

## FUTURE DIRECTIONS FOR RESEARCH

The following list recommends future directions for spine research. It is derived from gaps identified in the spine literature during clinical guideline development.

*Special Note to Researchers: Studies evaluating treatment outcomes should utilize validated outcome measures and include results specific to each of the treatment methods implemented in the study for all subgroups studied.*

### Antibiotic Prophylaxis in Spine Surgery

#### Efficacy

##### Use of Antibiotic Prophylaxis vs. Patients Who Do Not Receive Prophylaxis

- Further study is needed on the use of collagen or other carriers for local antibiotic treatments.
- A case controlled study utilizing available national databases to determine the relative efficacy of antibiotic prophylaxis in single-level, instrumented cases.
- A series of randomized, controlled studies each dealing with a specific subpopulation defined by diagnosis and procedure.

#### Protocol

- Prospective, randomized, clinical trials to compare the efficacy of cephalosporins to aminoglycosides and other antibiotics.
- Prospective, randomized, clinical trials to compare different timing and dosage protocols, for example, single perioperative dose versus multiple dose protocols.
- Prospective, comparative drug studies to determine optimal antibiotic prophylaxis regimen.
- Prospective, comparative studies to determine optimal dosing regimens for antibiotic prophylaxis.
- A case controlled study utilizing available national databases to determine the relative efficacy of different antibiotic prophylactic protocols in single-level, uninstrumented cases.
- A case controlled study utilizing available national databases to determine the relative efficacy of different antibiotic prophylactic protocols in single-level, instrumented cases.
- Case controlled studies to evaluate rates of polymicrobial infection stratified by comorbidities to identify other high risk populations.
- Prospective, randomized studies to evaluate the effect of broad spectrum antibiotic coverage in reducing infection rates in various high risk populations treated with instrumented fusion.

#### Redosing

- A case controlled study utilizing available national databases to determine the relative efficacy of redosing antibiotic prophylaxis in specific patient populations undergoing spine surgery.
- A series of randomized controlled studies evaluating dosing regimens. Each study could address a specific subpopulation defined by diagnosis, procedure and comorbidity.

#### Discontinuation

- Controlled studies comparing infection rates in spinal surgical patients who received antibiotics which were discontinued at 24 hours as compared with groups who received antibiotics for a longer period of time.

#### Wound Drains

- Controlled studies comparing infection rates in nonfusion and nonimplanted spinal surgical patients with drains and discontinuation at 24 hours as compared with longer duration prophylaxis.
- Controlled studies comparing infection rates in spinal surgical patients receiving spinal implants with drains and discontinuation at 24 hours as compared with longer duration prophylaxis.

#### Body Habitus

- Prospective, randomized clinical trials to evaluate the effect of antibiotic choice and altered dosing on infection rates in obese patients.

### Comorbidities

- Prospective, randomized clinical trials to evaluate the effect of antibiotic choice and altered dosing on infection rates in potentially high risk patients.
- A case controlled study to help identify other potential comorbidities leading to higher infection rates in patients undergoing spine surgery.

## Antithrombotic Therapies in Spine Surgery

### Efficacy

- A randomized, controlled trial comparing mechanical prophylaxis alone (i.e. pneumatic compression boots or compression stockings) with combined LMWH and mechanical prophylaxis in high-risk patients to assess the respective incidence of DVT, PE, neurological deterioration secondary to epidural hematoma, postoperative bleeding and wound complications.
- A randomized, controlled trial comparing mechanical prophylaxis alone (i.e. pneumatic compression boots or compression stockings) with combined low-dose warfarin and mechanical prophylaxis in high-risk patients to assess the respective incidence of DVT, PE, neurological deterioration secondary to epidural hematoma, postoperative bleeding and wound complications.
- A prospective, uncontrolled, prognostic, multicenter study of a high number of patients undergoing a wide variety of spine surgeries to quantify the relative risk of a number of suspected predisposing factors for VTE that include, but not be limited to, length of surgery, number of levels fused, underlying diagnosis, traumatic injury, paralysis and SCI. In addition, the relative risks of postoperative neurological deterioration from epidural hematoma, bleeding, wound complications, and transfusion requirements should be scrupulously defined for each subgroup.

### Chemoprophylaxis

- A randomized, controlled trial of LMWH vs. heparin as a bridge therapy for patients on long term warfarin prophylaxis for cardiac or other vascular conditions.
- A comparative study identifying the risks of perioperative bleeding complications in spinal surgery patients with clopidogrel-coated stents compared with those taking ASA and controls.
- A comparative study investigating the rate of bleeding complications in patients discontinuing clopidogrel ten days, seven days and one day prior to elective spinal surgery.
- A prospective study investigating optimum duration of postoperative prophylaxis comparing three groups of spine surgery patients treated with LMWH, ASA or clopidogrel for one week and another three groups of patients treated with LMWH, ASA or clopidogrel for four weeks.
- A comparative study investigating the incidence of bleeding complications in spinal patients receiving LMWH immediately postoperatively with another group of patients receiving LMWH three days postoperatively.

### Wound Complication

- Controlled studies documenting rates of wound complications in spinal surgical patients who received specific chemoprophylaxis protocols. Data recorded for each patient should include type of procedure as well as specific chemoprophylaxis protocol (chemoprophylaxis agent, dosage, timing and duration).

## Degenerative Lumbar Spondylolisthesis

### Natural History

- Prospective study of untreated patients, all with degenerative lumbar spondylolisthesis without neurologic compromise to provide Level I evidence regarding the natural history of the disease. This study could include stratification as to the type of spondylolisthesis and evaluate progression of radiographic severity and clinical severity over time.
- Any systematic study of patients with untreated spondylolisthesis who presented with varying degrees of neurologic deficit to provide evidence regarding the natural history of the disease in this patient population. For example, defining and following a group of patients with lumbar spondylolisthesis and sensory deficits as compared with those who present with motor deficits that have not been treated would yield Level I evidence.

### History and Physical Exam

- A high quality, prospective study identifying specific aspects of the history and physical examination and characterizing the subgroups of patients with degenerative spondylolisthesis. Ideally the study would enroll a large number of patients, screen for symptomatic and asymptomatic degenerative lumbar spondylolisthesis, and have greater than 80% follow-up. Subgroups for evaluation could include patients with or without instability, radiculopathy, neurogenic intermittent claudication and back pain.

### Diagnostic Tests

- A prospective, appropriately powered study assessing the utility of supine (gold standard), standing and dynamic flexion-extension lateral radiographs in the evaluation of patients with degenerative spondylolisthesis. NOTE: These studies should assess a set of diagnostic criteria established a priori.
- A prospective, appropriately powered study assessing the utility of supine recumbent (gold standard), axial loaded and positional MRI in the detection and evaluation of stenosis via analysis of the dural sac area in patients with degenerative spondylolisthesis. NOTE: These studies should assess a set of diagnostic criteria established a priori.

### Outcome Measures

- Further studies are needed to validate additional outcome measures (Stenosis Bothersome Index, LBP Bothersome Index, Oxford Claudication Score, Shuttle Walking Test, JOA and calculated Recovery Rate) for the treatment of degenerative lumbar spondylolisthesis. Currently, the best outcome measure for degenerative spondylolisthesis with symptoms of spinal stenosis is the ZCQ/SSS as a disease-specific outcome tool. General health outcome tools that are appropriate for degenerative lumbar spondylolisthesis are the SF-36 and ODI.
- Degenerative lumbar spondylolisthesis with back pain alone needs to be defined as a stand-alone clinical entity by outcomes research. The use of these outcome measures in this subgroup of patients needs to be studied.

### Medical/Interventional Treatment

- The SPORT study demonstrated the intrinsic difficulties in conducting RCTs comparing surgical to medical/interventional treatment in the North American patient population. It is unlikely that higher quality data are achievable for the comparison of surgical and medical/interventional treatment. Future studies are needed to assess the effects of medical, noninvasive interventions for degenerative lumbar spondylolisthesis. These studies should include an untreated control group when ethically possible and should include results specific to each of the medical/interventional treatment methods implemented, presenting results stratified by patient symptomatology (e.g., axial back pain only, combination of axial back pain and radiculopathy).
- A randomized controlled study comparing the benefits of physical therapy with directional preference versus nonpreferential therapy for the treatment of degenerative lumbar spondylolisthesis.

### Surgical Treatment

- Independent randomized controlled trials to validate what appears to be an effective and minimally invasive means (interspinous spacers) of decompressing the spinal canal in patients with symptomatic spinal stenosis and degenerative lumbar spondylolisthesis.
- A high quality randomized controlled trial to provide meaningful information about the clinical benefits of achieving a solid fusion in patients treated with instrumented and noninstrumented fusion for symptomatic spinal stenosis and degenerative lumbar spondylolisthesis. This study should utilize validated, functional, disease-specific outcome measures with long-term follow-up of four years or more.
- A high quality RCT comparing decompression with instrumented posterolateral fusion to decompression with 360° (circumferential) instrumented fusion.
- Future long-term studies of the effects of surgical interventions for patients with symptomatic spinal stenosis and degenerative lumbar spondylolisthesis are needed and should include an untreated control group, when ethically feasible. Continued follow-up of patients already enrolled in ongoing randomized controlled trials or prospective comparative studies will yield higher quality data regarding the relative efficacy of surgery compared to medical/interventional treatments.
- Future long-term outcome studies are necessary to compare different surgical techniques for the treatment of patients with symptomatic spinal stenosis and degenerative lumbar spondylolisthesis.

## Degenerative Lumbar Spinal Stenosis

### Natural History

- A prospective study of untreated patients, all with lumbar stenosis of a moderate degree, would provide Level I evidence regarding the natural history of the disease. This study could include stratification as to type of stenosis (i.e., central vs. subarticular vs. foraminal), and evaluate progression of radiographic severity and clinical severity over time.
- Any systematic study of patients with untreated severe stenosis would provide evidence regarding the natural history of the disease in this patient population. For example, defining and following a group of patients with severe lumbar stenosis that has not been treated would yield Level I evidence.

### History and Physical Findings

- A sufficiently powered observational study of the predictive value of historical and physical findings in patients with the diagnosis of lumbar spinal stenosis is proposed. The study should utilize validated outcome instruments, such as the Zurich Claudication Questionnaire (ZCQ) and the VAS for back and leg pain, and CT myelography or MRI as the gold standard.

### Diagnostic Tests

- Develop reliable and reproducible criteria for the diagnosis by cross-sectional imaging of central, subarticular recess and foraminal stenosis.
- Repeat interobserver and intraobserver variability studies with MRI and CT myelography using dural sac area as a measure of central canal stenosis.
- Evaluate the significance of lateral recess and neuroforaminal size, effacement of perineural fat, nerve root sleeve anatomy and nerve root or ganglion displacement and compression with respect to symptomatic radiculopathy and the outcome with surgical decompression.
- A prospective study is proposed evaluating the significance of additional findings on axial loaded cross-sectional imaging on patient prognosis and surgical decompression in patients with neurogenic intermittent claudication and radiculopathy.

### Outcome Measures

- Further studies are needed to validate additional outcome measures for the treatment of lumbar spinal stenosis. Currently, the best and most specific outcome measure for spinal stenosis appears to be the Zurich Claudication Questionnaire (Swiss Spinal Stenosis Questionnaire). In future studies of specific outcome measures for the treatment of lumbar spinal stenosis, this questionnaire could be considered to be a potential gold standard.

### Medical/Interventional Treatment

- The role of routine pharmacological treatment including NSAIDS, muscle relaxants and analgesics, used extensively in the treatment of spinal stenosis as well as other back conditions, needs to be investigated in patients with spinal stenosis using untreated control groups with spinal stenosis.
- A large, double-masked, randomized controlled trial with a long-term observation period to examine the potential benefits of intramuscular calcitonin for the treatment of lumbar stenosis.
- An appropriately powered, randomized controlled trial comparing physical therapy to the natural history of lumbar spinal stenosis using standardized techniques and validated outcome measures.
- A controlled trial comparing manipulation to natural history of lumbar spinal stenosis using standardized techniques and validated outcome measures.
- Use of validated outcome measures to compare manipulation to other medical/interventional treatments for spinal stenosis, and assessment of long-term effectiveness and cost effectiveness.
- A large double-masked, randomized, controlled clinical trial with at least one-year follow-up in patients with unilateral leg pain from lumbar spinal stenosis treated by fluoroscopically-guided contrast-enhanced transforaminal epidural steroid injections in which the control group receives saline placebo injections.
- A large double-masked, randomized, controlled clinical trial with at least two-year follow-up in patients with neurogenic claudication from lumbar spinal stenosis treated by fluoroscopically-guided interlaminar or caudal epidural steroid injections in which the control group receives saline placebo injections.

- A randomized, controlled trial comparing the use of individual ancillary treatments to a control, preferably masked, in patients with lumbar spinal stenosis.
- An appropriately powered study containing three groups with symptomatic lumbar spinal stenosis comparing soft bracing, rigid bracing and untreated controls (no bracing). Outcome measures could include the ZCQ, VAS, walking distance and a validated, health-related quality of life measure such as the SF-36 or ODI.
- Future long-term studies of the effects of medical, noninvasive interventions for lumbar spinal stenosis are needed and should include an untreated control group, when ethically feasible. These studies should include results specific to each of the medical/interventional treatment methods utilized.

### **Surgical Treatment**

- A large, multicenter, three-arm, randomized, controlled trial using a well-defined group of patients with moderate clinically symptomatic stenosis, comparing lumbar decompression to a well-defined medical/interventional treatment program and a natural history group of untreated patients.
- A large, multicenter, three-arm, randomized, controlled trial using a well-defined group of patients with moderate stenosis, comparing the use of interspinous spacers to a microlaminotomy decompression and a well-defined medical/interventional treatment program.
- A multicenter, randomized, controlled trial with sufficient power and appropriate validated outcome tools to determine the effectiveness of lumbar decompression as compared to medical/interventional management for moderate to severe lumbar stenosis. This study could include stratification of patients based on demographics and comorbidities.
- A large, multicenter, three-arm, randomized, controlled trial using a well-defined group of patients with mild to moderate clinically symptomatic stenosis, comparing the use of interspinous spacers to a microlaminotomy decompression and a well-defined medical/interventional treatment program.
- A randomized, controlled trial of sufficient power is proposed with validated outcome instruments and long-term follow-up evaluating the results of decompression, decompression with fusion and decompression with fusion and instrumentation.