What's new in spine surgery

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**Specialty Update**

**What’s New in Spine Surgery**

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**What’s New in the Treatment of the Cervical Spine**

The treatment of cervical myelopathy continues to be debated, with more data suggesting that mildly symptomatic or asymptomatic patients can be observed and that, if surgery is performed, both anterior and posterior approaches have similar outcomes. Similarly, the results of a large prospective study analyzing the outcomes for geriatric patients with odontoid fractures may provide insight into the best treatment, either nonoperative or operative. Positive movement in the regulatory status of posterior cervical fixation has occurred, and a better understanding of a simple method to prevent surgical site infection has emerged.

**Cervical Myelopathy**

Two surgical approaches are commonly used for the treatment of cervical spondylotic myelopathy: (1) anterior decompression and arthrodesis and (2) laminoplasty. In most cases, the former directly decompresses the offending ventral abnormality, but it can be associated with the complications of dysphagia, graft extrusions, and complex cerebral spinal fluid leaks. Laminoplasty is more extensible, but, in general, requires a neutral or lordotic spine in the sagittal plane and is associated with a higher rate of C5 nerve root palsy. Recently, multiple clinical trials have demonstrated that both treatments have resulted in substantial functional, neurologic, and quality-of-life improvements, but no differences have been found between the two treatments. Reoperation rates have been greater following anterior treatment.

**Odontoid Fractures**

Geriatric odontoid fractures are difficult to treat, having substantial morbidity and a one-year mortality rate of >20%. In a multicenter study, 159 patients were followed for twelve months. Treatment decisions were based on shared decision-making between surgeons and patients. One-third of patients were managed conservatively. The two groups were similar in terms of age, demographic characteristics, and baseline medical status. The overall mortality rate was 18.1%, with a rate of 25.9% in the conservative treatment group and 13.9% in the surgical treatment group. Statistical analysis that controlled for confounding variables showed that conservative treatment, older age, and more comorbidities were associated with higher mortality rates. In the nonoperative treatment group, seventeen of fifty-nine patients had development of non-union, of whom thirteen required later C1-C2 arthrodesis. In this nonoperative treatment group, clinical outcomes were similar regardless of whether healing occurred or not. No patient who was managed nonoperatively had neurologic deterioration.

**Lateral Mass Fixation**

Posterior cervical screw fixation is widely used and is considered standard care. The regulatory status of these devices is problematic as they are currently unclassified and their use is considered off-label. This has several negative consequences. Training at hands-on courses in their proper use is prohibited, and therefore training usually only occurs in the operating room. Other negative effects are that payment for procedures involving “non-approved devices” may be denied, research and development is stifled, and medicolegal and informed consents are complicated. In September 2012, the U.S. Food and Drug Administration (FDA) was petitioned to classify these devices to a Class-2 status. Independent systematic reviews were performed by the FDA and the Cervical Spine Research Society. In both cases, a fusion rate of >98% was found and low complication rates were noted. Currently, the FDA is preparing a proposed rule to change the classification

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to Class 2, meaning that the screws will be approved for their intended purpose.

**Surgical Site Infection**
Prevention of surgical site infection is an essential component of patient safety. With use of a large database, the rates of surgical site infection after various cervical spine surgical procedures were determined. The prevalence of surgical site infection was 0.45% for anterior cervical discectomy and arthrodesis, 0.97% for posterior decompression, and 1.82% for posterior spinal arthrodesis. Surgical site infections resulted in a fourfold increase in mortality, a fifteen-day longer duration of hospitalization, and a mean increased cost of $32,000. One method that has been proposed to prevent surgical site infection is the placement of vancomycin powder into the wound at the time of closure. In an animal study, spinal wounds containing instrumentation were inoculated with *Staphylococcus aureus*. The placement of vancomycin powder into the wound eliminated infection in all animals, whereas all control animals had positive wound cultures. No cytotoxic effects were observed in association with vancomycin. In a clinical cohort study, patients undergoing posterior decompression and arthrodesis for the treatment of myelopathy who were managed with vancomycin powder were compared with historical controls. The rate of surgical site infection was reduced from 15% to none. Systemic distribution of vancomycin and adverse events were not seen. These findings are consistent with those of other reports documenting reduction of the rate of surgical site infection with use of vancomycin powder. The risks to the local tissue in association with the use of vancomycin powder appear to be minimal, although the likelihood of development of resistant organisms over time with long-term use is unknown.

**What’s New in Biologic Topics Related to the Spine**
The trend toward decreased use of second-site iliac crest bone graft harvest and increased use of bone graft substitutes continued in 2012.

**Recombinant Osteoinductive Proteins**
In 2012, there was a continued focus around potential local adverse events associated with recombinant human bone morphogenetic protein-2 (rhBMP-2). In June 2011, a series of articles, editorials, press releases, and letters to the editor highlighted major safety risks potentially associated with rhBMP-2. In June 2011, publications suggested three main concerns: (1) that rhBMP-2 increased the rate of retrograde ejaculation in patients managed with anterior lumbar interbody arthrodesis (the approved indication), (2) that rhBMP-2 resulted in increased rates of radiculitis, infections, and seromas, and (3) that rhBMP-2 was associated with a higher incidence of cancer. Subsequent studies suggested that many of the potential side effects seem to be approach-specific, if not approach-related.

Whether rhBMP-2 increases the rate of retrograde ejaculation remains unclear. A ten-year cohort controlled study from the Stanford University experience demonstrated a twofold increase in retrograde ejaculation in the rhBMP-2 cohort, similar to the findings of the original rhBMP-2 FDA clinical trial. Another study, from Denver, compared patients undergoing total disc replacement with those undergoing anterior interbody arthrodesis with rhBMP-2 and showed no difference in the incidence of retrograde ejaculation related to rhBMP-2. An alternative explanation is related to surgical exposure (transperitoneal versus retroperitoneal) and technique, suggesting that rhBMP-2 was not responsible for higher rates of retrograde ejaculation. There has been further clouding of this issue related to the lack of an exact definition of retrograde ejaculation and how it is measured.

The issue of radiculitis, presumably due to neuroinflammation as reported in some basic science studies, initially was raised on the basis of reanalysis of relatively small clinical trials. Most recent analyses have suggested that there is not an increased incidence of transient radiculitis following posterolateral use of rhBMP-2.

A recent review of nearly 1400 patients who were managed over seven years showed that seroma formation was slightly higher among patients managed with rhBMP (3.2%) as compared with demineralized bone matrix (2.0%) and autograft (1.4%), but these differences were not significant. The same study showed an overall infection rate of 3.1%, with no differences due to BMP. These data support the 55,000-patient Scoliosis Research Society (SRS) study and the 16,000-patient Medicare database study that showed no increases in the incidences of infection, hematoma/seroma, or overall complications due to BMP. These studies did show higher hospital charges, but fewer patients were discharged to skilled nursing facilities.

Perhaps the most concerning issue that has been raised is the potential association of rhBMP-2 with cancer. The approved formulation of 6 to 12 mg delivered on an absorbable collagen sponge is not associated with any increased risk of cancer according to the manufacturer’s analysis and there is no FDA warning, although an external analysis of a relatively small data set led to a different conclusion. A review of 93,000 patients in the Medicare database who had undergone lumbar arthrodesis showed no increased risk of pancreatic cancer. In late 2012, the Wisconsin group presented a study of 467,000 Medicare patients and found a 6.2% decreased (not increased) risk of cancer associated with the use of BMP at the time of spinal arthrodesis.

Work continues on more efficient delivery strategies for BMPs that presumably will avoid the large early burst phase of release off current carriers. The early release, while important to initiate the healing cascade, if too great, can result in excessive vascular permeability, leading to many of the local side effects discussed above.
Other Bone Graft Substitutes
Although much focus remains on rhBMPs, their relatively high cost has continued to encourage research involving other bone graft solutions. Another animal study showed that platelet-rich plasma, with or without bone marrow, does not promote posterolateral spine fusion. Silicate-substituted calcium phosphate, various bone marrow/ceramic combinations, and bioglass continue to be studied for spine fusion bone graft extenders. Most studies have suggested that these approaches, including mesenchymal stem cells, still do not reach the osteoinductive potency of rhBMPs.

Biologic Treatments for Disc Degeneration
Progress toward biologic treatments to prevent or retard disc degeneration or to heal anular defects continues at a slow pace. Most studies in the past year have been in vitro proof-of-concept studies, which are difficult to translate into the in vivo setting.

What’s New in Spinal Deformity Surgery
There were 129 papers presented from the podium at the recent SRS annual meeting, held from September 5 to 8, 2012, in Chicago, Illinois.

Idiopathic Scoliosis
There remains considerable interest in selective thoracic arthrodesis for the treatment of false double-major curve patterns, in which the thoracic curve is bigger than the lumbar curve but the lumbar curve is quite structural with substantial rotation and apical deviation. Several presentations at the recent SRS annual meeting in Chicago addressed this point. The only conclusions that could be made were that there was substantial variability among surgeons with regard to the decision to perform a selective thoracic arthrodesis and quite a bit of variability in terms of the outcome. It was very difficult to predict outcome on the basis of “rules.” At least one paper strongly suggested that surgical treatment of adolescent idiopathic scoliosis is cost-effective, with a cost of $8182 per quality-adjusted life-year (QALY), which compares favorably with coronary artery bypass surgery and total knee arthroplasty.

One interesting study compared pedicle screw constructs with hybrid constructs and investigated whether patients managed with mostly pedicle screw constructs had fewer returns to the operating room. Patients managed with pedicle screw constructs had decreased rates of return to the operating room as compared with those managed with hybrid constructs (3.5% versus 12.6%).

Adult Spinal Deformity
There is quite a bit of work currently being done to assess the cost-effectiveness of adult spinal deformity surgery. Most studies have demonstrated that this group of patients has significantly improved outcomes at two years of follow-up. However, the prevalence of neurologic deficit is quite high, as is prevalence of both proximal junctional kyphosis and catastrophic failure at the proximal junction. At least one study demonstrated that adult spinal deformity impacts physical function to a similar degree as diabetes and heart disease.

With long fusions to the sacrum, it is mandatory to protect sacral screws with iliac fixation. Whether it is better to employ iliac fixation or what is considered S2 alar iliac fixation is not clear. The S2 alar iliac fixation technique has been compared with first-generation iliac screws and appears to be advantageous from the standpoint of less prominence posteriorly. Current iliac fixation techniques utilize third-generation, smaller iliac screws and more effective burial of the implants. With both techniques, the morbidity associated with either iliac or S2 alar iliac fixation seems to be small, and both techniques seem to be very effective for protecting sacral screws.

Three-column osteotomies are becoming increasingly popular for the treatment of severe deformity in adults. These procedures are associated with a substantially higher complication rate in adults than in children.

Neuromuscular Deformities
Surgical treatment in patients with cerebral palsy is associated with a very substantial wound infection rate (approximately 6.5%). Factors that increase risk of wound infection include the presence of a gastrostomy tube, large preoperative kyphosis, longer operative time, and increased age. The ability to walk and the presence of antibiotics in the bone graft are associated with a lower rate of infection. One important study compared life expectancy after surgical versus nonsurgical treatment of flacid neuromuscular scoliosis (Duchenne muscular dystrophy, spinal muscular atrophy, etc.). The study demonstrated that life expectancy was higher in the group managed with surgery than in the group managed without surgery.

Complications
Various strategies have been investigated in an effort to reduce the likelihood of deep wound infection following the reconstruction of a substantial spinal deformity. Most studies have suggested that intravenous administration of vancomycin as well as a cephalosporin is advantageous. Also, preoperative skin preparations are more popular now and the utilization of deep local antibiotics, especially vancomycin, seems to be beneficial.

Early-Onset Scoliosis
The concept of using instrumentation without arthrodesis for the treatment of spinal deformity in a pediatric patient with a progressive deformity that is not controllable with bracing or casting continues to be popular. The populations to which this concept most commonly applies are patients with congenital scoliosis and patients with juvenile or infantile scoliosis under the age of ten years in whom the triradiate cartilages are still open. There are many strategies,
The translational gap between animal models and clinical understanding of the signaling pathways associated with spinal cord injury continue to be a focus for clinical and translational research.

Timing of Surgical Intervention
The Surgical Treatment of Acute Spinal Cord Injury Study (STASCIS), a multicenter international prospective cohort study comparing change in American Spinal Injury Association (ASIA) Impairment Scale (AIS) following early or late surgical decompression for the treatment of cervical spinal cord injury, was recently completed. Early decompression was defined as that performed less than twenty-four hours after the injury, and late decompression was defined as that performed more than twenty-four hours after the injury. One hundred and thirty-one patients underwent early surgery at a mean of 14.2 hours after the injury, and ninety-one patients underwent late surgery at a mean of 48.3 hours. The groups were significantly different, with the early surgery group having a higher percentage of AIS grade-A and B patients and a higher rate of treatment with methylprednisolone. In multivariate analysis, adjusting for corticosteroid administration and injury severity (complete versus incomplete), there was no difference between the groups with respect to the odds of improving one AIS grade; however, there was a 2.8-fold increase in the odds of improving two AIS grades in favor of early surgical intervention. There were no differences between the groups in terms of the rates of complications or mortality. In subgroup analysis, patients who underwent early decompression and received methylprednisolone had the greatest neurologic improvement. Corticosteroids also improved outcomes regardless of the timing of surgical intervention. A major concern associated with methylprednisolone administration is the development of complications. However, based on the STASCIS data, a clinical prediction model of acute inpatient complications showed that not receiving methylprednisolone was correlated with a higher rate of complications.

Translational Research
There have been numerous recent advancements in our understanding of the signaling pathways associated with spinal cord injury and the regenerative potential of the spinal cord. The translational gap between animal models and clinical practice is daunting, but several studies are attempting to narrow this divide.

Although it was originally developed as an antibiotic more than thirty years ago, minocycline has demonstrated a consistent record as a neuroprotective agent in multiple human and animal models. A phase-I randomized clinical trial of the effects of high-dose minocycline on human spinal cord injury was recently completed. In this study, direct cerebrospinal fluid pressure monitoring with lumbar drains and early surgical decompression (performed less than twenty-four hours after the injury) were used in both groups. Very few side effects were attributed to the study agent. There were no differences between the groups among patients with thoracic spinal cord injury. Patients with cervical spinal cord injury who were managed with minocycline demonstrated a mean improvement of 14 points on ASIA motor scores in comparison with controls ($p = 0.05$). Patients with incomplete cervical injuries showed even greater improvement, although the difference was not significant. Although minocycline is promising, additional studies are needed to demonstrate its efficacy for the treatment of spinal cord injury.

Riluzole, a sodium channel blocker, potentially decreases neuronal injury after spinal cord injury by reducing cytotoxicity related to increasing calcium concentration and presynaptic release of glutamate. It has been approved by the FDA as a therapy for amyotrophic lateral sclerosis. A phase-I/II clinical trial completed enrollment in 2011. Although not published, the results are promising enough that a phase-III clinical trial is approved to start in 2013 (clinicaltrials.gov identifier NCT01597518).

Cellular-based therapies represent another target of translational research in multiple ongoing studies. A phase-I trial of intramedullary spinal cord transplantation of purified human neuronal stem cells in patients with complete (ASIA A) chronic thoracic spinal cord injury by StemCells (Newark, California) is currently enrolling patients in Switzerland. As the transplanted cells are not autologous, a period of immunosuppression is required. Preclinical data suggest that the transplanted cells localize to the area of injury, where they differentiate into perineurial cell lines, particularly oligodendrocytes, which can repair damaged myelin sheath and potentially can promote neural regeneration. TotipotentRX (Los Angeles, California/New Delhi, India) is currently enrolling patients for a phase-I/II study in India investigating the use of autogenous transplantation of hematopoietic-derived stem cells for the treatment of chronic spinal cord injury. The Miami Project to Cure Paralysis recently received FDA approval to begin a phase-I trial of autologous Schwann cell transplantation in humans with acute and chronic spinal cord injury. The study protocol requires biopsy of a sensory nerve, from which the Schwann cells are isolated and cultured prior to re plantation.

What’s New in the Treatment of the Lumbar Spine
Pathologies leading to lumbar spinal disorders continue to be one of the most challenging clinical problems.
Outcomes of Lumbar Spine Surgery

Outcomes following lumbar spine surgery are of high interest in this era of cost-effectiveness and utility of spinal surgery. One study examined the perioperative outcomes, complications, and costs associated with lumbar spinal arthrodesis in older patients with spinal stenosis and spondylolisthesis. The authors examined the United States Medicare claims database retrospectively. A final cohort of 1672 patients who had been managed with spinal arthrodesis was included. Fifty percent of the patients had spinal stenosis only, 10% had spondylolisthesis only, and 40% had both. The average age was seventy-one years, and the average length of hospital stay was 4.6 days. Forty-two percent of the patients had routine discharge, whereas the majority of patients (55%) were discharged to an outside facility. One in four patients underwent a reoperation on the lumbar spine within two years, and nearly half of the patients were readmitted because of a surgery-related complication. The authors highlighted the areas where improvements could be made in the effective delivery and costs of surgery for patients in this age group and with these diagnoses.

Other authors performed a comparative effectiveness and cost-utility analysis in which transfemoral lumbar interbody arthrodesis was compared with the medical treatment of lumbar spondylolisthesis. This was a prospective, longitudinal, observational cohort study of eighty patients at a single institution. The surgical treatment cohort had significant (p < 0.001) improvement in all outcome measures at two years, whereas comprehensive medical treatment failed to provide significant improvement. The two-year gain in QALYs was significantly greater after surgery than after medical treatment (mean, 0.43 compared with 0.06 QALY gained). The total two-year cost was significantly greater for surgical treatment. The authors concluded that lumbar arthrodesis, when compared with medical treatment, was cost effective and provided greater two-year improvement in terms of pain, disability, and quality of life.

Spinal Trauma

There have been several recent studies on traumatic injuries to the spine. One study compared the long-term results of operative and nonoperative treatment of thoracolumbar fractures in patients without neurological deficits. In this prospective, randomized, multi-institutional study, forty-seven consecutive patients with stable burst fractures were separated into two groups that received either operative or nonoperative treatment. After an average duration of follow-up of seventeen years (range, fifteen to twenty years), nineteen patients in the operative treatment group and twenty-three patients in the nonoperative treatment group were available for evaluation. The authors examined the United States Medicare claims database retrospectively. A final cohort of 1672 patients who had been managed with spinal arthrodesis was included. Fifty percent of the patients had spinal stenosis only, 10% had spondylolisthesis only, and 40% had both. The average age was seventy-one years, and the average length of hospital stay was 4.6 days. Forty-two percent of the patients had routine discharge, whereas the majority of patients (55%) were discharged to an outside facility. One in four patients underwent a reoperation on the lumbar spine within two years, and nearly half of the patients were readmitted because of a surgery-related complication. The authors highlighted the areas where improvements could be made in the effective delivery and costs of surgery for patients in this age group and with these diagnoses.

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Demographic Characteristics and Spinal Trauma

One group of authors presented a study that evaluated the effects of demographic characteristics, injury-specific factors, race/ethnicity, and insurance status on outcomes after spinal trauma with use data from the National Sample Program of the National Trauma Data Bank. The study involved a sample of 75,351 incidents of spine trauma in patients with an average age of 43.8 years. Increased age, male sex, Injury Severity Score, and blood pressure were significant predictors of mortality, whereas age, male sex, other mechanisms of injury, Injury Severity Score, and blood pressure influenced complications. Non-white and black/African-American race increased the risk of mortality. Lack of insurance was associated with an increased risk of mortality and with decreases in the number of days of hospitalization, the number of days in the intensive care unit, and ventilator time.

Appendix: Evidence-Based Orthopaedics

The editorial staff of The Journal reviewed a large number of recently published research studies related to the musculoskeletal system that received a Level of Evidence grade of I or II. Over 100 medical journals were reviewed to identify these articles, which all have high-quality study design. In addition to articles published previously in this journal or cited already in the Update, fourteen additional Level-I and II studies were identified that were relevant to spine surgery. A list of those titles is available with the online version of this article as a data supplement at jbjs.org. We have provided a brief commentary about each of the articles to help to guide your further reading, in an evidence-based fashion, in this subspecialty area.

Upcoming Meetings and Events Related to Spine Surgery

- The Scoliosis Research Society (SRS) Forty-seventh Annual meeting will be held on September 18 through 23, 2013, in Lyon, France. Web site: www.srs.org
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- The EuroSpine annual meeting will be held on October 2 through 4, 2013, in Liverpool, United Kingdom. Web site: www.eurospine.org
- The North American Spine Society (NASS) Twenty-seventh Annual Meeting will be held on October 9 through 12, 2013, in New Orleans, Louisiana. Web site: www.spine.org
- The Cervical Spine Research Society (CSRS) Forty-first Annual Meeting will be held on October 11 through 13, 2013, at the Century Plaza Hyatt Regency in Los Angeles, California. Web site: www.csrs.org
- The AANS/CNS (American Association of Neurological Surgeons/Congress of Neurological Surgeons) Section on Disorders of the Spine and Peripheral Nerves Annual Meeting will be held on March 5 through March 8, 2014, at Walt Disney World Swan and Dolphin Resort in Orlando, Florida. Web site: http://spinesection.org
- The Federation of Spine Associations will present the spine program at Specialty Day at the Annual Meeting of the American Academy of Orthopaedic Surgeons (AAOS) on March 14, 2014, in New Orleans, Louisiana. Web site: www.aaos.org
- The International Society for the Advancement of Spine Surgery (ISASS) Fourteenth Annual Meeting will be held on April 29 through May 2, 2014, in Miami, Florida. Web site: www.isass.org
- The International Society for the Study of the Lumbar Spine (ISSLS) annual meeting will be held on June 3 through 7, 2014 in Seoul, Korea. Web site: www.issls.org

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