followed up without further treatment as there was no further neurological deterioration and the MRI scans and angiography showed no changes during the follow-up period.

None of the 4 patients who underwent microsurgery as the initial treatment for sDAVF showed any follow-up evidence of persistent arteriovenous shunting. Hence, the initial success rate for endovascular treatment in our current study cohort was 38%, and the secondary success rate was 50%. In comparison, the initial and secondary success rates for microsurgical treatment were both 100% (Fig. 1).

2. Clinical Outcomes

Neurological improvements in both gait and micturition were determined by clinical outcome analysis using ALS scores. Subgroup analysis was performed according to the treatment modality (microsurgery vs. endovascular) and the initial treatment outcome (initial treatment success vs. initial treatment failure). In quantitative terms, the mean ALS gait score showed significant improvement in the final follow-up after treatment in all subgroups (microsurgery group: $p = 0.001$, embolization group: $p = 0.005$, initial treatment success group: $p < 0.001$) except for the initial treatment failure group ($p = 0.097$). In addition, the

Table 2. Pre- and final ALS score in the initial treatment success (n = 17) and initial treatment failure (n = 21) groups

Variable	Aminoff-Logue score			Group comparison†
	Pretreatment	Last follow-up	p-value	
Gait				0.002
Initial success group	2.62 ± 1.49	1.21 ± 1.06	< 0.001*	
Initial failure group	2.76 ± 1.53	2.15 ± 1.77	0.097	
Micturition				0.124
Initial success group	1.5 ± 1.18	0.71 ± 0.80	< 0.001*	
Initial failure group	1.53 ± 1.50	1.23 ± 1.64	0.375	

Values are presented as mean ± standard deviation.
*$p < 0.05$, statistically significant difference (as determined by the Wilcoxon signed-rank test). †Comparison between the groups. An improvement in gait but not micturition was significantly different between the 2 groups.

Table 3. Prognostic indicator analysis

Variable	Univariate analysis			Multivariate analysis		
	p-value	Odds ratio	95% CI	p-value	Odds ratio	95% CI
Sex, male:female	0.405	0.482	0.087–2.680	-	-	-
Age	0.263	1.033	0.976–1.093	-	-	-
Neurologic status				-	-	-
Gait	0.566	1.144	0.722–1.813	-	-	-
Micturition	0.457	1.239	0.705–2.177	-	-	-
Location of the feeding artery	0.696	0.861	0.407–1.821	-	-	-
No. of feeders	0.639	0.779	0.275–2.206	-	-	-
Feeder diameter	0.020*	0.015	0.000–0.511	-	-	-
Presence of collateral flow	0.114	4.278	0.706–25.919	-	-	-
Location of the proximal site of the RMV (dorsal: ventral)	0.877	1.182	0.142–9.827	-	-	-
Venous drainage flow direction (upward: downward: mixed)	0.552	1.400	0.462–4.238	-	-	-
Relationship between the feeder and ASA	0.999	Not estimated	Not estimated	-	-	-
Embolization site (artery, artery+vein)	0.008*	19.250	2.183–169.786	0.023*	14.034	1.448–136.003

CI, confidence interval; RMV, radiculomedullary vein; ASA, anterior spinal artery.
*$p < 0.05$, statistically significant difference.

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mean ALS micturition score was significantly improved after treatment in each subgroup (microsurgery group: p = 0.015, embolization group: p = 0.007, initial treatment success group: p < 0.001) except for the initial treatment failure group (p = 0.375) (Table 2). In addition, when we analyzed the degree of symptom improvement between subgroups (initial treatment success vs. initial treatment failure), there were statistically significant gait improvements in the initial treatment success group (p = 0.002). In terms of micturition, the comparison indicated no significant differences in the degree of symptom improvement between the groups (p = 0.124).

3. Prognostic Factors

We conducted prognostic factor analysis related to the initial treatment success of 34 patients who underwent embolization as the initial treatment (Table 3). Patients were first classified into 2 groups depending on this outcome. In univariate analysis, the diameter of the feeding artery (p = 0.020; OR, 0.015; 95% CI, 0.000–0.511) and embolization of the artery only (p = 0.008; OR, 19.250; 95% CI, 2.183–169.786) were identified as factors associated with initial treatment failure. In multivariate analysis, no variable other than embolization of the artery only (p = 0.023; OR, 14.0342; 95% CI, 1.448–136.003) was identified as statistically significant. There was no association between initial treatment success or failure and the age, sex, initial neurologic status, level of the fistula, number of feeders, dorsal or ventral location of the RMV, presence of collateral flow, venous drainage flow direction, or relationship between the feeder and ASA.

4. Complications

There were no surgical complications in the microsurgery group. In the embolization group, unintentional complications including arterial tear or endothelial injury occurred in 4 patients, and a fatal complication caused by posterior spinal artery (PSA) territory infarction occurred in 1 patient.

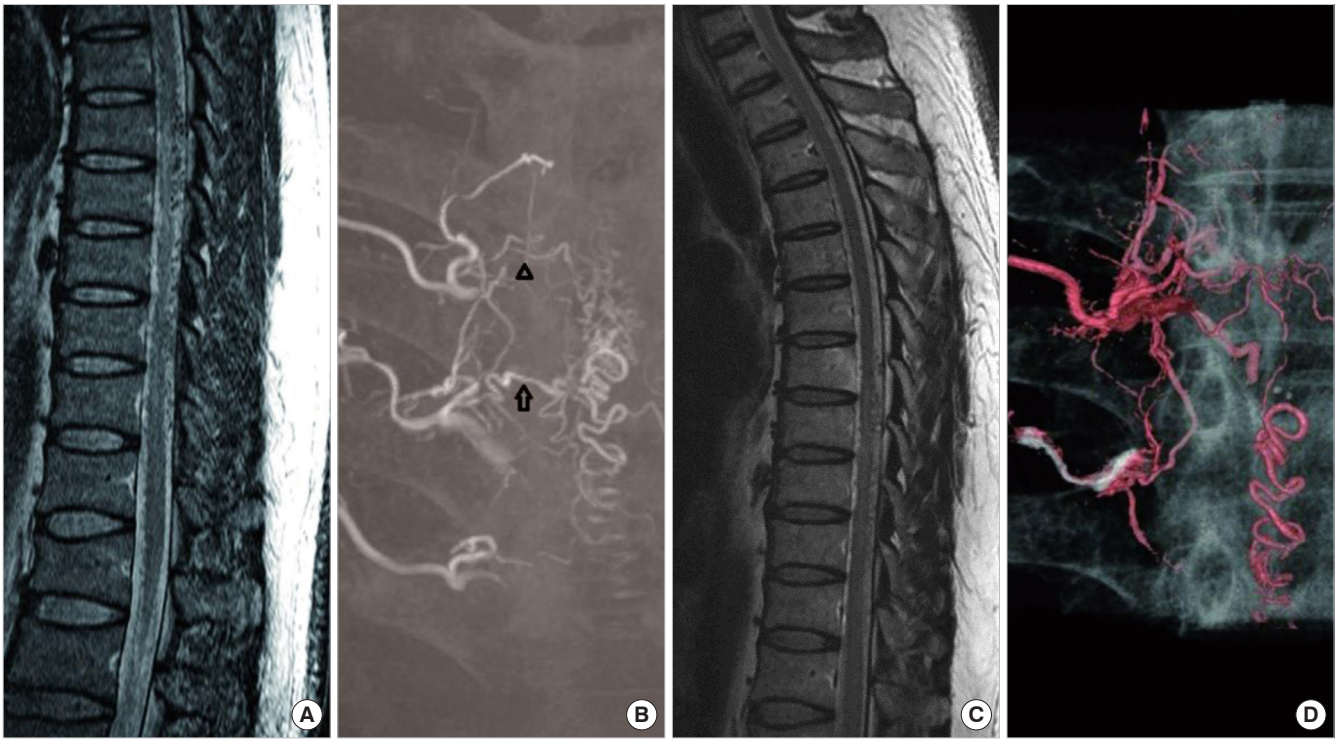

Fig. 2. Recurrence after initial complete obliteration of the fistula. (A) Pretreatment T2-weighted sagittal magnetic resonance image showing the flow voids of the enlarged pial vessels and the increased signal intensity of the spinal cord. (B) Reconstructed spinal angiography showing spinal dural arteriovenous fistula (sDAVF) filling from the right T7 pedicle (arrow) and suggesting the minor feeding of the sDAVF from the right T6 radicular artery (arrowhead). (C) The patient showed mild symptomatic improvements after the intervention; however, the symptoms worsened after 1 year. A sagittal T2-weighted magnetic resonance image taken at 24-month posttreatment indicated persistent increased signal intensity as well as enlarged pial vessels. (D) 3-dimensional reconstruction images showing complete occlusion of the feeder at the previous embolization site (right T7) and a recurred DAVF fed by the right T6 spinal artery.

5. Case Illustration

1) Case 1

A 46-year-old man was presented at our clinic with a history of progressive hypoesthesia, paraparesis, and urinary and fecal incontinence. The patient was diagnosed with sDAVF and undergone embolization at another hospital 2 years previously with similar symptoms (Fig. 2). The patient showed mild symptomatic improvements after the previous intervention; however, his symptoms worsened at 1-year posttreatment. The patient was recommended for an annual follow-up at the hospital where the initial treatment was given; however, his symptoms continued to progress, and he visited our hospital for further evaluation and treatment.

There was a questionable component at T6 associated with the fistula on the pretreatment DSA from the previous institution (Fig. 2B). Selective spinal angiography at our hospital showed the recurrent fistula at the right T6 (Fig. 2D). We attempted another embolization procedure for the recurrent lesion but decided to perform surgical ligation because of inaccessibility with the microcatheter. The patient underwent a T6–7 laminotomy for obliteration of the sDAVF. A midline durotomy was performed, and the right T6 artery was identified with a clear fistula point (Fig. 3). Successful obliteration of the fistula was achieved using ICG and an MV Doppler. Postoperative spinal angiography performed 7 days later revealed no residual sDAVF (Fig. 4). Periodic follow-ups at our outpatient clinic for 6 months indicated that the patient showed signs of hypoesthesia and gait improvements; however, urinary and fecal incontinence improvements were somewhat marginal.

2) Case 2

A 62-year-old man visited the Emergency Department with headache and neck pain. A brain computed tomography (CT) scan revealed SAH, and angiography showed sDAVF at the craniocervical junction. The main feeder was the ASA originating from the left vertebral artery. Another fistula was observed from the left C2 segmental artery (Fig. 5).

We tried embolization as the first treatment. The feeding artery from the left C2 segmental artery was completely blocked but the feeding artery from the ASA was partially occluded. After embolization, the patient's neurological findings indicated severe paralysis of the left upper and lower limbs and sensory disturbance of touch and position sensations on the left side of his body from the neck downward.

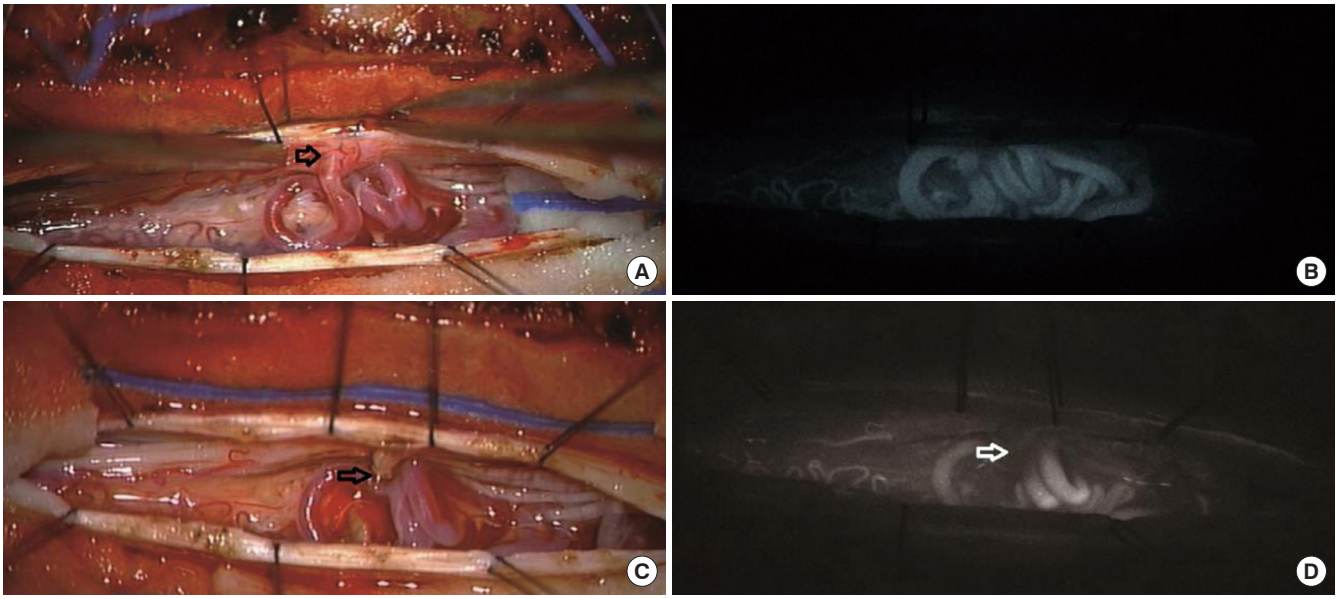

Fig. 3. Intraoperative photographs. (A) Dilated arteries and arterialized perimedullary veins along the spinal cord. The fistula point could be identified at the dorsolateral portion of the dura mater as the feeding artery enters the intradural space (arrow). (B) Indocyanine green (ICG) angiography revealed the gradual filling of the dilated perimedullary vein, indicating the presence of spinal dural arteriovenous fistula at that level. (C) Bipolar coagulation and disconnection of the fistulous point (arrow) were performed, resulting in the immediate darkening of the blood in the draining vein. (D) ICG angiography revealed that the previously injected dye remained in the dilated perimedullary vein and that the feeding artery was no longer in contrast (arrow). This confirmed the successful obliteration of the fistula. Persistent dye filling in the dilated veins indicated existing venous hypertension.[20]

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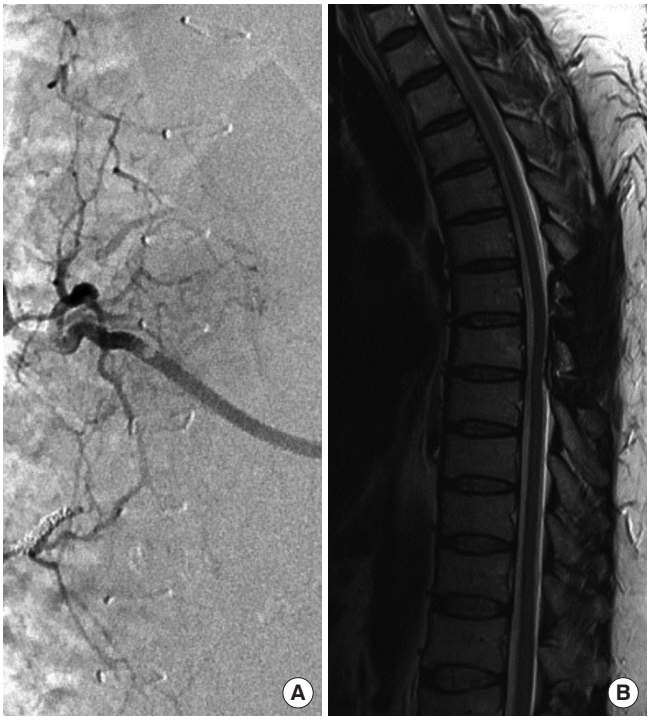

Fig. 4. (A) DSA showing no further filling of the fistula from the radiculomedullary junction of the right T6 vertebral level of the thoracic cord. (B) Posttreatment (4 months) sagittal T2-weighted magnetic resonance image showing markedly decreased cord swelling without the engorgement of pial vessels.

T2-weighted MRI images showed high signal intensity areas in the left upper cervical PSA from the C1 to the C4 levels that were consistent with spinal cord infarction (Fig. 6).

He received comprehensive rehabilitation treatment. His left limb strength was restored to grade 4 and he was able to walk without assistance on his own. About 2 years later, he underwent surgical treatment for sDAVF recurrence and was diag-

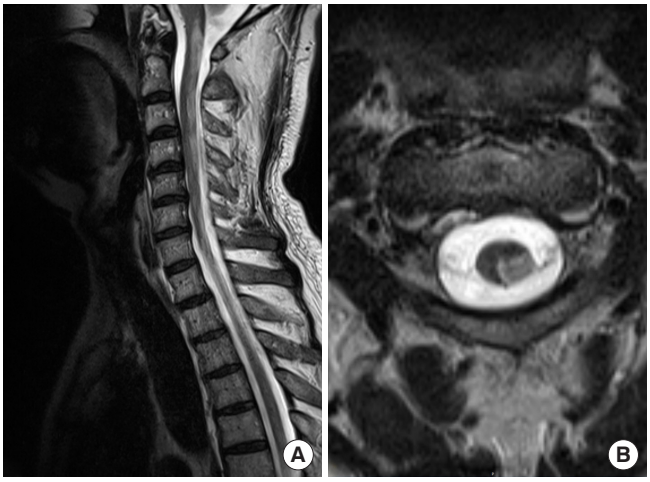

Fig. 6. T2-weighted magnetic resonance imaging sagittal (A) and axial (B) images show high signal intensity areas in the left upper cervical posterior spinal artery from C1 to C4 level.

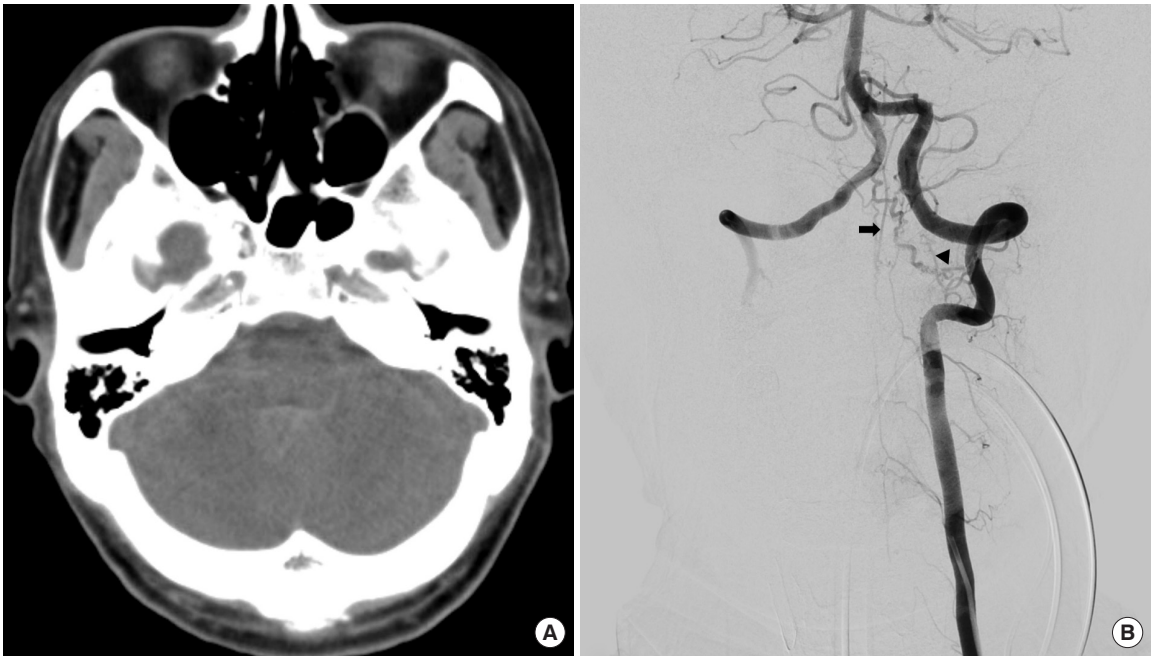

Fig. 5. (A) A brain computed tomography scan shows the subarachnoid hemorrhage in the perimedullary cistern and intraventricular hemorrhage in the 4th ventricle. (B) Angiography shows the subarachnoid hemorrhage. Anterior spinal artery (arrow) and left C2 segmental artery (arrowhead) form the feeding artery of the fistula.

nosed with complete obliteration.

DISCUSSION

1. Treatment of Choice for sDAVF

The choice between endovascular and surgical interventions for sDAVF remains somewhat controversial in the current literature. In a meta-analysis of spinal AVF cases published by Steinmetz et al.[2] in 2004, the treatment success rate for the endovascular treatment group was 46%; however, another meta-analysis published in 2015 reported a 72.2% success rate.[11] In our current study, the total success rate was 69%. However, the surgical success rates reported in several studies have been consistently high.[6-13] The surgical success rate in our case series was 100%.

Consistently, the results of other studies have indicated that initial embolization has limitations for successful treatment and that additional treatment is frequently needed.[2,3,10] Some studies suggest that even though additional treatment may be needed after an incomplete initial therapy, patient outcome would improve.[15,16] However, it is also well established that occlusion may be temporary as sDAVF can have a high rate of recurrence, and recanalization of the fistula can lead to secondary clinical deterioration; thus, early definitive treatment is important.[7,18] A previous study revealed that a shorter duration of symptoms was linked to better clinical outcomes.[19] In our study, the duration from onset to treatment in the initial success group ranged from 0 to 96 months (average, 26 months).

Although this was not statistically significant, patients with shorter duration of symptoms before treatment had better clinical outcomes. If patients were symptomatic for less than 24 months before treatment, gait function improved by 1.7 grades at last follow-up, while in those with longer duration of preoperative symptoms, gait function improved by 1.1 grades at last follow-up ($p = 0.48$).

In our current study, quantitative analysis of the clinical symptoms of sDAVF demonstrated the importance of initial treatment success in improving the patients' neurologic status.

Other studies have described surgery for AVF as a definitive treatment with stable long-term results and low levels of procedure-related morbidity.[2,20] Endovascular techniques have continued to improve in recent years. However, advances in intraoperative microscopy and the use of ICG have augmented the ability to resolve this type of lesion surgically.[20,21] In addition, minimally invasive spine surgery has been developed, which can produce similarly excellent results and allow faster patient discharges.[11] Moreover, surgery is an effective intervention when the segmental feeding artery also supplies a spinal cord artery—a relative contraindication for endovascular treatment.[6] Indeed, our current case series included a case of inadvertent occlusion causing PSA territory infarction.

The development of 3-dimensional rotational angiography has facilitated the examination of the angioarchitecture in sDAVF patients prior to treatment. This method may also be helpful in choosing the right working angle and feeder prior to embolization and assist with the decision to change the treatment modality if embolization is likely to fail or incomplete occlusion is possible. In our present study, the treatment decision for 3 of the 4 sDAVF patients who underwent microsurgery as the initial intervention was attributed to the relationship between the feeding artery and ASA on diagnostic angiography. In the remaining initial microsurgery case, the selection of the feeding artery was regarded as difficult. Owing to sound decision-making in this case, the patient achieved neurological recovery without recurrence after only one operation. Although embolization materials or other endovascular devices have undergone considerable advances over the years, endovascular treatment may not be curative. Typically, in sDAVF cases with enhanced angioarchitecture complexity on diagnostic angiography, no endovascular attempts are made, and patients would be immediately referred for microsurgical treatment.[6,11,22-24]

2. Prognostic Indicators of Initial Treatment Success

Initial treatment success and recanalization in spinal AVF are related to the complexity of the angioarchitecture and rich collateral networks.[3,6,9,23] In our current study cohort, 6 of 8 cases of failed embolization were attributed to the severe tortuosity of the feeding artery, thus making surgery a favorable option for these patients. We also found a statistically significant association between a narrow feeding artery diameter and initial treatment success ($p = 0.020$). In our present study, 5 of 16 patients with complete occlusion at initial embolization developed subsequent recurrence. If the glue penetrates only the feeding artery and does not penetrate the draining vein, recanalization occurs through the newly opened or existing collateral vessel.[3]

Discontinuous and uneven glue distribution between the arterial and venous segments tends to cause the fistula to recur.[6,23] Furthermore, our prognostic factor analysis revealed a statistically significant association between initial treatment success and venous occlusion of the embolization material ($p = 0.008$). The development of the collateral network was also greater in the initial treatment failure group (38%) than in the initial treat-

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ment success group (15%), which could be caused by an additional supply from anywhere from the segmental artery or a dural collateral with low flow at pretreatment that could not be determined as a feeder or was not visible. However, this limited flow could change over time to a feeder after embolization.[25]

However, this was not statistically significant (p = 0.114; OR, 4.278; 95% CI, 0.706–25.919). There was no correlation between the venous drainage flow direction and treatment outcome (p = 0.696; OR, 0.861; 95% CI, 0.407–1.821). The association between fistula location and treatment success remains a subject of controversy in the current literature.[6,23,26] As indicated by a previous study, an ASA arising from the same level could limit the ability to embolize.[15] However, no statistically significant association was found between the ASA and treatment failure in our current case series (p = 0.999); most of the patients with sDAVF and ASA of the same origin underwent microsurgery.

3. Limitations

There were some limitations in our current study. First, it was a retrospective design. Second, the patient population was small. However, in terms of rare disease entities, our study sample size was comparable to that of many other studies. Third, the number of patients who underwent microsurgery as the initial treatment was significantly lower, and the success rate of microsurgery was 100%, thus limiting treatment failure analysis. Fourth, the angioarchitecture of the spinal vessels in our cases was very small and complex and thus did not allow for the quantitative analysis of tortuosity. Further studies are required to address these limitations.

CONCLUSION

Although the natural course of sDAVF is progressive, it can be considered as a treatable and curable disease due to advances in imaging diagnosis and treatment techniques. Endovascular treatment is the preferred intervention for sDAVF because it is safer and less invasive than surgery. However, there is a higher tendency for recurrence, which can be accompanied by neurological deterioration. Therefore, the success of the initial treatment of sDAVF is essential for improving the patient's symptoms. A detailed pretreatment evaluation and proper decision-making for each individual sDAVF patient are important, and endovascular therapy should be attempted if it is likely that a single embolization session could treat sDAVF. Despite the continued development of endovascular techniques, microsurgical occlusion still produces superior outcomes, especially in terms of initial complete obliteration.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Minimally Invasive Spine Surgery With Midline Cortical Bone Trajectory Screw Fixation for Lumbar Degenerative Disease in a Retrospective Study of 200 Patients

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Objective: Midline lumbar interbody fusion is performed for treatment of various lumbar degenerative diseases, with good clinical outcomes and few complications. However, there are no large-scale or long-term studies regarding midline lumbar interbody fusion. Therefore, the purpose of this study was to evaluate the clinical results of midline lumbar interbody fusion and to compare the results according to surgical level.
Methods: Between January 2013 and December 2015, 200 patients with lumbar degenerative disease undergoing midline lumbar interbody fusion surgery were enrolled. The mean patient age was 69.9 ± 15.8 years (range, 40–85 years). The patients were divided into groups according to surgical level: (1) level 1 operation (136 patients), (2) level 2 operation (43 patients), (3) level 3 operation (12 patients), and (4) level 4 or higher (9 patients). Clinical outcomes, fusion rates, and complications were compared among the 4 groups.
Results: All clinical outcomes significantly improved after surgery (measured at 3 years postoperatively) in all groups. Mean fusion rate was 90.5% ± 5.21%. Fusion rate was highest in group I (95.8%) and lowest in group IV (85.2%). There were complications in 17 cases (8.5%). Adjacent segment disease occurred in 16 cases, 5 of which required surgery. Group 1 had 1 case, and group 4 had 4 cases. Screw loosening occurred in 1 case in group 4. There were no cases of infection or mechanical complications.
Conclusion: This large, single-institution, retrospective study demonstrates favorable clinical outcomes after midline lumbar interbody fusion for lumbar degenerative disease regardless of surgical level.

Keywords: Lumbar spinal stenosis, Posterior lumbar interbody fusion, Cortical bone trajectory screw technique, Clinical outcome, Fusion rate

INTRODUCTION

Posterior lumbar screw fixation and fusion are conservative surgeries that are performed for treatment of degenerative diseases of the lumbar spine with instability.[1,2] Most lumbar fusions are performed using pedicle screw (PS) fixation. Lateral muscle dissection is required to insert the PS and requires a long surgical incision and retraction of the paravertebral tissue. These methods can cause severe postoperative pain at the surgical site and iatrogenic muscle damage. PS insertion also causes superior facet joint violation and injury to the medial branch of the posterior ramus of the spinal nerve. This procedure can cause mechanical pain around the screw insertion point and adjacent segment degeneration. The cortical bone trajectory (CBT) screw

fixation method was first introduced by Santoni et al.[3] in 2009 to overcome the limitations of PS fixation. Since 2009, several articles and a meta-analysis have been published regarding cortical screw insertion.[4-7]

However, there have been no large-scale or long-term studies performed at a single institution involving surgeries performed by a single surgeon. In addition, none of the prior studies have compared outcomes by surgical level. Therefore, the purpose of this study was to evaluate the clinical results of midline lumbar interbody fusion with CBT screw fixation for lumbar degenerative diseases and to compare the results based on surgical level.

MATERIALS AND METHODS

1. Patients

This study was approved by the Institutional Review Board at National Health Insurance Service Ilsan Hospital (2019-044). Three hundred sixty-nine patients with lumbar degenerative disease underwent surgery between January 2013 and December 2015 at our institution. Among them, 80 patients were excluded because they had PS fixation. In addition, 20 patients were excluded due to need for a second operation, and 69 patients were excluded because they were lost to follow up (Fig. 1). Two hundred patients underwent conventional posterior lumbar interbody fusion with cortical screw fixation by a single surgeon. Clinical outcomes, radiologic studies, and surgical methods were reviewed and analyzed retrospectively. The inclusion criteria are described below. First, all patients were diagnosed with spinal stenosis, degenerative or spondylolytic spondylolisthesis, or degenerative disc diseases based on clinical symptoms, physical examination, and imaging (with x-ray, computed tomography [CT], and magnetic resonance imaging [MRI]). All of the included patients had received conservative treatments

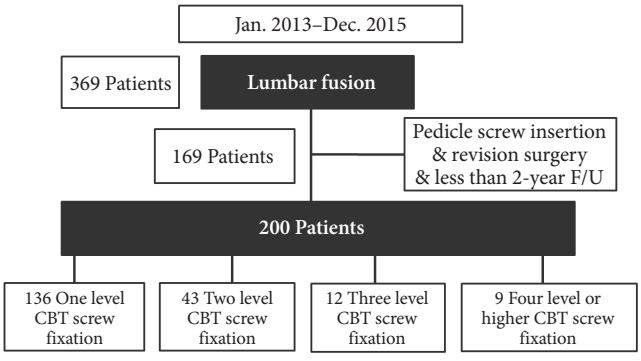

Fig. 1. Flow chart of the patients in our study. F/U, follow-up; CBT, cortical bone trajectory.

(including medication, physiotherapy, and injection therapy) for >6 months prior to inclusion. We also included patients who required surgery due to significant clinical symptoms. Only cases that employed cortical screws with midline lumbar interbody fusion were included. Only patients with >3 years of follow-up were included. The exclusion criteria are as follows: patients with tumors, congenital disease, fractures, or repeat surgeries; patients who underwent PS fixation; and patients who had <3 years of follow-up. The mean patient age was 69.9±15.8 years (range, 40–85 years). The patients were divided into 4 groups according to surgical level: (1) level 1 operation (136 patients), (2) level 2 operation (43 patients), (3) level 3 operation (12 patients), and (4) level 4 or higher operation (9 patients). The mean follow-up period was 48.9±10.8 months (range, 38–72 months).

2. Operative Method

The patients were placed under general anesthesia in the prone position. All operations were performed by a single surgeon (HYZ) using the same surgical technique. A midline skin incision was made, and posterior decompression was achieved by laminectomy and bilateral partial medial facetectomy. Discectomy was performed, and an interbody cage was inserted. We used 2 PEEK cages (CAPSTONE; Medtronic, Memphis, MN, USA) per disc level. The cortical screw was inserted into the pedicle under fluoroscopic guidance. We used a bilateral screw-rod system with CS (MIDLF; Medtronic Sofamor Danek, Memphis, TN, USA). If there were no surgical complications, the patient was allowed to sit upright and walk on the first postoperative day. Clinical and radiographic results were obtained by an independent observer for 6 days postoperatively. The patients were continuously followed in the outpatient clinic.

3. Clinical Outcome Evaluations

We examined the visual analogue scale (VAS), Oswestry Disability Index (ODI), 36-item Short Form health survey (SF-36) mental component summary score (MCS), and physical component summary score (PCS) at preoperative, postoperative, and final follow-up to determine the clinical outcomes. We also reviewed and analyzed the following parameters retrospectively: operative time, intraoperative bleeding, length of incision, days of hospitalization, and surgical complications.

4. Radiological Evaluation

Preoperatively, patients underwent x-ray, CT, and MRI imaging. Plain radiographs were obtained postoperatively at 6 months,

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1 year, and at the final follow-up. Imaging with CT and MRI was performed in patients with adjacent segment disease (ASD) after surgery. The criteria for radiological ASD were as follows: (1) decrease of disc height >10%; (2) translation >3 mm and rotation changes >10° on flexion and extension lateral x-rays; and (3) worsening by 2 or more grades as noted on postoperative lumbar lateral x-rays (based on the University of California, Los Angeles grading scale for intervertebral disk degeneration[8] at an adjacent level); and (4) identification of spinal stenosis or disc herniation at an adjacent level on follow-up MRI. The height of the intervertebral discs was measured on neutral lumbar lateral x-rays according to the Frobin method.[9] The surgical indications for ASD were extreme low back pain, severe radiculopathy, or limitation of daily activities caused by radicular or neurogenic intermittent claudication and that was refractory to at least 3 months of conservative treatment of at least 3-month duration. Fusion was determined at the final follow-up examination by the first author (SHN). Fusion was defined as absence of movement at the surgical level on dynamic x-rays and osseous continuity between the vertebra and the grafted bone on CT without loosening of the PSs.[10]

5. Statistical Analysis

The findings are expressed as mean value±standard deviation or count, as indicated. One-way analysis of variance and chi-square tests were used to compare the results from the 4 groups after adjusting for age and sex. A p-value of <0.05 was considered to indicate statistical significance. All statistical analyses were performed using IBM SPSS Statistics ver. 23.0 (IBM Co., Armonk, NY, USA) and SAS ver. 9.2 (SAS, Cary, NC, USA).

RESULTS

1. Patient Demographics

Two hundred patients underwent midline lumbar interbody fusion with CBT screw insertion at the author's institution. Table 1 shows the detailed demographics of the 4 groups of patients, which were comparable. This study comprised 63 male (31.5%)

Table 1. Patient demographics

Variable	One level (n=136)	Two level (n=43)	Three level (n=12)	Four level or higher (n=9)	p-value
Sex					
Female	91	33	9	4	
Male	45	10	3	5	0.623
Age (yr)	67.2±7.21	66.3±6.18	67.3±8.61		0.628
Follow-up (mo)	39.4±2.91	40.3±3.12	39.3±2.75		0.866
BMD (g/cm^2)					
T-score	-1.75±0.47	-1.69±0.29	-1.81±0.42	-	0.756
BMI (kg/m^2)	23.4±4.31	23.5±3.78	23.8±5.75		0.852
Operation level					
L1/2	0	1	0	2	
L2/3	3	2	3	9	
L3/4	15	28	12	9	
L4/5	84	37	12	9	
L5/S1	34	18	9	7	
Thoracic	0	0	0	1	0.404
Preoperative diagnosis					
Spinal stenosis without spondylolisthesis	80	15	4	3	
Degenerative spondylolisthesis	45	20	8	3	
Spondylolytic spondylolisthesis	11	8	0	0	
Deformity	0	0	0	3	

Values are presented as number or mean±standard deviation.
BMD, bone mineral density; BMI, body mass index.

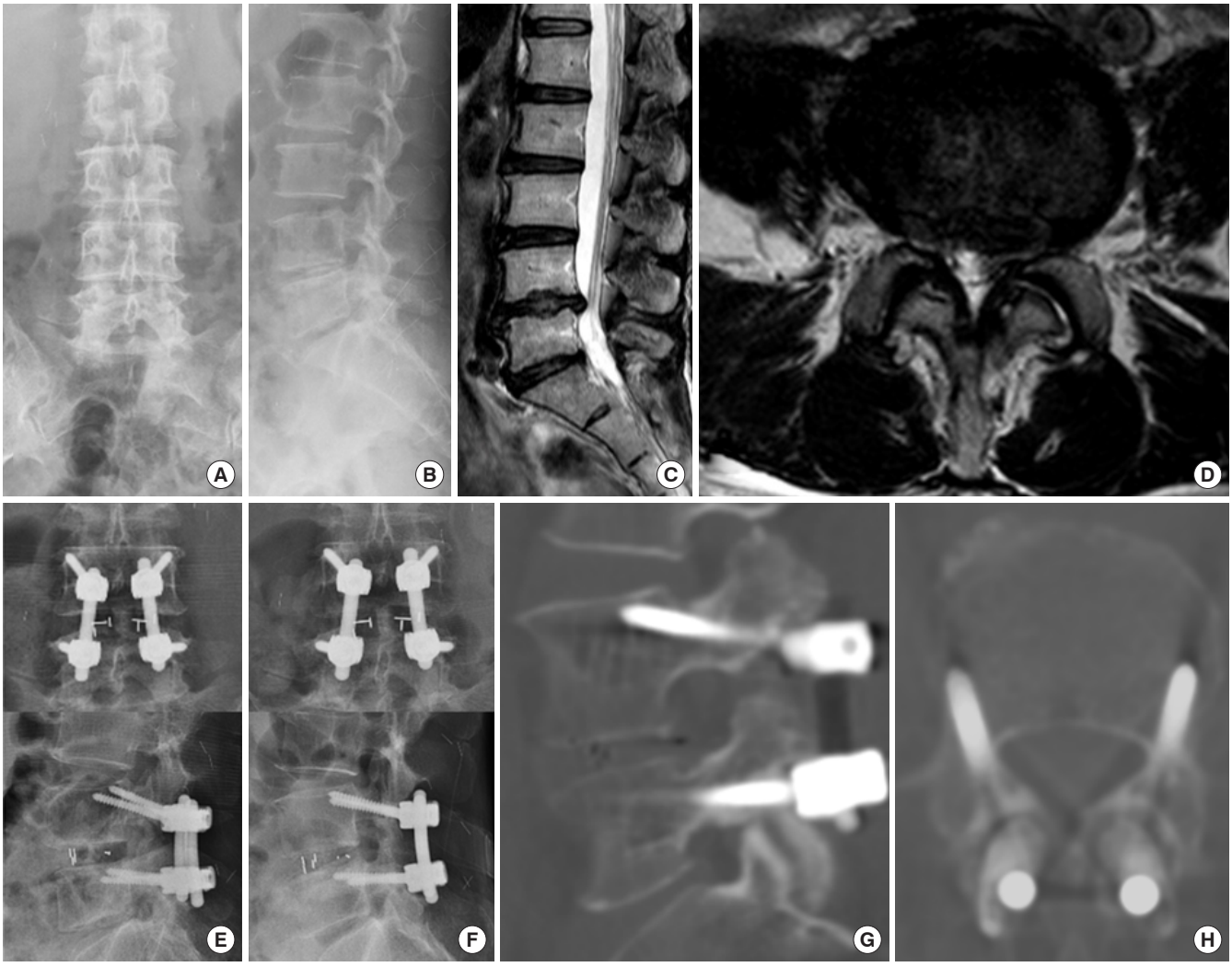

Fig. 2. A case from one level cortical bone trajectory screw fixation group. (A-D) A 78-year-old woman had L4/5 stenosis. (E) She underwent L4/5 posterior interbody fusion with cortical bone trajectory screw fixation. (F-H) After 5 years, there were no specific complications on follow-up radiologic examination.

and 137 female patients (68.5%). Patient age ranged from 40 to 85 years (average age, 69.9 ± 15.8 years). The patients were followed for an average of 48.9 ± 10.8 months. The most frequent surgical site was L4/5, followed by L5/S1. The preoperative diagnoses were spinal stenosis without spondylolisthesis (102 patients), degenerative spondylolisthesis (76 patients), spondylolytic spondylolisthesis (19 patients), and deformity (3 patients). Radiographs of representative 2 cases are shown in Figs. 2 and 3.

2. Comparison of Clinical Outcomes

All clinical outcomes improved significantly after 3 years in all groups (Table 2). Back VAS, leg VAS, ODI, SF-36, SF-36 MCS, and SF-36 PCS improved significantly (in all groups) after 3 years ($p < 0.05$) (Fig. 4).

3. Comparisons of Intraoperative Blood Loss, Operative Time, Hospital Day, Fusion Rate, and Complications

Intraoperative blood loss, operation time, days of hospitalization, complications, and fusion rate of the 4 groups are shown in Table 3. Fusion rate was highest in group I (95.8%) and lowest in group IV (85.2%). Complications occurred in 17 cases (8.5%). ASD occurred in 16 cases, of which 5 required surgeries with ASD. Group 1 had 1 case of ASD, and group 4 had 4 cases. Screw loosening occurred in 1 case in group 4. There were no cases of infection or mechanical complications.

DISCUSSION

The new CBT method was initially supported by Santoni et

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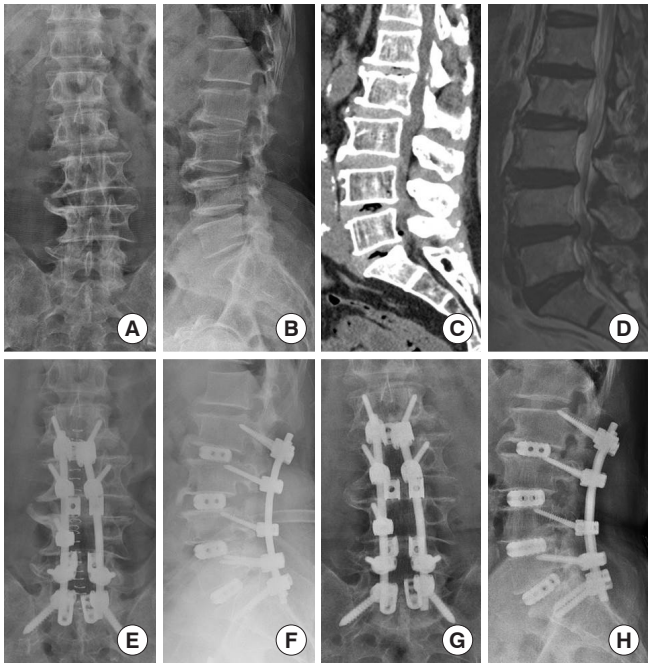

Fig. 3. A case from 4 level cortical bone trajectory screw fixation group. (A-D) A 75-year-old man had multiple stenosis L2/3/4/5/S1. (E, F) He underwent L2/3/4/5/S1 posterior interbody fusion with cortical bone trajectory screw fixation. In the process of inserting the left L4 cortical bone trajectory screw, the pedicle was damaged, so the L4 screw could not be inserted. (G, H) After 5 years, there were no specific complications on follow-up radiologic examination.

al.[3] In Matsukawa et al.,[11] CBT screws provided a 30% increase in uniaxial yield pullout strength compared to that of conventional PS. In addition, in vivo insertion torque of the CBT screws increased by 1.71 times compared to that of conventional PS. Zhang et al.[12] found that CBT screws had better biomechanical performance in pullout strength and toggle tests than did conventional PS. It is known that CBT screw/rod structures provide almost the same stability as conventional PS-rod structures.[13] Prior studies have shown good results for CBT screws in the laboratory. However, prior to this study, there were no long-term or large-scale clinical studies. In addition, no prior studies regarding CBT screws addressed the results by surgical level. In this study, we will discuss the clinical efficacy of CBT fixation.

Most clinical outcomes, such as VAS, ODI, and Japanese Orthopaedic Association, improved after CBT screw fixation in prior studies.[14] There were no differences identified between CBT screw fixation and PS fixation. In our study, back VAS, leg VAS, ODI, and SF-36 improved at the final follow-up in all groups.

The CBT screw fixation technique of inserting a screw into the caudomedial entry point near the pars articularis has been widely used. This technique maximizes the interface between the screw and the cortical bone and provides enhanced screw bone bonding strength.[15] The paths from the inside to the outside and from the caudal to the cephalad portions of the cortical screw can reduce the risks of nerve damage and superior facet violation. This technique may also allow for shorter skin incisions, less muscle dissection, less intraoperative bleeding, shorter operation time, and shorter hospitalization. And this also reduced postoperative infection. Sakaura et al.[10,16] and Lee et al.[17] found that operative time, bleeding amount, hospital days, and incision length were all shorter/smaller with CBT fixation than with PS fixation. Although it was not discussed in this study, operative time, incision length, bleeding amount, and length of hospital stay were all lower with CBT fixation than with PS fixation in out institution. And there was no infection case.

Many studies have previously addressed the complication and fusion rates of CBT fixation.[14,16,18] The fusion rate of CBT fixation was not significantly different from that of PS fixation. In our study, the fusion rate was good at surgical levels 1–3 but poor above level 4. The potential complications of CBT fixation include intraoperative nerve injury, dura tear, screw malpositioning, postoperative surgical site infection, screw loosening, and adjacent segment degeneration. In Keorochana et al.,[14] the intraoperative complication rate was lower with CBT fixation than it was with PS fixation, although the difference was not statistically significant. In our study, there was 1 case of screw malposition and 5 cases of dura tear. Shorter operative times improve a surgeon's concentration and reduce the rate of intraoperative complications. Postoperative complications were significantly less frequent with CBT than they were with PS fixation. In Hu et al.,[18] complications of CBT fixation were not significantly different from those of PS fixation. Among these complications, ASD occurred twice as often with PS fixation than it did with CBT fixation.[16] CBT fixation allows for a smaller incision of the superior facet and paraspinal muscles and less violation of the superior facet than does PS fixation.[10] Superior facet violations increase biomechanical stress and consequently cause instability in the adjacent segments.[19] In our study, ASD occurred in one case of level one and in 4 cases above level 4. Keorochana et al.[14] reported about the loss of reduction as a disadvantage of CBT. Compared to PS, it is difficult to obtain sufficient lordosis when surgery is performed with CBT level 3 or higher. PS is the most common and reliable tool for correcting spinal deformity.[14] So, in our cases, Smith-Petersen Osteotomy was performed to obtain sufficient lordosis through CBT.

Table 2. Comparison of clinical parameters according to fusion levels

Variable	One level (n = 136)	Two levels (n = 43)	Three levels (n = 12)	Four levels or higher (n = 9)	p-value
Back VAS					
Preoperation	7.8 ± 0.36	7.5 ± 0.12	7.9 ± 0.15	8.2 ± 0.51	0.471
Postoperation	2.7 ± 0.15#	2.8 ± 0.18#	2.8 ± 0.51#	3.1 ± 0.48#	0.687
Last follow-up	1.9 ± 0.27#	1.7 ± 0.39#	1.8 ± 0.54#	1.9 ± 0.37#	0.269
Leg VAS					
Preoperation	8.2 ± 0.16	8.1 ± 0.27	8.3 ± 0.28	8.1 ± 0.62	0.271
Postoperation	2.5 ± 0.24#	2.4 ± 0.12#	2.6 ± 0.73#	2.5 ± 0.58#	0.259
Last follow-up	1.4 ± 0.71#	1.3 ± 0.68#	1.4 ± 0.71#	1.5 ± 0.42#	0.321
ODI					
Preoperation	43.9 ± 2.13	41.7 ± 2.32	45.2 ± 2.71	46.7 ± 1.75	0.461
Postoperation	15.1 ± 2.01#	14.6 ± 1.13#	13.7 ± 2.27#	14.5 ± 1.21#	0.103
Last follow-up	5.7 ± 1.54#	4.9 ± 0.12#	3.6 ± 1.12#	5.1 ± 1.75#	0.363
SF-36 MCS					
Preoperation	30.5 ± 9.12	29.7 ± 8.15	28.8 ± 5.17	28.2 ± 6.27	0.335
Postoperation	42.1 ± 8.13#	43.2 ± 7.22#	41.9 ± 9.14#	40.8 ± 10.1#	0.825
Last follow-up	45.7 ± 8.15#	46.5 ± 9.13#	45.8 ± 7.54#	44.7 ± 9.77#	0.433
SF-36 PCS					
Preoperation	28.8 ± 6.33	29.5 ± 7.27	28.2 ± 8.15	29.2 ± 4.89	0.541
Postoperation	40.1 ± 8.12#	41.2 ± 8.12#	42.8 ± 7.19#	40.8 ± 5.12#	0.358
Last follow-up	48.8 ± 7.59#	47.5 ± 6.19#	47.8 ± 5.85#	47.8 ± 7.91#	0.256

Values are presented as mean ± standard deviation.
VAS, visual analogue scale; ODI, Oswestry Disability Index; SF-36 MCS, 36-item Short Form health survey mental composite score; SF-36 PCS, 36-item Short Form health survey physical composite score.
#$p < 0.05$, comparison with the preoperative value.

Table 3. Comparisons of intraoperative blood loss, operative time, hospital day, fusion rate, and complications

Variable	One level (n = 136)	Two levels (n = 43)	Three levels (n = 12)	Four levels or higher (n = 9)	p-value
Operation time (min)	131.21 ± 22.46	152.74 ± 31.91	281.67 ± 57.57	332.67 ± 42.12	0.021*
Bleeding loss (mL)	153.17 ± 20.12	230.15 ± 31.75	812.24 ± 204.53	1,383.48 ± 257.32	0.001*
Hospital day (day)	9.15 ± 0.57	9.45 ± 0.28	12.37 ± 3.12	14.12 ± 3.78	0.037*
Fusion rate (%)	95.8 ± 1.21	95.3 ± 0.98	94.1 ± 2.71	85.2 ± 4.21	0.043*
Complications					
ASD	1	0	0	4	
Screw loosening	0	0	0	1	
Dura tear	3	3	2	0	
Postoperative infection	0	0	0	0	

Values are presented as mean ± standard deviation or number.
ASD, adjacent segmental disease.
*$p < 0.05$, statistically significant difference.

However, screw loosening that occurs in patients with severe osteoporosis can be minimized by using CBT.[20] CBT increases pullout strength of screw by maximizing the contact surface between screw and cortical bone.[11] Biomechanical study reported that the pullout load of CBT was increased by 30% compared to PS.[3] In our study, there was 1 case of screw loosening in group

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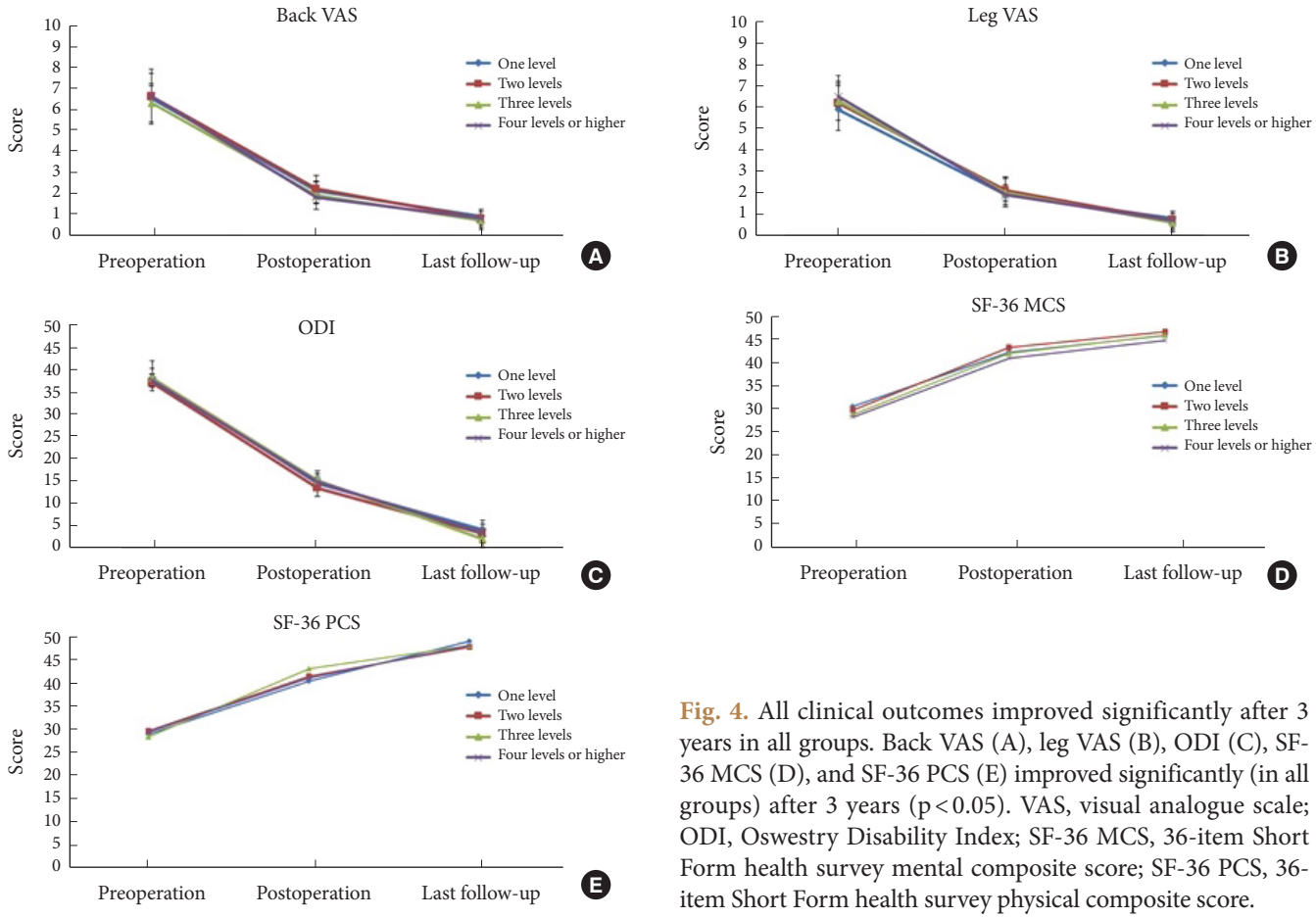

Fig. 4. All clinical outcomes improved significantly after 3 years in all groups. Back VAS (A), leg VAS (B), ODI (C), SF-36 MCS (D), and SF-36 PCS (E) improved significantly (in all groups) after 3 years ($p < 0.05$). VAS, visual analogue scale; ODI, Oswestry Disability Index; SF-36 MCS, 36-item Short Form health survey mental composite score; SF-36 PCS, 36-item Short Form health survey physical composite score.

4. In case of severe osteoporosis, CBT is a good surgical method.

Our study has several limitations. It has inherent risk of selection bias given its retrospective design. In addition, because our study size was small, we were limited in our ability to make comparisons between the groups for several factors known to affect prognosis. Regardless of these limitations, the results of this study suggest that the operative results according to surgical level must be considered when performing CBT fixation. Prospective studies must be conducted using well-guided evidence-based protocols with adequate controls.

CONCLUSION

The large, single-institution, retrospective cohort of the present study showed favorable clinical outcomes after midline lumbar interbody fusion with CBT screw insertion for lumbar degenerative disease regardless of number of fusion levels.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Original Article

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Metric Evaluation of Reliability and Transparency of the Videos About Carpal Tunnel Syndrome Surgery in the Online Platforms: Assessment of YouTube Videos' Content

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Objective: To evaluate the quality and reliability of carpal tunnel syndrome surgery videos on YouTube.
Methods: A keyword set of "carpal tunnel syndrome surgery" was searched on YouTube. The DISCERN scoring system, *Journal of the American Medical Association* (JAMA) scoring system, and Health on the Net (HON) ranking systems were used to evaluate the quality and reliability of the first 50 videos appeared in the search results. The characteristics of each video, such as the number of likes, dislikes and views, upload days, video length, and the uploader, were collected retrospectively. The relationships between the video quality and these factors were investigated statistically.
Results: All of the featured videos sorted were found to be of poor content (mean DISCERN score [n = 1.71 of 5], mean JAMA score [n = 1.76 of 4], mean HON score [n = 5.65 of 16]). Yet, DISCERN scores of the videos uploaded by medical centers were higher than that of the others (p = 0.022). No relationship was detected between the other variables and video quality.
Conclusion: Healthcare professionals and organizations should be more cautious when recording and uploading a video to the online platforms. As those videos could reach a wide audience, their content should provide more information about possible complications of a treatment and other treatment modalities.

Keywords: YouTube, Carpal tunnel syndrome surgery, Patient education

INTRODUCTION

Today, YouTube is the largest online video hosting platform in the world, and it has been increasingly popular in gathering medical information.[1] Usually, patients and their relatives visit YouTube to search for readily available information about their illness and possible treatment methods.[2] They are used to watch online videos to get information before undergoing a planned operation and find out potential risks and complications. Even some healthcare professionals like surgery residents and junior surgeons are known to have been making use of this platform to improve their knowledge or learn new techniques in the field of surgery. As YouTube is easily accessible, patients too are used to watch online videos to get information before undergoing a planned operation and find out potential risks and complications. Thus, in evaluating the quality of the YouTube videos, our target audience is not only patients and their relatives but also surgery residents and junior surgeons.

On the other hand, given their function and role in educating both patients and surgeons, these videos should be examined

regularly, and their reliability should be evaluated. There exist more than 1,500 studies in the literature that examine YouTube videos in medical content. Many studies suggest that the majority of those videos can be categorized as unreliable educational material. Although the reliability of the YouTube videos about medical issues has become a popular topic of interest in recent years, there is no study investigating the quality and reliability of the YouTube videos about carpal tunnel syndrome surgery (CTSS). Within this information, the purpose of this study is to evaluate quality of the videos about CTSS that are available on YouTube.

MATERIALS AND METHODS

In September 2020, a search was made on YouTube with the English keywords "carpal tunnel syndrome surgery." No filters were applied. "Relevance-based ranking" was applied as the ranking criterion and the first 50 videos in the search results were selected, similar to the method of a previous study.[3]

The following data were collected for each video: the time passed since upload of the video, the uploader, the number of views, likes, and dislikes. The uploaders were divided into 3 categories: (1) doctor, (2) medical center (institute, hospital, or clinic), (3) medical media agency. Those categories were determining as such: those including only a doctor's name in the video title or information were put in the "doctor" category; the videos including name of a hospital, institute, or clinic were put in the "medical center" category, and lastly, the videos uploaded by agencies were put in the "medical media agency" category.

The videos were retrospectively reviewed by 3 independent senior clinicians (OO, FD, OB) using DISCERN, the *Journal of the American Medical Association* (JAMA), and Health on the Net (HON) ranking systems. Each video was scored separately and the mean score of each video was calculated.

DISCERN is a questionnaire designed to evaluate the quality and reliability of health information. The videos are labelled as "poor," "moderate," and "good" in terms of their quality and then scored on a scale of 15 questions with 5 items in each. Each question is scored out of 5 and the mean score in 15 questions is pointed out the video's final score.[4] The first 8 questions focus on reliability of the information while the last 7 questions examine the treatment options offered (Table 1). DISCERN score is evaluated as "good" if it is higher than 3, "moderate" if it is 3, and "poor" if it is less than 3.

The JAMA evaluation criteria were used to evaluate video accuracy and reliability.[5] The JAMA comparison criterion is a nonspecific and objective assessment consisting of 4 different criteria (Table 2). Each criterion stands for 1 point. After the scores are calculated, a score of 4 indicates high accuracy and reliability of the source, while a score of 0 indicates poor accuracy and reliability. These criteria have been applied extensively in previous studies to evaluate the reliability of online resources.[3]

The HON is an assessment method that aims to improve the quality of health information on the internet including YouTube

Table 1. The DISCERN Instrument

No.	The DISCERN Instrument
1	Are the aims clear?
2	Does it achieve its aims?
3	Is it relevant?
4	Is it clear what sources of information were used to compile the publication (other than the author or producer)?
5	Is it clear when the information used or reported in the publication was produced?
6	Is it balanced and unbiased?
7	Does it provide details of additional sources of support and information?
8	Does it refer to areas of uncertainty?
9	Does it describe how each treatment works?
10	Does it describe the benefits of each treatment?
11	Does it describe the risks of each treatment?
12	Does it describe what would happen if no treatment is used?
13	Does it describe how the treatment choices affect overall quality of life?
14	Is it clear that there may be more than one possible treatment choice?
15	Does it provide support for shared decision-making?

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Table 2. JAMA Scoring System

Section	JAMA Scoring System	Yes	No
Authorship	Authors and contributors, their affiliations, and relevant credentials should be provided	1	0
Attribution	References and sources for all content should be listed clearly, and all relevant copyright information should be noted	1	0
Disclosure	Website "ownership" should be prominently and fully disclosed, as should any sponsorship, advertising, underwriting, commercial funding arrangements or support, or potential conflicts of interest	1	0
Currency	Dates when content was posted and updated should be indicated	1	0

JAMA, *Journal of the American Medical Association.*

Table 3. HONcode principles

Principle	Characteristic
1. Authoritative	Indicate the credentials of the authors
2. Complementarity	Support, not replace, the physician-patient relationship
3. Privacy	Respect the site visitor's privacy and confidentiality regarding any personal data submitted
4. Attribution	Cite the source(s) of published information, data, and medical and health pages
5. Justifiability	Back up claims relating to benefits and performance
6. Transparency	Present accessible, accurate email contacts
7. Financial disclosure	Identify funding sources
8. Advertising policy	Clearly distinguish advertising from editorial content

HON, Health on the Net.

Table 4. Analysis of video streaming source and DISCERN score, JAMA Scoring System, and HONcode

Video classification scale	Doctor	Medical Center	Medical media agency	p-value†
DISCERN score	1.62 ± 0.06	1.80 ± 0.22	1.74 ± 0.19	0.022
JAMA Scoring System (score)	1.72 ± 0.83 (0–3)	2.17 ± 0.94 (0–3)	1.55 ± 0.83 (0–3)	0.160
HONcode (score)	5.78 ± 2.16 (2–10)	6.67 ± 2.53 (3–11)	4.95 ± 2.39 (1–9)	0.114

Values are presented as mean ± standard deviation (range).
JAMA, *Journal of the American Medical Association*; HON, Health on the Net.
†Kruskal-Wallis test.

and other online platforms.[6] HON examines transparency and accuracy of the online information. The HON score primarily includes the following ethical aspects: author credentials, date of latest modification of clinical documents, data confidentiality, source data references, funding, and advertising policy (Table 3). The HON score has a maximum score of 16: 5 points for accessibility and transparency of information including valid contact information; 5 points for referring to authors' credentials; 3 points for accountability; 1 point for the privacy policy for user information; 1 point to reference when the information was last updated; and 1 point for accessibility.[6,7] A HON score of 12 or above out of 16 indicates that a YouTube video is fairly reliable.[6,7]

The IBM SPSS Statistics ver. 25.0 (IBM Co., Armonk, NY, USA) is used for statistical analysis. The Kolmogorov-Smirnov test was used to examine the normal distribution. According to the results of normality analyses, the data was not normally distributed. The descriptive statistical methods (frequency, percentage, mean, standard deviation) were used to evaluate the demographic data. The Kruskal-Wallis test was used in the comparison of quantitative data of 3 groups. The Spearman correlation analysis was performed for analyzing the association of the quantitative data. The results were evaluated at a confidence interval of 95% and a significance level of $p < 0.05$.

RESULTS

Of the 50 videos analyzed, all scored less than 3 out of 5 according to the DISCERN score. The mean DISCERN score was 1.71 out of 5. The average JAMA score was 1.76 out of 4, with a range of 0–3. The average HON score was 5.65 out of 16, with a

Table 5. Analysis of other variables and DISCERN score, JAMA Scoring System, and HONcode

Variable	Duration (sec)	Like	Unlike	Upload days	Views
Overall (n = 50), mean ± SD (range)	391.8 ± 442.3 (57–2,114)	831.6 ± 2.540.7 (0–13,000)	34.5 ± 54.7 (0–242)	1,713 ± 1,173 (362–4,342)	119,491.9 ± 190,850.2 (1,060–822,260)
Video classification DISCERN score correlations, p-value (r)*	0.267 (-0.160)	0.466 (0.115)	0.771 (-0.042)	0.425 (0.115)	0.957 (-0.008)
JAMA correlations, p-value (r)*	0.238 (-0.170)	0.871 (0.023)	0.541 (0.089)	0.132 (-0.216)	0.539 (-0.089)
HON correlations, p-value (r)*	0.341 (-0.138)	0.572 (-0.082)	0.566 (-0.083)	0.356 (0.133)	0.583 (-0.079)

SD, standard deviation; JAMA, *Journal of the American Medical Association*; HON, Health on the Net.
*Spearman correlation test.

range of 1–11. None of the videos scored 12 points or above.

It was determined that 36% of the videos were produced and uploaded by doctors, 24% by the medical center, and 40% by the medical media agency. Although all of the videos were in the poor-quality group, a statistically significant difference was found between their scores and uploaders according to DISCERN (p = 0.022) (Table 4). The DISCERN score of videos made by health centers was higher than the others. There was no statistically significant difference between the uploaders of the videos and JAMA and HON (Table 4) (p = 0.160 and p = 0.114, respectively).

The videos examined were uploaded at varying dates between 2009–2019. The mean upload days was 1,713 ± 1,173 days, with a range of 362–4,342, the mean video length was 391.8 ± 442.3 seconds, with a range of 57–2,114, the total number of views of 50 videos was 5,974,598, and; the mean number of views was 119,491.9 ± 190,850.2, with a range of 1,060–822,260. While the mean number of likes was 831.6 ± 2,540.7, with a range of 0–13,000, the number of dislikes was 34.5 ± 54.7, with a range of 0–242, respectively. Consistent with the results of the other studies, those results show that the common criteria applied in ranking videos such as the time passed since the upload date, number of views, likes, or dislikes, and the length of a video indeed have no effect on the quality of a video (Table 5).

DISCUSSION

In the present study, videos about CTSS on YouTube, the leading online video sharing platform, were evaluated. The sampled videos on this subject were found to be unreliable and unchecked. There exist a sound literature examining the reliability of the YouTube videos watched by patients to gather medical information, including the subject of neurosurgery.[3,8-13] In those studies reliability of the videos posted on YouTube regarding the subjects like spinal surgery, brain tumors, intracranial aneurysms, and deep brain stimulation surgery was investigated.[3,8-13] Those studies generally suggest that the YouTube videos usually fall short of providing complete medical information.

To the best of our knowledge, there is no study evaluating the reliability and accuracy of the information in the CTSS-related videos on YouTube. In our study, we examined 50 videos on this topic that we sampled according to the method of "relevance-based ranking." The first 50 videos that appeared in the keyword search results were selected because of 2 reasons: First, YouTube search engine seems to show the videos with highest number of views first. So, a sample of those videos could give a true picture of the impact of the videos on healthcare professionals and the general public. Second, any person seeking information about CTSS on YouTube should search the same or similar keywords to get the most relevant results. So, we think that our search criteria provided us with the accurate sample to evaluate the CTSS-related videos with highest impact and widest reach. The results showed that all videos had a DISCERN score below 3 (poor), HON scores below 12, and very low JAMA scores (1.76 of 4). The reliability of the videos containing preoperative medical information was also low. Only a small number of videos, for example, mentioned source of the information featured. Besides, it was not clear when the information discussed in the videos was produced. No details of the additional sources of information were disclosed either. Some videos discussing a treatment method of an illness mentioned alternative methods as well but their approaches to the other alternatives seemed neither well-balanced nor impartial. Potential risks or benefits of a discussed treatment method were not thoroughly described and compared with alternative therapies. The issue of how a proposed treatment method options would affect overall quality of life of a patient was neglected. Thus, the reliability of those videos was considered to be low. Nevertheless, overall, medical centers make relatively better quality and more reliable videos. It was observed that the videos featured

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by medical centers had higher DISCERN score, while there was no significant difference as far as JAMA and HON scores are concerned. No other factors were found to be significantly associated with a higher DISCERN score, JAMA score, and HON score.

The standard deviation values for video features like length, views, and dislikes were determined higher than their mean values. These results also suggested that the CTSS-related videos on YouTube have no standards, unreliable and unchecked by a professional.

In this regard, healthcare professionals should notice that there are thousands of readily available videos about diseases and their treatment methods on YouTube and many patients watch those videos. As it is impossible to edit those videos or undo their impact uploaders should at least be more sensitive and conscious about the impact their videos make especially on general public. In a health-related video aiming to make positive impact and contribute to the public health following categories of information should be discussed professionally: pathophysiology of the relevant disease, the natural course of the disease if untreated, treatment options, unbiased comparison of treatment options, potential complications of treatment options, possible complications related to anesthesia if used, clear mention of all sources of the information, and expected effects of the treatment on general quality of life.

On the other hand, these videos are watched by residents and junior surgeons for their surgical development and training. Thus, missing or misleading information in these videos can lead to unrepairable consequences. It is possible that a video containing partial information about a surgery could be considered by junior surgeons as practical and time-saving thereby misleading and misinforming them. For example, while the decompression of the median nerve takes at least 10 minutes, a video that fast-forwards and shortens this duration to attract more viewers might make the healthcare professional think that indeed this operation could be competed in less than 10 minutes. However, it is highly likely that shortened videos may not cover all essential aspect of a surgery. In such cases, maintaining an operation with insufficient hemostasis, or rushing to finish an operation in shorter than ideal duration would equip the junior surgeons with at best incomplete and misleading information ultimately undercutting their training. The downside of those videos for surgery residents and junior surgeons are summarized in Table 6. Negative impacts of the problematic videos are shown in the range of 24%–74%. The problems in the medical videos may be neglected as long as their target audience is patients and general public. However, as they have also been used by residents and junior surgeons as training materials the problems should be addressed properly. So, there is need for further research to raise awareness about this problem and device ways to end healthcare professional's exposure to misleading information. In Table 6, it was listed some basic issues to contribute to this discussion and there is room for new studies to further develop these topics.

Table 6. Negative issues in videos for surgeons

Negative issues in videos for surgeons	No. (%)
Over editing of videos	37 (74)
Quick surgery	12 (24)
Insufficient exposure	21 (42)
Insufficient or excessive hemostasis	17 (34)
Misleading surgical anatomy	21 (42)
Not showing whole surgical steps	33 (66)
Insufficient decompression	19 (38)

It is a fact that that most of medical-related YouTube videos have been made and uploaded by some health professionals and medical centers for the purpose of advertising. In addition, there is a legitimate concern that most of the videos have been made public without obtaining consent for the patients' surgical images or any other scenes involving them and ethical rules protecting privacy and personal information of the patients have not been respected duly. There is no information that the procedures performed in these videos comply with the ethical standards of relevant institutional and/or national research committees and but also the 1964 Declaration of Helsinki or any other comparable ethical standards. We believe that in the near future we may have new online open-source media forums under YouTube's lead or within alternative platforms that commit to the Helsinki Declaration and comply with the ethical principles and international scientific publication standards.

It should also be noted that YouTube hosts numerous high-quality medical resources and thereby could offer useful options in informing patients and the general public, training health professionals and last but not least providing a connection between professionals and patients. However, because of the shortcomings in videos and lack of an effective mechanism to separate fact from fiction, it seems that this is not possible for the time being.[5] As far as providing reliable medical information is concerned, YouTube is comparable to a dinner chat rather than an effective healthcare communication and decision-making platform.

CONCLUSION

YouTube provides patients and health professionals with an easy access to a large amount of information on CTSS. However, the poor quality and unreliability of the medical videos constitute one reason to be cautious. Health professionals should inform patients about the limitations of YouTube videos and refer them to appropriate sources of information to reduce their exposure to misinformation. Besides, health professionals too should avoid using online videos as training material for the same reason. Yet, given the global impact of online platforms such as YouTube, health professionals, and medical centers should make use of this opportunity to disseminate correct and easily digestible medical information for the general public. Such efforts would certainly contribute to protection of the public health in general and prevention of spread of misinformation in particular.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Original Article

Patient Health Questionnaire-9 Is a Valid Assessment for Depression in Minimally Invasive Lumbar Discectomy

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Objective: The Patient Health Questionnaire-9 (PHQ-9) is a screening tool for evaluating depressive symptoms. Research is scarce regarding the validity and correlation of PHQ-9 scores with other patient-reported outcomes of mental health after minimally invasive lumbar discectomy (MIS LD). We aim to validate PHQ-9 as a metric for assessing mental health in MIS LD patients.
Methods: A database was retrospectively reviewed for patients who underwent elective, single-level MIS LD. Patients were excluded if they had incomplete preoperative PHQ-9, 12-item Short Form Health Survey (SF-12), or Veterans RAND 12-item health survey (VR-12). Survey scores were collected preoperatively and postoperatively through 1 year. Mean scores were used to calculate postoperative improvement from preoperative scores. Correlation of PHQ-9 with SF-12 mental composite score (MCS) and VR-12 MCS scores was also calculated. Correlation strength was assessed by the following categories: $0.1 \leq |r| < 0.3$ = low; $0.3 \leq |r| < 0.5$ = moderate; $|r| \geq 0.5$ = strong.
Results: A total of 239 patients underwent single-level MIS LD. PHQ-9, VR-12 MCS, and SF-12 MCS all demonstrated statistically significant increases from preoperative scores at all postoperative timepoints ($p \leq 0.001$). SF-12 MCS and VR-12 MCS were each observed to have strong and significant correlations with PHQ-9 at all timepoints when evaluated with both Pearson correlation coefficients and partial correlation coefficients.
Conclusion: We observed that PHQ-9, SF-12 MCS and VR-12 MCS all significantly improve following lumbar discectomy and that PHQ-9 scores strongly correlated with these previously established measures. Our results substantiate evidence from other surgical fields that PHQ-9 scores are a valid tool to evaluate pre- and postsurgical depressive symptoms.

Keywords: Lumbar discectomy, Patient Health Questionnaire-9, Lumbar, Outcomes, Depression

INTRODUCTION

According to a recent report by the National Center for Health Statistics, approximately 8.1% of United States adults experienced significant depressive symptoms lasting for at least 2 weeks between 2013 and 2016.[1] Past studies have emphasized the prevalence of mental health disorders in spine patients, reporting that 59% of individuals with chronic low back pain presented with current symptoms of one or more psychiatric diagnoses.[2] These findings are especially important to note in the context of observations regarding the impact of depression on spine surgery outcomes. For example, Menendez et al.[3] reported that spine surgery patients with preoperative depression had a higher risk of perioperative adverse events over those without depressive symptoms. Another study by Miller et al.[4] demonstrated that higher preoperative depression was correlated with diminished

improvement in quality of life following lumbar spine surgery. These studies emphasize the importance of a reliable and valid means of assessing depressive symptoms in the clinical spine setting.

Patient Health Questionnaire-9 (PHQ-9) is a self-reported questionnaire that quantifies depression severity using 9 questions based on the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) criteria for major depressive disorder. Scores can range from 0 to 27, as each question is scored from 0 (not at all) to 3 (nearly every day), based on the frequency with which patients experience various effects of depressive symptoms. The PHQ-9 has been validated in a variety of clinical settings and has demonstrated several advantages over other mental health assessment tools, such as 12-item Short Form health survey (SF-12) and Beck Depression Inventory (BDI).[5] For example, PHQ-9 may be less time consuming than SF-12 and BDI, which have 12 and 21 questions, respectively. Additionally, its frequency-based responses allow clinicians to assess severity of depressive symptoms, and its basis on DSM-IV diagnosis provides logical validity.[6] Furthermore, the widespread use of this survey in both primary care and spine surgery settings means this data may be readily available for many patients.[7,8] Patel et al.[9] utilized PHQ-9 scores to assess the relationship between preoperative depression and postoperative outcomes following transforaminal lumbar interbody fusion and found that patients experiencing depressive symptoms reported greater pain, higher narcotic consumption, and poorer postoperative improvement. As the use of PHQ-9 continues to expand, it is critical to validate this tool on a procedure-specific level against other empirically supported mental health measures.

Parrish et al.[10] previously validated PHQ-9 in the cervical spine and reported strong correlations between PHQ-9, SF-12 mental composite score (MCS), and Veterans RAND 12-item health survey (VR-12) MCS in patients undergoing either anterior cervical discectomy and fusion or cervical disc replacement. While PHQ-9 has also been validated in lumbar fusions,[11] the drastic differences in indications, duration of symptoms, and outcomes among different spinal procedures necessitates that its use be validated for the specific populations, pathologies, and techniques associated with additional procedures.

Minimally invasive lumbar discectomy (MIS LD) has been established as a reliable intervention with positive long-term results for the treatment of disc herniation,[12] which is a common cause of lower back pain, sciatica, and neurological deficits.[13] However, depression may substantially interfere with this procedure's effectiveness and place patients at further risk for neurological complications. Additionally, Chaichana et al.[14] also demonstrated that patients with preoperative depression did not experience meaningful improvement in disability and quality of life at the same rates as others following LD. While the mental health psychometric SF-12 MCS has been extensively investigated for its validity in a wide variety of populations,[15-18] there still a dearth of studies that validate the use of PHQ-9 in both pre- and postoperative settings. Moreover, due to the frequency with which LDs are performed and their relationship with preoperative depression, it is important to assess the validity of PHQ-9 in this procedure-specific manner. This study aims to validate PHQ-9 as an appropriate metric for assessing mental health in patients undergoing MIS LD.

MATERIALS AND METHODS

1. Patient Population

Prior to study commencement, approval by the Institutional Review Board of Rush University Medical Center (ORA #1405-1301) and informed patient consent were obtained. A prospectively maintained surgical registry was retrospectively reviewed for patients who underwent primary, single-level MIS LD for degenerative spinal pathology from March 2016 until May 2019. Patients were excluded if they had not completed a PHQ-9, SF-12, or VR-12 survey at the preoperative timepoint or if their procedure was indicated due to trauma, malignancy, or infection. All MIS LD procedures were performed by the same fellowship-trained spine surgeon at a single academic institution.

2. Data Collection

Demographic and perioperative information was collected including age, sex, smoking status, body mass index categorized as <30 kg/m^2 (nonobese) or ≥ 30 kg/m^2 (obese), Charlson Comorbidity Index (CCI), operative duration (from incision to skin closure, in minutes), estimated blood loss (in mL), and postoperative length of stay (in hours). Patient mental health was assessed using PHQ-9, SF-12 MCS, and VR-12 MCS surveys at preoperative and postoperative (6 weeks, 12 weeks, 6 months, 1 year) timepoints. Surveys were completed either in the clinic using a provided tablet device or at the patient's home using a personal device. All surveys were administered and recorded through a secure, online Outcomes Based Electronic Research Database platform (OBERD, Columbia, MO, USA). Regular email-based reminders as well as outreach by clinical and/or research staff were utilized to maximize survey compliance.

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Table 1. Baseline characteristics of study population

Characteristic	Value
Age (yr)	42.4 ± 12.1
Sex	
Female	77 (32.2)
Male	162 (67.8)
Smoking status	
Nonsmoker	212 (88.7)
Smoker	27 (11.3)
Body mass index	
< 30 kg/m^2 – nonobese	145 (60.7)
≥ 30 kg/m^2 – obese	94 (39.3)
Charlson Comorbidity Index	0.8 ± 1.1
Operative time (min)	41.2 ± 11.8
Estimated blood loss (mL)	25.8 ± 5.3
Hospital length of stay (hr)	5.3 ± 7.0

Values are presented as mean ± standard deviation or number (%).

Table 2. Postoperative changes in survey scores

Variable	Score	Change	p-value†
PHQ-9			
Preoperative	6.7 ± 6.0 (239)	-	-
6 Weeks	3.6 ± 4.8 (177)	-3.2 ± 5.3 (177)	< 0.001*
12 Weeks	3.8 ± 5.5 (101)	-3.0 ± 5.8 (101)	< 0.001*
6 Months	3.8 ± 5.0 (82)	-3.5 ± 4.9 (82)	< 0.001*
1 Year	4.1 ± 6.1 (51)	-3.6 ± 6.8 (51)	< 0.001*
SF-12 MCS			
Preoperative	47.9 ± 11.2 (239)	-	-
6 Weeks	53.3 ± 10.0 (166)	5.3 ± 11.0 (166)	< 0.001*
12 Weeks	53.8 ± 10.3 (90)	5.6 ± 11.3 (90)	< 0.001*
6 Months	53.6 ± 9.1 (72)	7.0 ± 11.0 (72)	< 0.001*
1 Year	51.5 ± 11.2 (49)	5.9 ± 12.8 (49)	< 0.001*
VR-12 MCS			
Preoperative	50.0 ± 10.5 (239)	-	-
6 Weeks	56.0 ± 10.2 (166)	6.0 ± 10.1 (166)	< 0.001*
12 Weeks	57.0 ± 10.4 (90)	6.5 ± 11.1 (90)	< 0.001*
6 Months	56.6 ± 10.0 (72)	7.3 ± 10.4 (72)	< 0.001*
1 Year	54.4 ± 12.9 (49)	6.5 ± 13.2 (49)	0.001*

Values are presented as mean ± standard deviation (number).
PHQ-9, Patient Health Questionnaire-9; SF-12 MCS, 12-item Short Form health survey mental composite score; VR-12 MCS, Veterans RAND 12-item health survey mental composite score.
*$p < 0.05$, statistically significant difference. †p-value calculated using paired t-test comparing scores at each timepoint to preoperative values.

3. Statistical Analysis

All calculations and statistical analyses were performed using Stata 16.1 (StataCorp, College Station, TX, USA). Descriptive statistics were performed for all demographic and perioperative variables (Table 1). Mean scores were calculated for PHQ-9, SF-12 MCS, and VR-12 MCS at all timepoints and used to determine the mean change from baseline for each survey at each postoperative timepoint (Table 2). A paired Student t-test assessed improvements in each postoperative survey from preoperative baseline. Pearson correlation coefficient and time-controlled partial correlation coefficient were used to evaluate the relationship of PHQ-9 with SF-12 MCS and VR-12 MCS scores at each timepoint (Table 3). Correlation strength was assessed by the following categories: $0.1 \leq |r| < 0.3$ = low; $0.3 \leq |r| < 0.5$ = moderate; $|r| \geq 0.5$ = strong. Scatterplots were constructed to demonstrate relationships of PHQ-9 with SF-12 MCS and VR-12 MCS. PHQ-9 was further evaluated for discriminant validity using a 1-way analysis of variance. The threshold value for depression was set at 41.4 for SF-12 MCS based on prior clinical validity studies.[17] A p-value of < 0.05 was considered the threshold for statistical significance in all analyses.

Table 3. Correlation of PHQ-9 with SF-12 and VR-12 MCS for MIS lumbar discectomy

Variable	Pearson, r	p-value†	Partial, r	p-value‡
PHQ-9 vs. SF-12 MCS				
Preoperative	-0.647	< 0.001*	-0.658	< 0.001*
6 Weeks	-0.728	< 0.001*	-0.734	< 0.001*
12 Weeks	-0.761	< 0.001*	-0.765	< 0.001*
6 Months	-0.756	< 0.001*	-0.755	< 0.001*
1 Year	-0.898	< 0.001*	-0.898	< 0.001*
PHQ-9 vs. VR-12 MCS				
Preoperative	-0.702	< 0.001*	-0.778	< 0.001*
6 Weeks	-0.776	< 0.001*	-0.778	< 0.001*
12 Weeks	-0.796	< 0.001*	-0.802	< 0.001*
6 Months	-0.842	< 0.001*	-0.842	< 0.001*
1 Year	-0.909	< 0.001*	-0.908	< 0.001*

MIS, Minimally Invasive Surgery; PHQ-9, Patient Health Questionnaire-9; SF-12 MCS, 12-item Short Form health survey mental composite score; VR-12 MCS, Veterans RAND 12-item health survey mental composite score.
*$p < 0.05$, statistically significant difference. †p-value calculated using Pearson correlation. ‡p-value calculated using time-independent partial correlation.

RESULTS

A total of 310 patients who underwent primary, single-level MIS LD were initially identified. Of these, 239 met full inclusion/exclusion criteria, as outlined in Fig. 1. The patient cohort had an average age of 42.4 years, 32% were female, 39% were obese, and mean CCI was 0.8 (Table 1). Mean operative duration was 41 minutes, mean estimated blood loss was 25.8 mL, and mean postoperative length of stay was 5.3 hours (Table 1).

A summary of postoperative changes in all PROMs is found in Table 2. A total of 58 patients had completed one or more surveys at the final, 1-year timepoint. Mean baseline preoperative scores were 6.7 ± 6.0 for PHQ-9, 47.9 ± 11.2 for SF-12 MCS, and 50.0 ± 10.05 for VR-12 MCS. Following lumbar discectomy, PHQ-9 mean values demonstrated a significant improvement from baseline values at the 6-week (3.6 ± 4.8), 12-week (3.8 ± 5.5), 6-month (3.8 ± 5.0), and 1-year (4.1 ± 6.1) postoperative timepoint ($p < 0.001$, all). This corresponded to a mean postoperative change in PHQ-9 which ranged from 3.0 ± 5.8 at 12 weeks to 3.6 ± 6.8 at 1 year.

For SF-12 MCS, mean values significantly improved from baseline at the 6-week (53.3 ± 10.0), 12-week (53.8 ± 10.3), 6-month (53.6 ± 9.1), and 1-year (51.5 ± 11.2) postoperative timepoint ($p < 0.001$). This also corresponded to changes in SF-12 MCS that ranged from the smallest change of 5.3 ± 11.0 at 6-week to the largest change of 7.0 ± 11.0 at 6-month.

Lastly, for VR-12 MCS, a significant improvement in postoperative values was demonstrated at the 6-week (56.0 ± 10.2), 12-week (57.0 ± 10.4), 6-month (56.6 ± 10.0), and 1-year (54.4 ± 12.9) timepoint ($p < 0.001$, all). These improvements in VR-12 MCS ranged from 6.0 ± 10.1 at its smallest and 7.3 ± 10.4 at its largest.

Pearson correlation coefficient and time-controlled partial

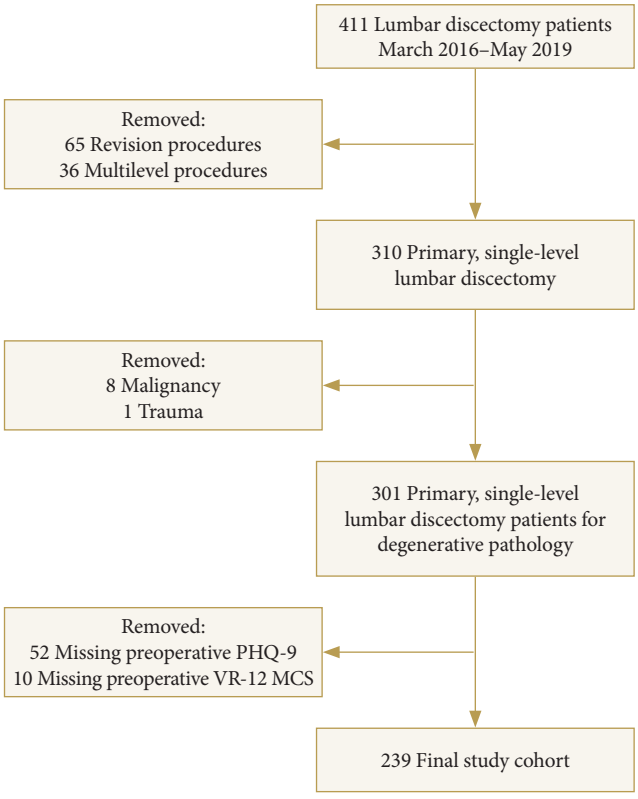

Fig. 1. Flowchart detailing patient inclusion and exclusion process for final study cohort.

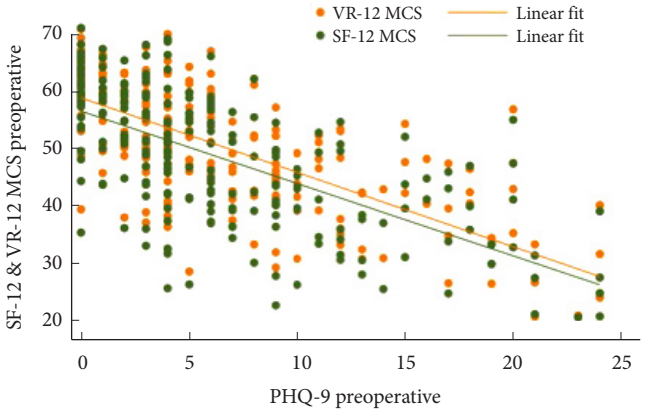

Fig. 2. Correlation of PHQ-9 with both SF-12 MCS and VR-12 MCS at the preoperative timepoint. PHQ-9, Patient Health Questionnaire-9; SF-12 MCS, 12-item Short Form health survey mental composite score; VR-12 MCS, Veterans RAND 12-item health survey mental composite score.

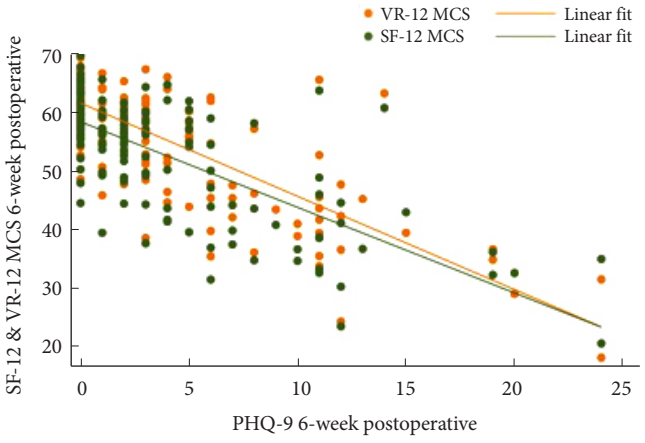

Fig. 3. Correlation of PHQ-9 with both SF-12 MCS and VR-12 MCS at the 6-week postoperative timepoint. PHQ-9, Patient Health Questionnaire-9; SF-12 MCS, 12-item Short Form Health Survey mental composite score; VR-12 MCS, Veterans RAND 12-item health survey mental composite score.

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correlation both demonstrated statistically significant correlations of PHQ-9 with SF-12 MCS at the preoperative (Fig. 2), 6-week (Fig. 3), 12-week (Fig. 4), 6-month (Fig. 5), and 1-year (Fig. 6) postoperative timepoints ($p < 0.001$, all) with all coefficients categorized as strong ($|r| \geq 0.647$, all). A similar result was observed for the relationship between PHQ-9 and VR-12 MCS with both Pearson correlation coefficient and time-controlled partial correlation demonstrating significant ($p < 0.001$, all) and strong ($|r| \geq 0.778$, all) at the preoperative (Fig. 2), 6-week (Fig. 3), 12-week (Fig. 4), 6-month (Fig. 5), and 1-year (Fig. 6) timepoints. A summary of these relationships can be found in Table 3.

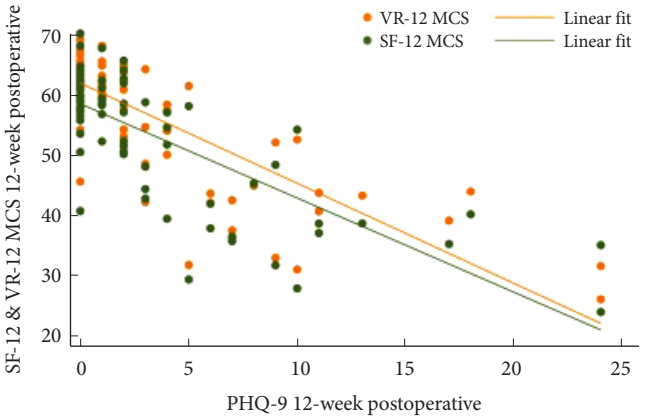

Fig. 4. Correlation of PHQ-9 with both SF-12 MCS and VR-12 MCS at the 12-week postoperative timepoint. PHQ-9, Patient Health Questionnaire-9; SF-12 MCS, 12-item Short Form Health Survey mental composite score; VR-12 MCS, Veterans RAND 12-item health survey mental composite score.

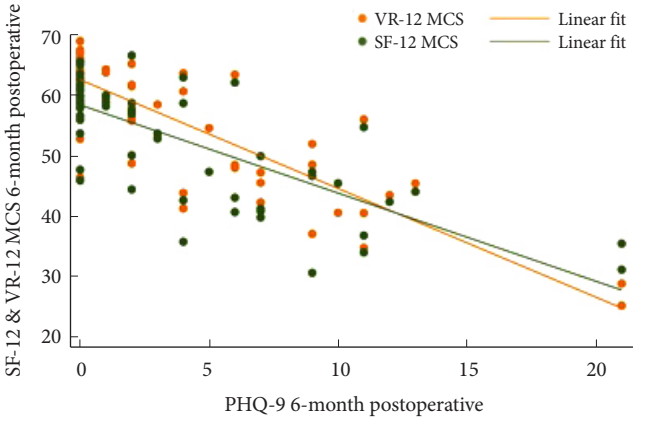

Fig. 5. Correlation of PHQ-9 with both SF-12 MCS and VR-12 MCS at the 6-month postoperative timepoint. PHQ-9, Patient Health Questionnaire-9; SF-12 MCS, 12-item Short Form health survey mental composite score; VR-12 MCS, Veterans RAND 12-item health survey mental composite score.

Discriminant validity was established for PHQ-9 at all timepoints ($p < 0.001$, all) (Table 4). At the preoperative timepoint, PHQ-9 values demonstrated a sig nificant difference in mean values between depressed and non-depressed groups (4.3 ± 4.2 vs. 11.5 ± 6.3). Again, PHQ-9 mean values demonstrated a significant difference at the 6-week (2.1 ± 3.0 vs. 11.3 ± 5.9), 12-week (1.4 ± 2.2 vs. 10.8 ± 6.9), 6-month (2.3 ± 3.4 vs. 10.4 ± 5.9), and 1-year (1.8 ± 2.9 vs. 12.9 ± 6.7) postoperative timepoints.

DISCUSSION

Psychiatric disorders are highly prevalent among patients living with spinal pathology, with rates of depression ranging from 21.5% to 49.3% reported in those undergoing LD.[19] Depression has previously been associated with worse outcomes for lumbar

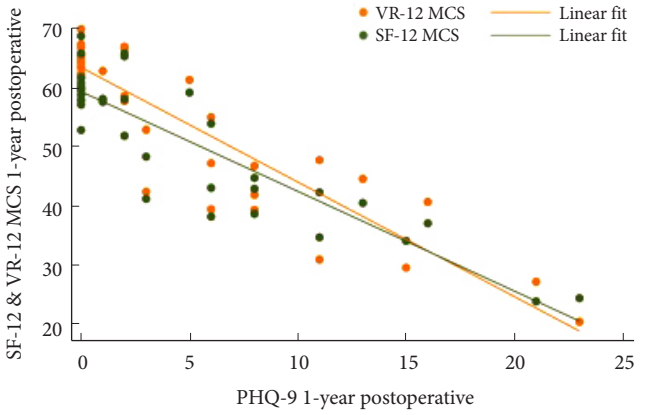

Fig. 6. Correlation of PHQ-9 with both SF-12 MCS and VR-12 MCS at the 1-year postoperative timepoint. PHQ-9, Patient Health Questionnaire-9; SF-12 MCS, 12-item Short Form Health Survey mental composite score; VR-12 MCS, Veterans RAND 12-item health survey mental composite score.

Table 4. Discriminant validity of PHQ-9

PHQ-9	Not depressed† SF-12 MCS ≥ 41.4	Depressed† SF-12 MCS < 41.4	p-value‡
Preoperative	4.3 ± 4.2 (171)	11.5 ± 6.3 (68)	< 0.001*
6 Weeks	2.1 ± 3.0 (129)	11.3 ± 5.9 (25)	< 0.001*
12 Weeks	1.4 ± 2.2 (67)	10.8 ± 6.9 (16)	< 0.001*
6 Months	2.3 ± 3.4 (56)	10.4 ± 5.9 (10)	< 0.001*
1 Year	1.8 ± 2.9 (33)	12.9 ± 6.7 (9)	< 0.001*

Values are presented as mean ± standard deviation (number).
PHQ-9, Patient Health Questionnaire-9; SF-12 MCS, 12-item Short Form health survey mental composite score.
*$p < 0.05$, statistically significant difference. †Threshold for depression was set using an SF-12 MCS value reported by Vilagut et al.[17] ‡p-values calculated using 1-way analysis of variance.

spine surgery,[4,9] and correlated with decreased rates of meaningful improvement in disability specifically for patients undergoing LD.[14] The PHQ-9 offers a number of advantages as a tool for assessing depression[5,6] and has previously been validated for use in the cervical spine[10] and for lumbar fusion surgeries.[11] The robust relationship between depressive symptoms and LD surgery makes validation of PHQ-9 a priority for this patient population.

The influence of depressive symptoms on postoperative outcomes of lumbar spine surgery has been well described in the literature. Patel et al.[9] used preoperative PHQ-9 scores to categorize patients undergoing transforaminal lumbar interbody fusions based on their level of depressive symptoms. The authors reported that patients with more severe depression not only reported greater levels of pain and increased narcotic consumption in the immediate postoperative period, but also demonstrated reduced improvement in pain, disability, and physical function 6-months after surgery. Similarly, in a study of LD patients, Chaichana et al.[14] also observed an association of depressive symptoms with poorer outcomes in terms of quality of life and disability.

Lumbar discectomy has demonstrated clear clinical benefits for patients with disc herniations and low back pain, in terms of both physical and mental health outcomes.[20] Lebow et al.[20] studied 100 patients undergoing microdiscectomy for lumbar disc herniation resulting in radiculopathy and found that depression, as measured by the Zung Self-Rating Depression Scale, significantly improved following surgery. Patients in our study demonstrated significant improvements in depression as measured by PHQ-9, as well as SF-12 and VR-12 MCS scores at 6-week through 1-year follow-up. In contrast, while LD patients in the study of Lebow et al.[20] did demonstrate improvements in depressive symptoms, these changes required 12-months following surgery to reach statistical significance.

Jenkins et al.[11] have previously validated PHQ-9 for use in patients undergoing lumbar fusion surgeries and found that PHQ-9 was strongly correlated with SF-12 and VR-12 MCS scores at all timepoints through 1 year. However, given possible differences in indications, symptomatology, and underlying spinal pathology associated with lumbar fusion, it is important to provide separate validation of PHQ-9's utility for assessment of LD patients. LD is typically performed to correct herniations of the nucleus pulposus, which can result in acute radicular pain and neurological deficits.[21] While lumbar fusion can be indicated for recurrent herniations, it can also be indicated for a wider variety of structural issues of the spine which may be chronic and progressive in nature, such as spondylolisthesis and scoliosis.[22] Furthermore, time courses for these disorders can differ significantly. Lumbar disc herniations may present rather acutely, with rapid onset of pain and neurological symptoms and LD may be indicated for these patients after just a few weeks of failed conservative therapy.[21] In contrast, degenerative pathology such as spondylolisthesis may develop more chronically over the course of a patient's life and fusion surgery may not be recommended until the patient has participated in conservative treatment for at least several months.[23] These differences may be especially important to consider for the usage of PHQ-9 as they may relate to substantial differences in the way patients' spinal pathologies and treatments interplay with depressive symptoms.

We were able to demonstrate significant, strong correlations of PHQ-9 with SF-12 and VR-12 MCS scores at all timepoints through 1-year in our cohort of patients undergoing MIS LD. Our use of a time-controlled partial correlation allows us increased confidence that these strong correlations represent true relationships between measures and were not simply related to the temporal proximity of survey completion. Additionally, PHQ-9 scores differed significantly between patients categorized as "depressed" vs "not depressed", as measured by SF-12 MCS, at all timepoints, confirming strong discriminant validity for PHQ-9 to differentiate between patients with differing mental health status. These findings are in line with those of previous studies validating the use of PHQ-9 and provide further support for its utility as a measure of depressive symptoms for this patient population.[10,11]

Originally adapted from their longer, 36-item predecessor, SF-12 and VR-12 MCS have been validated by a number of previous studies for the assessment of spine patients as well as the general population.[17,24,25] In particular, the ability of SF-12 MCS to demonstrate postoperative changes in patients undergoing LD surgery was verified by Vishwanathan and Braithwaite.[26] However, while these measures have demonstrated strong internal validity and responsiveness to change, their question designs lend themselves more to a general assessment of mental well-being. Conversely, the PHQ-9 is designed based on the DSM-IV and DSM-V to specifically assess patients for symptoms of major depression. Given the clear importance of understanding and quantifying depression in spine patients, the use of such a focused measure may be preferable.

Although our results allow us to confidently recommend the use of PHQ-9 to quantify depressive symptoms, our methodology is not without limitations. First, all procedures were performed by a single attending surgeon with extensive experience

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in MIS procedures at a single academic institution. This may limit the generalizability of our validation of PHQ-9 to other surgeons and patient populations. A follow-up study utilizing similar methodology, but with a multicenter design could significantly enhance the generalizability of these results. Additionally, our cohort was subject to significant attrition by the 1-year timepoint which may introduce an element of bias to our results if patients who continued to follow up significantly differed from those who did not. Furthermore, depressive symptoms were only characterized in terms of self-reported survey data. Diagnosis by a licensed mental health professional is considered the gold-standard for classification of depression and could have provided additional validity to our analysis. Finally, the power of our analysis was limited by lower survey completion rates at long-term follow-up.

CONCLUSION

Significant improvements in mental health were demonstrated in all 3 included measures through 1-year following MIS LD. Scores for PHQ-9 were strongly correlated with those of SF-12 and VR-12 MCS from the preoperative timepoint through 1 year. These results, considered alongside those of previous studies examining the use of PHQ-9 in spine surgery, allow us to confidently substantiate the validity of this measure to quantify depressive symptoms in patients undergoing MIS LD.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Original Article

Preoperative Neck Disability Severity Limits Extent of Postoperative Improvement Following Cervical Spine Procedures

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Objective: Our study aims to evaluate the impact of severity of preoperative Neck Disability Index (NDI) on postoperative patient-reported outcome measures (PROMs).
Methods: A retrospective review of primary, elective, single or multilevel anterior cervical discectomy and fusion or cervical disc arthroplasty procedures between 2013 and 2019 was performed. Visual analogue scale (VAS) neck and arm, NDI, 12-item Short Form physical and mental composite score (SF-12 PCS and MCS), Patient-Reported Outcome Measurement Information System physical function, and 9-item Patient Health Questionnaire (PHQ-9) were collected preoperatively and postoperatively. Patients were categorized by preoperative NDI: none-to-mild disability (< 30); moderate disability (≥ 30 to < 50); severe disability (≥ 50 to < 70); complete disability (≥ 70). The impact of preoperative NDI on PROM scores and minimum clinically important difference (MCID) achievement rates were evaluated.
Results: The cohort included 74 patients with none-to-mild disability, 95 moderate, 76 severe, and 17 with complete disability. Patients with greater preoperative disability demonstrated significantly different scores for NDI, VAS neck, SF-12 MCS, and PHQ-9 at all timepoints ($p < 0.001$). Patients with more severe disability demonstrated different magnitudes of improvement for NDI (all $p < 0.001$), VAS neck ($p \leq 0.009$), VAS arm ($p = 0.025$), and PHQ-9 ($p \leq 0.011$). The effect of preoperative severity on MCID achievement was demonstrated for NDI and for PHQ-9 ($p \leq 0.007$).
Conclusion: Patients with severe neck disability demonstrated differences in pain, disability, physical and mental health. MCID achievement also differed by preoperative symptoms severity. Patients with more severe neck disability may be limited to the degree of improvement in quality of life but perceive them as significant changes.

Keywords: Cervical fusion, Neck Disability Index, Outcomes

INTRODUCTION

Degenerative cervical myelopathy is one of the leading causes of spinal cord dysfunction worldwide with areas such as North America recording a prevalence of around 605 individuals per million.[1] Arising due to the compression of the spinal cord, myelopathy is characterized by weakness, loss of manual dexterity, gait dysfunction, and extensive disability.[2] Due to such adverse effects on an individual's physical and mental health, the number of patients electing to receive surgeries such as anterior cervical discectomy and fusion (ACDF) and cervical disc arthroplasty (CDA), rather than relying on conservative treatments for relief, is steadily rising.

Myelopathy has been cited as a major cause of disability, leading clinicians to place greater importance on following patients' functional and mental statuses preoperatively and postopera-

tively. These are measured using patient-reported outcome measures (PROMs) such as the Neck Disability Index (NDI), Japanese Orthopaedic Association scores (JOA), and modified JOA (mJOA). The NDI, specifically, contains 10 domains about daily life that quantify the level of disability present in those with neck pain.[3] NDI scores have been found to significantly improve following cervical spine surgery in myelopathy patients as well as to correlate with other quality of life measures.[4-8]

Although studies have considered postoperative improvements from baseline, the question of whether the extent of preoperative disability modulates postoperative recovery still exists. A past study reported that while a majority of those with severe or progressive myelopathy improve following surgery, there may be 15%–30% who do not experience recovery.[9,10] With varying outcomes, it is vital to consider postoperative improvement in the context of preoperative symptom severity. Prior analyses have established that preoperative disability may be a predictor for postoperative outcomes in myelopathy patients by using the JOA and mJOA.[11,12] Goh et al.[13] further stratified severity by JOA scores to demonstrate that severe preoperative myelopathy patients reported greater postoperative improvement and ability to attain a minimum clinically important difference (MCID) in functional and mental health outcomes following surgery. Though not categorized by severity, there has been a report of higher baseline JOA scores significantly reducing the odds of achieving MCID in myelopathy patients as well.[14] Although a few of these studies evaluate severity, they have not considered this topic or its implications on the attainment of a clinically perceivable difference in symptoms through the NDI measure. Although this measure was originally validated in the outpatient setting,[15] its use in spine surgery is pervasive across the globe and previous studies have established both its reliability and appropriateness among patients with cervical myelopathy.[5,16,17]

Currently, there is controversy surrounding whether surgery is the best and most efficacious option for severe myelopathy patients, as some report the existence of residual disability postoperatively, while others find only substantial improvements.[7,18,19] Our study may shed more light on this conversation through analysis of a widely utilized PROM that captures disability severity. With this information, physicians may reference a larger variety of PROMs to screen for the distinct preoperative symptoms caused by cervical myelopathy. In doing so, spine surgeons may preemptively account for the extent of an individual's disease manifestation and possibly predict their potential to obtain optimal outcomes following elective cervical procedures. Therefore, our aim is to evaluate the impact of the severity of preoperative NDI on postoperative PROMs.

MATERIALS AND METHODS

1. Study Design

A retrospective review of a prospectively maintained single-surgeon surgical database was performed to identify patients who underwent a cervical spine procedure between December 2013 and December 2019. Inclusion criteria were set as patients who underwent a primary, elective, single or multilevel ACDF or CDA. Exclusion criteria were set as revision procedures or procedures indicated for trauma, infection, or malignancy. Additionally, patients missing a preoperative NDI score were excluded. All procedures were performed at a single institution and both approval by the Institutional Review Board of Rush University Medical Center (ORA #14051301) and patient informed consent were obtained prior to the commencement of this study.

2. Data Collection

The surgical database used for this study contained information for each patient regarding demographics, perioperative characteristics, complications and PROMs. Demographic information was collected for age, body mass index (BMI), reported gender, ethnicity, diabetic and smoker status, and insurance collected. Patient fitness for surgery was evaluated using the American Society of Anesthesiologist physical status classification and comorbidity burden was scored as the Charlson Comorbidity Index. Perioperative characteristics were defined as the associated spinal pathology, number of operative levels, operative duration (skin incision to closure), estimated intraoperative blood loss (EBL), postoperative length of hospital stay (LOS), and day of discharge.

PROMs were collected as NDI, visual analogue scale (VAS) for neck and arm pain, Patient-Reported Outcome Measurement Information System physical function (PROMIS PF), 12-item Short Form physical composite score (SF-12 PCS) for physical health, and both 9-item Patient Health Questionnaire (PHQ-9) and SF-12 mental composite score (MCS) for mental health. All PROMs were collected preoperatively and at 6 weeks, 12 weeks, 6 months, and 1 year postoperatively. Assessment of significant improvements as perceived by the patient was collected through MCID achievement by comparing the improvement from preoperative to postoperative scores (Delta) with established thresholds from the literature: 2.6 (VAS neck);[20] 4.1 (VAS arm);[20] 17.3 (NDI);[20] 8.1 (SF-12 PCS);[20] 4.7

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(SF-12 MCS);[20] 4.5 (PROMIS PF);[21] 3.0 (PHQ-9).[22]

3. Severity of Disability

Preoperative disability was evaluated using the NDI, which is a self-reported questionnaire adapted from the Oswestry Disability Index. The questionnaire consists of 10 equally weighted domains that are scored from 0–5. The total score is multiplied by 2 and divided by 100 to reach a final score with larger scores indicating worse disability and a score of 0 indicating absent disability. To further assess the severity of disability, the NDI score was categorized into 5 separate groups based on the score: none-to-mild disability (NDI < 30); moderate (30 ≤ NDI < 50); moderately severe disability (50 ≤ NDI < 70); complete disability (70 ≤ NDI).

4. Statistical Analysis

The study cohort was evaluated for differences in baseline demographics and perioperative characteristics between severity groups using either chi-square analysis for categorical variables or an unpaired t-test for continuous variables. Differences in mean absolute postoperative PROM scores and magnitude of postoperative improvement between NDI severity groups was evaluated using a 1-way analysis of variance and *post hoc* Tukey test. The impact of preoperative NDI severity on PROM

Table 1. Patient demographics

Characteristic	Total (n = 262)	None (n = 74)	Moderate (n = 95)	Severe (n = 76)	Complete (n = 17)	p-value†
Age (yr)	49.3 ± 10.0	51.2 ± 10.9	49.3 ± 9.9	47.5 ± 9.0	49.2 ± 10.2	0.166
BMI (kg/m^2)	29.4 ± 5.6	29.2 ± 5.7	29.2 ± 5.9	29.5 ± 5.1	30.9 ± 6.7	0.724
Sex						0.093
Female	98 (37.4)	22 (29.7)	40 (42.1)	26 (34.2)	10 (58.5)	
Male	164 (62.6)	52 (70.3)	55 (57.9)	50 (65.8)	7 (41.2)	
Ethnicity						0.235
African-American	24 (9.2)	7 (9.5)	8 (8.4)	6 (7.9)	3 (17.7)	
Asian/Other	12 (4.6)	3 (4.1)	7 (7.4)	1 (1.3)	1 (5.9)	
Hispanic	22 (8.4)	7 (9.5)	4 (4.2)	9 (12)	2 (11.8)	
White	203 (77.8)	57 (77.0)	76 (80.0)	59 (78.7)	11 (64.7)	
Diabetic status						0.257
Nondiabetic	238 (90.8)	68 (91.9)	82 (86.3)	72 (94.7)	16 (94.1)	
Diabetic	24 (9.2)	6 (8.1)	13 (13.7)	4 (5.3)	1 (5.9)	
Smoker status						0.039*
Nonsmoker	234 (89.3)	71 (95.9)	86 (90.5)	62 (81.6)	15 (88.2)	
Active smoker	28 (10.7)	3 (4.1)	9 (9.5)	14 (18.4)	2 (11.8)	
ASA PS classification						0.482
≤ II	201 (87.8)	60 (85.7)	72 (87.8)	58 (92.1)	11 (78.6)	
> II	28 (12.2)	10 (14.3)	10 (12.2)	5 (7.9)	3 (21.4)	
CCI score						0.896
< 1	82 (36.6)	24 (38.1)	29 (35.4)	25 (38.5)	4 (28.6)	
≥ 1	142 (63.4)	39 (61.9)	53 (64.6)	40 (61.5)	10 (71.4)	
Insurance						< 0.001*
Medicare/medicaid	6 (2.3)	3 (4.1)	2 (2.1)	0 (0)	1 (5.9)	
WC	72 (27.6)	9 (12.3)	18 (18.9)	37 (48.7)	8 (47.1)	
Private	183 (70.1)	61 (83.6)	75 (79.0)	39 (51.3)	8 (47.1)	

Values are presented as mean ± standard deviation or number (%).
ASA PS, American Society of Anesthesiologists physical status; CCI, Charlson Comorbidity Index; VAS, visual analogue scale; WC, workers' compensation.
*p < 0.05, statistically significant difference. †p-value was calculated using a chi-square test (categorical) or a t-test (continuous).

scores was assessed using a multiple linear regression to account for radiculopathy (VAS arm and VAS neck) and any significant baseline characteristics. Similarly, the impact of preoperative NDI severity on rates of MCID achievement was evaluated using a simple logistic regression and a multiple logistic regression to account for radiculopathy. To control for False Discovery Rates, a Benjamini Hochberg correction was applied and an alpha value was set to 0.05.

RESULTS

Following the application of inclusion and exclusion criteria, a total of 262 patients were included in the study cohort, of whom 74 had none-to-mild disability, 95 moderate, 76 severe, and 17 with complete disability. Mean age was 49.3 years with 62.6% being male and having an average BMI of 29.4 kg/m^2. Except for smoker status and insurance collected (both $p \leq 0.29$), there were no significant differences in baseline characteristics between all groups (Table 1).

Perioperative characteristics are detailed in Table 2. Majority of patients had a preoperative spinal pathology of herniated nucleus pulposus, which was similar across all groups ($p = 0.781$), with most operations conducted at the single level (58.5%, $p = 0.205$). Similar EBL, LOS, and day of discharge were demonstrated for all groups, but the operative duration was significantly shorter in the severe group as compared to the none-to-mild group (53.8 ± 21.3 minutes vs. 63.1 ± 21.6 minutes, $p = 0.028$).

Comparisons of PROMs between neck disability severity groups is detailed in Table 3. At the preoperative timepoint, mean NDI demonstrated significantly higher values for moderate, severe, and complete disability groups as compared to the none-to-mild group ($p < 0.001$). A significantly higher disability re-

Table 2. Perioperative characteristics

Characteristic	Total (n = 262)	None (n = 74)	Moderate (n = 95)	Severe (n = 76)	Complete (n = 17)	p-value†
Spinal pathology						
Central stenosis	167 (63.7)	52 (70.3)	59 (62.1)	45 (59.2)	11 (64.7)	0.541
HNP	222 (84.7)	60 (81.1)	80 (84.2)	68 (89.5)	14 (82.3)	0.781
Foraminal stenosis	25 (95.0)	7 (9.5)	9 (9.5)	8 (10.5)	1 (5.9)	0.830
No. of levels						0.138
1 Level	152 (58.0)	40 (54.1)	56 (58.9)	49 (64.5)	7 (41.2)	
2 Levels	92 (35.1)	25 (33.8)	34 (35.8)	23 (30.3)	10 (58.8)	
3 Levels	18 (6.9)	9 (12.2)	5 (5.3)	4 (5.3)	0 (0)	
Most common levels						-
C5–6	66 (25.2)	18 (24.3)	26 (27.4)	20 (26.3)	2 (11.8)	
C5–7	63 (24.1)	17 (23.0)	23 (24.2)	17 (22.4)	6 (35.3)	
C6–7	61 (23.3)	17 (23.0)	21 (22.1)	21 (27.6)	2 (11.8)	
Operative time						
1 Level	50.6 ± 12.7	51.2 ± 14.3	52.5 ± 13.3	47.8 ± 10.6	51.4 ± 11.6	0.308
2 Levels	70.8 ± 13.2	75.0 ± 18.0	70.6 ± 8.8	70.9 ± 13.0	60.4 ± 7.3	0.038*
3 Levels	89.3 ± 11.7	91.0 ± 10.2	84.0 ± 15.8	92.7 ± 9.3	-	0.495
Estimated blood loss (mL)	31.6 ± 14.5	31.0 ± 13.5	31.5 ± 12.3	32.8 ± 18.2	29.7 ± 10.1	0.844
Length of stay (hr)	12.8 ± 12.1	12.3 ± 10.8	12.3 ± 10.1	13.3 ± 15.0	15.2 ± 13.9	0.776
Day of discharge						0.487
POD 0	189 (74.1)	56 (75.7)	68 (73.1)	54 (78.1)	11 (64.7)	
POD 1	58 (22.7)	16 (21.6)	24 (25.8)	13 (18.3)	5 (29.4)	
POD 2	6 (2.4)	2 (2.7)	1 (1.1)	2 (2.8)	1 (5.9)	
POD 3	2 (0.8)	0 (0)	0 (0)	2 (2.8)	0 (0)	

Values are presented as number (%) or mean ± standard deviation.
HNP, herniated nucleus pulposus; POD, postoperative day.
*$p < 0.05$, statistically significant difference. †p-value was calculated using a chi-square test (categorical) or a t-test (continuous).

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Table 3. Mean PROM scores by neck disability severity

Variable	None	Moderate	Severe	Complete	p-value†
NDI					
Preoperative	16.7 ± 7.2 (74)	38.3 ± 5.5 (95)*	58.0 ± 5.8 (76)*	78.2 ± 8.4 (17)*	< 0.001*
6 Weeks	19.8 ± 14.5 (66)	25.5 ± 14.0 (85)	43.9 ± 17.1 (61)*	62.8 ± 20.9 (11)*	< 0.001*
12 Weeks	14.4 ± 14.3 (55)	21.0 ± 12.6 (79)	37.8 ± 18.9 (58)*	50.7 ± 26.4 (14)*	< 0.001*
6 Months	11.9 ± 15.4 (46)	20.1 ± 12.7 (59)	34.0 ± 20.8 (50)*	44.8 ± 25.1 (10)*	< 0.001*
1 Year	14.7 ± 15.7 (24)	19.5 ± 14.4 (43)	36.8 ± 22.9 (21)*	45.3 ± 22.2 (6)*	< 0.001*
VAS neck					
Preoperative	4.2 ± 2.5 (74)	6.0 ± 1.9 (95)*	7.6 ± 1.6 (75)*	9.0 ± 1.5 (17)*	< 0.001*
6 Weeks	2.5 ± 2.3 (66)	2.8 ± 2.2 (85)	4.3 ± 2.3 (60)*	7.3 ± 2.1 (11)*	< 0.001*
12 Weeks	1.9 ± 2.2 (55)	2.2 ± 1.8 (81)	4.2 ± 2.4 (58)*	5.8 ± 3.2 (14)*	< 0.001*
6 Months	1.8 ± 2.4 (46)	2.5 ± 2.0 (59)	3.7 ± 2.6 (52)*	5.2 ± 3.6 (10)*	< 0.001*
1 Year	1.8 ± 2.0 (24)	2.7 ± 2.4 (43)	5.1 ± 2.8 (21)*	6.2 ± 3.3 (6)*	< 0.001*
VAS arm					
Preoperative	4.2 ± 2.7 (74)	5.6 ± 2.4 (95)*	7.2 ± 2.0 (75)*	9.0 ± 1.4 (16)*	< 0.001*
6 Weeks	1.9 ± 2.2 (66)	2.2 ± 2.5 (85)	3.8 ± 2.8 (60)*	6.0 ± 2.6 (11)*	< 0.001*
12 Weeks	2.0 ± 2.7 (55)	2.3 ± 2.7 (79)	3.3 ± 2.8 (58)	5.4 ± 3.4 (14)*	< 0.001*
6 Months	2.3 ± 3.0 (46)	2.2 ± 2.3 (59)	3.5 ± 2.9 (50)	5.4 ± 3.7 (11)*	0.001*
1 Year	2.8 ± 3.2 (24)	2.8 ± 2.8 (43)	4.9 ± 3.3 (22)	3.7 ± 3.0 (6)	0.060
PROMIS PF					
Preoperative	44.9 ± 7.1 (51)	40.3 ± 4.5 (63)*	34.3 ± 5.4 (39)*	33.6 ± 8.5 (6)*	< 0.001*
6 Weeks	45.1 ± 8.9 (43)	43.9 ± 5.5 (53)	38.3 ± 6.7 (29)*	29.5 ± 1.8 (4)*	< 0.001*
12 Weeks	49.9 ± 11.2 (32)	46.3 ± 8.0 (46)	40.2 ± 6.7 (26)*	33.7 ± 9.0 (6)*	< 0.001*
6 Months	51.0 ± 10.8 (23)	47.1 ± 8.7 (28)	42.3 ± 5.8 (20)*	33.1 ± 7.4 (5)*	< 0.001*
1 Year	49.9 ± 6.9 (20)	49.9 ± 10.3 (30)	43.4 ± 9.1 (14)	40.1 ± 0.0 (1)	0.101
SF-12 PCS					
Preoperative	40.4 ± 8.9 (65)	34.9 ± 7.6 (82)*	29.7 ± 5.2 (68)*	26.1 ± 7.0 (16)*	< 0.001*
6 Weeks	39.0 ± 10.0 (50)	38.1 ± 8.5 (65)	32.0 ± 6.0 (46)*	26.1 ± 3.3 (8)*	< 0.001*
12 Weeks	45.8 ± 10.2 (43)	40.5 ± 10.0 (54)*	36.1 ± 8.8 (44)*	34.5 ± 9.6 (9)*	< 0.001*
6 Months	47.6 ± 10.1 (36)	41.8 ± 9.7 (43)	37.3 ± 9.5 (33)*	32.0 ± 11.0 (6)*	< 0.001*
1 Year	47.0 ± 8.0 (28)	43.0 ± 10.3 (42)	36.1 ± 12.2 (20)*	40.6 ± 13.8 (4)	0.005*
SF-12 MCS					
Preoperative	53.1 ± 9.6 (65)	49.7 ± 11.4 (82)	40.7 ± 12.4 (68)*	37.3 ± 13.7 (16)*	< 0.001*
6 Weeks	56.5 ± 7.9 (50)	53.9 ± 8.3 (65)	45.0 ± 12.9 (46)*	38.9 ± 9.7 (8)*	< 0.001*
12 Weeks	55.8 ± 7.5 (43)	54.1 ± 8.5 (54)	44.4 ± 12.8 (44)*	39.7 ± 9.7 (9)*	< 0.001*
6 Months	55.6 ± 7.3 (36)	54.4 ± 8.9 (43)	45.6 ± 12.8 (33)*	38.2 ± 16.1 (6)*	< 0.001*
1 Year	55.4 ± 8.2 (28)	53.1 ± 9.1 (42)	42.7 ± 16.7 (20)*	36.5 ± 4.9 (4)*	< 0.001*
PHQ-9					
Preoperative	2.9 ± 3.2 (53)	6.7 ± 5.2 (58)*	10.6 ± 6.6 (49)*	13.4 ± 5.8 (9)*	< 0.001*
6 Weeks	3.1 ± 3.2 (47)	3.1 ± 3.1 (56)	8.8 ± 7.1 (35)*	15.5 ± 5.2 (6)*	< 0.001*
12 Weeks	2.3 ± 3.0 (45)	2.5 ± 2.5 (45)	6.8 ± 7.0 (38)*	12.8 ± 7.8 (6)*	< 0.001*
6 Months	1.4 ± 2.3 (35)	3.5 ± 3.1 (35)	7.7 ± 6.1 (35)*	14.8 ± 6.9 (6)*	< 0.001*
1 Year	2.5 ± 3.8 (18)	3.6 ± 4.7 (28)	7.3 ± 7.3 (14)	14.5 ± 4.2 (4)*	< 0.001*

Values are presented as mean ± standard deviation (number).
PROM, patient-reported outcome measure; NDI, Neck Disability Index; VAS, visual analogue scale; PROMIS PF, Patient-Reported Outcome Measurement Information System physical function; SF-12 PCS, 12-item Short Form health survey physical composite score; SF-12 MCS, 12-item Short Form health survey mental composite score; PHQ-9, 9-item Patient Health Questionnaire.
*$p < 0.05$, statistically significant difference. †p-value calculated using analysis of variance with *post hoc* Tukey testing.

Table 4. Regression analysis of NDI severity as predictors of PROMs

Variable	Moderate			Severe			Complete		
	β	SE	p-value†	β	SE	p-value†	β	SE	p-value†
NDI									
Preoperative	19.10	0.962	<0.001*	36.7	1.18	<0.001*	54.7	1.89	<0.001*
6 Weeks	5.76	2.73	0.037*	23.2	3.45	<0.001*	43.6	6.04	<0.001*
12 Weeks	7.39	3.07	0.017*	24.1	3.91	<0.001*	38.5	6.07	<0.001*
6 Months	8.53	3.61	0.020*	20.9	4.65	<0.001*	30.7	7.14	<0.001*
1 Year	5.21	4.72	0.272	22.5	6.50	0.001*	32.3	9.17	0.001*
VAS neck									
Preoperative	1.17	0.270	<0.001*	2.05	0.321	<0.001*	2.55	0.523	<0.001*
6 Weeks	0.05	0.394	0.891	1.09	0.499	0.030*	4.00	0.869	<0.001*
12 Weeks	0.03	0.405	0.936	1.56	0.519	0.003*	3.12	0.805	<0.001*
6 Months	0.499	0.520	0.338	1.41	0.669	0.036*	2.84	1.02	0.006*
1 Year	0.602	0.671	0.371	2.62	0.924	0.006*	3.72	1.30	0.005*
VAS arm									
Preoperative	0.274	0.328	0.405	0.961	0.402	0.018*	2.00	0.634	0.002*
6 Weeks	0.347	0.450	0.441	1.86	0.569	0.001*	4.00	0.993	<0.001*
12 Weeks	0.400	0.529	0.522	1.21	0.674	0.074	3.30	1.04	0.002*
6 Months	-0.155	0.610	0.800	0.991	0.785	0.209	2.91	1.21	0.017
1 Year	-0.089	0.788	0.910	1.99	1.06	0.063	1.15	1.53	0.454
PROMIS PF									
Preoperative	-5.04	1.21	<0.001*	-10.9	1.56	<0.001*	-11.1	2.77	<0.001*
6 Weeks	-0.34	1.56	0.825	-5.19	2.02	0.012*	-14.0	3.88	<0.001*
12 Weeks	-5.14	2.31	0.028*	-12.1	3.03	<0.001*	-19.2	4.69	<0.001*
6 Months	-4.19	3.00	0.167	-8.75	3.71	0.021*	-17.7	5.72	0.003*
1 Year	-0.94	3.03	0.757	-8.34	4.22	0.053	-10.4	9.75	0.289
SF-12 PCS									
Preoperative	-5.63	1.31	<0.001*	-10.9	1.62	<0.001*	-14.6	2.51	<0.001*
6 Weeks	-1.90	1.71	0.269	-9.05	2.21	<0.001*	-16.1	3.74	<0.001*
12 Weeks	-6.87	2.14	0.002*	-13.2	2.62	<0.001*	-14.8	4.31	0.001*
6 Months	-5.26	2.56	0.042*	-9.39	3.24	0.005*	-14.5	5.11	0.006*
1 Year	-4.46	2.66	0.097	-11.8	3.61	0.001*	-6.87	6.3	0.279
SF-12 MCS									
Preoperative	-2.47	2.05	0.231	-11.1	2.53	<0.001*	-13.2	3.92	0.001*
6 Weeks	-2.00	2.05	0.331	-10.1	2.64	<0.001*	-16.3	4.47	<0.001*
12 Weeks	-3.06	2.21	0.170	-13.1	2.71	<0.001*	-18.5	4.46	<0.001*
6 Months	-3.97	2.59	0.129	-13.8	3.29	<0.001*	-21.7	5.19	<0.001*
1 Year	-3.01	2.85	0.294	-14.3	3.86	<0.001*	-23.0	6.74	0.001*
PHQ-9									
Preoperative	3.15	1.07	0.004*	6.26	1.33	<0.001*	8.04	2.21	<0.001*
6 Weeks	-0.193	0.983	0.844	5.10	1.28	<0.001*	12.9	5.58	<0.001*
12 Weeks	0.688	1.10	0.534	5.17	1.33	<0.001*	11.6	2.45	<0.001*
6 Months	2.27	1.21	0.064	6.55	1.48	<0.001*	13.7	2.29	<0.001*
1 Year	1.33	1.71	0.438	3.42	2.33	0.148	11.9	3.23	0.001*

NDI, Neck Disability Index; PROMs, patient-reported outcome measures; SE, standard error; VAS, visual analogue scale; PROMIS PF, Patient-Reported Outcome Measurement Information System physical function; SF-12 PCS, 12-item Short Form health survey physical composite score; SF-12 MCS, 12-item Short Form health survey mental composite score; PHQ-9, 9-Item Patient Health Questionnaire.
*$p < 0.05$, statistically significant difference. †p-value calculated using multiple linear regression to determine effect of NDI severity while accounting for VAS arm, VAS neck and significant baseline confounders.

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Table 5. Delta PROM by neck disability severity

Variable	None	Moderate	Severe	Complete	p-value†
ΔNDI					
6 Weeks	3.6 ± 14.4	-12.8 ± 13.7*	-13.6 ± 16.9*	-16.1 ± 20.9*	< 0.001*
12 Weeks	-2.9 ± 15.0	-16.9 ± 13.2*	-19.5 ± 19.3*	-28.6 ± 24.5*	< 0.001*
6 Months	-4.7 ± 15.9	-18.3 ± 13.6*	-23.2 ± 20.8*	-33.8 ± 24.1*	< 0.001*
1 Year	-1.0 ± 15.8	-18.8 ± 13.7*	-20.5 ± 21.9*	-31.7 ± 25.7*	< 0.001*
ΔVAS neck					
6 Weeks	-1.6 ± 2.9	-3.1 ± 2.9*	-3.2 ± 2.3*	-1.8 ± 2.7	0.001*
12 Weeks	-2.1 ± 3.1	-3.7 ± 2.7*	-3.4 ± 2.6*	-3.1 ± 2.8	0.009*
6 Months	-1.8 ± 3.4	-3.3 ± 2.7	-4.1 ± 2.9*	-3.5 ± 4.4	0.003*
1 Year	-2.2 ± 3.3	-2.8 ± 2.9	-2.6 ± 2.7	-1.9 ± 4.6	0.829
ΔVAS arm					
6 Weeks	-2.1 ± 3.2	-3.2 ± 3.6	-3.3 ± 3.3	-3.0 ± 3.3	0.124
12 Weeks	-2.2 ± 3.5	-3.0 ± 3.6	-3.7 ± 3.3	-3.7 ± 4.1	0.107
6 Months	-1.6 ± 4.2	-3.1 ± 3.0	-3.8 ± 3.7*	-3.4 ± 3.6	0.025*
1 Year	-1.1 ± 3.9	-2.5 ± 3.9	-2.3 ± 3.4	-5.0 ± 2.2	0.141
ΔPROMIS PF					
6 Weeks	4.3 ± 9.7	9.2 ± 8.9	8.1 ± 7.0	6.9 ± 2.1	0.080
12 Weeks	7.9 ± 9.3	11.0 ± 10.2	10.3 ± 9.2	6.9 ± 14.4	0.515
6 Months	10.1 ± 7.3	12.1 ± 9.2	11.3 ± 7.4	4.3 ± 11.9	0.287
1 Year	8.8 ± 6.8	13.3 ± 9.9	12.3 ± 7.2	18.4 ± 0.0	0.290
ΔSF-12 PCS					
6 Weeks	0.5 ± 10.1	3.7 ± 9.9	1.9 ± 5.8	3.1 ± 3.8	0.106
12 Weeks	5.1 ± 9.4	5.9 ± 10.1	5.4 ± 8.4	5.6 ± 11.1	0.986
6 Months	7.6 ± 8.2	8.3 ± 11.4	7.3 ± 9.5	5.2 ± 13.8	0.902
1 Year	7.4 ± 8.1	9.1 ± 9.7	6.1 ± 11.5	15.7 ± 19.5	0.416
ΔSF-12 MCS					
6 Weeks	16.4 ± 10.9	19.6 ± 11.5	14.8 ± 13.6	15.9 ± 12.8	0.229
12 Weeks	15.3 ± 9.9	19.8 ± 11.3	14.3 ± 13.3	11.9 ± 15.0	0.084
6 Months	15.9 ± 9.9	21.0 ± 11.7	15.2 ± 12.8	11.5 ± 21.3	0.097
1 Year	16.1 ± 8.2	18.3 ± 1.4	12.5 ± 17.0	15.0 ± 7.5	0.429
ΔPHQ-9					
6 Weeks	0.3 ± 3.3	-3.6 ± 5.5*	2.9 ± 5.8*	0.4 ± 4.5	0.001*
12 Weeks	0.7 ± 4.2	-3.7 ± 4.7*	-4.4 ± 5.9*	-2.8 ± 6.7	0.011*
6 Months	0.8 ± 4.0	-3.4 ± 6.9	-2.7 ± 6.9	1.8 ± 9.4	0.257
1 Year	0.4 ± 5.1	-2.6 ± 4.1	-4.7 ± 10.1	1.7 ± 6.0	0.195

Values are presented as Δmean ± standard deviation.
PROM, patient-reported outcome measure; NDI, Neck Disability Index; VAS, visual analogue scale; PROMIS PF, Patient-Reported Outcome Measurement Information System physical function; SF-12 PCS, 12-item Short Form health survey physical composite score; SF-12 MCS, 12-item Short Form health survey mental composite score; PHQ-9, 9-Item Patient Health Questionnaire.
*$p < 0.05$, statistically significant difference. †p-value calculated using analysis of variance with *post hoc* Tukey testing.

Table 6. Achievement of MCID by neck disability severity

Variable	None	Moderate	Severe	Complete	p-value†	p-value‡
NDI						
6 Weeks	4 (6.1)	34 (40)	24 (39.3)	5 (45.5)	<0.001*	<0.001*
12 Weeks	12 (21.8)	37 (468)	32 (55.2)	9 (64.3)	<0.001*	<0.001*
6 Months	8 (17.4)	28 (47.5)	35 (70)	7 (70)	<0.001*	<0.001*
1 Year	2 (8.3)	25 (58.1)	11 (52.4)	3 (50)	<0.001*	<0.001*
Overall	15 (22.1)	60 (66.7)	48 (69.6)	12 (75)	<0.001*	<0.001*
VAS neck						
6 Weeks	25 (37.9)	46 (54.1)	35 (58.3)	4 (36.4)	0.072	<0.001*
12 Weeks	26 (47.3)	52 (64.2)	39 (67.2)	7 (50)	0.107	<0.001*
6 Months	21 (45.7)	35 (59.3)	38 (73.1)	7 (70)	0.043	<0.001*
1 Year	9 (37.5)	24 (55.8)	9 (42.9)	2 (33.3)	0.419	<0.001*
Overall	39 (56.5)	70 (76.9)	54 (76.1)	11 (73.3)	0.028	<0.001*
VAS arm						
6 Weeks	17 (25.8)	40 (47.1)	21 (35)	3 (30)	0.053	<0.001*
12 Weeks	17 (30.9)	35 (44.3)	23 (39.7)	6 (46.1)	0.433	<0.001*
6 Months	13 (28.3)	24 (40.7)	23 (46)	3 (30)	0.294	<0.001*
1 Year	5 (20.8)	16 (37.2)	7 (31.8)	3 (50)	0.419	<0.001*
Overall	25 (37.3)	49 (54.4)	35 (50)	8 (53.3)	0.181	<0.001*
PROMIS PF						
6 Weeks	11 (28.9)	25 (52.1)	11 (44)	0 (0)	0.091	0.112
12 Weeks	11 (40.7)	24 (57.1)	13 (59.1)	3 (75)	0.383	0.162
6 Months	13 (59.1)	16 (57.1)	9 (60)	2 (50)	0.985	0.828
1 Year	11 (57.9)	21 (75)	6 (66.7)	1 (100)	0.468	0.802
Overall	25 (54.3)	44 (74.6)	22 (70.9)	4 (80)	0.145	0.298
SF-12 PCS						
6 Weeks	12 (25.5)	18 (31)	7 (15.6)	2 (25)	0.328	0.357
12 Weeks	15 (39.5)	21 (43.7)	12 (29.3)	3 (37.5)	0.558	0.282
6 Months	14 (45.2)	22 (55)	14 (43.7)	2 (33.3)	0.649	0.754
1 Year	11 (42.3)	17 (48.6)	9 (50)	1 (33.3)	0.908	0.794
Overall	25 (44.6)	43 (58.9)	25 (46.3)	4 (36.4)	0.251	0.400
SF-12 MCS						
6 Weeks	16 (34)	22 (37.9)	21 (46.7)	4 (50)	0.581	0.700
12 Weeks	12 (31.6)	17 (35.4)	19 (46.3)	4 (50)	0.482	0.471
6 Months	10 (32.4)	13 (32.5)	18 (56.3)	2 (33.3)	0.152	0.003*
1 Year	13 (50)	13 (37.1)	6 (33.3)	1 (33.3)	0.665	0.594
Overall	25 (44.6)	38 (52.1)	34 (62.9)	7 (64.6)	0.235	0.398
PHQ-9						
6 Weeks	7 (15.6)	30 (55.6)	18 (52.9)	1 (20)	<0.001*	<0.001*
12 Weeks	10 (25.6)	21 (51.2)	23 (63.9)	4 (66.7)	0.005*	0.005*
6 Months	4 (14.3)	12 (40)	11 (36.7)	1 (25)	0.122	0.006*
1 Year	5 (27.8)	13 (48.1)	7 (58.3)	1 (33.3)	0.344	0.262
Overall	13 (34.2)	34 (64.1)	28 (70)	4 (50)	0.007*	0.007*

Values are presented as number (%).
MCID, minimum clinically important difference; NDI, Neck Disability Index; VAS, visual analogue scale; PROMIS PF, Patient-Reported Outcome Measurement Information System physical function; SF-12 PCS, 12-item Short Form health survey physical composite score; SF-12 MCS, 12-item Short Form health survey mental composite score; PHQ-9, 9-Item Patient Health Questionnaire.
*$p < 0.05$, statistically significant difference. †p-value calculated using simple logistic regression. ‡p-values calculated using multiple logistic regression.

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mained for both the severe and complete disability groups as compared to the none-to-mild group for all postoperative timepoints ($p < 0.001$, all). The moderate, severe, and complete disability groups demonstrated significantly worse values for VAS neck, VAS arm, PROMIS PF, SF-12 PCS, and PHQ-9 as compared to the none-to-mild group at the preoperative timepoint, whereas, only the severe and complete disability groups demonstrated significantly worse scores for SF-12 MCS ($p < 0.001$, all). Postoperatively, VAS neck and SF-12 MCS demonstrated significantly worse scores among the severe and complete disability groups compared to the none-to-mild group at 6 weeks through 1 year and 6 weeks through 6 months for PROMIS PF ($p < 0.001$, all). VAS arm scores were significantly worse for the severe disability group at the 6-week timepoint only and for the complete group from 6 weeks through 6 months ($p < 0.001$, all). SF-12 PCS scores were significantly worse than the none-to-mild group for patients categorized with complete disability from 6 weeks through 6 months, severe disability at all postoperative timepoints, and for moderate disability at 12 weeks only ($p < 0.001$, all). Lastly, mean PHQ-9 values were significantly worse for the severe-to-complete disability group at all postoperative timepoints and from 6 weeks through 6 months for the severe group ($p < 0.001$, all).

A summary of all multiple linear regression analyses is found in Table 4. Regression analysis demonstrated that relative to the none-to-mild group, preoperative NDI severity groups were significant effectors of preoperative NDI, VAS neck, PROMIS PF, SF-12 PCS, and PHQ-9 ($p < 0.001$, all). Similarly, severe and complete groups were also significant effectors of preoperative VAS arm and SF-12 MCS ($p < 0.001$, both). Postoperatively, the moderate severity group was significantly associated with NDI from 6 weeks through 6 months ($p \leq 0.037$, all), 12 weeks only for PROMIS PF ($p = 0.028$), and 12 weeks through 6 months for SF-12 PCS ($p \leq 0.042$, both). The severe disability group was a significant effector of NDI, VAS neck, SF-12 PCS, and SF-12 MCS at all postoperative timepoints ($p \leq 0.036$, all) as well as VAS arm at 6 weeks ($p = 0.001$), PROMIS PF at 6 weeks through 6 months ($p \leq 0.021$, all), and PHQ-9 from 6 weeks through 6 months ($p < 0.001$, all). Complete disability was a significant effector of all postoperative PROM scores ($p \leq 0.017$, all) except for at 1 year for VAS arm, PROMIS PF, and SF-12 PCS ($p \geq 0.279$, all).

Evaluation of differences in the magnitude of improvement from the preoperative to all postoperative timepoints is summarized in Table 5. Mean improvement (delta) was significantly different between groups from 6 weeks through 1 year for NDI ($p < 0.001$, all). Additionally, a significant difference in mean delta VAS neck between groups was demonstrated at the 6-week through 6-month timepoints ($p \leq 0.009$, all). Delta VAS arm and delta PHQ-9 demonstrated significantly different mean values at 6 months only ($p = 0.025$), and both 6 weeks and 12 weeks ($p \leq 0.011$), respectively.

Preoperative neck disability severity had a significant impact on rates of MCID achievement at all postoperative timepoints for NDI ($p < 0.001$, all) and at 6 weeks, 12 weeks, and overall for PHQ-9 ($p \leq 0.007$, all). When accounting for VAS neck and VAS arm, multiple logistic regression demonstrated a significant association with the achievement of MCID at all postoperative timepoints for NDI, VAS neck, and VAS arm ($p < 0.001$, all). The same was observed for SF-12 MCS at 6-months ($p = 0.003$) and PHQ-9 from 6 weeks to 6 months and overall ($p \leq 0.007$). A summary of MCID achievement by severity group is summarized in Table 6.

DISCUSSION

Patients suffering from cervical spondylotic myelopathy or myeloradiculopathy often seek invasive treatments to alleviate their symptoms. While patients with severe symptoms typically find relief of pain and disability following surgery, past studies have indicated that surgical treatment for patients suffering from milder symptoms is similarly efficacious and safe.[8,19] However, it remains to be established whether the preoperative severity of symptoms may impact the extent of postoperative recovery of pain, disability, and both physical and mental health. The current study was able to establish that individuals suffering from more severe preoperative disability demonstrate similar changes in postoperative pain, physical and mental health, but not disability. Additionally, these individuals may also be restricted in the degree to which they improve, reporting worse postoperative PROMs compared to those with milder disability.

Evaluating the impact of the severity of preoperative disability on postoperative outcomes, whether surgical or patient-reported, has been seldom reported among spine literature. Patients in our study's cohort reported worse preoperative and postoperative pain, disability, physical function, and mental health when compared to individuals with none-to-mild disability. Few other studies have evaluated outcomes by severity groups, but among published studies, patients were categorized according to their preoperative mJOA. At the preoperative timepoint, both Goh et al.[13] and Fehlings et al.[19] were able to demonstrate that patients with severe neck disability (mJOA < 9) had significantly worse NDI, Nurick Score, mJOA, and SF-36 PCS

and MCS. Although we used NDI in place of mJOA for preoperative severity categorization, our study demonstrated a similar finding where patients in the moderate, severe, and complete disability groups had a significantly worse disability (NDI), physical function (PROMIS PF and SF-12 PCS), and mental health (SF-12 MCS and PHQ-9). Additionally, our study demonstrated that both arm and neck pain were significantly worse, a finding which was not reported by either study. In many regards, these results were expected as a number of studies have established the significant correlations between NDI and a variety of PROMs.[23,24]

Postoperatively, patients with more severe preoperative disability demonstrated significantly worse postoperative outcomes as compared to the milder severity groups. While past studies align well with our preoperative results, the current literature is somewhat split on the impact neck disability has on outcomes. A prospective study of patients with severe degenerative myelopathy reported residual symptoms and disability following decompression surgery,[7] which was similarly observed among our severe and complete disability groups. Other investigators have similarly established that a more severe preoperative neck disability translated into worse Nurick Scale, NDI, mJOA, and SF-36 PCS at the 2-year follow-up.[13] Interestingly, Goh et al.[13] observed no difference in these same outcomes at 6 months and their patient cohort reported no difference in pain among all groups irrespective of postoperative timepoint, which is in contrast to our results. While our study and others were able to establish differences among severity groups, a large-scale multicenter study of cervical spondylotic myelopathy patients contrarily reported that severity of neck disability, as measured by mJOA, had no impact on mean values for NDI, SF-36 PCS and MCS, with the exception of mJOA, out to 1 year. These differences may be due, in part, to the heterogeneity associated with the large-scale multicenter design (8 different centers) the study implemented. Whereas, comparatively, our study and the study of Goh et al.[13] were able to demonstrate minimal differences in study cohort demographics. On a more basic science level, our results may also be reflective of the biological changes to the central nervous system as a result of more severe neck disability. Holly et al.[25] was able to observe that cervical spondylotic patients with a higher NDI demonstrated significant functional connectivity changes to the pre- and postcentral gyri, the superior frontal gyrus, and supplementary motor area, all of which have implications in chronic pain and motor dysfunction,[26] which are common symptoms among myelopathy and myeloradiculopathy patients. It may then be inferred that patients with worse disability at the preoperative level may inherently be limited to the extent they will recover postoperatively and surgeons may need to counsel patients on expected improvements.

Although patients may have demonstrated worse postoperative outcomes among the more severe neck disability groups, the magnitude of improvement was largely not affected. Given the close association NDI has with physical function outcomes,[24,27-29] it was hypothesized that all three, the absolute score, degree of improvement, and MCID, should be limited by the extent of neck disability; however, delta values were only significantly different between groups for NDI and PHQ-9. In terms of delta values, our results align well with those of Fehlings et al.,[19] where the degree of improvement in disability, physical and mental health (SF-36 PCS and MCS) were unaffected by preoperative severity. While our results regarding the achievement of MCID mirror those of Goh et al.,[13] where a large proportion of patients achieved the threshold value for NDI and PCS, other investigators have also alluded that a higher JOA acted as a significant predictor of MCID achievement.[14] While our results largely are similar to these previous studies, it was interesting to observe that the only differences in mean delta and MCID achievement rates occurred for both NDI and PHQ-9. Differing results between mental health outcomes may stem from the specificity of the 2 psychometrics, with PHQ-9 better suited to capture depressive symptoms as it is based on the Diagnostic and Statistical Manual of Mental Disorders. These results may reflect the significant association of NDI with depressive symptoms reported by several previous studies.[23,30-32] Collectively, these results support the notion that the ability to achieve a significantly improved PROM score may not be influenced by preoperative severity of neck disability. There may be limitations to the extent of these improvements, but patients may not necessarily perceive this as an unfavorable outcome.

Given that patients with more severe disability largely demonstrated a similar level of postoperative improvement in pain, disability, physical function, and mental health, there is one possible explanation that may not be inherently clear. While myelopathy has its own set of symptoms, there is a number that does overlap with symptoms associated with radiculopathy. Previous studies have also demonstrated significant improvements in overall health-related quality of life and could be the underlying factor that may explain the similar improvements among patients who have a more severe disability.[33] However, the current study has accounted for signs of radiculopathy by way of VAS arm and VAS neck and largely found similar significant associations with NDI severity with PROM scores and

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MCID achievement. These results place a larger emphasis on the notion that a patient's disability may not impede the ability to achieve a significant improvement in pain, disability, physical function, mental health, and overall quality of life. This will provide both patient and provider with the confidence to move forward with surgery for treatment of disabling cervical spine pathologies.

This study is not without limitations, which may affect the interpretation of results. The current study categorized patients according to preoperative NDI to represent the extent of neck disability severity as a result of myelopathy or myeloradiculopathy. However, radiographic analysis was not conducted for the purposes of this study, but may benefit future studies looking at the translational effect of spinal cord compression on postoperative outcomes. Another limitation is related to the use of health-related questionnaires completed by patients, which are prone to the responder and recall bias and could affect the values reported in this study. Additionally, the impact of duration of symptoms prior to surgical therapy may also influence how a patient responds to health questionnaires and ultimately may affect preoperative and postoperative outcomes. Future studies should calculate the duration of symptoms to determine the effects, if any, on preoperative NDI. Lastly, the generalizability of this study is limited as patients received treatment from a single surgeon at the same institution.

CONCLUSION

Patients suffering from varying degrees of neck disability severity due to cervical spondylotic myelopathy or myeloradiculopathy demonstrated significantly different preoperative pain, disability, physical function, and mental health. Postoperatively, differences in pain, disability, physical function, and mental health continued between severity groups. While postoperative PROM values demonstrated significant differences, the magnitude of improvement from preoperative values was not significantly different between severity groups except for neck disability and depressive symptoms. The same differences were observed for achievement of an MCID of NDI and PHQ-9. These results suggest patients with worse preoperative neck disability may be unable to achieve a similar level of improvement following cervical spine surgery.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Original Article

Are Lumbar Fusion Guidelines Followed? A Survey of North American Spine Surgeons

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Objective: To evaluate the use of guidelines for lumbar spine fusions among spine surgeons in North America.
Methods: An anonymous survey was electronically sent to all AO Spine North America members. Survey respondents were asked to indicate their opinion surrounding the suitability of instrumented fusion in a variety of clinical scenarios. Fusion indications in accordance with North America Spine Society (NASS) guidelines for lumbar fusion were considered NASS-concordant answers. Respondents were considered to have a NASS-concordant approach if ≥ 70% (13 of 18) of their answers were NASS-concordant answers. Comparisons were performed using bivariable statistics.
Results: A total of 105 responses were entered with complete data available on 70. Sixty percent of the respondents (n = 42) were considered compliant with NASS guidelines. NASS-discordant responses did not differ between surgeons who stated that they include the NASS guidelines in their decision-making algorithm (5.10 ± 1.96) and those that did not (4.68 ± 2.09) ($p = 0.395$). The greatest number of NASS-discordant answers in the United States. was in the South (5.75 ± 2.09), with the lowest number in the Northeast (3.84 ± 1.70) ($p < 0.01$). For 5 survey items, rates of NASS-discordant answers were ≥ 40%, with the greatest number of NASS-discordant responses observed in relation to indications for fusion in spinal deformity (80%). Spine surgeons utilizing a NASS-concordant approach had a significant lower number of NASS-discordant answers for synovial cysts ($p = 0.03$), axial low back pain ($p < 0.01$), adjacent level disease ($p < 0.01$), recurrent stenosis ($p < 0.01$), recurrent disc herniation ($p = 0.01$), and foraminal stenosis ($p < 0.01$).
Conclusion: This study serves an important role in clarifying the rates of uptake of clinical practice guidelines in spine surgery as well as to identify barriers to their implementation.

Keywords: Lumbar fusion indications, North America Spine Society, AO Spine North America

INTRODUCTION

The prevalence of lumbar pain due to spinal disorders is increasing around the world, and instrumented fusion procedures are widely used as an option of treatment.[1-3] Despite the increasing utilization of instrumented fusion for the treatment of lumbar pathology, there is still a lack of medical literature detailing concrete fusion indications and studies validating guidelines as predictors of outcomes.[4-6] This is largely secondary to heterogeneity in clinical decision-making amongst spine surgeons and surgical indications in lumbar spine pathology management.

Improving the quality of care under a patient-centered per-

spective is an effort that drives medical initiatives like the construction of evidence-based medical (EBM) guidelines. The North American Spine Society (NASS), in an attempt to improve surgical outcomes and patient care, published diagnosis and indications for lumbar fusion as well as qualifying criteria.[7] These guidelines provide a tool to guide clinical decision-making in the treatment of lumbar pathology.

This study is an initiative to evaluate and gain insight into the use of the NASS criteria for indications of lumbar spine fusions among spine surgeons in North America. The results of this survey aim to inform and contribute to future discussions of the applicability of EBM guidelines in assisting surgical decision-making for lumbar spine fusions. The main objective of this study is to evaluate the use of EBM guidelines for lumbar spine fusions among spine surgeons in North America.

MATERIALS AND METHODS

An online electronic survey was generated using Qualtrics software (Provo, UT, USA). The survey questions consisted of 18 clinical vignettes to elucidate participating surgeons' indications for lumbar spine fusion. Each clinical vignette was framed and discussed by a panel of senior neurosurgeons and spine surgeons at a quaternary university hospital and intended to evaluate the acceptance of the specific indications for arthrodesis published by the NASS as a coverage policy for lumbar fusions after conducting a comprehensive literature review by multidisciplinary experts.[7] All panel members agreed that each clinical vignette had a clear indication for or against lumbar spine fusion based on the NASS guidelines.[7]

The survey was available in English, participation was voluntary, without remuneration, anonymized, and was distributed

Table 1. Definition of the U.S. regions

U.S. region	U.S. states
Region 1 (Northeast)	Connecticut; Maine; Massachusetts; New Hampshire; Rhode Island; Vermont; New Jersey; New York; Pennsylvania
Region 2 (Midwest)	Indiana; Illinois; Michigan; Ohio; Wisconsin; Iowa; Nebraska; Kansas; North Dakota; Minnesota; Missouri; South Dakota
Region 3 (South)	Delaware; District of Columbia; Florida; Georgia; Maryland; North Carolina; South Carolina; Virginia; West Virginia; Alabama; Kentucky; Mississippi; Tennessee; Arkansas; Louisiana; Oklahoma; Texas
Region 4 (West)	Arizona; Colorado; Idaho; New Mexico; Montana; Utah; Nevada; Wyoming; Alaska; California; Hawaii; Oregon; Washington

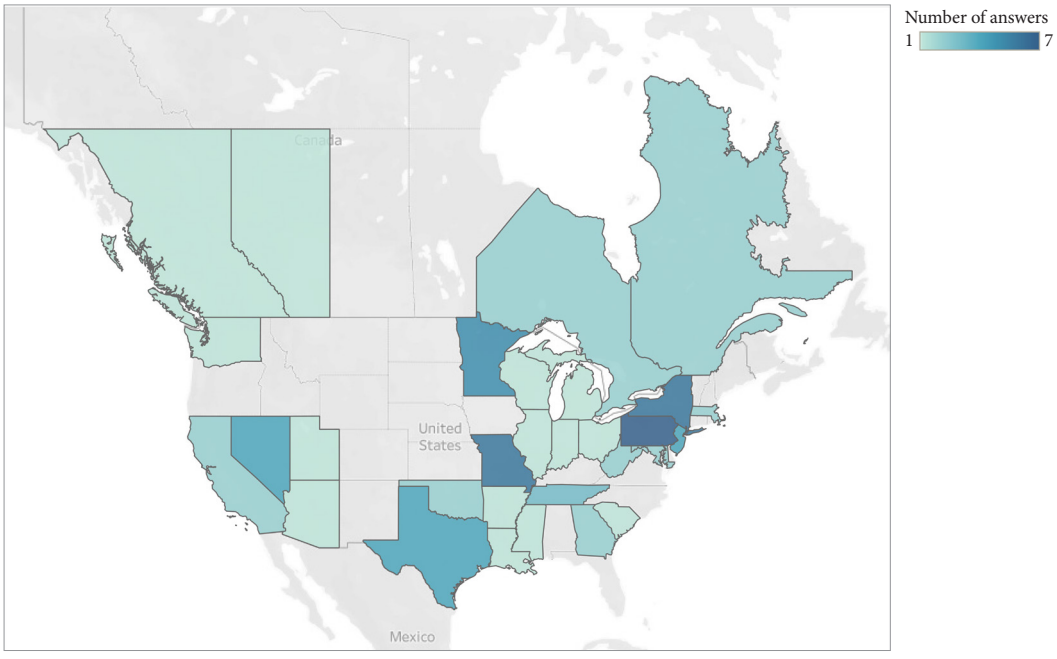

Fig. 1. Geographic distribution of survey respondents. The color gradient represents the number of answers per state/province.

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electronically to spine surgeon members of the AO Spine North America (AOSNA). The study was approved by the research committee of the AOSNA and distributed through an electronic invitation that was sent on 4 separate occasions between July and August 2020 to the spine surgeons. The introductory electronic communication with the respondents consisted of an email specifying study objectives, the survey structure, and an online link to the Qualtrics platform (Supplementary material 1). In an effort to eliminate bias, none of the surgeons involved in the study panel filled out the survey.

The first part of the survey consisted of demographic questions about the spine surgeon residency specialty, fellowship training, number of years in practice, and the approach to indicate a lumbar spine fusion (Supplementary material 1). The second part of the survey was based on 18 items with clinical vignettes and radiological images, followed by whether or not the surgeon felt a spine fusion was indicated in the treatment of the patient (Supplementary material 3). The major outcome investigated was the number of answers (fusion indications) in accordance with the NASS guidelines (NASS-concordant answer), assessed with the 18 clinical items of the survey.[7] The participating surgeon was considered to have a NASS-concordant approach if ≥ 70% (13 of 18) of their answers to the survey cases were NASS-concordant. Due to the study design, the study protocol was initially exempted from Institutional Review Board approval.

The survey data was exported from Qualtrics into a tabulated Microsoft Excel file, and data were analyzed with IBM SPSS Statistics ver. 22.0 (IBM Co., Armonk, NY, USA). Continuous variables were reported as means and standard deviation, and categorical variables were reported as frequency and percentage. Differences in frequencies between the groups of responses

Table 2. Comparison of the Neurosurgeon and Orthopedic Surgeon group of responses

Variable	All answers (N = 70)	Neurosurgeon (N = 21)	Orthopedic surgeon (N = 49)	p-value†
Total no. of NASS-discordant answers	4.93 ± 2.01	4.62 ± 1.85	5.06 ± 2.07	0.403
Fellowship training	68 (97.1)	20 (95.2)	48 (97.9)	0.513
Years in practice				
0–5	28 (40)	6 (28.6)	22 (44.9)	0.288
6–10	14 (20)	4 (19)	10 (20.4)	1.000
11–15	9 (13)	4 (19)	5 (10.2)	0.437
16–20	7 (10)	6 (28.6)	1 (20.4)	< 0.01*
> 20	12 (17.1)	1 (4.7)	11 (22.4)	0.09
Approach to indicate lumbar fusion				
I do not use a specific criteria	5 (7.1)	1 (4.8)	4 (8.2)	1.000
I consider the evidence-based NASS criteria in my evaluation	42 (60)	13 (61.9)	29 (59.2)	0.831
I use another criteria	9 (12.9)	4 (19)	5 (10.2)	0.259
My indication is only based on my clinical experience	14 (20)	3 (14.3)	11 (22.4)	0.529
Region				
South	20 (28.6)	6 (28.6)	14 (28.6)	1.000
Northeast	19 (27.1)	5 (23.8)	14 (28.6)	0.776
Midwest	16 (22.9)	4 (19)	12 (24.5)	0.761
West	9 (12.9)	3 (14.3)	6 (12.2)	1.000
Canada	6 (8.6)	3 (14.3)	3 (6.1)	0.355
NASS-concordant approach (≥ 70% of NASS-concordant answers)	44 (62.8)	14 (66.7)	30 (61.23)	0.79

Values are presented as mean ± standard deviation or number (%).
NASS, North America Spine Society.
*$p < 0.05$, statistically significant difference. †Fisher exact test, t-test, or Mann-Whitney test, comparing the group of Neurosurgeons with Orthopedic Surgeons.

analyzed were evaluated using a chi-square test and the Fisher exact test based on frequency table cell count. The unpaired 2-tailed Student t-test and the Mann-Whitney U-tests for non-parametric data were used to compare continuous variables as appropriate based on assumptions of normality. A p-value of <0.05 was set for statistical significance.

RESULTS

A total of 515 AOSNA members were invited to participate in the survey, 105 responses were received, 35 were excluded due to an incomplete survey, thereby 70 were included in the final analysis. Ninety-one percent (n = 64) of the survey participants practice in the United States (US). Respondents were distributed across 4 provinces in Canada and 27 states in the US, in which the greatest number of responses was in Pennsylvania (n = 7). The 2 regions of the US with the most number of responses were the South (n = 20, 28.6%), followed by the Northeast (n = 19, 27.1%)[8] (Table 1, Fig. 1).

The majority of the responses were from orthopedic surgeons (n = 49, 70 %), 68 participants (97.1%) stated that they have fellowship training in spine surgery, and 41 participants (58.5%) practice in an academic medical center. Out of the 70 participants, 28 (40%) have less than 5 years of clinical practice as a spine surgeon, followed by 14 respondents (20%) that are in practice between 6–10 years. The majority of the spine surgeons (n = 42, 60%) stated that they follow the EBM NASS guidelines in their evaluation of the lumbar fusion indication.[7] Twenty-eight participants reported that the NASS guidelines are not considered in their evaluation of fusion indication; of those 28 responses, 14 (20%) utilize arthrodesis indications based only on their clinical experience, 9 (12.9%) use other criteria, and 5 (7.1%) do not use a specific criteria to indicate a lumbar fusion.

There was no statistical difference in the mean number of NASS-discordant answers between the group of neurosurgeons (4.62 ± 1.85) and the orthopedic surgeons (5.06 ± 2.07) (p = 0.403). The only significant difference between the 2 groups of specialties is the number of respondents who have 16–20 years in practice ($p<0.01$), no other variable considered in this survey, was significantly different between the neurosurgery and the orthopedic group ($p>0.05$) (Table 2).

The group of participants who answered that they use the NASS criteria in their clinical evaluation was compared with the respondents who answered they do not use the NASS criteria. The mean number of NASS-discordant answers were not significantly different between the group who consider the NASS criteria (5.10 ± 1.96) with the group who do not consider it (4.68 ± 2.09) (p = 0.395). All the other variables compared between both groups were also not significantly different ($p>0.05$) (Table 3).

The number of NASS-discordant answers was only significantly different when the regions analyzed were compared ($p<0.01$). The region associated with the greatest number of NASS-discordant answers in the US was the South (5.75 ± 2.09), while the region with the lowest number was the Northeast (3.84 ± 1.70) (Table 4, Fig. 2). The comparison between the group of respondents who were considered to have a NASS-concordant approach (≥ 70% of NASS-concordant answers) with the group who have a NASS-discordant approach also confirmed the association of participants from the South with a NASS-discordant approach (p = 0.01) and participants from the Northeast with a NASS-concordant approach (p = 0.02) (Table 5). The mean number of NASS-discordant answers of the spine surgeons who had most of their practice in an academic medical center (4.63 ± 1.75)

Table 3. Comparison between the respondents who stated that consider the NASS criteria in their lumbar fusion indication algorithm and the respondents who do not consider

Variable	All answers (N = 70)	Consider NASS (N = 42)	Do not consider (N = 28)	p-value†
Total no. of NASS-discordant answers	4.93 ± 2.01	5.10 ± 1.96	4.68 ± 2.09	0.395
Fellowship training	68 (97.1)	41 (97.6)	27 (96.4)	1.000
Years in practice				0.212
0–5	28 (40)	15 (35.7)	13 (46.4)	0.457
6–10	14 (20)	11 (26.2)	3 (10.7)	0.138
11–15	91 (12.9)	4 (9.5)	5 (17.8)	0.468
16–20	7 (10)	6 (14.3)	1 (3.5)	0.23
> 20	12 (17.1)	6 (14.3)	6 (21.4)	0.524
Region				
South	20 (28.6)	13 (30.9)	7 (25)	0.788
Northeast	19 (27.2)	12 (28.6)	7 (25)	0.79
Midwest	16 (22.9)	7 (16.7)	9 (32.1)	0.155
West	9 (12.9)	7 (16.7)	2 (7.1)	0.299
Canada	6 (8.6)	3 (7.1)	3 (10.7)	0.677
NASS-concordant approach (> = 70% of NASS-concordant answers)	44 (62.9)	25 (59.5)	19 (67.9)	0.615

Values are presented as mean ± standard deviation or number (%).
NASS, North America Spine Society.
†Fisher exact test, t-test, or Mann-Whitney test, comparing the group who consider the NASS criteria with the group who do not consider.

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Table 4. Analysis of the number of NASS-discordant answers stratified by specialty, fellowship training, years in practice, and region

Variable	NASS-discordant answers	p-value
Specialty		0.403
Neurosurgery	4.62 ± 1.85	
Orthopedic Surgery	5.06 ± 2.07	
Fellowship		0.762
Yes	4.94 ± 2.02	
No	4.5 ± 2.12	
Years in practice		0.335
0–5	5.11 ± 1.66	
6–10	4.29 ± 1.63	
11–15	5.22 ± 1.92	
16–20	4.00 ± 2.38	
> 20	5.58 ± 2.81	
Region		< 0.01*
South	5.75 ± 2.09	
Northeast	3.84 ± 1.70	
Midwest	4.06 ± 1.34	
West	5.67 ± 1.50	
Canada	6.83 ± 2.13	

Values are presented as mean ± standard deviation.
NASS, North America Spine Society.
*$p < 0.05$, statistically significant difference.

was also compared with the ones who had in the private practice (5.34 ± 2.30), and they were not statistically different ($p = 0.148$).

The specific items of the survey that the spine surgeons did not agree were also evaluated. Five items of the survey had an average of NASS-discordant answers ≥ 40% (Table 6). The question item with the greatest number of NASS-discordant responses was the indication of fusion in cases of deformity (80%), followed by synovial cysts (78.6%), degenerative spondylolisthesis (47.1%), axial lumbar pain (41.4%), and adjacent level disease (40%). When the answers were stratified by the respondents who had an overall NASS-concordant approach (≥ 70% NASS-concordant answers in the survey), the items with the greatest number of NASS-discordant answers were the same. Spine surgeons utilizing a NASS-concordant approach had a significantly lower number of NASS-discordant responses in comparison with respondents utilizing a NASS-discordant approach in the following items: synovial cysts ($p = 0.03$), axial low back pain (LBP) ($p < 0.01$), adjacent level disease ($p < 0.01$), recurrent stenosis ($p < 0.01$), recurrent disc herniation ($p = 0.01$), and foraminal stenosis ($p < 0.01$) (Table 6).

DISCUSSION

Spinal fusion utilization, frequency, and hospital charges in the US have been increasing disproportionately compared to

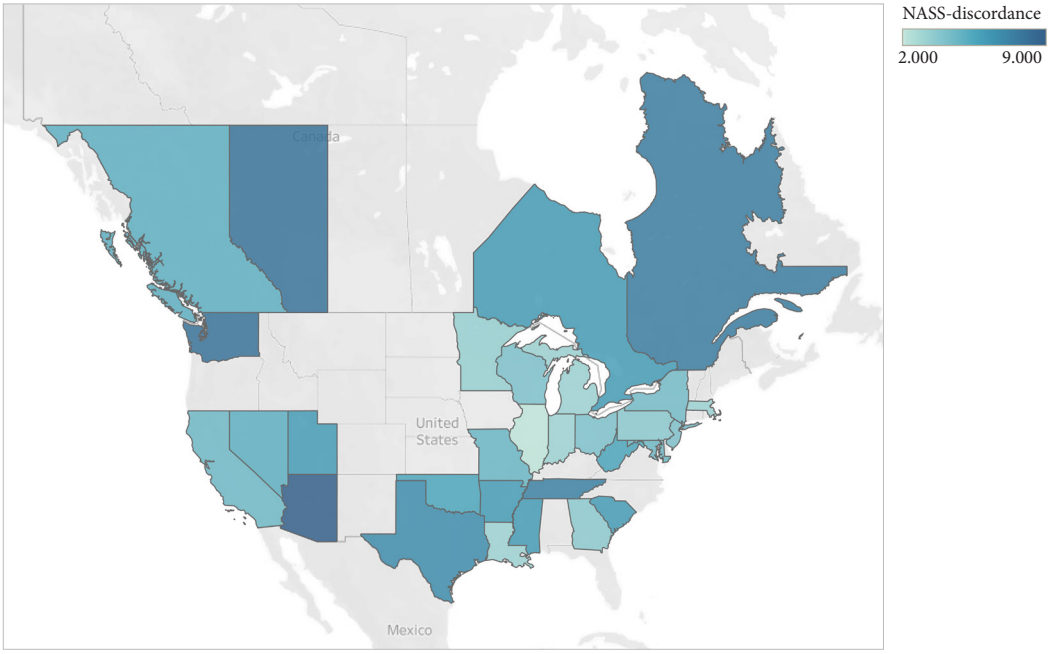

Fig. 2. Geographic distribution of NASS-discordant answers. The color gradient represents the number of NASS-discordant answers per state/province. NASS, North America Spine Society.

Table 5. Analysis of respondents who met a NASS-concordant approach compared to those that did not

Variable	NASS-concordant approach (≥70% of NASS-concordant answers) (N=44)	NASS-disconcordant approach (<70% of NASS-concordant answers) (N=26)	p-value
Fellowship, yes	43 (97.7)	25 (96.1)	1.000
Years in practice			
0–5	19 (43.2)	9 (34.6)	0.615
6–10	10 (22.7)	4 (15.4)	0.548
11–15	4 (9.1)	5 (19.2)	0.277
16–20	5 (11.3)	2 (7.7)	1.000
>20	6 (13.6)	6 (2.3)	0.341
Region			
South	8 (18.2)	12 (46.3)	0.01*
Northeast	16 (36.3)	3 (11.5)	0.02*
Midwest	12 (27.3)	4 (15.4)	0.139
West	5 (11.4)	4 (15.4)	0.718
Canada	2 (4.6)	4 (15.4)	0.186

Values are presented as number (%).
NASS, North America Spine Society.
*$p < 0.05$, statistically significant difference.

other inpatient surgical procedures.[3] Despite this increase in utilization, outcomes in patients undergoing lumbar fusion greatly vary.[9-11] As the armamentarium of lumbar fusion options for LBP grows,[3,12] an evidence-based criteria for which spinal pathology to perform fusion on must be established to address the wide variability in treatment and technique. This study attempts to evaluate the role of the NASS criteria in surgical decision-making.

Establishing evidence-based surgical criteria in practice is a necessary part of unifying outcomes and controlling quality in surgical specialties. For instance, even with strong evidence in the literature supporting beneficial outcomes in patients undergoing decompression and fusion for degenerative spondylolisthesis,[13-15] there may be non-uniform decision-making by surgeons when addressing these patients.[16]

In our experience, it was noted that 60% of surgeons surveyed utilize NASS criteria in surgical decision-making. Despite 40% of surgeons stating they do not consider NASS criteria in surgical decision-making, there was no overall statistically significant difference in the percentage of NASS-concordant answers

Table 6. Survey item components with the respective number of NASS-discordant answers stratified by respondents who had a NASS-concordant approach

No.	Question item	No. of NASS-discordant answers			
		All answers (N=70)	NASS-concordant approach (N=44)	NASS-discordant approach (N=26)	p-value†
1	Deformity and no physical therapy	56 (80.0)	36 (81.1)	20 (76.9)	0.759
2	Synovial cyst	55 (78.6)	31 (70.4)	24 (92.3)	0.037
3	Degenerative spondylolisthesis	33 (47.1)	18 (40.9)	15 (57.7)	0.219
4	Axial LBP	29 (41.4)	12 (27.3)	17 (65.4)	<0.01*
5	Adjacent level disease	28 (40.0)	12 (27.3)	16 (61.5)	<0.01*
6	Recurrent stenosis	26 (37.1)	8 (18.2)	18 (69.2)	<0.01*
7	Burst fracture	24 (34.2)	13 (29.5)	11 (42.3)	0.307
8	Recurrent disc herniation	20 (28.6)	8 (18.2)	12 (46.1)	0.016*
9	Foraminal stenosis	19 (27.1)	2 (4.5)	17 (65.4)	<0.01*
10	Degenerative spondylolisthesis	17 (24.3)	9 (20.4)	8 (30.1)	0.393
11	Deformity	9 (12.9)	4 (9.1)	5 (19.2)	0.277
12	Pseudoarthrosis	9 (12.9)	3 (6.8)	6 (23.1)	0.068
13	Transverse process fracture	8 (11.4)	3 (6.8)	5 (19.2)	0.137
14	Axial LBP with a trial of nonsurgical therapy	7 (10.0)	2 (4.5)	5 (19.2)	0.093
15	Discitis	3 (4.3)	1 (2.3)	2 (7.7)	0.551
16	Lumbar stenosis	1 (1.4)	0 (0)	1 (3.8)	0.371
17	Disc herniation	1 (1.4)	1 (2.3)	0 (0)	1.000
18	Axial LBP without a trial of nonsurgical therapy	0 (0)	0 (0)	0 (0)	ND‡

Values are presented as number (%).
NASS, North America Spine Society; LBP, low back pain; ND, not done given the total cell count of the 2 groups analyzed.
*$p < 0.05$, statistically significant difference. †Fisher exact test, comparing the group who had a NASS-concordant approach with those who had a NASS-discordant approach. ‡Fisher-exact test was not performed.

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between surgeons who consider NASS guidelines in decision-making versus those who do not.[7] This was interesting to the authors as it may represent that the NASS criteria serve as a valuable summary or representation of evidenced-based medicine in lumbar spine fusion. Even surgeons who do not consciously use NASS guidelines in decision-making, but indicate surgery based on their understanding of literature, clinical experience, and training, have a similar concordance with the criteria as those surgeons who consider NASS in their surgical indication.

Interestingly, surgeon experience, fellowship training, academic setting, and specialty did not affect the use of NASS guidelines in surgical decision-making, neither the adoption of a NASS-concordant approach.[7] This is contrary to the study Irwin et al.,[16] showing that both younger surgeons and orthopedic surgeons exhibited different surgical management strategies, leading to higher fusion rates.

When examining the geographic distribution of NASS-concordant decision-making, this study noted a statistically significant difference in NASS-concordant answers based on region. The Northeast had the lowest mean number of NASS-discordant responses, while the South had the highest mean number of NASS-discordant answers in the US. This regional variability was interesting, given the fact that it seems to correlate with the incidence of surgical treatment of lumbar degenerative disease.[3] As the treatment incidence rises, weaker concordance with EBM criteria such as the NASS criteria may be seen.

Finally, when examining the NASS-concordant approach versus the NASS-discordant approach to surgical management, we noted several pathologies with significant differences in management. NASS concordance was significantly greater in synovial cyst, axial LBP, adjacent level disease, recurrent stenosis, recurrent disc herniation, and foraminal stenosis when comparing surgeons who actively use NASS criteria versus those who do not. Prospectively examining differences in outcome in these groups of patients would be beneficial in assessing NASS criteria as a tool to improve surgeons' outcomes since these pathologies showed the greatest differences in management decisions between the 2 groups of surgeons.

This study is not without limitations. The current study aimed to compare NASS-concordant versus NASS-discordant responses to spinal indications; however, the indications based upon the NASS guidelines are not solely based on level I evidence. Responses to each clinical vignette may have been biased given the survey's electronic nature and that a participant can easily compare their responses to NASS guidelines online.[7] We attempted to mitigate this bias by anonymizing each participant. We identified a regional disparity in the study, although this may have been limited by the survey's response rate of each region. In an attempt to mitigate any regional institutional bias, none of the authors participated in the survey. The demographic information was self-declared by the participants. Lastly, the small sample size and regional distribution may not necessarily correlate with actual regional practices.

CONCLUSION

NASS criteria is a set of EBM guidelines pertaining to lumbar fusion decision-making. When surveying 70 AOSNA members, 60% use the NASS criteria in their decision-making algorithm. Overall, experience, training, specialty did not affect NASS concordance in decision-making. However, geographical differences were seen in survey results. In addition, NASS criteria was met more frequently by surgeons utilizing a NASS-concordant approach for pathology such as synovial cyst, axial LBP, adjacent level disease, recurrent stenosis, recurrent disc herniation, and foraminal stenosis. These pathologies may serve as starting points for further investigation of outcomes associated with NASS criteria and the usefulness of its implementation.

CONFLICT OF INTEREST

The authors have nothing to disclose.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.14245/ns.2142136068.

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Editorial

Commentary on "Are Lumbar Fusion Guidelines Followed? A Survey of North American Spine Surgeons"

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I read the article titled "Are Lumbar Fusion Guidelines Followed? A survey of North American Spine Surgeons" with great interest, as these guidelines are extremely popular on an international basis. As a Past-President of the North American Spine Society, this article gives me a personal window into the effect of the guidelines on the clinical practice of spine surgeons in North America. I recall that as a member of the North America Spine Society (NASS) Board of Directors, and as President, I was constantly being asked to review the guidelines, give feedback, approve ideas, and ultimately approve the guidelines. In reading this article, I now get a sense of the effect that these guidelines have on the clinical practice of spinal surgeons.

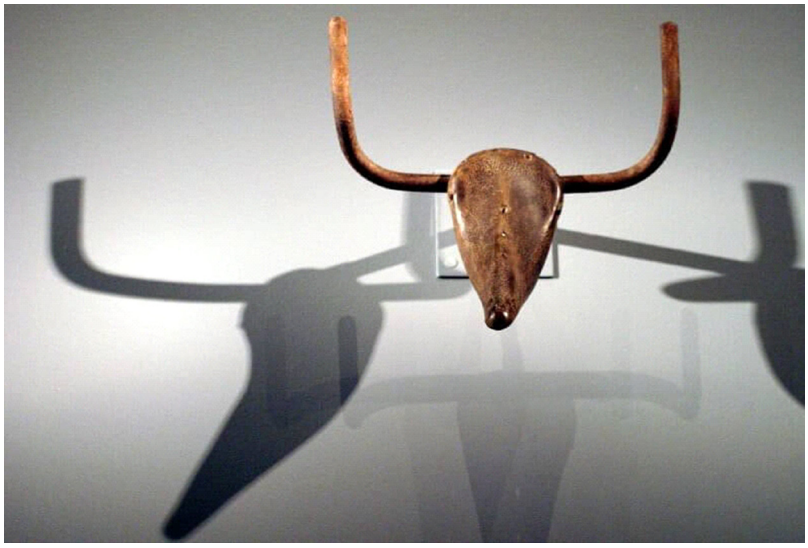
As I read this article, the survey, and the results, I am delighted to see the results of the guidelines amongst those that follow the guidelines. However, I am perhaps even more interested in the results of those who do not report following the guidelines. When I see the data, I am extremely satisfied with the results. These guidelines were designed to put forth the current evidence to determine suggestions for best practices in the modern environment. To see that the discordance was similar in those who follow the guidelines as those who do not follow the guidelines, allows me to see that the guidelines follow clinical practice. In addition, these guidelines are not meant to be concrete rules, but rather evidence-based guidelines or suggestions for the management of certain pathologies. Each patient is different, and will have individualized aspects to their own clinical scenario, which requires that each surgeon evaluate their own patients as unique individuals. The variations in management of certain pathologies, falls along the lines of critical debates about patient management, which should exist and should continue. We should not fall into one predetermined protocol for the management of groups of patients as hard-fast rules, but rather use evidence-based guidelines to help guide decision-making for our individualized and different patients we treat on a daily basis. I believe many of the differences in management reflect actual various opinions that exist between surgeons today, and is a healthy concept that should not change. We must continue to think critically about our patients, and not conform completely to a strict set of rules.

I will finish by giving some inside information on these guidelines. There are a substantial number of NASS volunteers and staff, who put countless hours of exceedingly hard work into the creation of these guidelines. These guidelines are a top priority for the NASS

organization, and I am both pleased and delighted to see that they are being used appropriately. I do believe that the NASS folks who helped to create these guidelines, would be very pleased with the results of this study.

CONFLICT OF INTEREST

Royalties – Biomet, Seaspine, Synthes/Investments; Options – Bone Biologics, Pearldiver, Electrocore, Surgitech; Board of Directors - AO Foundation, Society for Brain Mapping and Therapeutics; Editorial Boards - Global Spine Journal Editor-in-Chief; Fellowship Funding (paid to institution): AO Foundation.



Title: Bull's Head
Artist: Pablo Picasso
Year: 1942
© 2021 - Succession Pablo Picasso - SACK (Korea)

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Technical Note

Transumbilical Retroperitoneal Lumbar Interbody Fusion: A Technical Note and Preliminary Case Series

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Objective: Anterior lumbar interbody fusion (ALIF) has advantages over posterior lumbar interbody fusion or transforaminal lumbar interbody fusion techniques in that it minimizes damage to the anatomical structure of the posterior spinal segment and enables indirect decompression of the foramen by insertion of a tall cage. However, the predominant abdominal scar tissue reduces patients' satisfaction after ALIF. Herein, we describe the technique of transumbilical lumbar interbody fusion (TULIF) and its preliminary results in a case series.
Methods: A retrospective review of 154 consecutive patients who underwent TULIF between the L2–3 and L4–5 levels was performed. After preoperatively selecting patients by evaluating the location of the umbilicus and vessel anatomy, a vertical skin incision was made on the umbilicus to minimize the abdominal scar tissue.
Results: There were 120 single-level (110 L4–5 and 10 L3–4), 31 two-level, and 3 three-level surgeries. All patients were very satisfied with their postoperative abdominal scars, which were noticeably faint compared to those after conventional ALIF.
Conclusion: TULIF is a feasible, minimally invasive surgical option that can achieve both the treatment of degenerative spinal disease and satisfactory cosmesis. Although it is technically demanding, patients obtain sufficient benefits.

Keywords: Anterior lumbar interbody fusion, Transumbilical lumbar interbody fusion, Scar less surgery, Lumbar interbody fusion

INTRODUCTION

From its first introduction by Dr. Cloward in the 1950s, anterior lumbar interbody fusion (ALIF) has been widely performed for treating degenerative spine disease (including spondylolisthesis), deformity, infection, and trauma.[1] The anterior approach has advantages over conventional posterior lumbar interbody fusion and transforaminal lumbar interbody fusion techniques as it minimizes damage to the anatomical structure of the posterior spinal segment[2] and enables indirect decompression of the foramen by insertion of a tall cage.[3]

Aside from these advantages, however, undergoing spinal surgery through laparotomy is a great psychological burden for some patients, and the predominant abdominal scar tissue resulting after the procedure, reduces patients' satisfaction after ALIF. Given that many surgical techniques are now minimally invasive and aim to cause as few scars as possible postoperatively, this disadvantage of ALIF should be addressed.

The transumbilical approach already has been widely used for laparoscopic surgeries and plastic surgeries, such as breast augmentation, to minimize abdominal scars[4-6]; however, its application for spinal surgery has rarely been reported. Herein, we describe the transumbilical lumbar interbody fusion (TULIF) technique for addressing the disadvantage of the retroperitoneal approach for ALIF via a small incision on the umbilicus and its preliminary results in a case series of TULIF for degenerative lumbar disease.

MATERIALS AND METHODS

A retrospective review of consecutive patients who underwent TULIF between the L2–3 and L4–5 levels from November 2012 to December 2015. This study was approved by the Institutional Review Board of Wooridul Spine Hospital (IRB No. 2019-12-WSH-009) and informed consent was obtained from the patients. The inclusion criteria were the following: (1) instrumented TULIF and (2) clinical and radiological follow-up duration for a minimum 6 months. Indication of surgery included patients who presented with spondylolisthesis (n = 84), discogenic low back pain (n = 22), disc herniation (n = 21), spinal stenosis with instability (n = 16), foraminal stenosis (n = 6), degenerative scoliosis (n = 4), and pseudoarthrosis (n = 1) between the L2–3 and L4–5 levels (Table 1), and did not respond to intensive conservative treatments. Exclusion criteria were spondylodiscitis, a history of previous abdominal surgery or radiotherapy, inappropriate vascular anatomy for the anterior approach, and severe obesity (body mass index [BMI] ≥ 30 kg/m^2).

Table 1. Patients' demographic and clinical data

Characteristic	Value
Age (yr)	58.3 ± 10.2
Sex, male:female	41:113
Body mass index (kg/m^2)	25.4 ± 3.2
Bone mineral density (T-score, lumbar)	-0.84 ± 1.47
Surgical levels	
1 Level	
L3-4	10
L4-5	110
2 Levels	
L2-3-4	1
L3-4-5	30
3 Levels	
L2-3-4-5	3
Diagnosis	
Spondylolisthesis	84
Discogenic low back pain	22
Disc herniation	21
Spinal stenosis with instability	16
Foraminal stenosis	6
Degenerative scoliosis	4
Pseudarthrosis	1

Values are presented as mean ± standard deviation or number.

1. Radiological and Clinical Evaluation

Follow-up dynamic lumbar radiographs were evaluated in all patients. At 12-month follow-up, computed tomography (CT) scan was performed. Fusion was defined as solid when there was osseous continuity observed in CT reconstruction images and mobility less than 4 degree as seen in flexion-extension lateral radiographs. Nonunion was defined as the presence of a visible gap, instrument loosening and mobility greater than 4 degree. Clinical outcomes were assessed by the visual analogue scale (VAS; 0–10, with 0 reflecting no pain) and functional outcomes were measured by the Oswestry Disability Index (ODI; 0%–100%) score.

2. Surgical Technique

Before the surgery, preoperative magnetic resonance image (MRI) and sagittal scout CT were evaluated to identify the location of the umbilicus centered on the index levels (Fig. 1A, B). Under general anesthesia, patients were placed in the supine position. Sterile skin preparation and surgical draping were done. To detect over traction of the abdominal or left common iliac artery during the surgery, an oximeter was placed on the patient's left great toe. C-arm-guided marking was conducted to evaluate the index level. Anterior retroperitoneal surgical approach was made by approach surgeon. An approximately 3-cm (1.5 inch) long vertical skin incision was made into the dermal layer on the midline of the umbilicus with an 11th or 15th blade (Fig. 2). The subcutaneous fat under the umbilicus was carefully exfoliated to reach the linea alba and anterior sheath of the rectus muscle using Adson forceps and Bovie cautery. Then the anterior fascia was incised and retracted laterally with the rectus

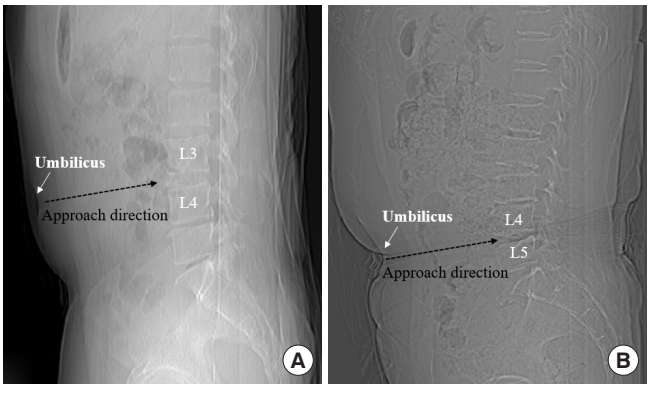

Fig. 1. Preoperative sagittal scout computed tomography view used to identify the location of the umbilicus centered on the index levels. These images show examples of cases where the position of the patient's umbilicus is parallel to the L3–4 levels (A) or parallel to the L4–5 levels (B).

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muscle using the light retractor (Fig. 3). The rectus muscle was elevated to reveal the posterior sheath of the rectus muscle and arcuate line (linea semicircularis). Next, the peritoneal sac was separated from the posterior sheath by blunt dissection, starting from the lateral border of the arcuate line (approximately 4 cm lateral from the midline). In order to prevent peritoneal sac injury, we cut the posterior sheath vertically toward the index disc level (Fig. 4). If a peritoneal injury occurred, we evaluated whether peritoneal organ injury occurred and performed primary repair of the organ with an absorbable suture. The surgical procedures performed after accessing the peritoneum are the same as those used in conventional ALIF. The intraperitoneal contents were bluntly displaced from the retroperitoneal space from the left side toward the midline (Fig. 5A). When the index disc level was reached, the field of view was secured using the level retractor (Fig. 5B). Suture after discectomy and cage insertion is the same as typical ALIF. However, in order to suture the skin layer and subcutaneous layer of umbilicus without

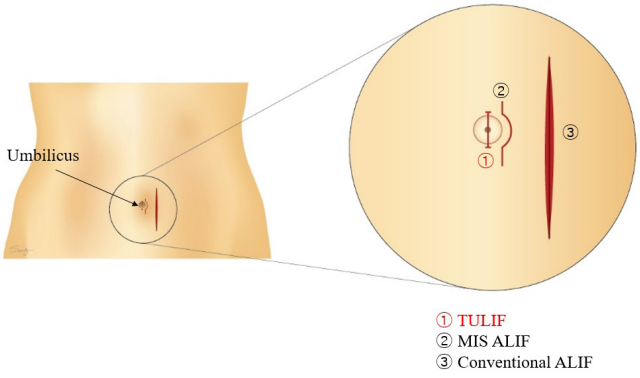

Fig. 2. Comparison of the incisions in transumbilical lumbar interbody fusion (TULIF), minimally invasive spine (MIS) anterior lumbar interbody fusion (ALIF), and conventional ALIF.

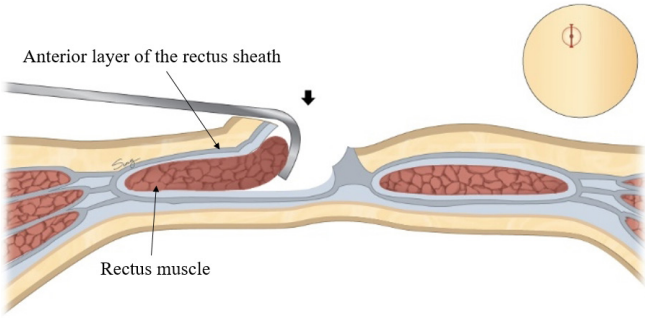

Fig. 3. The anterior fascia is incised and retracted laterally with the rectus muscle using the light retractor.

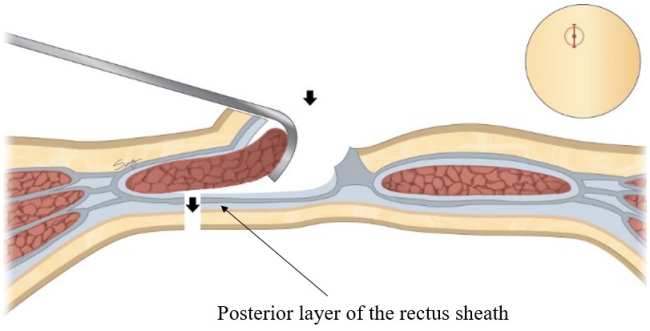

Fig. 4. Axial illustration showing the procedure of cutting the posterior sheath.

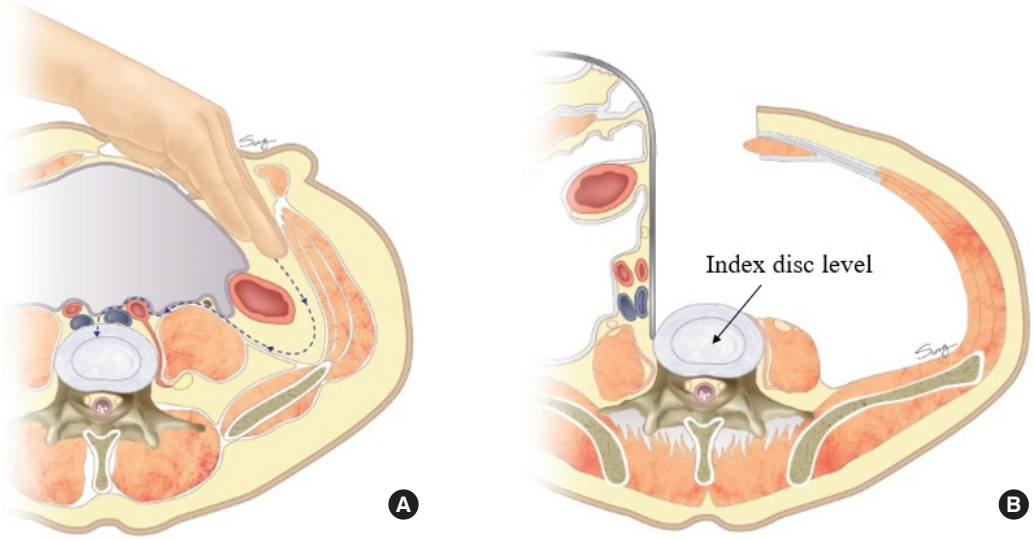

Fig. 5. (A) The intraperitoneal contents are bluntly displaced from the retroperitoneal space from the left side toward the midline. (B) When the index disc level is reached, the field of view is secured using the level retractor.

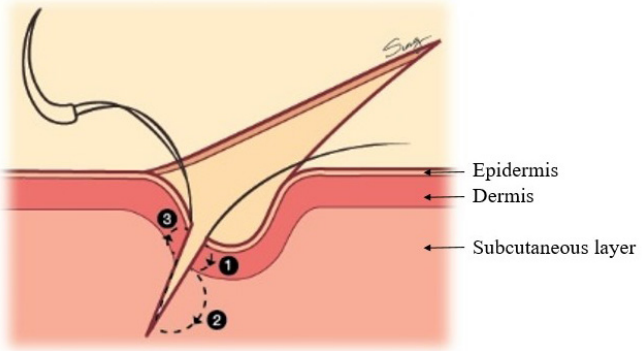

Fig. 6. Illustration showing the technique of suturing the abdominal layer.

dimpling, the connection between layers must be appropriate. After the suture needle passes through the skin and subcutaneous layer of the medial part of umbilicus, the subcutaneous layer of the lateral part is skipped and the skin layer is then connected (Fig. 6). It is important not to include the subcutaneous layer of the lateral part, which is to preserve the belly naturally present in the umbilicus. If the suture is connected as layer by layer like a normal surgery, the navel will be pitted downwards to restore flatness, leaving an unnatural look.

Suturing after discectomy and cage insertion are the same as those performed in conventional ALIF. However, in order to suture the skin layer and subcutaneous layer of the umbilicus without causing dimpling, the 2 layers must be aligned with each other.

After completion of the ALIF, the patient was turned to prone position. Percutaneous pedicle screw fixation was performed under the C-arm guidance. In selected patients with severe stenosis, additional decompressive laminectomy/facetectomy was performed.

RESULTS

A total 154 patients (41 males; mean follow-up, 21.3 ± 12.6 months) were evaluated. Patients' mean age was 58.3 ± 10.2 years, and mean BMI was 25.4 ± 3.2 kg/m^2 (Table 1). Mean bone mineral density was -0.84 ± 1.47 (T-score, lumbar). There were 120 single-level (110 L4–5 and 10 L3–4), 31 two-level, and 3 three-level surgeries. The most common cause of surgery was spondylolisthesis (n = 84). Among the 84 patients who diagnosed with degenerative spondylolisthesis, 18 patients had additional decompressive laminectomy after the pedicle screw fixation. Mean operative time was 90.9 ± 34.3 minutes with a mean blood loss of 189.7 ± 146.9 mL for the anterior surgery. The amount of drainage (anterior drainage) was 175.3 ± 60.6 mL. There was 1 case (0.6%) of intraoperative peritoneal tear and 1 case (0.6%) of wound revision (Table 2). Radiographs of all patients at the last follow-up showed fusion. All patients were very satisfied with their postoperative abdominal scars (recorded through a questionnaire at follow-up after 6 months), which were noticeably faint compared to those after conventional ALIF. VAS for back and leg pain and ODI demonstrated statistically significant differences between the preoperative and postoperative periods (Table 3).

Table 2. Patients' operative data

Variable	Value
Operative time (min) (anterior)	90.9 ± 34.3
Blood loss (mL) (anterior)	189.7 ± 146.9
Drain output (mL) (anterior)	175.3 ± 60.6
Complication	
Peritoneal tear (intraoperatively)	1 (0.6)
Wound revision (postoperatively)	1 (0.6)

Values are presented as mean ± standard deviation or number (%).

Table 3. Clinical and functional outcomes

Variable	Preoperative	Postoperative	p-value
VAS (back)	8.4 ± 1.3	2.3 ± 1.6	< 0.0001
VAS (leg)	7.3 ± 1.7	1.8 ± 0.9	< 0.0001
ODI (%)	63.4 ± 16.8	17.5 ± 12.8	< 0.0001

1. Case Examples

1) Case 1

A 61-year-old man suffered from low back pain and leg numbness in both legs for 5 years (Fig. 7). He experienced neurogenic intermittent claudication at 100 m. The physical examination showed hypoesthesia of both legs, and heel gait was impossible due to motor weakness. The radiological examination revealed degenerative spondylolisthesis with spinal stenosis at the L4–5 levels (Fig. 7A). He underwent TULIF of the L4–5 levels using the described technique, followed by percutaneous pedicle screw fixation. Postoperatively, he showed improvement without any complication (Fig. 7B). At 6 months postoperatively, his scars were very faint (Fig. 7C).

2) Case 2

A 72-year-old woman had low back pain and radiating pain in her right leg for 3 years (Fig. 8). The physical examination showed hypoesthesia of her right leg and foot drop of her right ankle. The radiological examination revealed right foraminal

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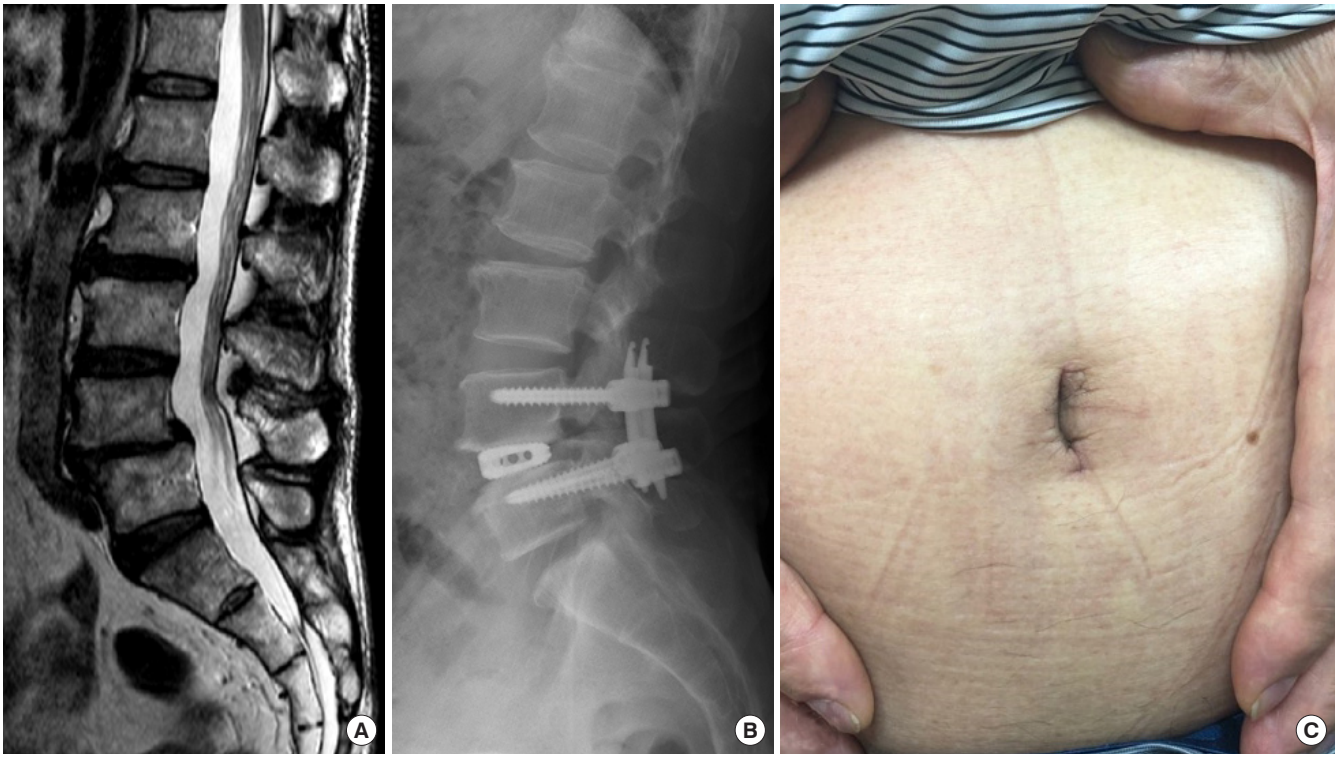

Fig. 7. (Case 1) Preoperative magnetic resonance imaging scan (A), postoperative x-ray (B), and photograph of the abdominal scar after 6 months postoperatively (C).

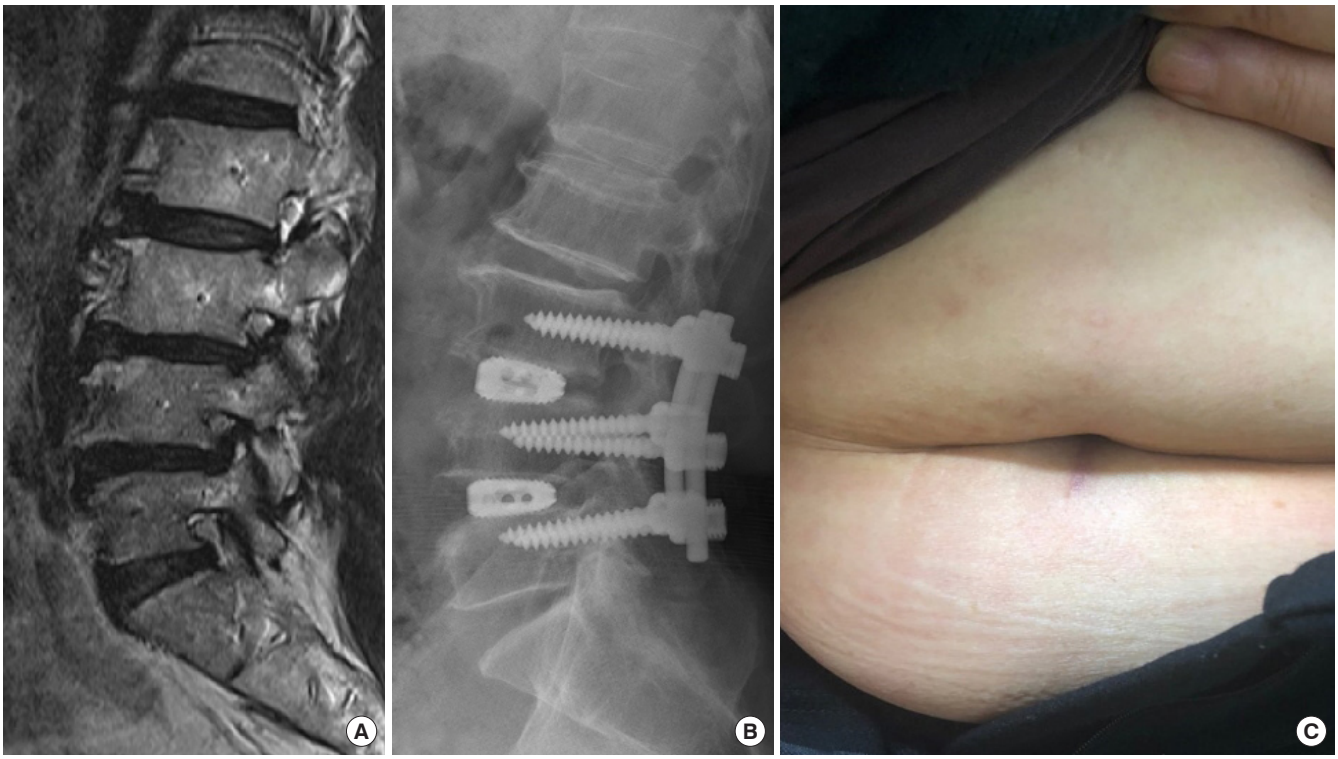

Fig. 8. (Case 2) Preoperative magnetic resonance imaging scan (A), postoperative x-ray (B), and photograph of the abdominal scar after 6 months postoperatively (C).

stenosis at the L3-4-5 levels (Fig. 8A). She underwent TULIF of the L3-4-5 levels using the described technique, followed by percutaneous pedicle screw fixation. At 2 months postoperatively, her leg pain improved from a VAS score of 8 to 1, and she showed improvement in motor function of her right ankle from grade 2 to 3+ (Fig. 8B). At 6 months postoperatively, her scars were very faint and only visible slightly below the navel (Fig. 8C).

DISCUSSION

Currently, many techniques of spine surgeries are pursuing minimally invasive spine (MIS) procedures.[7,8] The concept of MIS procedure includes shortening the surgical time, preserving normal tissue, and minimizing the length of the incision, which lead to rapid recovery of the patient. Fusion through the anterior approach is one of these MIS techniques in that it can minimize injury of the posterior spinal segment.

Conventional ALIF is a mini-laparotomy concept that typically starts with a 3- to 5-inch long incision on the left side of the abdomen.[9] As aforementioned, this approach results in a noticeable scar and is associated with postoperative abdominal pain. A surgical technique for performing ALIF with as small of an incision as possible next to the navel needs developed in order to reduce this complication. Brau[10] introduced a "mini-open approach" for performing an incision transversely parallel to the index level. Although the size of the incision is smaller than that of conventional ALIF, there is a possibility that wound healing may be affected by blood vessel damage and supply, as most blood suppliers in the abdomen are vertically distributed. Recently, Bassani et al.[11] introduced the "keyhole approach" using a perinavel incision, which creates a rounded incision under the navel to create a skin lid and is then closed again postoperatively. This type of incision reduces postoperative scars more than the conventional "mini-open approach." However, all of the existing methods cause some incision scar because they require incision of the normal skin tissue area of the abdomen.

TULIF described herein is a surgical operation through the navel rather than the abdominal skin. The first advantage of this approach is that most of the incisions are performed in the navel, leaving a minimal sign of surgery. Based on the recently reported keyhole approach,[11] incision scars are still noticeable postoperatively. Scarring induced by TULIF is trivial enough to be barely discernible (Figs. 7C, 8C). The second advantage of TULIF is that unlike the "mini-open approach," the incision is performed vertically and parallel to the vessel, thus reducing the risk of vascular damage, which will be helpful for wound recovery.[12,13] The third advantage is that this surgical approach uses a natural orifice. Surgery through the natural orifice transluminal approach has already been performed a lot in the general surgery fields. The advantages this surgical approach are faster recovery, fewer adhesions, fewer postoperative ileus, avoidance of incisional hernias, fewer abdominal wound infections, less postoperative pain, and better cosmetic results.[14,15]

Conventional ALIF has already been proven in many papers as a surgery with high fusion rate and good surgical outcome.[16-20] TULIF is revised technique of conventional ALIF only at the initial abdominal approach stage, and the basic retroperitoneal approach and fusion method are the same as the existing ALIF. Therefore, fusion rate and clinical outcome are thought to be the same as the existing ALIF. This will be verified in an additional clinical article after the technical note is published in the future.

However, since TULIF can be performed within a much smaller window than conventional surgery, an understanding of the normal anatomy of the abdomen is essential and technically, a longer training period is required. Considering the small operation field of abdomen and emergent management for the major vessel injury, co-operation with the approach surgeon can be an ideal solution for this difficulty. Additionally, because each patient has a different anatomy, the index level may be difficult to access through the navel in some patients, and an additional incision may be required for multilevel fusion surgery (more than 3 levels). According to our experience, appropriate level of this technique is mainly L3–4 and L4–5 level. Before the surgery, it is necessary to review preoperative MRI or sagittal scout CT to ensure that the index level is a level that can be approached with TULIF. Despite some limitations, the scar after TULIF improved dramatically, compared to those after previous approaches. TULIF seems to have developed the conventional ALIF into a more suitable approach for MIS procedures.

CONCLUSION

TULIF is a feasible, minimally invasive surgical option that can achieve both treatment of degenerative spinal disease and satisfactory cosmesis. Although it is technically demanding (e.g., extensive experienced with ALIF is needed and skin closure takes longer than that in conventional ALIF), patients obtain sufficient benefits. Within its limited indication, TULIF seems to be an alternative surgical option for better cosmetic satisfaction after using the anterior spinal approach.

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CONFLICT OF INTEREST

The authors have nothing to disclose.

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Technical Note

Simultaneous Robotic Single Position Oblique Lumbar Interbody Fusion With Bilateral Sacropelvic Fixation in Lateral Decubitus

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Single position lateral fusion reduces the need for a secondary surgery and robotic guidance allows for potentially higher accuracy of screw placement. We expand the role of robotics with a simultaneous workflow where 2 surgeons can work in single position surgery and discuss the technical feasibility of placement of S2-alar-iliac (S2AI) screws in the lateral position. A 70-year-old male presented with chronic back pain and bilateral leg pain with the left side worse than the right. He subsequently underwent an L3–S1 oblique lumbar interbody fusion (OLIF) with a minimally invasive L3-ilium robotic posterior spinal fixation simultaneously in single lateral position with S2AI screws. The software planning requisite of robotics allowed for a preoperative plan where lumbar cortical screws were used to line up with bilateral S2AI screws. Intraoperatively, the OLIF was performed anterior to the patient which allowed for a second surgeon to perform the posterior stage of screw placement simultaneously in overlapping fashion during OLIF exposure. Once all screws were placed, the OLIF discectomy and cage placement were completed. As the OLIF incision is closed, rodding proceeds posteriorly with subsequent closure simultaneously as well. Operative time from skin incision to skin closure was 3 hours and 47 minutes. We present here a novel technical report on the recommended workflow of simultaneous robotic single position surgery OLIF and demonstrate the feasibility of placement of sacroiliac fixation in the lateral decubitus position. We believe this technique to be minimally invasive, effective, with the benefit of shortening valuable operating room case time.

Keywords: Minimally invasive surgical procedures, Robotics, Mazor, Sacropelvic fixation, S2-alar-iliac

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BACKGROUND AND IMPORTANCE

The oblique lumber interbody fusion (OLIF) approach, which allows access to the spine via a small corridor between the psoas muscle and the aorta, was introduced by Mayer in the late 1970s as an alternate to the anterior lumbar interbody fusion.[1] Indications include amelioration of degenerative diseases of the spine in L1–S1, as well as coronal and sagittal alignment correction.[2] Studies have shown a decreased risk of psoas muscle and lumbar plexus injury, higher rates of vertebral body fusion and thorough disc clearance, and quicker mobilization after surgery compared to newer techniques such as the extreme lateral indirect fusion.[3-5] Risks of the OLIF procedure include iliac vessel injury, transient neurological damage, and sympathetic chain injury.[3]

Recently, Huntsman et al.[6] reported successful pedicle screw

placement with navigated robot-assisted single position lateral lumbar interbody fusion. There is a paucity of studies of robot-assisted single position OLIF procedures, and none yet describing either a 2-surgeon simultaneous approach or the technical feasibility of robotic-assisted placement of S2-alar-iliac (S2AI) screws. We report a novel 2-surgeon simultaneous robotic single position surgery (SR-SPS) OLIF with bilateral sacropelvic fusion in lateral decubitus.

CLINICAL PRESENTATION

1. Patient Presentation

A 70-year-old male presented with chronic back pain and bilateral leg pain with the left side worse than the right. Informed consent was obtained from the patient. Having failed conservative management of physical therapy, trigger point injections, and epidural steroid injections, he sought surgical care. His preoperative Oswestry Disability Index (ODI) was a 48/100. Magnetic resonance imaging demonstrated degenerative change with disc height collapse causing bilateral neuroforaminal stenosis at L3–4, L4–5, and L5–S1 (Fig. 1). Due to his equal distribution of back pain and leg pain, he was offered an L3–S1 OLIF with a minimally invasive L3-ilium robotic posterior spinal fixation simultaneously in single lateral position with S2AI screws (Mazor X Stealth Edition, Medtronic Sofamor Danek, Memphis, TN, USA). Sacropelvic fixation was chosen to reduce the risk of postoperative sacroiliac joint pain after multilevel stabilization and fusion in light of the patient's body mass index of 38.4 kg/m^2.[7]

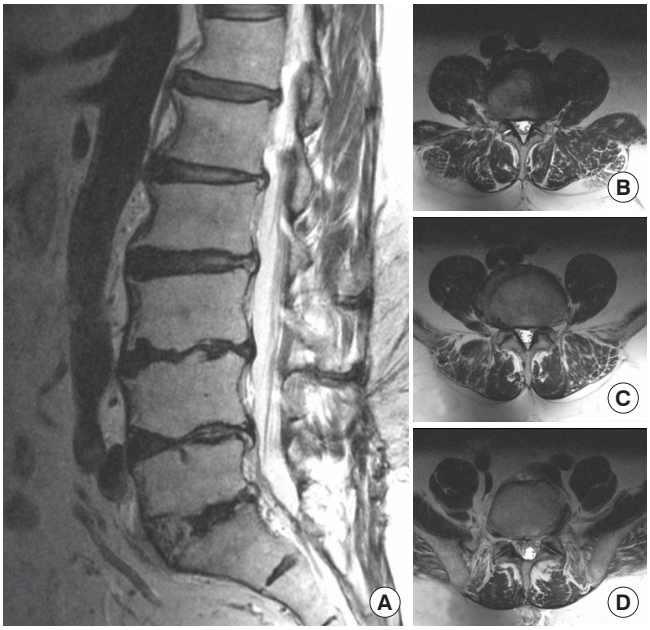

Fig. 1. (A) Sagittal T2-weighted magnetic resonance imaging showing collapse of disc spaces and degenerative change from L3–S1 with axial section of L3–4 (B), axial section of L4–5 (C), and axial section of L5–S1 (D).

2. Software Planning

The Mazor X planning software is used to prepare the targets and trajectories of the patient's construct design based on a

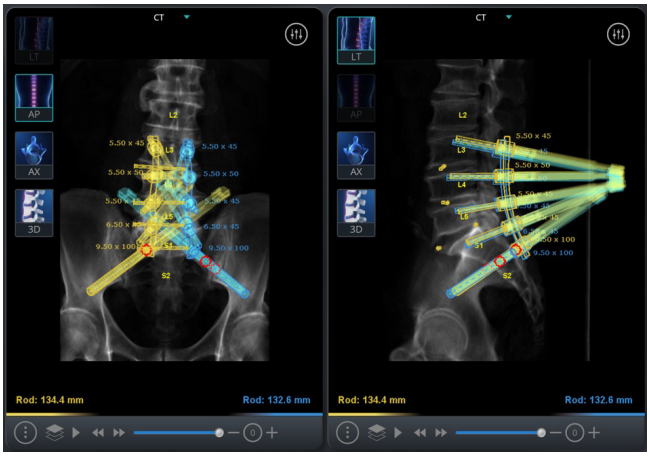

Fig. 2. Mazor X software robotic plan showing planned screw trajectories from L3 to S2AI, as well as the marked disc space levels from L3–4 to L5–S1. Note that the cortical lumbar screws line up well with the S2AI screws for a straight planar rod design.

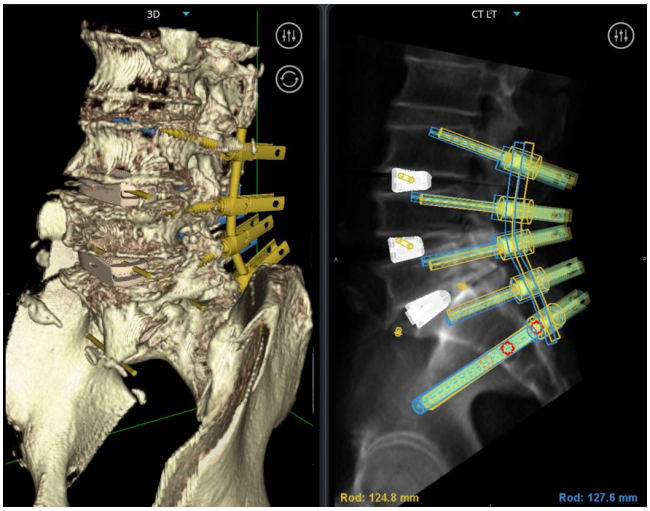

Fig. 3. Mazor X software robotic plan with simulated view of oblique interbody cage placement from L3–4 to L5–S1 and anticipated "ideal" correction.

thin-cut preoperative computed tomography (CT). Because the L3-ilium construct is planned as a minimally invasive design, cortical screw trajectories are planned which allow for better rod line-up (Fig. 2).[8] In addition, the L3–4, L4–5, and L5–S1 disc spaces can be targeted so that the robotic arm can be used for intraoperative guidance for direction down to the respective disc spaces while minimizing intraoperative fluoroscopy. Additionally, the predictive software alignment can simulate a variety of cage footprints for surgeon clinical decision making (Fig. 3).

3. Operative Technique

The patient is positioned in right lateral decubitus with the left side facing up (Fig. 4). The back is positioned as close to the edge of the table as possible to allow for reach of the posterior pedicle screw and iliac screw instruments. Because the surgical technique allows both surgeons to work near simultaneously, there are various stages where it is advised that the posterior (pedicle screw) surgeon or anterior (OLIF) surgeon pause and wait to maximize robotic accuracy and guidance. These steps are outlined below.

1) Registration

The robotics platform is rigidly attached to the bed and to the patient's spine via the posterior superior iliac spine. Two fluoroscopic images are then taken to align the patient's *in situ* positional anatomy to the segmented preoperative CT anatomy. Once registration has occurred, great care is taken to minimize motion to the patient so as not to introduce error into the registration. This includes avoiding leaning against the patient, avoiding any heavy-handed maneuvers, and minimizing somatosensory evoked potentials signals if neuromonitoring is being used.

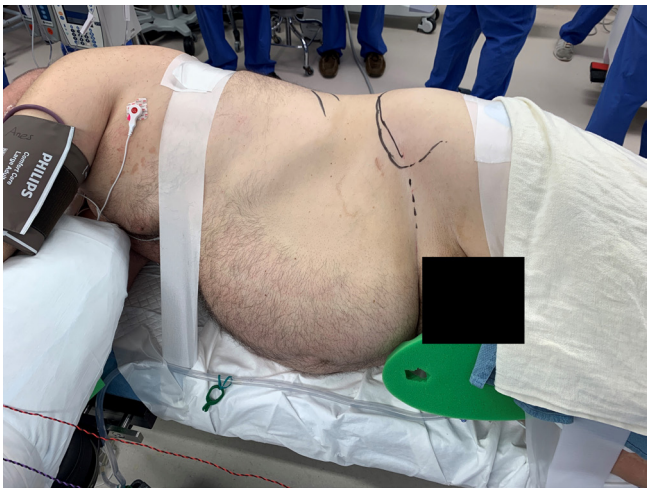

Fig. 4. Lateral decubitus positioning of the patient with the back positioned as close to the posterior edge as possible, and the abdomen allowed to fall away to the bed without anterior bolsters to allow freedom for the oblique trajectory.

2) Posterior surgeon

Once the robotics platform is attached and registered, the robotic arm is first sent to the anterior surgeon's disc space trajectories so that incisions can be planned. The arm is then sent back to the posterior screws. Due to the long segment nature of this construct, we performed a single midline skin incision for cosmesis and performed all screws transfascially. Screws were placed in the following sequence: right-sided L3, L4, L5, S1; left-sided L3, L4, L5, S1; right-sided S2AI; left-sided S2AI. Screw placement proceeds proximal to distal to maximize accuracy of the screws furthest away from the robotics platform which may have the higher risk of error. The right-side is performed first because any incisional bleeding will drain downwards, and performing the right-side last may be hindered by blood draining down from the left side. S2AI screws are both performed last because the amount of force and torque required for placement exceeds that of regular pedicle screws, which again may increase risk of mismatch error. Because of the preplanning design of the S2AI screws as well as the rigid guidance of the robotic arm, placement of the S2AI screws bilaterally is not a technically laborious task. Robotic technique for placement of screws using the Mazor X Stealth Edition platform includes the robotic knife which is inserted down to the bone, followed by the navigated dilator and cannula. Subsequently, the navigated drill, tap, and pedicle screw are placed down the robotic arm with real-time navigation on-screen to confirm an appropriate trajectory as compared to the preoperative plan. As a technical note, we use continuous power for our instruments to avoid the "start-stop" movement of hand drivers. Also, drills, taps, and screws are started just slightly above the bone before being driven down the bony path to avoid skive error.

Once all screws are placed, the posterior surgeon pauses while the anterior surgeon performs the discectomy and cage placement at all the appropriate levels. Once this is finished, the posterior surgeon can resume placement of the rods and set screws using standard minimally invasive technique. Although the surgical view of a "forest of towers" may initially be daunting, the preoperative planning has already taken into account the alignment of the screws for the rods, and rod placement is done with minimal difficulty (Fig. 5). Closure then proceeds in usual fashion.

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3) Anterior surgeon

The robotic arm is sent to all disc spaces that had been preplanned on the software. This is then marked on the skin as a guide for the surgical corridor. Because the OLIF is performed under direct visualization of the disc space, skin incisions are marked anterior to the level of the disc and the iliac crest can be avoided for all levels. The robotic arm is then sent back to the posterior surgeon for placement of screws, and the anterior surgeon can proceed simultaneously with exposure down to the disc space at all levels (Fig. 6). Great care is taken not to shift or move the patient during this time to avoid introducing mismatch error in robotic guidance posteriorly. The L5–S1 disc space is exposed first via an oblique corridor, and then subsequently to save time, the L4–5 and L3–4 disc space corridors can be dilated and exposed if the posterior surgeon is still working (Fig. 7).

The anterior surgeon must then pause until all the posterior screws have been placed. Once screw placement has finished, the anterior surgeon then proceeds with the OLIF discectomy and cage placement at all levels with fluoroscopic guidance. When all cages have been placed, anterior closure then pro-

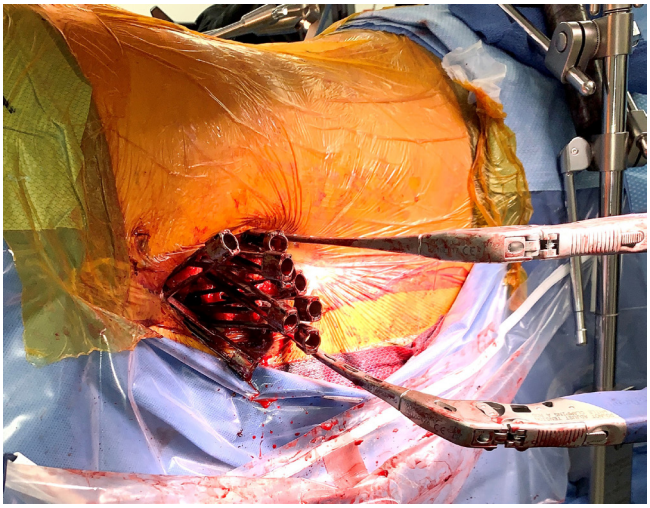

Fig. 5. Posterior view with all screws placed causing a "forest of towers" in the surgical field. Also shown is placement of bilateral rods using minimally invasive technique and inserters.

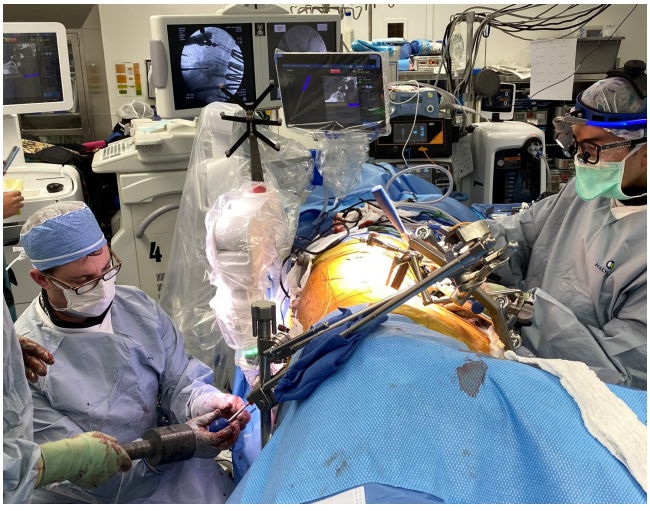

Fig. 6. Operating room view showing both the posterior surgeon (right) and anterior surgeon (left) simultaneously overlapping in their workflow.

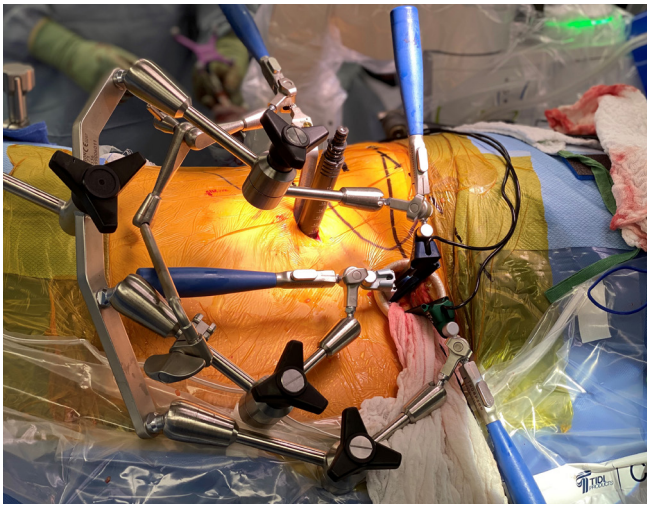

Fig. 7. Anterior view showing the L5–S1 surgical corridor with 3 minimally invasive retractor blades, and the L3–4 surgical corridor with the L3–4 minimally invasive dilators. The anterior surgeon is paused now awaiting complete placement of all posterior screws.

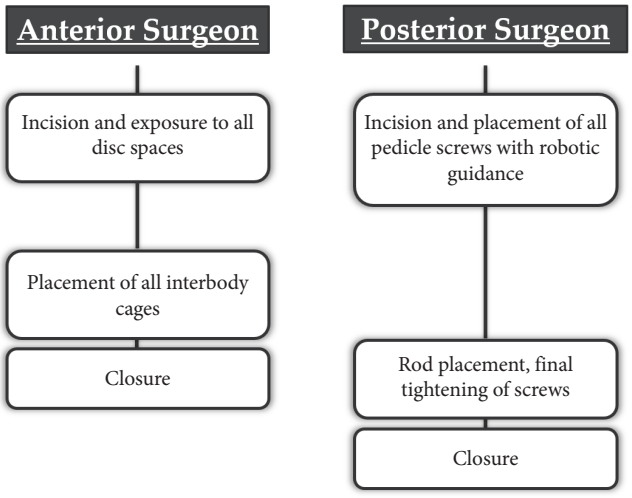

Fig. 8. Workflow diagram of anterior and posterior surgeon.

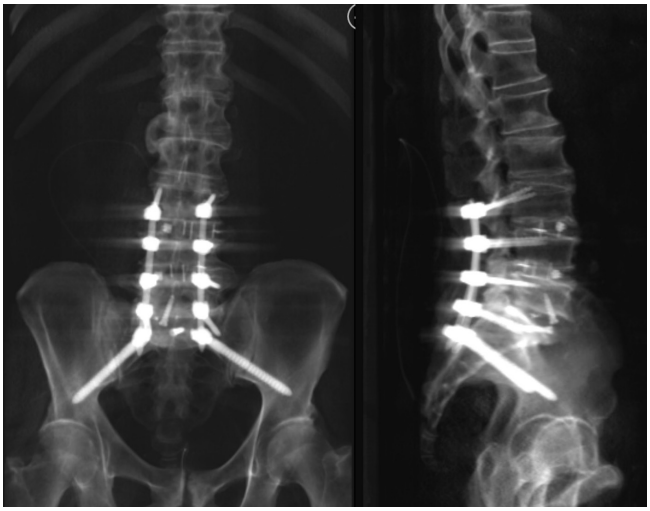

Fig. 9. Postoperative computed tomogarphy-constructs showing anteriorposterior and lateral view of the final L3-ilium construct.

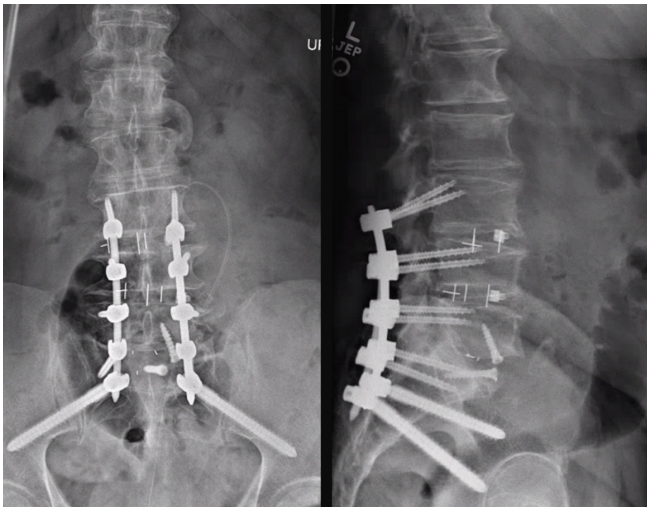

Fig. 10. Postoperative imaging showing anteriorposterior and lateral x-rays of the construct.

ceeds simultaneously as the posterior surgeon begins the final rodding (Fig. 8).

4. Clinical Outcome

Due to the simultaneous exposure and overlapping workflow, total operative time from skin incision to skin closure for placement of 8 lumbosacral screws, 2 S2AI screws, and 3 interbody cages including L5–S1 was 3 hours and 47 minutes. Blood loss was estimated to be 100 mL. Postoperative imaging demonstrated implants to all be in good position (Figs. 9, 10). He was discharged on the third postoperative day. At 8-month follow-up, he has complete resolution of his leg pain and significant improvement in his axial back pain. There have been improvements in his visual analogue scale and ODI scores with decreases of 6 points and decreased by 34 points respectively.

DISCUSSION

Single position lateral fusions reduce the need for a secondary surgery, and robotic guidance allows for potentially higher accuracy of screw placement. Additionally, completing the procedure in a single position reduces OR time, redraping, and cost of surgery.[9] We demonstrate here this technical case to build upon the role of robotics in expanding a simultaneous workflow which allows for single position surgery to be performed in an overlapping manner, as well as the technical feasibility of placement of S2AI screws now in lateral position as well.

Preoperative planning is required for all robotics platforms, which allows for input of the desired targets and trajectories which make up the patient's construct design. The preoperative planning itself is key to the success of the construct design, as screws can be lined up beforehand to minimize frustration and difficulty in passage of the rod down to the S2AI screws. Similar to PACS (picture archiving and communication system) systems and other software programs, there is some up-front learning required for appropriate use. However, the learning curve is similarly not steep and a quick familiarity can be obtained due to intuitive directions and controls.

The benefits of performing SR-SPS are unique to both robotics and OLIF. Because the OLIF is performed anterior to the patient, this allows for the opportunity to perform the posterior stage of screw placement simultaneously in overlapping fashion to maximize efficiency and reduce both anesthesia and operating room time. Because of the accuracy and rigidity of robotic guidance, placement of S2AI screws becomes no more difficult a task than the planning design and placement of any other pedicle screw. For surgeons who are comfortable with OLIF, this technique demonstrates the feasibility of not only placement of pedicle screw instrumentation in the single lateral position, but also that extension down to the ilium is not an impediment or reason to flip to prone. This workflow provides an opportunity for tremendous efficiency and time savings while still providing the surgical goals. Although we describe here the feasibility of placement of sacroiliac fixation in the lateral decubitus position, this technical description also offers a recommended workflow for SR-SPS OLIF in general.

Over the past few years, robotic assistance in spinal surgery has also grown. Benefits of robotic aid include increased accu-

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racy of screw placement and decreased radiation exposure. A systematic review article noted that of the 22 studies evaluating the accuracy of spinal instrumentation with robotic assistance, only one resulted in lowered accuracy in screw placement using a robot.[10,11] The literature supports the benefits of robotic assistance in reducing radiation exposure and time under fluoroscopy. Kantelhardt et al.[12] concluded that average x-ray exposure per screw was significantly lower in robotic aided surgery (34s vs 77s) in comparison to conventional methods; Lieberman et al.[13] reported lower fluoroscopy time per screw as well.

Recent studies have outlined the possibility of keeping the patient in a single position for spinal fusion surgeries. While keeping the patient in a single position, Huntsman reported a 98% success rate of pedicle screw placement with the lateral lumbar interbody fusion approach. The study also noted that there were no screw revisions needed, hence supporting the procedure's efficacy.[6] Lamartina introduced the feasibility of conducting the extreme lateral interbody fusion with posterior fixation in the prone position.[14] This study outlined a reduced mean surgical time of 133.8 ± 26.6 minutes in the prone position, as compared to 182.8 ± 47.9 minutes in standard lateral decubitus. Walker et al.[15] report a similar lengthened mean surgical time of 203.6 ± 64.8 minutes in standard lateral decubitus, as well as similar rates of known complications.[14]

CONCLUSION

We present here a novel technical report on the recommended workflow of SR-SPS OLIF and demonstrate the feasibility of placement of sacroiliac fixation in the lateral decubitus position. We believe that we have stated the advantages in terms of time savings and efficiency. The use of robotic guidance in bilateral iliac fixation in the single lateral position would significantly reduce operative and anesthesia times, without the need to flip patients.

CONFLICT OF INTEREST

Dr. Pham reports consultant fees with Medtronic. Dr. Diaz-Aguilar reports no financial disclosures. Dr. Lehman reports consultant fees with Medtronic; speaking and/or teaching arrangements with Medtronic, DePuy, Stryker; grants from the Department of Defense, Defense Medical Research Development Program. Other authors have nothing to disclose.

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Letter to the Editor

Commentary on "Impact of Nonlordotic Sagittal Alignment on Short-term Outcomes of Cervical Disc Replacement"

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To the editor,

With great interest, we read the article titled "Impact of Nonlordotic Sagittal Alignment on Short-term Outcomes of Cervical Disc Replacement" written by Jung, et al. in *Neurospine*.[1] The authors conducted a retrospective study to evaluate outcomes of cervical disc replacement (CDR) in patients with nonlordotic alignment. The conclusion is that CDR has the potential to generate and maintain lordosis and improve patient-reported outcome measures (PROMs) in the short term, and can be an effective treatment option for patients with nonlordotic alignment. We highly appreciate their contribution to this topic; however, some issues in the article may confuse the readers, which needs further clarification.

First, cervical kyphosis can be divided into reversible kyphosis and irreversible kyphosis. For many patients with reversible kyphosis, the neck pain was so torturous that they had to hold the relatively kyphotic position to relax the posterior neck muscle, thus leading to preoperative kyphosis. But after pain relief, the neck muscle spasm was immediately and remarkably relieved. Then, the cervical spine automatically returned to a relatively lordotic position; whereas the irreversible kyphosis was frequently associated with serious cervical degeneration or congenital bone malformation, cervical kyphosis in these patients may not improve after pain relief.[2] Therefore, the authors should measure the curvature of the cervical spine after pain relief. We think that the real purpose of this study was to examine the short-term outcomes of CDR in patients with irreversible kyphosis who had no improvement in cervical alignment after pain relief. PROMs recommend to be collected for analysis after pain relief, immediately after surgery, and postoperative follow-up <6 months, ≥ 6 months.

Second, the baseline characteristics may be incomparable and confounding factors such as the professional types, the presence or absence of adjacent segment degeneration,[3] the occipital orientation[4] and whether to undergo traction treatment should also be included. The consistency of patient data between groups can be assessed more comprehensively, so that subsequent studies can be more comparable.

Third, the method used by the authors to measure cervical curvature may be controversial, the C2–7 Cobb method and local surgical segments method were deemed to affect the definition of cervical alignment remarkably. These 2 methods obtained all their information locally at the endpoints but inferred a conclusion about the entire cervical region.

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Hu et al.[2] mentioned that no existing study proposed an exact degree range concerning the definition of straight cervical spine, as opposed to the modified Toyama method that could determine the 3 types of cervical alignment quantitatively. Meanwhile, the modified Toyama method was regarded as a reliable and accurate method for the classification of cervical alignment.[5]

In conclusion, we believe that future studies should give more details concerning other confounding factors and try to control baseline comparable. A reasonable cervical alignment measurement method should be used and those appropriate target population should be included in future study subjects, so as to draw a conclusion with more credibility. Once again, we appreciate the authors for their great work and hope that the readers can benefit from it.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Letter to the Editor

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Reply to Commentary on "Impact of Nonlordotic Sagittal Alignment on Short-term Outcomes of Cervical Disc Replacement"

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To the editor,

We would like to thank you for the opportunity to respond to the letter to the editor. We would also like to thank the authors of this letter for their interest in our research and hope that the additional information provided here addresses their concerns and questions.

With regard to the first point of the difference between reducible and irreducible kyphosis, we agree that the underlying mechanisms for the two are different, and thus outcomes of surgery, cervical disc replacement or otherwise, may be different in these patient populations as well. This study included patients with passively reducible kyphosis and thus our findings are applicable to this subset of patients with nonlordotic alignment, as mentioned in the discussion section of our paper. In terms of patient-reported outcome measures (PROMs), we have included a comprehensive list of PROMs for cervical spine surgery,[1] covering disease-specific measures, pain scores and general health measures. Additionally, these PROMs were obtained preoperatively and at multiple postoperative timepoints, with the early follow-up timepoint including PROMs from 2 weeks up to 3 months after surgery, thus ensuring that PROMs and pain scores in the early postoperative were effectively captured and analyzed.

As a second point, the authors propound concerns with regard to incomparable baseline characteristics and potential confounders. We agree that having similar baseline characteristics is an important consideration when performing comparative analyses, and we made efforts to ensure that our groups were comparable. As seen in the results section of the manuscript and the tables, there were no statistically significant difference in any patient demographics or operative factors, except age, thus demonstrating that the cohorts in our study were comparable. Furthermore, the study by Yang et al.,[2] cited by the authors, demonstrates an association between adjacent segment (ASD) and occipito-cervical inclination (OCI), but shows no association between ASD and C2–7 Cobb angle, SVA or T1 slope. The current study did not analyze OCI but analyzed C2–7 Cobb angle, SVA and T1 slope, which are not associated with ASD. Additionally, as mentioned by the authors of this letter, numerous parameters, including occipital orientation, can impact cervical alignment. However, in the study by Zhu et al.,[3] cited by the others, although the correlation between the occipital orientation parameters and C2–7 lordosis was statistically significant, it was a weak

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correlation, with the correlation coefficients ranging from 0.23 to 0.30. Additionally, this study was performed in asymptomatic healthy individuals without any degenerative spinal pathology. Thus, it is not clear whether this association would be present in patients with spinal pathology and how it would affect outcomes following cervical spine surgery. Thus, we believe that our findings are valid and remain unchanged regardless of ASD or occipital orientation. Nevertheless, we agree that these are important topics that should be explored further in future studies. Traction treatment was not used for any patients prior to surgical intervention, and thus does not impact our findings.

Thirdly, as the authors rightly point out, numerous methods exist to characterize alignment of the cervical spine,[4,5] each with its limitations and advantages. We chose the Cobb angle method because it is an established, simple and reproducible method that can be performed quickly and easily in a clinical setting, without the need for sophisticated software or numerous measurements. Furthermore, it has been used in a number of published studies,[6-9] thus allowing for comparison of results across studies as well as pooling of results for meta-analyses. Additionally, although Hu et al.,[10] cited by the authors, do not use a particular angular measurement to determine spinal alignment, our methodology was based on the studies by Kim et al.[11] and Le Huec et al.,[12] which define lordosis and kyphosis based on the C2–7 Cobb angle being less than or greater than 0 degree. This method provides a simple way to classify patients and has been used in numerous studies in the literature.

We appreciate the interest the authors of this letter have shown in our work and thank them for their valuable comments and insightful feedback. We hope that the additional information provided here better explains our methodology and the rationale for it, and further supports the findings reported in our study.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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• Journal article

1. Sakai K, Okawa A, Takahashi M, et al. Five-year follow-up evaluation of surgical treatment for cervical myelopathy caused by ossification of the posterior longitudinal ligament. Spine (Phila Pa 1976) 2012;37:367-76.

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2. Sweitzer S, Arruda J, DeLeo J. The cytokine challenge: Methods for the detection of central cytokines in rodent models of persistent pain. In: Kruger L, editor. Methods in pain research. Boca Raton, FL: CRC Press; 2001:109-32.

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This journal follows the data sharing policy described in "Data Sharing Statements for Clinical Trials: A Requirement of the International Committee of Medical Journal Editors" (https://doi.org/10.3346/jkms.2017.32.7.1051). As of July 1, 2018 manuscripts submitted to ICMJE journals that report the results of interventional clinical trials must contain a data sharing statement as described below. Clinical trials that begin enrolling participants on or after January 1, 2019 must include a data sharing plan in the trial's registration. The ICMJE's policy regarding trial registration is explained at http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html. If the data sharing plan changes

Table. **Examples of Data Sharing Statements That Fulfill These ICMJE Requirements***

	Example 1	Example 2	Example 3	Example 4
Will individual participant data be available (including data dictionaries)?	Yes	Yes	Yes	No
What data in particular will be shared?	All of the individual participant data collected during the trial, after deidentification.	Individual participant data that underlie the results reported in this article, after deidentification (text, tables, figures, and appendices).	Individual participant data that underlie the results reported in this article, after deidentification (text, tables, figures, and appendices).	Not available
What other documents will be available?	Study Protocol, Statistical Analysis Plan, Informed Consent Form, Clinical Study Report, Analytic Code	Study Protocol, Statistical Analysis Plan, Analytic Code	Study Protocol	Not available
When will data be available (start and end dates)?	Immediately following publication. No end date.	Beginning 3 months and ending 5 years following article publication.	Beginning 9 months and ending 36 months following article publication.	Not applicable
With whom?	Anyone who wishes to access the data.	Researchers who provide a methodologically sound proposal.	Investigators whose proposed use of the data has been approved by an independent review committee (learned intermediary) identified for this purpose.	Not applicable
For what types of analyses?	Any purpose.	To achieve aims in the approved proposal.	For individual participant data meta-analysis.	Not applicable
By what mechanism will data be made available?	Data are available indefinitely at (*Link to be included).*	Proposals should be directed to xxx@yyy. To gain access, data requestors will need to sign a data access agreement. Data are available for 5 years at a third party website (*Link to be included).*	Proposals may be submitted up to 36 months following article publication. After 36 months the data will be available in our University's data warehouse but without investigator support other than deposited metadata. Information regarding submitting proposals and accessing data may be found at (*Link to be provided*).	Not applicable

* These examples are meant to illustrate a range of, but not all, data sharing options.

after registration this should be reflected in the statement submitted and published with the manuscript, and updated in the registry record. All of the authors of research articles that deal with interventional clinical trials must submit data sharing plan of example 1 to 4 in Table 1. Based on the degree of sharing plan, authors should deposit their data after deidentification and report the DOI of the data and the registered site.

For the policies on the research and publication ethics not stated in this instructions, International standards for editors and authors (https://publicationethics.org/resources/resources-and-further-reading/international-standards-editors-and-authors) can be applied.

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