Future Advances in Spine Surgery: The AOSpine North America Perspective

This focus issue highlights state-of-the-art techniques, equipment, and practices in the modern era of spine surgery while providing a glimpse into the next generation of patient care. A broad range of topics are presented to cover the full spectrum of the field. Degenerative diseases are discussed in a series of 3 articles on (1) pathophysiology, management, and surgical approaches to degenerative cervical myelopathy; (2) novel approaches to degenerative thoracolumbar disease (eg, interspinous process spacers, minimally invasive/endoscopic approaches); and (3) animal models and emerging therapeutics in degenerative disk disease. Also included is a unique study aiming to establish the critically important cost–benefit relationship for spine procedures with perspectives on how value is defined and how to address variability.

Primary and metastatic spine oncology are reviewed with a focus on upcoming targeted biologics, subspecialized radiotherapy (eg, proton-beam, carbon-ion, stereotactic radiosurgery), genetic profiling to stratify risk, and morbidity-reducing surgical approaches (eg, minimally invasive/endoscopic resections, percutaneous instrumentation). Trauma is discussed in 2 high-quality papers on controversies in spinal trauma and neuromoductive/neuroregenerative interventions for traumatic spinal cord injury. A stimulating article on cervical, thoracolumbar, and pediatric deformity highlights the rapid evolution of deformity surgery with a look at innovative tools (eg, high-fidelity 3-dimensional reconstructions, magnetically controlled growing rods) and their impact on quality of life. Additionally, a must-read article on surgical site infections discusses key risk factors and evidence-based preventative techniques to remain aware of. Finally, cutting-edge technologies, including computer-assisted navigation, shared-control robotics, neuromodulation, novel osteobiologics, and biomaterials, are covered in detail in a series of 3 fascinating papers on the next generation of the field.

Each section intends to highlight the salient literature and afford insights from multiple key thought leaders in an effort to minimize bias and provide varied perspectives. Overall, we hope this issue provides high-quality, evidence-based data relevant to trainees and practicing surgeons while also stimulating excitement about the future of spine surgery.

KEY WORDS: Trauma, Oncology, Degenerative, Neuromodulation, Spine, Surgery, Review, Biomaterials, Deformity, Myelopathy, Robotics, Infection
DEGENERATIVE DISEASE

Degenerative Cervical Myelopathy

Degenerative cervical myelopathy (DCM) is a recently coined term encompassing degenerative pathologies (eg, spondylosis, ossification of the posterior longitudinal ligament, degenerative disk disease [DDD], etc) resulting in compression of the spinal cord and a clinical syndrome characterized by decreased dexterity, gait imbalance, and possible sphincter dysfunction. Substantial variability in the underlying etiology of DCM and its natural history has generated heterogeneity in practice patterns across geographic regions, specific institutions, and individual surgeons. Debates in management most commonly center around the timing of intervention and the ideal surgical approach. Two key multicenter studies, the AOSpine North America Cervical Spondylotic Myelopathy (CSM) study (n = 278) and the AOSpine International CSM study (n = 479), found surgical decompression to be effective in moderately or severely myelopathic patients with a low rate of serious complications. Based on these results and several subsequent comparative studies, an upcoming 2017 AOSpine guideline will recommend surgical intervention for individuals with moderate or severe DCM. With regard to the ideal surgical technique, a recent systematic review of retrospective studies found no consistent difference in outcomes for anterior vs posterior approaches. Similarly, there is currently no consensus around the relative efficacy of laminoplasty vs laminectomy, minimally invasive surgery (MIS) vs open surgery, and the role of adjuvant pharmacological treatments. The “State of the Art in Degenerative Cervical Myelopathy: An Update on Current Clinical Evidence” article discusses these important topics while also outlining the salient pathophysiological features of DCM, the present understanding of its natural history, and key ongoing clinical trials to remain aware of.

Degenerative Thoracolumbar Surgery

Several complementary fields of spine surgery, including deformity, osteobiologics, biomaterials, computer-assisted navigation (CAN), and robotics, are actively being combined to deliver the next generation of treatments for degenerative thoracolumbar disease. Lumbar decompression, for example, has been typically avoided in elderly patients with substantial medical comorbidities due to significant perioperative morbidity and mortality. However, the risk–benefit balance has shifted with the introduction of interspinous process spacers (eg, X-stop, Coflex, Superion, etc), MIS tubular/endoscopic approaches, and percutaneous instrumentation, allowing the inclusion criteria for degenerative thoracolumbar surgery to be broadened. Even the historically challenging insertion of intervertebral fusion cages has become safer using less invasive transforminal (TLIF), extraforaminal, and oblique lumbar interbody fusion techniques to reduce blood loss and infection rates.

Furthermore, the increasing availability of large-scale registry and clinical trial data has facilitated more precise patient selection and allowed refinement of treatment algorithms. As an example, the Spine Patients Outcomes Research Trial (n = 304) assessed nonoperative vs surgical treatment for degenerative spondylolisthesis finding surgery to be associated with reduced disability (Oswestry Disability Index) and improved quality of life (short form-36), even in patients over 80 years old. Similarly, recent trials have shown that patients with back pain due to sacroiliac (SI) joint degeneration are more likely to see improvements with MIS SI fusions vs conservative treatment alone. These and other key studies are discussed in the “Emerging Techniques in Degenerative Thoracolumbar Surgery” article along with expert interpretations of the data and insights into the next breakthroughs coming down the research pipeline.

Intervertebral Disks

Degeneration of intervertebral disks (IVD) is a major contributor to the $253 billion USD spent on direct medical costs for back pain in the USA each year. Understanding the pathophysiology of DDD and how to regenerate disks is therefore a crucial part of spine care. The fibrocartilaginous IVD loses endplate vascular supply with age leading to a procatabolic state with decreasing proteoglycan and type II collagen composition. This is compounded in patients with risk factors such as high body mass index, smoking, and genetic predispositions. Multiple animal models have been developed to mimic DDD; however, some critical anatomical differences still exist including bipedal biomechanics, disk geometry, and nonlinear scale-up of forces. Despite this, the molecular pathophysiological cascade observed in several species does approximate human biology allowing novel therapeutics to be effectively tested at the preclinical stage. Growth-stimulating protein injections (eg, bone morphogenetic protein-2 [BMP-14]), virus-mediated in vivo gene therapy, and cell therapies (eg, mesenchymal stem cells, chondrocytes, etc) are some of the upcoming strategies showing promise in either preventing degeneration of disks or regenerating them after failure. “Intervertebral Disc Degeneration and Repair” provides a deeper look at these and other
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<th>Degenerative disease</th>
<th>“State of the Art in Degenerative Cervical Myelopathy: An Update on Current Clinical Evidence”</th>
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<td>• DCM is an overarching term for cervical spinal cord compression from degenerative pathologies resulting in gait imbalance, decreased hand dexterity, and possible sphincter dysfunction.</td>
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<td>• This article covers the role of these new approaches in degenerative thoracolumbar surgery, the importance of registry and large-scale trial data, and provides insight into the next breakthroughs in the research pipeline.</td>
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<td>Oncology</td>
<td>“Spine Oncology—Primary Spine Tumors”</td>
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<td>• Targeted biologics, proton-beam therapy, stratification of tumor subtypes, and the delivery of precision medicine are transforming primary spine oncology.</td>
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<td>• This article reviews these important approaches and provides an overview of the basic tenets of managing a primary spinal tumor and the evolving role of surgery.</td>
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<td>“Spine Oncology—Metastatic Spine Tumors”</td>
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<td>• Modern metastatic spine oncology relies on early tissue diagnosis to permit genetic analyses, risk stratification (eg, BRAF mutation in melanoma) and provide personalized treatment plans.</td>
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<td>• This article discusses the pertinent medical and surgical management of these patients with an emphasis on techniques to reduce treatment-related morbidity (eg, MIS/endoscopic resections, percutaneous instrumentation, SRS, etc).</td>
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<td>Trauma</td>
<td>“Controversies in Spinal Trauma and Evolution of Care”</td>
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<td>• A synthesized literature review on 8 of the most relevant and rapidly evolving topics in spine trauma:</td>
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<td>“Traumatic Spinal Cord Injury—Repair and Regeneration”</td>
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<td>• The direct lifetime cost for an individual with a traumatic spinal cord injury exceeds $1.1 to 4.6 million USD making the development of neuroprotective (eg, riluzole, minocycline, hypothermia, etc) and neuroregenerative (eg, stem cell therapies, Cethrin [BioAxone BioSciences Inc.], anti-NOGO antibody) therapies especially critical.</td>
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<td>• This article provides a concise overview of the pathophysiology of SCI, current management paradigms based on AANS/CNS guidelines, and promising therapeutics of the next decade.</td>
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therapies with a focus on the pathophysiology of DDD. The article also reviews the current status of important clinical trials and highlights a pressing need to better understand the complex interplay of cell signaling within the IVD to continue generating effective therapeutics.

**ONCOLOGY**

**Primary Tumors**

The challenging management of primary spinal tumors has resulted in unprecedented collaboration across disciplines to
improve patient survival, enhance quality of life, and decrease treatment-related morbidity. Advanced percutaneous diagnostic techniques combined with targeted biologics (eg, RANKL for giant cell tumors) have transformed the management of many pathologies previously treated with extensive resection.24,25 Patients with classically radioresistant tumors are now increasingly becoming candidates for treatments such as stereotactic radiotherapy (SRS), proton-beam therapy, and carbon-ion therapy.26,27 Furthermore, our ability to deliver precision medicine is rapidly evolving as molecular markers (eg, RUNX3 in chondrosarcomas) increasingly provide stratification of tumor subtypes to guide treatments and prognostication.28 Recently, the AO Spine Tumor Knowledge Forum published a seminal series of multicenter analyses finding that adherence to Ennekens principles resulted in a >25% reduction in local recurrence of chordomas, osteosarcomas, and chondrosarcomas.29-31 Important oncological principles such as this are covered in “Spine Oncology – Primary Spine Tumors,”32 which provides an overview of the basic tenets of managing a primary spinal tumor followed by an insightful discussion into recent advances across all domains of primary spinal oncology.

Metastatic Tumors

Our understanding of metastatic spinal tumors has been greatly advanced by countless high-impact discoveries in cancer research throughout the body including paradigm shifts in the role of radiotherapy, new combinatorial chemotherapies, and the advent of tumor-specific antibodies. The modern treatment era places increased emphasis on early tissue diagnosis to permit genetic analysis, risk stratification (eg, BRAF mutation in melanoma), and to develop personalized treatment plans (eg, nonsmall cell lung cancer with an EGFR mutation may respond better to erlotinib and pemetrexed–cisplatin).33-35 While the integration of these data with existing prognostic scores (eg, Tomita, Tomita, Tokuhashi, etc) is ongoing, it is critical for all care providers to remain aware of relevant markers as they can substantially alter patients’ long-term treatment plan. From a surgical perspective, several techniques have decreased morbidity and made interventions more acceptable to patients. An example is polymethylmethacrylate augmentation which has been shown to reduce pain in a study (n = 47) of patients with spinal metastases.36 Other strategies include MIS tubular/endoscopic resections, polyetheretherketone (PEEK) cages, and percutaneous instrumentation.37 These important topics are discussed in depth in the “Spine Oncology - Metastatic Spine Tumors”38 article along with a thorough review of the literature and meaningful perspectives from key opinion leaders in the field.

TRAUMA

Spine Trauma

Tremendous advances in our understanding of biomechanics, materials engineering, and critical insights into the pathophysiology of injury have driven a rapid evolution in how we manage individuals with spinal trauma. Unfortunately, this makes remaining up-to-date evermore challenging. The unique “Controversies in Spinal Trauma and Evolution of Care”39 article synthesizes the literature on 8 of the most relevant and rapidly evolving topics in spine trauma including (1) historical and modern classification schemes, such as the Thoracolumbar Injury Classification and Severity scale; (2) early vs late surgery for spinal canal compression; (3) the management of thoracolumbar burst fractures; (4) the management of vertebral compression fractures (eg, medical therapy vs vertebroplasty vs surgical stabilization); (5) the importance of global sagittal balance and spine pelvis of alignment in trauma; (6) therapeutic hypothermia for spinal cord injury; (7) lumbar cerebrospinal fluid (CSF) drainage to enhance cord perfusion pressure; and (8) microstructural magnetic resonance imaging (eg, diffusion tensor imaging). Each section provides a discussion of pertinent studies and outlines key ongoing controversies to remain aware of. The article also highlights critical knowledge gaps where additional data will be required before clear management algorithms can be defined.

Spinal Cord Injury

Traumatic spinal cord injuries have a devastating impact on patients, caregivers, and society as a whole with direct lifetime costs exceeding $1.1 to 4.6 million USD per patient.40 This underscores the need to generate effective neuroprotective and neuroregenerative therapies by aligning clinical, translational, and basic science research.41-42 “Traumatic Spinal Cord Injury – Repair and Regeneration”43 outlines the pathophysiology of spinal cord injury and provides a working knowledge of current management paradigms aligned with the American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) joint section committee recommendations and an upcoming 2017 AOSpine guideline. Discussions on steroids for spinal cord injury, blood pressure augmentation, and the importance of early surgical decompression are expanded to reflect ongoing debates in the field. The article also explores exciting pharmacological therapies on the cusp of translation including riluzole, minocycline, fibroblast growth factor, anti-Nogo antibody, Cethrin (BioAxone Biosciences, Cambridge, Massachusetts), hepatocyte growth factor, and granulocyte colony-stimulating factor. This is followed by an overview of cutting-edge nonpharmacological strategies such as CSF drainage, spinal cord stimulation, biomaterials, and promising cell-based therapies (eg, neural precursor cells, mesenchymal stem cells, olfactory ensheathing cells, etc). Overall, readers are provided with an all-encompassing look at current and future approaches to managing traumatic spinal cord injury.

INFECTION

With the advancing age of patients worldwide and the increasing burden of chronic illnesses, surgical site infections (SSIs) continue to represent a significant source of readmission and morbidity for patients undergoing spine surgery. The “Prevention of Surgical Site Infection in Spine Surgery”44 article is a must-read primer on the epidemiology, pathogenesis, costs,
Complication rates continue to be lower for device procedures, such as betadine wound irrigation, aseptic showers, vancomycin powder, and silver-impregnated dressings. Overall, this engaging review provides a comprehensive look at SSIs with new information to be gleaned for readers at all levels.

DEFORMITY

The management of pediatric and adult deformity has dramatically changed over the last 2 decades across the spectrum from initial radiographic assessment and surgical planning through postoperative care. For example, recognition of the importance of multiplanar alignment has driven the evolution of pre-, intra-, and postoperative imaging as we move into the era of high-fidelity 3-dimensional reconstructions and automated radiographic measurements.45,46 Complication rates also continue to be reduced by identifying critical risk factors (eg, frailty) and stratifying patients using predictive analytics.47,48 This has been achieved by closely aligning biotechnology and surgical research to generate innovative tools such as magnetically controlled growing rods for children, reinforced rod techniques for pedicle subtraction osteotomies, and MIS approaches to deformity.49-51 The “Recent and Emerging Advances in Spinal Deformity”52 article provides a comprehensive overview of adult thoracolumbar, cervical, and pediatric deformity with an emphasis on quality-of-life outcome metrics. The article also highlights key terms and measurements relevant to all spine surgeons with outstanding illustrations to distil complex concepts.

COST ANALYSIS

Establishing the cost–benefit relationship for spine procedures is paramount as the economic burden of degenerative spinal pathologies rises and pay-for-performance reimbursement becomes commonplace.53 The question is complex, however, as real-world benefits can be challenging to accurately quantify using patient-reported outcome measures. Moreover, variability in clinical outcomes and treatment costs can be substantial between individuals undergoing spine surgery. “Bending the Cost Curve – Establishing Value in Spine Surgery”54 is a unique retrospective analysis (n = 1454) of prospective, longitudinal registry data on adults with degenerative lumbar spine disease where nonoperative treatment was not successful. Quality-adjusted life years, derived from validated scores, were analyzed against total costs (ie, both direct and indirect costs to society) to establish the cost curve and guide analyses. The study found that at a population level (based on Quality Outcome Database data), disability and quality of life substantially improved 1 year after lumbar spine surgery; however, the effects were highly variable. Importantly, at the individual level, one-eighth of patients did not benefit from surgery at all and one-third found no meaningful benefit creating a challenge for spine surgeons in an era of increasing scrutiny. The article provides an insightful interpretation of the data and a thought-provoking discussion around how value is defined, the relevance of perspective, how to address variability, and the importance of granularity in cost analyses.

TECHNOLOGICAL ADVANCES

Robotics and Navigation

CAN has revolutionized spine surgery by providing real-time data based on intraoperative radiography (eg, CT, MRI, etc), fiducials, and/or registration points. The benefits are particular apparent in oncological resections with distorted anatomy and unclear margins where MRI coregistration often provides data beyond the realms of direct vision.35 Other applications, such as thoracolumbar pedicle screw placement, continue to be a source of debate as several meta-analyses of thousands of screws have shown superior accuracy with CAN vs freehand techniques but no statistically significant difference in patient outcomes.56,57 Nonetheless, the applications for CAN continue to broaden, which, combined with the digitization of patient anatomy, has facilitated the introduction of robotic surgical technologies into spine operating rooms. A pioneer of this space is the shared-control SpineAssist/Renaissance (MAZOR Robotics Inc., Orlando, Florida) robot which has been shown in certain studies to insert percutaneous or open pedicle screws with greater accuracy than fluoroscopic- or navigation-guided techniques.58 “Navigation and Robotics in Spinal Surgery: Where Are We Now?”59 discusses the utility of SpineAssist, ROSA (Medtech, Montpellier, France), and the Da Vinci Surgical System (Intuitive Surgical, Norcross, Georgia) in detail as they relate to patient outcomes, surgical time, and surgeon safety. The article also provides an exciting look into the future of our operating rooms and how ongoing advances in engineering will impact surgical practice.

Neuromodulation

Dorsal epidural spinal cord stimulation has emerged as an effective therapy for refractory neuropathic pain, hyperalgesia, and allodynia. While the mechanism of action continues to be investigated, level I recommendations exist to support spinal cord stimulation for persistent postoperative neuropathic pain, chronic inoperable limb ischemia, complex regional pain syndrome, painful diabetic neuropathy, and treatment refractory angina.60-62 Complication rates remain relatively low for device migration (12%), loss of treatment effect (4%), wound complications (5%), and more serious epidural hematomas (0.19%) and spinal cord contusions (0.1%).63 Furthermore, efficacy continues to improve through technological advances such as novel pulse waveforms, high-density stimulation, dorsal root ganglion targeting, feedback loops, and innovative MIS techniques. “The Advancing Role of Neuromodulation for the Management of
Chronic Treatment-Refractory Pain covers these important topics in depth while also providing thoughtful algorithms to guide clinicians in appropriate device selection for their patients.

Osteobiologics and Biomaterials

Osteobiologics and biomaterials have become an integral part of modern spine surgery bringing advances in engineering directly to patients. Interbody cages, for example, have been used since the 1980s but their composition has gradually evolved from the stainless steel Bagby cage to fusion-promoting titanium-PEEK composites, hydroxyapatite-coated implants and silicon nitride ceramics. BMP-2 is another prime example of a novel product which activates serine-threonine kinase receptors on cells to induce robust osteogenesis even in patients with otherwise poor bone quality. While its use was curtailed after several studies identified complications associated with rhBMP-2, there remain select cases where it is an important adjunct. With advances in stem cell technology, biomaterials are also seeing a renaissance as vectors for delivering cells and slow-release growth factors. Collagen, poly-L-lactic acid (PLLA), hyaluronan-methylcellulose, demineralized bone matrix, and self-assembling peptides have all seen increased integration into spine surgery at a clinical or research level. The “Novel Osteobiologics and Biomaterials in the Treatment of Spinal Disorders” article covers these topics in detail and provides fascinating discussions on injectable biomaterials for radiculopathy, the role of tumor necrosis factor-α inhibitors for pain, and where we are moving with stem cell technologies for regenerating IVDs.

CONCLUSION

This “AOSpine North America: Future Advances in Spine Surgery” issue is a collaborative effort bringing together expertise from a diverse group of institutions with the hope of disseminating state-of-the-art techniques and stimulating excitement in the field. Each article is authored by several key thought leaders in an effort to minimize bias and provide varied perspectives. We hope the content will be thought provoking and provide insight into the future of spine care.

Disclosures

Dr. Hsu is a board or committee member with AAOS, Cervical Spine Research Society, Lumbar Spine Research Society, and North American Spine Society. He is a paid presenter/speaker and consultant for AONA. He is also a paid consultant of Baxter, Bioventus, CeramTec, Globus, Graily, Lifenet, Medtronic Sofamor Danek, Mirus, Relievant, Rti, SI Bone, and Stryker, and receives research support from Medtronic. The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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