What's new in spine surgery

Keith H. Bridwell
Washington University School of Medicine in St. Louis
Paul A. Anderson
University of Wisconsin Hospital
Scott D. Boden
Emory University School of Medicine
Alexander R. Vaccaro
Rothman Institute at Jefferson
Jeffrey C. Wang
University of California - Los Angeles

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**Specialty Update**

**What’s New in Spine Surgery**

By Keith H. Bridwell, MD, Paul A. Anderson, MD, Scott D. Boden, MD, Alexander R. Vaccaro, MD, and Jeffrey C. Wang, MD

| What’s New in the Treatment of the Cervical Spine | Six-year outcomes from Europe are encouraging, with patients maintaining clinical improvement and motion. Adjacent-segment disease appears to progress in patients with preexisting disease but not in its absence.

From outside the United States, there have been case reports of complications, including the late development of central stenosis secondary to osteophyte formation, fracture of a vertebral body during insertion, spontaneous fusion, expulsion of the device, and kyphotic angulation. Despite these cases, the results of disc arthroplasty are encouraging, but longer follow-up is needed.

Early return to function is a hypothetical benefit of arthroplasty. In general, arthroplasty does not require immobilization and patients are allowed to rapidly return to full function. The median time to return to work is significantly better following arthroplasty than it is following fusion. This effect is even greater in patients receiving Workers’ Compensation. From a socioeconomic perspective, this may mitigate the additional cost of the implant and the additional surgical time.

**Complications**

Wang et al. reported on the complications and mortality associated with surgical treatment in patients with degenerative cervical spine disease. That study was a retrospective analysis of the Nationwide Inpatient Sample (a sample of hospital discharges). Over a ten-year period, 0.3% of hospital admissions were for the treatment of cervical spine disease. Complications based on specific disease codes were present in 3.9% of the patients, with an overall mortality rate of 0.14%. Multivariate analysis identified risk factors for complications, including age (more than seventy-four years), a diagnosis of myelopathy, a posterior fusion alone, or combined anterior-posterior fusion.

Dysphagia is an under-recognized morbidity after anterior cervical surgery. Using an accepted outcome instrument, patients maintain clinical improvement and motion.

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**Disclosure:** The authors did not receive any outside funding or grants in support of their research for or preparation of this work. One or more of the authors or a member of his or her immediate family received, in any one year, payments or other benefits in excess of $10,000 or a commitment or agreement to provide such benefits from a commercial entity (Medtronic, Stryker, Pioneer Surgical Technology, St. Francis Medical Technologies). Also, a commercial entity (Medtronic, Osteotech, Synthes, Abbott Spine, DePuy) paid or directed in any one year, or agreed to pay or direct, benefits in excess of $10,000 to a research fund, foundation, division, center, clinical practice, or other charitable or nonprofit organization with which one or more of the authors, or a member of his or her immediate family, is affiliated or associated.

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Specialty Update has been developed in collaboration with the Council of Musculoskeletal Specialty Societies (COMSS) of the American Academy of Orthopaedic Surgeons.
Lee et al. found that dysphagia was present in >50% of patients at one month and as many as 15% at two years. Risk factors included female gender, revision procedures, and multilevel procedures. Ischemia of the upper esophageal sphincter mucosa resulting from the use of soft-tissue retractors may be the cause of postoperative dysphagia. Maintaining the endotracheal balloon pressures at <20 mm Hg, intermittent relaxation of retractors, and cuff reinflation after the retractors are place are all strategies that may decrease dysphagia.

Myelopathy
Expansive laminoplasty for decompression in patients with multilevel spinal cord stenosis and myelopathy generally has been shown to have an outcome similar to that of anterior decompression and fusion. Laminoplasty avoids problems with fusion but has been associated with kyphotic deformity and chronic neck pain. A number of strategies have been described to decrease this tendency. Liu et al. preserved the spinous process-ligament-muscle complex with use of an osteotomy at the base of the spinous process reconstructed with wire fixation. Thirty patients had a mean increase of 9° of lordosis, and no patient had increased kyphosis. Other approaches to minimize neck pain include avoiding C7 laminoplasty altogether and performing a laminectomy rather than a laminoplasty at C3; this affords greater retention of the musculature attachments to C2. These techniques have been associated with diminished axial pain in case series. Their acceptance will require better-designed studies to prove their safety and efficacy.

In the study by Miyata, forty patients who had postoperative ossification of the posterior longitudinal ligament following a French-door type of laminoplasty were evaluated with dynamic magnetic resonance imaging. The author found that the cord had shifted posteriorly and was adequately decompressed. This study again validates that posterior decompression allows posterior cord translation away from the ventral pathway.

Despite surgical treatment, ossification of the posterior longitudinal ligament appears to progress in the majority of patients and can lead to recurrent symptoms. No means to decrease this tendency have been developed. Furthermore, it is not known if fusion will likely increase or decrease this phenomenon.

An important controversy is how to treat and counsel patients who have cervical stenosis but are asymptomatic. Recent reports from the Cervical Spine Research Society have shown that 30% of patients with stenosis experienced minor trauma and that half of those will deteriorate neurologically. Future studies should determine if a much more aggressive surgical approach can prevent neural damage.

Spinal Cord Monitoring
Intraoperative neurophysiologic monitoring during cervical spine surgery has not been shown to increase patient safety or to have a positive cost benefit. Smith et al. reviewed 1039 cases of decompression for non-myelopathy monitored with somatosensory evoked potentials and found a 1% incidence of any changes. All changes in somatosensory evoked potentials were corrected by normalizing blood pressure. There was one nondetected cord deficit, and no differences were identified between patients who were monitored and those who were not. In patients with myelopathy, transcranial motor evoked potentials appear to identify C5 nerve root lesions in a majority of cases, although they have not been shown to be useful in preventing injury to this nerve root.

What’s New in Biologic Topics Related to the Spine
Biologic tools for reconstruction and regeneration continue to be an important focus of research related to the spine today. There are continued efforts to enhance the process of achieving spine fusion and to eliminate the need for autogenous iliac crest bone graft harvest. Since the United States Food and Drug Administration’s (FDA) post-marketing approval of recombinant human bone morphogenetic protein-2 (rhBMP-2) in 2002 and the creation of a Humanitarian Device Exemption for rhBMP-7 late in 2004, the era of recombinant bone morphogenetic proteins for use in spine fusion has continued to blossom. Given the limited access (with only two companies producing approved BMPs) as well as their relatively high cost, there has been renewed interest in promoting less expensive and potentially unvalidated alternative bone-graft substitutes. Finally, while an increasing amount of research continues to be focused on understanding the biology of the intervertebral disc and on developing biologic strategies to retard or reverse degeneration, these treatments still seem to be quite far from clinical practice.

Recombinant Osteoinductive Proteins
The initial clinical studies on the use of rhBMP-7 (OP-1; Stryker Biotech, Hopkinton, Massachusetts) for posterolateral spine fusion yielded fusion success rates of 50% to 70% on radiographs, and these modest fusion rates were attributed to the use of a “more challenging” noninstrumented spine fusion model. In 2006, nineteen patients with degenerative spondylolisthesis were entered into a prospective, randomized, controlled study of instrumented fusion. Patients were randomized to receive OP-1 putty alone (3.5 mg of OP-1 per side) or local autograft with hydroxyapatite-tricalcium phosphate granules. The fusions were evaluated with plain radiographs and computed tomographic scans. Sixteen patients who showed radiographic evidence of fusion underwent instrumentation removal and surgical exploration of the fusion site. Although seven of the nine patients managed with OP-1 were thought to have fusion on the radiographs, only four of the seven actually had fusion at the time of exploration, for an overall OP-1 fusion rate of four of nine. In contrast, nine of the ten control patients who were managed with local bone grafts showed fusion. Long-term follow-up is required to determine the clinical significance of these findings.
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graft were thought to have fusion on radiographs and seven of the nine actually had fusion at the time of exploration, for an overall autograft fusion rate of seven of ten. Although this difference was not significant because the study was under-powered, the fusion rate of approximately 50% associated with the use of OP-1 in patients managed with an instrumented fusion is consistent with the numbers reported in studies of uninstrumented fusion and is still not at a level equal or superior to that of autograft. It is believed that the data from the OP-1 posterolateral United States clinical trial will remain under review by the FDA for consideration for post-marketing approval.

Although rhBMP-2 (INFUSE; Medtronic Sofamor Danek, Memphis, Tennessee) has been approved by the FDA for anterior lumbar interbody fusion, much physician-directed use has occurred in the posterolateral spine. A subset of data from an investigational device exemption study involving the use of a higher concentration of rhBMP-2 (20 mg BMP-2 per side) on a compression-resistant matrix (AMPLIFY; Medtronic) has been published. The report included ninety-eight patients from a prospective, randomized study in which AMPLIFY was compared with iliac crest bone graft in patients undergoing a single level instrumented posterolateral lumbar fusion. In this subset of patients, the radiographic fusion rate was 88% for the AMPLIFY group and 73% for the iliac crest bone graft group (p = 0.05). This was the first time that a recombinant BMP demonstrated superiority over autogenous bone graft. With the outcome measures used, no substantial clinical benefit was detected in association with the avoidance of harvesting an iliac crest bone graft. Readers should note that the BMP formulation comprising AMPLIFY is different (with respect to dose and carrier) than the currently available INFUSE formulation. In another study, the approved INFUSE kit was used in addition to iliac crest cancellous bone graft for instrumented posterolateral fusion. The use of INFUSE in combination with iliac crest bone improved the fusion success rate (as determined with thin-slice computed tomography scans) from 77% with iliac crest graft alone to 97% with iliac crest graft plus one large Infuse kit (6 mg BMP-2 per side) wrapped around local bone as a bulking agent. This finding suggests that the current kit, while likely not sufficient as a stand-alone graft substitute for the posterolateral spine, can provide a significant enhancer effect, improving the success of autogenous bone graft.

A primary concern with off-label use of recombinant BMPs relates to local adverse events. The three most commonly reported local side effects have been heterotopic bone formation in the surgical approach track, transient bone resorption when used near exposed cancellous bone, and sterile seroma fluid collections and/or local edema. Most of these local side effects are believed to be related to the surgeon’s use of too much BMP either by increasing the concentration of the growth factor or by overstuffing the defect, which can result in a higher concentration or leakage of BMP into the surrounding tissues. Two reports have described perioperative swelling in the cervical spine, again most often in association with excessive BMP doses and with the implant being placed outside the structural cage or ring. Surgeons who are encountering these local side effects with any regularity should carefully examine their technique to limit the exposure of BMP directly to cancellous bone (e.g., through less aggressive end plate decortication) and should avoid the use of excessive amounts of BMPs in small spaces or overpacking of the BMP implants.

Other Bone-Graft Substitutes

Although much focus remains on recombinant osteoinductive proteins, their relatively high cost has continued to encourage research involving other bone-grafting solutions. A recently published study demonstrated the failure of platelet concentrates to improve spine fusion healing. This study adds to a growing body of literature suggesting that platelet gels either inhibit or have no effect on spine fusion healing. In addition, an animal study confirmed that platelet-derived growth factor, transforming growth factor-beta, and platelet gel inhibited the BMP activity in demineralized bone when implanted together in animals. While platelet gels may serve a purpose for impaired wound-healing, their role in promoting bone formation remains in question.

A recently published animal study investigated the role of simvastatin in achieving posterolateral spine fusion in rabbits. Statins have been shown to increase the expression of BMPs and may enhance bone formation in certain situations. In this study, the systemic administration of simvastatin did not positively or negatively affect spine fusion. It is possible that local administration of statins may have more profound effects.

Interest in mesenchymal stem cells has increased with the introduction of two mineralized allograft products that are claimed to have cryopreserved stem cells. These products are claimed to immunodeplete the non-stem cells from allograft and to provide a mineralized scaffold with allogeneic stem cells. Since these products are regulated as “minimally manipulated tissues,” little outcome data are available. The studies that are under way may not include the proper controls to assess whether the stem cells are providing any increased healing in comparison with the allograft alone. These, as well as other, minimally manipulated products that are claimed to have bone-healing potential must be carefully evaluated by surgeons because the FDA does not require definitive proof of bone-enhancing capability. In general, the number of stem cells present in bone marrow is relatively small, and without specific signals (e.g., BMP) it is not clear whether sufficient numbers of cells are present to initiate bone formation de novo.

Biologic Treatments for Disc Degeneration

Progress toward biologic treatments to prevent or retard disc degeneration continued at a slow pace. Continued evidence of
beneficial effects of recombinant BMPs (BMP-7, BMP-2, growth differentiation factor-5) on disc metabolism in animals has prompted the planning of a clinical trial to investigate the response in humans. A majority of this preclinical work has been performed with OP-1, which can prevent disc height loss after needle puncture injury and can restore disc height that has been already lost after anular puncture in rabbits. Although this technology is a long way from clinical use, it is worth monitoring developments in this area, which could ultimately provide a groundbreaking technology for the treatment and prevention of many degenerative spine disorders.

What’s New in Spinal Deformity Surgery

Over the past year, many articles and presentations addressed the etiology of adolescent idiopathic scoliosis and the treatment of early-onset scoliosis as well as congenital spinal deformity, particularly thoracic insufficiency syndrome. There also have been advances in the treatment of kyphosis, neuromuscular scoliosis, and spondylolisthesis. The Scoliosis Research Society (SRS) continues to be very interested in investigating complications of surgical treatment.

Etiology of Adolescent Idiopathic Scoliosis

Investigators from two centers presented papers at the recent SRS meeting that further emphasized the potential genetic markers and familial characteristics of idiopathic scoliosis. Identification of the etiology of idiopathic scoliosis remains the number-one research goal of the SRS.

Early-Onset Scoliosis

Several new methods are evolving to allow for continued growth with intermittent surgical lengthening of the spine for patients with infantile and juvenile scoliosis. Such techniques utilize bilateral instrumentation, intermittent distraction, and multiple fixation points at the top and bottom and potentially at the apex of the deformity.

Congenital Spinal Deformity

The “titanium rib” technique with expansion thoracostomy has continued to gain popularity and momentum. Early data continue to suggest that distraction techniques associated with chest wall surgery can slowly lengthen the spine without creating a major neurologic deficit and with modest improvement in chest volumes. Documentation of changes in pulmonary function in these patients is not straightforward, however. One study, conducted at The Children’s Hospital of Philadelphia, did not demonstrate a significant improvement in lung function after expansion thoracostomy surgery. According to one multicenter study presented at the SRS meeting, patients with thoracic insufficiency syndrome clearly had marked reduction in their quality of life when compared with other children on the basis of the Child Health Questionnaire.

Kyphosis

One excellent paper that was presented at the SRS annual meeting emphasized the risk of increased kyphosis and pain following implant removal because of idiopathic scoliosis. Previous presentations have emphasized the problems associated with implant removal in the adult population. It appears that this is a substantial concern in the teenage population as well. The extent to which changes in the deformity reflected bending of the fusion mass as opposed to motion at undetected pseudarthroses was not entirely clear.

Neuromuscular Scoliosis

Assessment of the benefits of surgical treatment for patients with cerebral palsy and spinal deformity is quite complex. Most previous studies have only assessed radiographic parameters as opposed to a patient/parent evaluation. One paper that was presented at the SRS meeting focused on eighty-one children with cerebral palsy (and their families) who were undergoing spinal fusion. The postoperative complication rate was high (33%). However, the family satisfaction rate was quite high (92%). Eighty-seven percent reported improvement in sitting balance, and 66% believed that quality of life had improved. Unfortunately, at this time, health-related quality-of-life measures for this population of patients are not standardized and validated.

Spondylolisthesis

Classification of spondylolisthesis has remained elusive. Authors from Boston, Montreal, and France, as part of a multicenter study, have identified two distinct groups regarding the sagittal alignment of patients with high-grade spondylolisthesis. Critical factors appear to be the orientation of the pelvis and the sacrum, the obliquity of the L5-S1 disc, and the degree of dysplasia of the L5 element.

Adolescent Spinal Deformity

There continues to be a substantial effort to investigate the results associated with the use of pedicle screw implants, particularly in the thoracic spine, for the treatment of adolescent idiopathic scoliosis. Most data suggest that correction is somewhat better in association with this technique than in association with techniques involving the use of either hooks or wires or a combination of hooks, wires, and screws. It appears that Cobb angle correction, translational correction, and rotational correction are all slightly better with pedicle screws than with other implants. Furthermore, for curves of between 70° and 100°, it appears that anterior and thoracoscopic releases frequently are not required if pedicle screw implants are used to achieve fixation at all levels. In terms of cost analysis, pedicle screw implants are expensive, but if they obviate the need for open or thoracoscopic anterior releases, this is offset by the shorter operating time, decreased surgical morbidity, and fewer days spent in the hospital and the intensive care unit than is the case with a combined approach. One potential dis-
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Advantage of the pedicle screw technique is that the hypokyphotic thoracic spine remains hypokyphotic postoperatively as most of the pedicle screw derotational techniques being employed now push anteriorly on the posterior convex spine. Furthermore, there is no clear evidence that the increased correction achieved with pedicle screw implants translates to higher Health Related Quality of Life scores on SRS surveys.

Adult Spinal Deformity
An SRS classification system for adult spinal deformity continues to evolve. This work is being accomplished by the Adult Spinal Deformity Committee of the SRS, led by Thomas Lowe, MD. The aspects of the classification include curve type, sagittal modifiers, distal lumbar degenerative modifiers, and global balance parameters. In addition, Frank Schwab, MD, has a very similar classification scheme, which is reflective of the likelihood of surgical intervention. Factors that predict the need for surgical treatment of adult scoliosis include sagittal and coronal plane decompensation, substantial rotatory subluxations, spinal stenosis symptoms, and deformity progression. The coronal Cobb angle itself is not a primary determinant for surgical intervention. It does appear the SRS Health Related Quality of Life instrument is far more responsive to change following the surgical treatment of adult spinal deformity than it is following the surgical treatment of adolescent deformity. With adolescent deformity, it appears that the only domain that substantially changes after surgery is the self-image domain, whereas with adult spinal deformity, changes typically are identified in all domains.

Complications after surgery for the correction of spinal deformity are more common in adults than in adolescents. These complications include pseudarthrosis, proximal and distal junctional kyphosis, and an extended recovery. RhBMP is being considered as an alternative or adjunct to reduce the pseudarthrosis rate in adults with spinal deformity. However, use of these products for posterior surgery constitutes an off-label use and is prohibitively expensive for many centers.

Complications
The Morbidity and Mortality Committee report to the membership at the annual SRS meeting was an exhaustive study of the complications of spinal fusion for the treatment of adult scoliosis. Adult patients who had idiopathic scoliosis were compared with those who had scoliosis of a purely degenerative origin. From 2003 to 2005, 2852 patients underwent spinal fusion for the treatment of adult scoliosis. The complication rate was significantly higher in the degenerative group than in the idiopathic group (15.6% compared with 12.3%; p < 0.01). The death rate was the same in both groups. The neurologic complication rate was 1.3% overall, with six documented spinal cord deficits (0.21%), but only one deficit was complete (0.04%).

What’s New in Spinal Cord Injury
Research in the area of spinal cord injury is making strides in understanding the mechanisms of secondary injury and the factors inhibiting axonal regeneration. Cell death not only occurs at the time of injury but also is due to a cascade of secondary events that result in further neurologic dysfunction. Multiple biochemical processes, including the production of reactive oxygen species, excitotoxicity from neurotransmitter release, and imbalances in ion concentrations at a cellular level, culminate in the death of neurons and supporting glial cells.

Spinal cord injury is followed by changes that inhibit the regrowth of axons and the reestablishment of neural connections. It was once thought that axonal regeneration could not occur within the central nervous system, but it is now understood that central nervous system axons can regenerate in the proper environment. Formation of a glial scar and production of inhibitory compounds in the extracellular matrix impede the regrowth of axons across the site of injury.

As a result of a better understanding of the multiple biochemical processes that result in secondary cell injury and the inhibition of axonal regeneration, many new therapies are being studied. In addition, new strategies are being investigated to bridge the gap across a damaged spinal cord segment.

Therapies to Reduce Secondary Injury
Historically, the investigation of spinal cord injury therapies has focused on the inhibition of lipid peroxidation and the use of anti-inflammatory drugs, but through a better understanding of the mechanisms leading to secondary injury, new investigational agents have targeted multiple areas of the biochemical cascades that lead to cell death. Calpain and caspase proteases are both upregulated and associated with secondary injury cascades in spinal cord injury. Recent studies on 6-shogaol, an apoptotic inhibitor, have shown significant improvements in hind-limb function in rodent models. Erythropoietin (EPO) and derivatives of this compound exert an anti-apoptotic effect in the setting of hypoxia and have been shown to improve cell survival after ischemic brain injury and spinal cord injury in rodent models. Polyethylene glycol (PEG), which is thought to interact with and stabilize injured cell membranes, has been shown to have neuroprotective properties in spinal cord injury models. Minocycline has been shown to have potent anti-inflammatory and neuroprotective properties after spinal cord injury and is currently being investigated in a preliminary clinical trial in Canada. Growth factors also have been studied extensively as a means to reduce secondary injury and also to improve nerve regeneration. Growth factors administered directly at the site of experimental spinal cord injury or via gene therapies have been shown to reduce cell death and to improve axonal regeneration.

Therapies to Promote Axonal Regeneration
Two therapies to promote axonal regeneration have been evaluated in clinical trials over the last three years, and a number of other potential therapies are being evaluated.
in laboratory studies. Rho, a small signaling protein, has been shown to result in the inhibition of axonal regeneration after experimental spinal cord injury. C3 transferase (C3), an inhibitor of Rho, was shown to have neuroprotective and regenerative properties in animal models. Cethrin (BioAxone Therapeutic, Saint-Laurent, Quebec), a combination of C3 with a transport sequence that helps the protein to cross cell membranes, showed encouraging results in a recent Phase-I/IIa multicenter clinical trial. The application of Cethrin in the epidural space at the time of decompressive or stabilization surgery in thirty-seven patients with American Spinal Injury Association (ASIA) type-A injuries resulted in improvement of at least one ASIA grade in 30% of the patients within six weeks. Historically, <5% of patients with an ASIA type-A lesion will have any improvement. Obviously, that study was small, but it warrants further clinical studies.

Although much research has been focused on reducing the immune response to spinal cord injury, other approaches have involved the utilization of immune cells (macrophages) to facilitate axonal regeneration. Animal testing with genetically modified autologous macrophages showed encouraging results in rodent models and prompted human clinical studies. ProCord (Proneuron Biotechnologies, Los Angeles, California) therapy, involving the injection of “activated” autologous macrophages into the contused area of a spinal cord injury, was begun as a Phase-II clinical study in the United States and Israel. The trial, which enrolled twenty-four patients, was suspended from further patient recruitment because of funding issues, but the patients who were managed are still being followed.

Other investigations have targeted neurite growth inhibitory protein, Nogo-A, which is a cell surface protein, expressed after spinal cord injury, that inhibits neurite growth. Antibodies to Nogo-A have been administered intrathecally in rodent spinal cord injury models, with increasing axonal regeneration and improved neurologic recovery being noted. Rolipram, a specific inhibitor of phosphodiesterase 4, has also been shown to improve axonal regeneration after spinal cord injury in rodent models.

Cell-based therapies involving Schwann cells, olfactory ensheathing cells, and stem cells as well as other forms of implantable scaffolding have been shown to facilitate axonal regeneration and remyelination after spinal cord injury in animal models. Lima et al. recently reported on the implantation of olfactory mucosa at the site of injury in seven patients with an acute complete spinal cord injury and noted an improvement in the ASIA grade in all patients, with two patients having two grades of improvement. Implantation of stem cells has received substantial attention in the media as a potential cure for spinal cord injury. However, as encouraging as the results in animal studies have been, human clinical trials have not proven that these therapies are currently effective.

What’s New in the Treatment of the Lumbar Spine
Novel treatments and advances in the treatment of lumbar degenerative disorders continue to be of high interest to clinicians and researchers as these pathologies represent some of the more common musculoskeletal disorders. The development of novel technologies is very exciting, but we certainly need appropriate evidence of their efficacy.

Motion Preservation/Lumbar Disc Arthroplasty
The area of motion preservation of the lumbar spine—specifically, disc arthroplasty—continues to be a topic of high interest, and several studies have evaluated the efficacy of the treatments. Zigler et al., in a presentation of the slightly longer-term follow-up of their prospective randomized study of one prosthesis, compared the results of arthroplasty with those of fusion. The minimum duration of follow-up was two years, with some patients being followed for as long as three years. These early results showed that disc arthroplasty was as good as fusion, with some early differences favoring disc arthroplasty in terms of the pain score and patient satisfaction disappearing by the third year.

One group of investigators presented a systematic literature review on the efficacy and safety of intervertebral disc prostheses for the lumbar spine. This meta-analysis primarily examined two of the FDA-approved disc devices in comparison with fusion. The conclusions were that the scientific evidence presently available for these devices was not sufficient to recommend the use of either one for the treatment of lumbar disc pain in routine clinical practice. The authors recommended additional studies with larger numbers of patients.

Adjacent Segment Degeneration
Theoretically, the greatest benefit of motion preservation over fusion would be a decrease in or the avoidance of adjacent-segment disease. However, the delineation of the prevalence of adjacent-segment disease is critically important. In one prospective study of eighty patients undergoing an anterior interbody fusion at L5-S1, the two proximal adjacent levels were monitored for an average duration of follow-up of five years. The rate of advanced degeneration at either of these levels was not significantly changed from the initial preoperative rate. The authors concluded that adjacent-segment disease after anterior interbody fusion is not a clinical problem.

Two studies have examined the fate of the L5-S1 level following spine fusion to L5. One study evaluated nineteen patients with fusion to L5 and showed that 32% of the patients required revision of the fusion to the sacrum at the time of the five-year follow-up, and the investigators predicted a 60% survival rate at ten years of follow-up. Another center presented a study of thirty patients after five years of follow-up. The investigators noted a high rate (68%) of progressive degeneration at the L5-S1 level and noted a 20% rate of revision to the sacrum.
Biological Promoters of Fusion
In addition to the review of biologics earlier in this update, three studies are particularly pertinent to the lumbar spine and will be discussed here. Dimar et al. reported the results of a prospective randomized study of 463 patients in which the use of rhBMP-2 was compared with autograft bone graft for posterolateral lumbar fusion. The authors reported significant differences between the groups in terms of operative time and blood loss but not in terms of the length of hospital stay. The fusion rates were similar in the two groups, but the rate of nonunion failure was higher in the autograft group than in the rhBMP-2 group.

Vaccaro et al. presented their results after the use of rhBMP-7 for uninstrumented posterolateral spinal fusion. Twenty-six patients were followed to the five-year time-point, and the five-year results were compared with the earlier (two-year) results presented for a larger group. The authors reported that the fusion rates and clinical outcomes were maintained at the longer-term follow-up.

Angervine et al. studied the cost-effectiveness of the use of rhBMP-2 for the primary surgical treatment of adult scoliosis. This retrospective cohort cost-offset analysis examined the charges for each hospitalization at one institution for all adults undergoing this procedure. The investigators found that the use of rhBMP-2 increased the cost of the index procedure for adult idiopathic scoliosis, but was cost-neutral when controlling for the type of surgery, the number of levels, and the number of pedicle screws used. Furthermore, when taking into account the differential rate of pseudarthrosis and the associated costs, the use of rhBMP-2 was more cost-effective.

Nonoperative Care
Perhaps the most interesting and promising developments were related to the nonoperative treatment of lumbar spine abnormalities. One group of investigators presented the results of a prospective, randomized study of seventy-four patients with lumbosacral radiculopathy who were managed with oral administration of tumor necrosis factor-alpha (TNF-alpha) antagonists or placebo. Compared with placebo, the TNF-alpha antagonist showed a reduction in maximum daily leg pain over the first two weeks, but by three weeks there were no differences. Additional, longer-term study is needed to fully delineate the benefits of this approach.

One group reported on a prospective series of 346 patients receiving nerve root injections for the treatment of a variety of degenerative lumbar disorders. The investigators demonstrated efficacy and the avoidance of surgery in a large percentage of patients (in increasing order of efficacy) who had moderate disc herniations, degenerative spondylolisthesis, spinal stenosis, isthmic spondylolisthesis, foraminal stenosis, degenerative scoliosis, and failed back syndrome. Poor outcomes were found in association with stenosis, extraforaminal disc herniations, recurrent disc herniations, and failed back surgery when combined with instability.

Complications
Wound complications are always of concern. The identification of possible risk factors for prevention was the topic of one study of 18,352 patients, which examined risk factors for wound dehiscence and deep and superficial infections. Significant risk factors for wound complications, in order of increasing risk, included smoking, non-insulin-dependent diabetes mellitus, and insulin-dependent diabetes. The combination of smoking and diabetic status further increased the risk, and great care should be exercised when treating these patients.

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. 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 this Update, sixteen level-I articles were identified that were relevant to spine surgery. A list of those titles is appended to this review after the standard bibliography. We have provided a brief commentary about each of the articles to help guide your further reading, in an evidence-based fashion, in this subspecialty area.

Upcoming Meetings and Events
Related to Spine Surgery
The forty-second annual meeting of the Scoliosis Research Society (SRS) will be held on September 5 through 8, 2007, at the Edinburgh International Conference Center, Edinburgh, Scotland. It will be preceded by a one-day course entitled “Update on Congenital Spinal Deformity,” to be held on September 4, 2007. Web site: www.srs.org

The twenty-second annual meeting of the North American Spine Society (NASS) will be held on October 23 through 27, 2007, at the Austin Convention Center in Austin, Texas. It will be preceded by several precourses and two half-day meetings of the Biologics Research Section and the Motion Preservation Section, which are being developed by the society. Web site: www.spine.org

The thirty-fifth annual meeting of the Cervical Spine Research Society (CSRS) will be held on November 29 through December 1, 2007, at the Palace Hotel in San Francisco, California. It will be preceded by an Instructional Course sponsored by the Society on November 28, 2007. Web site: www.chrs.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), to be held on Saturday, March 8, 2008, in San Francisco, California. Web site: www.aaos.org

The annual meeting of the International Society for the Study of the Lumbar Spine (ISSLS) will be held May
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The thirty-fourth annual meeting of the American Spinal Injury Association (ASIA) will be held on June 19 through 22, 2008, at Loews Coronado Bay Resort in San Diego, California. Web site: www.asia-spinalinjury.org

The fifteenth annual International Meeting on Advanced Spinal Techniques (IMAST) will be held on July 8 through 11, 2008, at the Hong Kong Convention Center in Hong Kong, China. Web site: www.imastonline.com

Note: The authors thank Drs. Jim Harrop, Alan Hilibrand, Steve Mardjetko, Dan Riew, and Harvinder Sandhu for peer reviewing the sections of this manuscript.

Keith H. Bridwell, MD
Department of Orthopaedic Surgery, Washington University School of Medicine, One Barnes-Jewish Hospital Plaza, Suite 11300 West

Alexander R. Vaccaro, MD
University of California at Los Angeles Department of Orthopaedic Surgery and Neurosurgery, University of California at Los Angeles School of Medicine, 1230 16th Street, 7th Floor Tower, Room 715, Santa Monica, CA 90404. E-mail address: jwang@mednet.ucla.edu

Scott D. Boden, MD
The Emory Spine Center, Emory University School of Medicine, 59 Executive Park South, Suite 3000, Atlanta, GA 30329. E-mail address: scott_boden@emoryhealthcare.org

Jeffrey C. Wang, MD
University of California at Los Angeles Department of Orthopaedic Surgery and Neurosurgery, University of California at Los Angeles School of Medicine, 1230 16th Street, 7th Floor Tower, Room 715, Santa Monica, CA 90404. E-mail address: jwang@mednet.ucla.edu

Suggested Reading List


Evidence-Based Articles Related to Spine Surgery


In this study from Norway, spinal fusion was compared with a cognitive intervention and exercise program following the “failure” of previous disc herniation operation to relieve back pain. There was a 50% success rate in the fusion group and a 48% success rate in the cognitive intervention/exercise group. Depending on one’s perspective, either both modalities were equally effective or equally ineffective in this very difficult group of patients. This study suggests there is no “one answer” to the patient who has continued chronic low-back pain after previous surgery for the treatment of a disc herniation.


This study was a review of the literature on traction. There was not sufficient evidence to recommend traction for patients with low-back pain or sciatica. Because most studies were underpowered, the literature does not allow a negative conclusion that traction is not effective.


This paper identified twenty-four randomized clinical trials involving >2000 patients. Five of the trials were considered “high quality.” The authors concluded that there was conflicting evidence regarding the short-term effectiveness of either continuous or intermittent traction as compared with placebo, sham treatment, or other treatments when managing patients who have either chronic low-back pain or a mixture of low-back pain and sciatica. This finding suggests that there is nothing “magical” about employing traction when physical therapy is being used to treat low-back pain.


This was a review of the literature for published articles examining diagnostic studies for spinal stenosis. The authors found twenty-four articles (fifteen on imaging tests, seven on clinical tests, and two on other diagnostic studies). The authors found that the published studies were of poor quality and were not directly comparable, and they concluded that no firm conclusions could be made regarding the different tests. The results of this study are not surprising as spinal stenosis is a clinical syndrome with a large number of varying symptoms that may all not be present in any particular patient. The diagnosis of spinal stenosis is determined by the clinician on the basis of a combination of the test results, the clinical information and history, and the imaging studies.


The authors performed a randomized controlled trial evaluating the use of a single intravenous bolus of methylprednisolone (500 mg) for the treatment of acute sciatica (duration of symptoms, less than six weeks). The authors noted a significant decrease in sciatic pain in association with the intravenous administration of methylprednisolone over the first twenty-four hours but noted that the effects were transient and of small magnitude. This study demonstrates that a high-dose intravenous bolus of steroids may provide some short-term pain relief and, thus, may allow patients to better participate in physical therapy and other conservative modalities to relieve the symptoms of sciatica.


This was a randomized controlled study comparing intradiscal electrothermal therapy (IDET) with sham treatment for patients with chronic low back pain. Thirty-eight patients were randomized to IDET, and nineteen were randomized to sham treatment. All patients had one or two-level degenerative low-back pain confirmed with magnetic resonance imaging and discography. At six months, no improvement from baseline was observed in either group, and no differences were present between the IDET and sham groups. This was a well-done study that contradicted a previous randomized controlled study that had demonstrated a slight to moderate effect of IDET as compared with sham treatment. Taking these studies together, IDET appears to have little clinical efficacy.


The authors performed an extensive review of the literature on the surgical treatment of degenerative lumbar spondylolisthesis and concluded that there is a paucity of good studies on this topic. There is limited evidence to support some aspects of surgical practice. The authors underscored the importance of critical appraisal of the literature when formulating individual practice behaviors.


This was a prospective randomized trial, from two different centers, that included 120 women who were employed as health-care and social-care professionals and had low-back pain. The women were randomized to either a multidisciplinary group rehabilitation program for seventy hours or individual therapy for ten hours. The authors found no differences between the two groups at the time of the two-year follow-up, with both groups demonstrating favorable effects from the therapy that held up at the time of the final follow-up. The study shows that group therapy that is comprehensive is as effective as individual therapy and that both demonstrate positive effects at the time of two-year follow-up.


The authors set out to perform a meta-analysis of the literature on transcutaneous electrical nerve stimulation (TENS) for the treatment of low-back pain but only found two studies that met criteria to include in this analysis. They concluded that evidence to support the use of TENS treatment for low-back pain is limited.


This was a prospective randomized controlled study of forty patients with sciatica due to a lumbar disc herniation. Patients were managed with either a single infusion of the medication (antibody against TNF-alpha) or placebo. Both groups showed a significant reduction in leg pain, without any significant differences between the two groups. The authors concluded that there was no support for the use of this medication for lumbar disc herniation-induced sciatica. With the recent interest in TNF-alpha blockers for the treatment of sciatic pain, this study demonstrates that there was no difference between the medication and the placebo, which may reflect the positive natural history of the disorder itself.

What’s New in Spine Surgery
Subjects who used the booklet. The conclusions of the study are limited in that.

Both therapeutic groups had significantly better results than did the.

comes, but the differences were not significant compared with the exercise.

ment in both the exercise and yoga groups. The yoga group had superior out-

symptoms. At twenty-six weeks of follow-up, there was significant improve-

that emphasizes breathing and posture for the treatment of low-back pain.

Viniyoga is a safe technique for chronic low back pain, Viniyoga was compared with group exercise taught by a physi-

terapists or through an instructional booklet. Viniyoga is a safe technique

costs: a randomized, controlled clinical trial and health economic evaluation.

This randomized study demonstrated that for patients exposed to

whiplash trauma in a motor-vehicle collision, active involvement and inter-

vention were both less costly and more effective than a standard intervention.

There was reduced pain and less sick leave in the active involvement group.

Sherman KJ, Cherkin DC, Erro J, Miglioretti DL, Deyo RA. Comparing yoga,

exercise, and a self-care book for chronic low back pain: a randomized, con-


In this randomized controlled study of patients with prior episodic

low-back pain, Viniyoga was compared with group exercise taught by a physi-

cal therapist or through an instructional booklet. Viniyoga is a safe technique

that emphasizes breathing and posture for the treatment of low-back pain

symptoms. At twenty-six weeks of follow-up, there was significant improve-

ment in both the exercise and yoga groups. The yoga group had superior out-

comes, but the differences were not significant compared with the exercise

group. Both therapeutic groups had significantly better results than did the

subjects who used the booklet. The conclusions of the study are limited in that

the results cannot be generalized because the treatment population was

poorly defined. Furthermore, instructions were given in each group by one

practitioner who may have biased the outcome. The duration of follow-up

was short, and it is unknown if the observed effect will be lasting. Finally,

compliance with the program was not reported.

Singh K, Samartzis D, Strom J, Manning D, Campbell-Hupp M, Wetzel FT,

Gupta P, Phillips FM. A prospective, randomized, double-blind study evalu-

ating the efficacy of postoperative continuous local anesthetic infusion at the


Continuous infusion of local anesthetic has been developed to de-

crease postoperative pain and is used in many surgical disciplines. This study

tested its efficacy in patients undergoing spinal fusion with use of iliac crest

bone grafts. Thirty-seven patients were randomized to placebo (saline solu-

tion infusion) or Marcaine (90 mL of 0.5%) with use of a continuous infusion

technique. Significantly lower pain scores and less opioid consumption was

present in the anesthetic group. No complications occurred in either group.

The pump and anesthetics were cost-neutral. This was a well-done study

showing the efficacy of an inexpensive (cost-neutral) method in decreasing

postoperative pain. The use of this anesthetic technique should be considered

in other musculoskeletal surgical areas.

Steele EJ, Dawson AP, Hiller JE. School-based interventions for spinal pain: a


This was a systematic literature review of twelve papers. All twelve pa-

pers received a “weak quality rating”; therefore, no conclusions could be made

regarding the effectiveness of a school-based spinal health intervention pro-

gram. This paper strongly suggests there is no clear evidence that schools and

health-promotion programs help with the treatment of spinal pain. There is

simply not a clear answer in the current peer-review literature.

Yukawa Y, Kato F, Ito K, Terashima T, Horie Y. A prospective randomized study

of preemptive analgesia for postoperative pain in the patients undergoing poste-

rior lumbar interbody fusion: continuous subcutaneous morphine, continuous


The authors studied the use of preemptive and postoperative con-

tinuous subcutaneous morphine, continuous epidural morphine, and di-

clofenac sodium in a prospective randomized fashion. The diclofenac

treatment group had the lowest initial visual analog scale pain scores imme-

diately after surgery (p = 0.059) but required more supplemental analgesic

medications in the first seventy-two hours after surgery (p = 0.013). The epi-

dural group had more side effects, most commonly nausea and vomiting,

than the other groups (p = 0.015). This study is very relevant to the practice

of spine surgery as effective postoperative analgesia improves patient out-

comes, reduces secondary complications by allowing for early mobilization,

and shortens hospital stay. On the basis of the results of this study, it appears

that the administration of continuous subcutaneous morphine might be a

safe and useful approach for the treatment of postoperative pain after spinal

surgery and warrants further study.