

How much medicine do spine surgeons need to know to better select and care for patients?

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Received: 11 August 12

Accepted: 13 August 12

Published: 26 November 12

This article may be cited as:

Epstein NE. How much medicine do spine surgeons need to know to better select and care for patients?. *Surg Neurol Int* 2012;3:S329-49.

Available FREE in open access from: <http://www.surgicalneurologyint.com/text.asp?2012/3/6/329/103866>

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Abstract

Background: Although we routinely utilize medical consultants for preoperative clearance and postoperative patient follow-up, we as spine surgeons need to know more medicine to better select and care for our patients.

Methods: This study provides additional medical knowledge to facilitate surgeons' "cross-talk" with medical colleagues who are concerned about how multiple comorbid risk factors affect their preoperative clearance, and impact patients' postoperative outcomes.

Results: Within 6 months of an acute myocardial infarction (MI), patients undergoing urological surgery encountered a 40% mortality rate: similar rates may likely apply to patients undergoing spinal surgery. Within 6 weeks to 2 months of placing uncoated cardiac, carotid, or other stents, endothelialization is typically complete; as anti-platelet therapy may often be discontinued, spinal surgery can then be more safely performed. Coated stents, however, usually require 6 months to 1 year for endothelialization to occur; thus spinal surgery is often delayed as anti-platelet therapy must typically be continued to avoid thrombotic complications (e.g., stroke/MI). Diabetes and morbid obesity both increase the risk of postoperative infection, and poor wound healing, while the latter increases the risk of phlebitis/pulmonary embolism. Both hypercoagulation and hypocoagulation syndromes may require special preoperative testing/medications and/or transfusions of specific hematological factors. Pulmonary disease, neurological disorders, and major psychiatric pathology may also require further evaluations/therapy, and may even preclude successful surgical intervention.

Conclusions: Although we as spinal surgeons utilize medical consultants for preoperative clearance and postoperative care, we need to know more medicine to better select and care for our patients.

Key Words: Hematology, medical comorbidities, neurological/psychiatric disorders, obesity, pulmonary, spinal surgery: cardiac disease, stroke

Access this article
online

Website:

www.surgicalneurologyint.com

DOI:

10.4103/2152-7806.103866

Quick Response Code:



INTRODUCTION

Although we obtain preoperative clearance from our medical colleagues, spine surgeons need to know more medicine to better select (e.g., work up, reject) patients for spinal surgery, and to manage them postoperatively. Improved recognition of significant comorbid risk factors should decrease perioperative morbidity, and improve postoperative outcomes. This study attempts to provide a broad, although cursory, overview of multiple medical topics for spinal surgeons that include: cardiac disease, stroke, uncoated/coated stents (cardiac/carotid/peripheral vascular), diabetes, obesity, infection, gastrointestinal disease, hematological diseases, pulmonary disease, neurological disorders, and psychiatric conditions [Tables 1 and 2].

MORBIDITY AND MORTALITY OF SPINAL SURGERY

Multiple studies document varying levels of operative success, particularly for the more extensive surgical procedures requiring instrumented fusions. In order to better evaluate how multiple comorbidities interact with these operative procedures, the outcomes (successes and failures) of such procedures from selected large studies were analyzed.

Morbidity and mortality of spinal surgery for degenerative lumbar stenosis

Lumbar spinal fusions for degenerative lumbar stenosis are some of the most frequently performed operations. In Fu *et al.* study, the Scoliosis Research Society (SRS) database for lumbar surgery attributed to degenerative lumbar stenosis was prospectively assessed, and focus was placed on the attendant morbidity and mortality associated with these procedures [Table 1].^[22] The 10,329 patients in this database were aged over 21 years, averaged 63 years of age (range 21–96), and had no history of prior lumbar surgery. Operations included 6609 (64%) decompressions alone, 3720 (36%) underwent decompressions with fusions, with instrumentation utilized in 3377 (91%) of the latter population. There were 719 complications (7.0%); that included new neurological deficits (0.6%). The 13 (0.12%) deaths recorded were attributed to cardiac (4 cases), respiratory (5 cases), pulmonary embolus (2 cases), sepsis (1 case), and a perforated gastric ulcer (1 case) [Table 1]. Interestingly, complication rates were not positively correlated with patient age or the number of levels fused. Minimally invasive surgical (MIS) procedures were reportedly associated with fewer complications and fewer new neurological deficits.

Table 1: Summary of morbidity/complications and mortality of spine surgery

Author	% Deaths (total patients)	% Complications
Lee Spine 2011 ^[40]	1.8% (767 Patients)	13% Cardiac 7% Pulmonary 8.2% Neurological 17.5% Hematological 6.7% Gastric 10.3% Urological
Fu ^[22]	0.12% (10,329 Patients)	0.04% Cardiac 0.05% Pulmonary 0.02% Pulmonary Embolism 1% Sepsis
Sansur ^[55]	0.1% (10,242 Patients)	0.7%- 2.1% Dural Tears Wound Infections Implant Complications
Street ^[65]	1.5% (942 Patients)	85% 1 Complication 39% Increased Hospitalization 7% Pneumonia 3% Neurological 2.2% Estimated Blood Loss over 2L 10.5% Intraoperative Complications 4.5% CSF leak 1.9% Instrumentation Failure
Schoenfeld ^[59]	0.3% (3475 Patients)	7.6% (263 patients)
Acosta ^[11]	0% (29 patients)	38% Major 62% At Least 1 Complication 52% Long term Complications 14% Reoperations
Cho ^[10]	NA* (166 Patients)	34.4% Major Complications 19.3% Perioperative 18.7% Follow Up

NA*: Not available

Summary: The surgical complication rate for degenerative lumbar stenosis was 7%, and included new neurological deficits in 0.6% of patients, and a 0.12% mortality rate.

Morbidity and mortality attributed to lumbar surgery for spondylolisthesis

In a retrospective analysis of 10,242 adults with degenerative spondylolisthesis (DS) and isthmic spondylolisthesis (IS), Sansur *et al.* studied the morbidity/complication rates and mortality (M and M) rates obtained from the SRS database [Table 1].^[55] Complications were based on several variables: age (over 65 or under 65 years old), surgical approach, spondylolisthesis (type/grade), and history of previous surgery. There were 945 complications (9.2%) observed in 813 patients (7.9%). The most frequent complications included dural tears, wound infections,

Table 2: Presentation of topics and summary statements

Topic	Summary
Morbidity and Mortality of Spinal Surgery for Degenerative Lumbar Stenosis	The surgical complication rate for degenerative lumbar stenosis was 7%, and included new neurological deficits in 0.6% of patients, and a 0.12% incidence of deaths.
Morbidity and Mortality Attributed to Lumbar Surgery for Spondylolisthesis	Higher-grade degenerative spondylolisthesis (DS), and aged over 65, both significantly correlated with higher complication rates of spinal surgery for DS.
Prospectively Collected Morbidity and Mortality for Patients Undergoing Spinal Surgery	The incidence of perioperative morbidity increased from 23% to 87% when data were prospectively collected in a complex spinal surgery trauma center.
Morbidity and Mortality in Different Spinal Series	Varying morbidity and mortality rates have been reported for patients undergoing spinal surgery. These include: cardiac, pulmonary, gastrointestinal, neurological, hematological, urological, prior wound infection, corticosteroid use, history of sepsis, American Society of Anesthesiologists (ASA) classification of >2, and prolonged operative times.
Major Complications/Risk Factors Associated with Revision Spinal Deformity Surgery	Patients undergoing secondary procedures for scoliosis had a 34.4% major complication rate, and poorer outcomes.
Morbidity and Mortality in Spine Surgery (Including Deformity) in Older Patients	Following major (>5-level) spinal deformity surgery, the overall long-term complication rate was 52%, but only a history of hypertension positively correlated with a 10-fold increase in susceptibility to complications.
Complex Spine Surgery: Sometime Unnecessary, Too Much or Too Little	Increasingly, geriatric and other patients with significant attendant comorbid factors, are being offered extensive and often "unnecessary spinal procedures".
High Rate of Reoperation for Patients Undergoing Multilevel Instrumented Fusions With 96% "Off-Label" Use of INFUSE (Medtronic, Memphis, TN, USA)	The 170 (96%) of 177 patients undergoing instrumented fusions utilizing INFUSE were performed "off-label", and resulted in a 40% reoperation rate for geriatric patients (over age 65).
Learning Curve for Minimally Invasive Spinal Surgery (MIS)	Comparable long-term outcomes for MIS vs. open spinal surgical procedures are being reported, and some unique MIS techniques are associated with higher complication rates.
Cardiac Disease and Risk of Acute Myocardial Infarction with Early Surgery	The risk of perioperative mortality following an acute MI in a series of patients undergoing acute hip surgery was 28% at 1, but 40% at 6 postoperative months. These data may similarly be applied to other operative procedures.
Anti-platelet Aggregant Therapy for Various Coated and Uncoated Cardiac Stents	Spinal surgery may be performed within 2 months of placing an uncoated stent, but requires up to 6 months to 1 year following placement of a coated stent.
Coated Stents for Acute or Recent Myocardial Infarction	Following acute/recent MI (<6 months), performing spinal operations and the cessation of anti-platelet aggregants may lead to complications (mortality, major cardiac events) utilizing first and second-generation coated stents.
Greater Safety and Efficacy Demonstrated for Coated vs. Uncoated Stents	Six months following the placement of sirolimus coated vs. uncoated stents, the coated stents demonstrated greater retention of luminal diameter, no restenosis (vs. 26.6% uncoated), no thrombosis, and a lesser 5.8% incidence of cardiac events (vs. 28.8% for uncoated stents).
Time-Frames for Cessation of Anti-Platelet Therapy in Urological Surgery	Time frames for performing various urological procedures following the placement of an uncoated stent were typically 1 month for uncoated vs. 12 months for coated stents. Schedules for cessation/reinitiation of aspirin and/or clopidogrel bisulfate varied according to the severity of the procedure.
Cardioembolic Stroke Risk	Atrial fibrillation (AFIB), recent myocardial infarction, mechanical prosthetic valve (MVR), dilated cardiomyopathy, and mitral rheumatic stenosis, are all factors that increase the risk of cardioembolic stroke. Cessation of anticoagulants or anti-platelet aggregants prior to spine surgery increases the risk of these strokes that carry a 27.3% risk of in-hospital mortality.
Carotid Revascularization Techniques vs. Carotid Artery Stenting (CAS)	Patients with significant carotid disease who are about to undergo major spine surgery may require acute stent implantation which has been correlated with a 95% incidence of success. The timing of surgery will be dictated by the stent utilized with a minimum of 6 weeks of anti-platelet therapy for non-coated vs. up to one year for coated stents.
Morbid Obesity Increases the Morbidity of Spinal Surgery	Although only 1455 (1.72%) of 84,607 patients undergoing spinal fusions were morbidly obese, they accounted for 97% of the in-hospital complications including; longer LOS (4.8 vs. 3.5 days), higher average hospital costs (\$108,604 vs. \$84,861), and higher (0.41 vs. 0.13) mortality rates.
Obesity Risk with Spinal Surgery and Indications for Weight Reduction Including Bariatric Surgery	Morbid obesity poses an increased risk of; DVT/PE (increased levels of antiphospholipid activating Factor 1), wrong-level surgery, poorly executed procedures, wound seromas/hematomas, infection, and intraoperative blood loss.

Contd...

Table 2: Contd...

Topic	Summary
Bariatric Surgery Increases Bone Loss/Osteopenia/Osteoporosis	Morbidly obese patients undergoing bariatric surgery experience malabsorption of calcium and vitamin D resulting in decreased hip and bone densities.
Hypocoagulation; Genetic Syndromes vs. Medication, Food, Vitamin, or Supplement Induced Syndromes	Hypocoagulation may be attributed to von Willebrand's Disease, and Hemophilia, but it may also be due to multiple medications (aspirin-containing), vitamins (especially Vitamin E, Multivitamins), supplements (fish oils Glucosamine/Chondroitin Sulfate, Ginkgo biloba), or foods (nuts).
Hypocoagulation with von Willebrand's Disease: A Range of Genetic Disorders	Von Willebrand's Disease (VWD) consists of a range of genetic disorders contributing to excessive bleeding, and may be treated pre-, intra-, and post-spinal surgery with desmopressin (DDVAP) and/or the infusion of VWF concentrates.
Hypocoagulation Due to Hemophilia: On-Demand vs. Prophylaxis with Factor VIII (FVIII) May Reduce Annual Bleeding Rates (ABR)	Hemophilic patients who are Factor VIII deficient exhibited fewer annual bleeding rates (ABR) if treated prophylactically (keeping FVIII trough levels at or above 1%) vs. those receiving on demand therapy (none were ABR free).
Medications, Vitamins and Foods Promoting Hypocoagulation Should Ideally be Stopped Several Weeks Prior to Spine Surgery	Various medications (aspirin, Clopidogrel Bisulfate, Dipyridamole), Vitamin E containing compounds (multivitamins, nuts), Glucosamine Chondroitin Sulfate, Ginkgo biloba, fish/fish oils/Omega-3 supplements all increase bleeding risk; they should be stopped several weeks (preferably 3) prior to spine surgery.
Hypercoagulation Syndromes	There are a multitude of both intrinsic and acquired hypercoagulation syndromes that contribute to arterial/venous thrombosis.
Various Management Strategies for Preventing/Managing Phlebitis and Pulmonary Embolism in Spine Surgery	Intermittent compression stockings adequately reduce the risk of DVT/PE in neurosurgical patients. Avoiding the hemorrhagic complications of low dose heparin (LDH)/low molecular weight heparin (LMWH) regimens [2–4% (cranial), 3.4% minor and 3.4% major hemorrhages (cranial/spinal), and 0.7% major/minor hemorrhages (spinal series)].
Efficacy of Alternating Compression Stockings for DVT/PE Prophylaxis for Spine Surgery	Pneumatic compression stocking prophylaxis resulted in a 2.8% incidence of DVT and 0.7% frequency of PE in 139 patients undergoing complex lumbar fusions; these results were comparable to those reported in other spine series utilizing LDH/LMWH.
Efficacy of Low Molecular Weight Heparin (LMWH) for Prophylaxis Against Venous Thromboembolism (VTE) After Lumbar Surgery	Low molecular weight heparin prophylaxis, beginning with a half dose administered 6 hours postoperatively followed by full dose therapy once a day, reduced DVT/PE to 0, while only 2 patients exhibited minor bleeding complications.
Indications and Results of Prophylactic Inferior Vena Cava Filter (IVCF) Placement in High Risk Patients Undergoing Spine Surgery	Prophylactic IVCF were safely placed in high-risk patients undergoing spine surgery (history of DVT/PE, hypercoagulation, long operations (>5 levels), 360°, and/or staged operations over 8 hours), resulting in an 8.7% incidence of DVT, and 3.7% frequency of PE.
Low Threshold for Ordering Spinal Computed Tomography Contrast Angiography (CTA) for Diagnosing Pulmonary Embolism (PE)	Spine surgeons should have a low threshold for ordering CTA-PE protocols, as the incidence of positive CTA despite negative Doppler studies was 6.7% for cervical laminectomies/fusions, and 3.6% for lumbar laminectomies/noninstrumented fusion.
Transient Cessation of Warfarin in Chronically Anticoagulated Patients: Assessment of Peri-Procedural (Operative) Risks of Thrombosis and Bleeding	For patients on chronic anticoagulation for atrial fibrillation (AFIB), deep venous thrombosis (DVT), or mitral valve replacement (MVR), transient cessation of anticoagulants, and the utilization of LMWH bridging therapy (69%) resulted in a 3-month incidence of 2.1% of major bleeding, and an overall 5.1% of bleeding.
Safety of Anticoagulating High Risk Patients After Spinal Surgery	Patients undergoing spinal surgery at high risk for DVT/PE managed without prophylaxis developed PE in 5.3% of deformity, 6% of trauma, and 2.3% of degenerative disease cases. Fatal PE, major bleeding (0.0–4.3%), and hematomas (0.4%) were rare.
Cancer and Hypercoagulation Syndromes	Hypercoagulation syndromes (thrombophilia, DIC, thrombocytosis), and lower antithrombin III, C-protein and S-protein plasma levels in patients with cancer or paraneoplastic syndromes, are the second most prominent cause of death secondary to hemorrhages or thromboses.
Oncology: Differentiation of Leptomeningeal Carcinomatosis from Lumbar Disease	Leptomeningeal disease, particularly carcinomatosis (carcinomas, lymphomas, other), may mimic lumbar disc disease, and should be a diagnostic consideration.
Value of Asthma Assessment and Optimization Prior to Spine Surgery	At least one week prior to spine surgery, patients with significant asthma should undergo preoperative pulmonary assessment (spirometry) to determine whether they require "optimization" with bronchodilators, inhaled steroids, Cromalyn Sodium, Montelukast, or if other measures are warranted.
Chronic Obstructive Pulmonary Disease (COPD)	Utilization of bronchodilators for patients with COPD may help optimize them for spinal surgery.
Cessation of Smoking Prior to Spinal Surgery: Duration of 4–8 Weeks Correlates with Respiratory Benefits	Cessation of smoking >4–8 weeks prior to surgery reduced respiratory complications, cessation of smoking 3–4 weeks preoperatively improved wound healing, while the failure to quit smoking within <2–4 weeks of surgery did not reduce morbidity.

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Table 2: Contd...

Topic	Summary
Increased Risks of Sleep Apnea and Respiratory Complications in Diabetic Patients Undergoing Spinal Surgery	Sleep apnea is more prevalent in diabetic patients who, if undiagnosed prior to lumbar surgery, may be susceptible to hypoventilation, aspiration, and pneumonia while utilizing routine narcotic pain medication.
A Role For Spinal, Epidural, Combined Spinal/ Epidural, and Local Anesthesia in Spinal Surgery	Some authors have documented a reduced perioperative morbidity associated with lumbar surgery performed under spinal (bupivacaine) and/or epidural (clonidine) anesthesia supplemented with local anesthetics (0.5% bupivacaine).
Risk of Spinal Infections and Prophylaxis	The risk of postoperative spinal infections varies from 0.4% to 3.5%, but may be reduced utilizing multiple preoperative, intraoperative and postoperative measures.
Measures to Avoid Nosocomial Surgical Site Infection (SSI)	Measures required to avoid surgical site infection (SSI), especially nosocomial, include; proper skin preparation, adherence to sterile technique, (limiting) surgical duration, and (limiting) traffic in the operating room. This includes limiting noise levels in the operating room.
Comparative Efficacy of Two Skin Preparation Solutions (ChlorPrep and DuraPrep) Utilized for Spine Surgery	Two commonly utilized skin preparation solutions (ChlorPrep and DuraPrep) provided comparable skin prophylaxis for spinal surgery.
Preoperative Bathing with Hibiclens (Chlorhexidine Gluconate)	Daily bathing with chlorhexidine (CHG) avoids bloodstream infections (BSI). Many hospitals now provide CHG brushes for bathing the night before and the morning of surgery to reduce SSI.
Antibiotic Prophylaxis for Spinal Surgery Utilizing a Cephalosporin Efficacy of Cefuroxime and Gentamicin As Prophylaxis Against MRSA	Cefuroxime and Gentamicin provide increased prophylaxis against MRSA at the time of induction of anesthesia for patients undergoing spine surgery.
Silver Impregnated Dressings May Limit Postoperative Wound Infections	Silver impregnated dressings did not significantly limit/reduce the incidence of wound infections in a series of patients undergoing elective colon surgery. It does appear to reduce postoperative deep and superficial wound infections following lumbar-instrumented fusions.
Rare Esophageal Perforation Following Anterior Cervical Surgery and Thoracic Fractures/Trauma	Esophageal injuries/perforations are infrequently encountered following anterior cervical surgery or spinal trauma. Continued drainage, fever, infection, and dysphagia one week following anterior cervical surgery should prompt one to suspect an esophageal tear. The surgical approach, and the potential for major esophageal complications with anterior procedures, should prompt careful consideration of the posterior cervical surgical alternatives, when appropriate.
Establishing the Diagnosis of Multiple Sclerosis (MS)	Establishing the diagnosis of Multiple Sclerosis (MS) is often delayed and can take an average of 2.2 years before patients see a neurologist, and an average of 3.5 years (following the initial onset of symptoms) before MS is correctly diagnosed.
Differentiating Multiple Sclerosis (MS) from Cervical Spondylotic Myeloradiculopathy (CSM), and Recognizing MS- Deficits and Types	The symptoms and signs of Multiple Sclerosis (MS) that may "mimic" cervical spondylotic myeloradiculopathy (CSM), typically include; motor (33%), multisystem (33%), and cerebellar disorders (16%). Three major types of MS are primary progressive-MS (62%), secondary progressive-MS (22%), or relapsing-remitting-MS (16%).
Barkhof Criteria seen on MR Scans in MS Patients	The Barkhof Criteria applied to MR scans of MS patients include: (a) at least 1 gadolinium-enhancing lesion or at least 9 lesions on T2-weighted images, (b) at least 3 periventricular lesions, (c) at least 1 juxtacortical lesion, and (d) at least 1 infratentorial lesion.
Intramedullary Cervical Plaque (C4-C7) Consistent with Adolescent MS	Intramedullary spinal lesions may mimic intrinsic spinal cord tumors further investigation is warranted (e.g., biopsy).
Differentiation of CSM from Neuromyelitis Optica (NMO or Devic Syndrome)	Neuromyelitis Optica (Devic Syndrome) is a disabling inflammatory condition that targets astrocytes in the optic nerves and spinal cord, but unlike MS, only 50% experience isolated unilateral optic neuritis. Preventive measures include broad-spectrum or selective B-lymphocyte immune suppression, while acute attacks can be managed with high-dose intravenous steroids, and plasma exchange.
Differentiating Amyotrophic Lateral Sclerosis (ALS) from Spinal Disease	The diagnosis of ALS is often delayed for up to 11 months, and 31.1% of patients initially receive incorrect diagnoses.
Psychiatric Disorders and Spine Disease	Studies focusing on psychiatric comorbidities in patients with spinal complaints (pain alone vs. pain with significant neurological deficits/radiographic pathology) differ in terms of recommendations for or against surgical intervention.
Microdiscectomy (Surgery) Was Effective and Improved Depression	Microdiscectomy significantly improved pain-associated depression, somatic anxiety, and mental well-being in patients with herniated lumbar disc.
Depression and Anxiety Negatively Impact Outcomes of Instrumented Fusion for Failed Back Surgery	In patients with failed back syndromes, secondary spinal fusions have resulted in a high failure rate (65%), with nearly one-third of patients exhibiting anxiety/depression. Conservative management may be more beneficial and selective and careful assessment should be done in order to prevent unnecessary surgery.

implant complications, and neurological complications (rates varied from 0.7% to 2.1%); the mortality rate was 0.1%.^[55] Significantly more complications occurred for those with DS (8.5%) vs. IS (6.6%). Interestingly, higher-grade spondylolisthesis correlated with higher complication rates (22.9% vs. 8.3%), reflecting the greater extent of surgery and longer operative times. Age over 65 years also significantly correlated with higher complication rates, reflecting greater comorbid factors in this age group (despite presumed adequate preoperative medical clearance). Alternatively, prior surgery and the operative approach did not appear to adversely impact outcomes.

Summary: Higher-grade DS, and age over 65 years both significantly correlated with higher complication rates of spinal surgery for DS.

Prospectively collected morbidity and mortality data for patients undergoing spinal surgery yields more accurate results

In 2008, Street *et al.* prospectively analyzed (over a one-year period) all adverse events (AE) occurring in 942 adults undergoing complex spinal surgery in a major trauma center; these included morbidity (major/minor, medical and surgical) and mortality.^[65] They assessed the impact of: (1) weekly multidisciplinary rounds, (2) a formal abstraction tool (questionnaire/data collection), and (3) prospectively recording perioperative morbidities. Outcomes analysis included the prospective assessment of in-hospital deaths, length of stay, and morbidity; the latter included the recording of unplanned second operations (1st admission), wound infections warranting reoperations, readmissions within the same year, and all intraoperative and nonsurgical postoperative AE [Table 1]. Prior to this study, they retrospectively recorded a 23% perioperative morbidity (major and minor, medical and surgical) rate. Utilizing this prospective system, the perioperative morbidity rate increased to 87% (822 AE). At least one complication was observed in 39% of patients that increased the length of hospital stay (LOS). There were 14 deaths, and a 10.5% intraoperative surgical complication rate that included: 4.5% incidental durotomy, 1.9% hardware malposition requiring revision, and a 2.2% blood loss of greater than 2 liters [Table 1]. A 73.5% frequency of postoperative complications included: wound complications (13.5%), delirium (8%), pneumonia (7%), neuropathic pain (5%), dysphagia (4.5%), and neurological deterioration (3%). The authors concluded that the prospective collection of morbidity data more accurately depicted events as compared with the retrospective analyses that failed to identify such events. Additionally, identification of these complications, newly revealed in weekly conferences, better identified why certain patients incurred longer hospitalizations (LOS).

Summary: The incidence of perioperative morbidity increased from 23% to 87% when data were prospectively collected in a complex spinal surgery trauma center.

Morbidity and mortality in different spinal series

In a 2-year prospective (2003–2004) analysis involving 767 patients undergoing lumbar spine surgery, Lee *et al.* found the following medical complications: cardiac (13%), pulmonary (7%), gastrointestinal (6.7%), neurological (8.2%), hematological (17.5%), and urological (10.3%) [Table 1].^[40] Additionally, they found that mortality was most highly correlated with cardiac or respiratory complications while the extent of surgery was the largest risk factor for cardiac, pulmonary, neurological, and hematological complications.

Schoenfeld *et al.* prospectively examined risk factors contributing to immediate postoperative (within 30 days) morbidity/mortality in a large series of patients from the National Surgical Quality Improvement Program (2005–2008) undergoing spine surgery.^[59] The average age for the 3475 patients was 55.5 years (range 16–90 years). Older age and contaminated wounds were positively correlated with 10 mortalities (0.3%) [Table 1]. For the 407 morbidities/complications observed in 263 patients (7.6%), independent predictors for one or more complications included: older age, cardiac disease, preoperative neurologic abnormalities, prior wound infection, corticosteroid use, history of sepsis, American Society of Anesthesiologists (ASA) Classification of >2, and prolonged operative times.^[59] Note that the correlation of higher morbidity rates with more comorbid risk factors, particularly older age, and increased operative time are factors that may well deter informed elderly patients from choosing surgical intervention.

Summary: Varying morbidity and mortality rates have been reported for patients undergoing spinal surgery. These are correlated with the following factors/pathology: cardiac, pulmonary, gastrointestinal, neurological, hematological, urological, prior wound infection, corticosteroid use, history of sepsis, ASA classification of >2, and prolonged operative times.

Major complications/risk factors associated with revision spinal deformity surgery

Cho *et al.* retrospectively analyzed risk factors contributing to the major complications seen over an average of 3.5 years (follow-up/range of 2–5 years) for 166 patients (averaging 53.8 years of age) undergoing multilevel revisions following previous spinal deformity surgery [Table 1].^[10] Revision surgery predominantly addressed adjacent segment disease, fixed sagittal imbalance, and pseudarthrosis. Outcomes were analyzed utilizing the SRS, and the Oswestry Disability Index (ODI) scores. Major complications were observed in

34.3% of patients (e.g., 19.3% perioperative; 18.7% during follow-up), and were attributed to: age >60 years, medical comorbidities, obesity, and some were related to prior surgery (pedicle subtraction osteotomy, and three-column osteotomy involving the progressive loss of sagittal correction). Although initial postoperative outcomes were comparable, “those experiencing follow-up complications reported lower scores at the final follow-up”.^[10]

Summary: Patients undergoing secondary procedures for scoliosis had a 34.4% major complication rate, and poorer outcomes

Morbidity and mortality in spine surgery (including deformity) in older patients

Acosta *et al.* analyzed the morbidity/complications and mortality for 29 patients undergoing major 5 or more level (average 10 levels, with a range of 5–15) spinal deformity surgery accompanied by fusions.^[11] Patients averaged 77 years of age, and were followed an average of 41.2 months (range 24–81).^[11] A minimum of 1 comorbid factor was found in 15 patients. Of the 29 patients, 13 had at least 1 complication after surgery, and 8 were considered major [Table 1]. The overall long-term complication rate was 52%, but only a history of hypertension positively correlated with a 10-fold increase in susceptibility to complications.

Summary: Following major (>5-level) spinal deformity surgery, the overall long-term complication rate was 52%, but only a history of hypertension positively correlated with a 10-fold increase in susceptibility to complications.

Complex spine surgery: Sometimes unnecessary, too much or too little

Epstein found increased complication/morbidity and mortality rates reviewing the literature concerning the frequency of spinal surgical procedures performed in patients aged 65 and over (geriatric) with multiple overlapping comorbidities.^[18] Specific attention was focused on the increasing number of operations offered to geriatric patients with their increased comorbidities, and the offers for “unnecessary” spine fusions, including both major open and MIS procedures.

Epstein further highlighted the incidence of “unnecessary” spine surgery being offered to patients, including geriatric patients, with significant comorbidities with pain alone, but without focal neurological deficits or significant radiographic findings.^[16] Within a series of spinal consultations seen over a 1 year interval, 47 (17.2%) patients were told by other surgeons they needed operations that were deemed “unnecessary” by the author. The 21 “unnecessary” cervical operations included 1–4 level anterior discectomy/fusion [18 patients], laminectomies/fusions [2 patients], and a posterior cervical discectomy [1 patient]. The 26 “unnecessary” lumbar operations involved 1–5 level posterior lumbar

interbody fusions. Notably, 29 patients exhibited one or more major overlapping comorbidities.

Summary: Increasingly, geriatric and other patients with significant attendant comorbidity factors, are being offered extensive and often “unnecessary” spinal procedures. In Epstein’s series, the frequency was 17.2%.

High rate of reoperation for patients undergoing multilevel instrumented fusions with 96% “off-label” use of INFUSE (Medtronic, Memphis, TN, USA)

Epstein also reported on the frequency of complications (morbidity and mortality) arising from multilevel complex spinal fusions utilizing INFUSE (Medtronic, Memphis, TN, USA).^[19] The study focused on 177 instrumented spinal fusions performed at one hospital in 2010: the reoperation rate was 20% for patients in all age groups, but increased to 40% for those aged over 65 years. Of interest, 96% of cases (170/177) were performed “off-label”; the only “on-label” cases (7/177) were anterior lumbar interbody fusions (ALIF). Notably, INFUSE for the 170/177 “off-label” fusions cost \$4,547,822, while 4% (7 of 177 cases) of “on-label” cases cost \$296,419.

Summary: The 170 (96%) of 177 patients undergoing instrumented fusions utilizing INFUSE were performed “off-label”, and resulted in a 40% reoperation rate for geriatric patients (aged over 65).

Learning curve for minimally invasive spinal surgery

Ultimately, the value of MIS spine surgery vs. open spinal procedures relies on the comparison of long-term outcomes. While some studies document that MIS procedures’ learning curves “do no harm”, reduce operative time, blood loss, and short-term recovery (time to ambulation), others cite comparable long-term outcomes for MIS vs. open surgery.^[36,39,70] Lee *et al.* prospectively assessed the learning curve for minimally invasive transforaminal lumbar interbody fusion (TLIF) in 86 consecutive patients (e.g., utilizing a tubular retractor, unilateral transforaminal approach, an interbody cage, and pedicle/screw fusion) with degenerative lumbar disease (minimum 1-year follow up).^[39] Patients were divided into two groups: the “early group” included the first 30 patients having TLIF, while the “late group” consisted of the last 38 patients having TLIF.^[39] Although patients from both groups exhibited comparable outcome scores (Oswestry Disability Index [ODI] and visual analogue scale [VAS]), patients from the “late group” exhibited significantly shorter operative times (1-level TLIF: 254 minutes for the “early group” vs. 183 minutes for the “late group” patients), estimated blood loss (EBL in 1-level TLIF; “early” 508 ml vs. “late” 292 ml), and ambulation recovery times (“early” 2.4 days vs. “late” 2.0 days).^[39] When Lau *et al.* compared the MIS TLIF

in 10 patients vs. open TLIF in 12 patients, they found that although the MIS TLIF patients demonstrated significantly lower intraoperative transfusion rates, required fewer drains over shorter time periods, and ambulated earlier, they “tended to have a higher rate of complications, which might have been associated with the learning curve.”^[36] Wang *et al.* also evaluated the long-term results of MIS TLIF interbody fusion (41 cases) vs. open surgery (38 cases); they found that “in the short-term, MIS is superior to open surgery, but in the long-term there is no significant difference between the two procedures.”^[70]

Other MIS series cite major complications attributed to minimally invasive approaches. In Lindley *et al.* axial lumbar interbody fusion series involving L4-5 and L5-S1 fusions (followed average 34 months), 16 (23.5%) of 68 patients experienced 18 complications (26.5%).^[44] These included pseudarthrosis (8.8%), superficial infection (5.9%), sacral fracture (2.9%), pelvic hematoma (2.9%), failure of wound closure (1.5%), transient nerve root irritation (1.5%), and rectal perforation (2.9%). The two cases of rectal perforation prompted the recommendation for proper patient selection and operative planning, including preoperative magnetic resonance (MR) imaging, a detailed patient physical examination and history, full bowel preparation, and the use of live fluoroscopy.^[44] The authors concluded that MIS surgical techniques may in fact be associated with their own added unique complications, which may not be encountered with open procedures.

Summary: Comparable long-term outcomes for MIS vs. open spinal surgical procedures are being reported, but some unique MIS techniques are associated with higher complication rates.

CARDIAC DISEASE

Cardiac disease and risk of acute myocardial infarction with early surgery (defined as within less than 6 months of a myocardial infarction)

A history of a myocardial infarction (MI) within a prior 6 month interval is a relative contraindication to spinal surgery due to the increased risk of a possible fatal cardiac event. Thiagarajah *et al.* studied the perioperative mortality for 25 patients averaging 88 years of age (range 78–98) undergoing hip surgery (acute proximal femoral neck fractures) within 1–12 days following an acute MI; the mortality rate was 28% within the 1st postoperative month, but increased to 40% by the 6st postoperative month.^[67]

Summary: The risk of perioperative mortality following an acute MI in a series of patients undergoing acute hip surgery was 28% at 1, but 40% at 6 postoperative months.

These data may similarly be applied to other operative procedures.

Anti-platelet aggregant therapy for coated vs. uncoated cardiac stents

Increasingly, cardiac revascularization, rather than utilizing bypass procedures, now employs uncoated (bare) or coated stents. If uncoated stents are utilized, spinal surgery and/or other operations must be delayed by at least 6 weeks to 2 months to allow for sufficient endothelialization of the stented vessel to take place; at this point, in some cases, anti-platelet therapy may be safely discontinued. However, for patients receiving a coated stent, spinal surgery must typically be delayed for 6 months to 1 year, as the coating inhibits endothelialization, making anti-platelet therapy imperative to avoid thrombotic complications.

Summary: Spinal surgery may often be performed within 2 months of placing an uncoated stent, but typically requires up to 6 months to 1 year following placement of a coated stent.

Coated stents for acute or recent myocardial infarction

For patients with acute or recent MIs (e.g., within <6 months), performing spinal operations may prove life threatening. In De Servi *et al.*, first and second-generation drug-eluting (coated) stents were performed similarly.^[11] However, with the latter second generation stents, patients were able to tolerate the cessation of anti-platelet aggregants within 6 postoperative months. Nevertheless, for both stents, anti-platelet therapy cessation within less than 6 months, could result in “dramatic increases in mortality and major cardiac adverse events.” Furthermore, there was a marked increase in these events if medication was stopped within less than 1 month.^[11]

Summary: Following acute/recent MI (<6 months), the cessation of anti-platelet aggregants to perform spinal operations may lead to complications (mortality, major cardiac events) utilizing first and second-generation coated stents.

Greater safety and efficacy demonstrated for coated vs. uncoated stents

Several studies demonstrate the greater safety and efficacy of coated vs. uncoated stents. Morice *et al.* compared the efficacy of a sirolimus (rapamycin)-coated stent (that inhibits lymphocyte and smooth-muscle proliferation) vs. uncoated stents for treating patients with chest pain.^[48] In a double-blind trial involving 238 patients at 19 medical centers, the two stents, utilized in previously untreated coronary arteries, were trialed; the end point for each was immediate vs. 6 month postprocedural luminal diameter, the frequency of restenosis ($\geq 50\%$), and clinical outcomes (e.g., death, MI, and need for revascularization) at 1, 6, and 12 months.^[48] At 6 months,

the coated stent performed substantially better; (1) greater preserved luminal diameter, (2) no restenosis in the coated vs. 26.6% restenosis in the uncoated stents, (3) no thromboses for coated stents, (4) and over the first year, 5.8% major cardiac events for the coated vs. 28.8% for the uncoated stents.

Summary: Six months following the placement of sirolimus coated vs. uncoated stents, the coated stents demonstrated greater retention of luminal diameter, no restenosis (vs. 26.6% uncoated), no thrombosis, and a lesser 5.8% incidence of cardiac events (vs. 28.8% for uncoated stents).

Time-frames for cessation of anti-platelet therapy in urological surgery

In urological surgery, following the placement of uncoated vs. coated cardiac stents, the timing for utilizing anti-platelet therapies varies according to the complexity of the surgery being performed.^[24,28] In Gupta *et al.* series, this typically required a minimum of 1 month for a bare stent, and 12 months for drug eluting stents.^[24] For low risk procedures, aspirin therapy could be continued while clopidogrel bisulfate was stopped, but had to be restarted within 24–48 h. For medium risk operations, both aspirin and clopidogrel bisulfate could be stopped for 5–7 days, while for high-risk surgery; both aspirin and clopidogrel bisulfate were stopped for 10 preoperative days, and then restarted at 7–10 postoperative days. Jain *et al.* further determined that it was safer to continue anti-platelet therapy for many urological procedures, and that the only group at increased risk was for those wherein postoperative bleeding could occur in “closed spaces”.^[28]

Summary: Time frames for performing various urological procedures following the placement of an uncoated stent were typically 1 month for uncoated vs. 12 months for coated stents. However, schedules for cessation/reinitiation of aspirin and/or clopidogrel bisulfate varied according to the severity of the procedure.

STROKE

Lumbar surgery and stroke

When Wu *et al.* evaluated the incidence of stroke (hemorrhagic/ischemic) following lumbar spinal fusion in 2015 patients vs. 120 control subjects, they found that the overall frequency of stroke (9.99 per 1000 person-year) was comparable for both groups.^[72]

Stroke risk for taking patients off anti-platelet or anticoagulant therapy prior to spine surgery: Timing of cessation of medication

For patients with significant cardiac disease (e.g., atrial fibrillation [AFIB]) or carotid disease (stenosis) requiring anti-platelet aggregant therapy or anticoagulants, the risk of peri- and postoperative stroke must be considered

before “clearing” patients for spinal surgery. This requires an on-going interaction with medical consultants, as the decision when to safely stop these medications prior to surgery, and when to restart them following surgery, may prove critical to patient outcomes.

When Stieb *et al.* assessed continuing anticoagulants and antiplatelet aggregant therapies prior to major spine surgery, they found a 50–81% risk for major bleeding requiring transfusion, with a 0.2% to 0.4% incidence of postoperative spinal hematomas warranting surgery (this depended on whether low-molecular-weight heparin (LMWH) was utilized postoperatively.^[63] For patients with AFIB on anticoagulants they recommended utilizing bridging therapy (unfractionated heparin-UFH or LMWH) immediately prior to surgery, while for those on antiplatelet aggregants for bare or active stenting, secondary prevention of MI, stroke or peripheral ischemia, they offered limited interruption of treatment.^[63] A critical feature was that “the strategy should be jointly determined by surgeon, anesthesiologist, and cardiologist, to optimize individualized care taking into account each party’s requirements, with the patient in the central role.”^[63]

Cardioembolic stroke risk

For patients about to undergo major spinal procedures, factors contributing to the risk of cardioembolic stroke once anticoagulation or anti-platelet therapy are stopped include AFIB, recent MI, mechanical prosthetic valve (Mitral Valve Replacement [MVR]), dilated cardiomyopathy, and mitral valve rheumatic stenosis.^[2] The risk of stroke associated with the cessation of anti-platelet or anticoagulant therapy required to perform surgery must, therefore, be carefully weighed against the pros and cons of avoiding surgery altogether. As Arboix *et al.* emphasized, the risk of cardioembolic stroke with these conditions comprises 14–30% of all ischemic strokes, with an accompanying in-hospital mortality rate of 27.3%.^[2]

Summary: AFIB, recent MI, mechanical prosthetic valve (MVR), dilated cardiomyopathy, and mitral rheumatic stenosis are factors that increase the risk of cardioembolic stroke. Cessation of anticoagulants or anti-platelet aggregants prior to spine surgery increase the risk of stroke carrying a 27.3% risk of in-hospital mortality.

Carotid revascularization techniques vs. Carotid artery stenting

Carotid artery disease leading to stroke is the third-leading cause of adult mortality.^[62] Prevention of stroke, particularly in patients with significant carotid disease prior to major spinal surgery may require carotid revascularization vs. stent placement. Siddiqui *et al.* found in the “Carotid Revascularization Endarterectomy versus Stenting Trial (CREST),” that carotid artery stenting (CAS) was a “safe, equally effective, and durable

alternative to carotid endarterectomy (CEA) for all patients requiring carotid revascularization.”^[62]

In Papanagiotou *et al.*, successful revascularization of extracranial ICA with acute stent implantation was achieved in 95% of patients (21 patients); there were no acute stent thromboses, intracranial recanalization was achieved with thrombolysis in 61% (11 of 18 patients), and the recanalization rate (extracranial and intracranial) was 63% (14 of 22 patients).^[51] Waiting for 6 weeks for uncoated vs. up to 1 year for coated stents is typically warranted to allow adequate time for endothelialization of the vessel to occur prior to cessation of anti-platelet therapies. The timing for restarting medication following spinal operations should be a joint spinal surgeon/medical decision.

Summary: Patients with significant carotid disease who are about to undergo major spine surgery may require acute stent implantation which has been correlated with a 95% incidence of success. The timing of surgery will be dictated by the stent utilized with a typical minimum of 6 weeks of anti-platelet therapy for noncoated vs. usually up to 1 year for coated stents.

OBESITY

Assessing the impact of obesity on morbidity and/or mortality associated with spinal surgery is critical. Recognition of obesity as a major risk factor for spinal surgery allows spinal surgeons to (1) avoid operating on “high risk” individuals, or at least to (2) optimize (e.g., recommend weight loss/improve nutrition) patient selection for surgery. When spinal operations are absolutely necessary, (i.e., evolving neurological deficits) procedures should be as uncomplicated as possible, and should be accompanied by limited instrumentation.

Morbid obesity increases the morbidity of spinal surgery

Utilizing The “Healthcare Cost and Utilization Project’s California State Inpatient Databases (CA-SID) (California 2003–2007)” that included 84,607 admissions, Kalanithi *et al.* documented that morbid obesity increases the risks/complications of spinal fusions, especially for those undergoing anterior cervical or posterior lumbar surgery.^[32] Their retrospective analysis assessed the adverse impact of morbid obesity on morbidity/mortality for 4 types of spinal fusions: Anterior Cervical Fusion (ICD-9-CM procedure code 810.2), Posterior Cervical Fusion (810.3), Anterior Lumbar Fusion (810.6), and Posterior Lumbar Fusion (810.8).^[32] Although only 1,455 (1.72%) of the patients were morbidly obese, they accounted for 97% of in-hospital complications, and exhibited longer LOS (4.8 vs. 3.5 days), incurred higher average hospital costs (\$108,604 vs. \$84,861), and higher (0.41 vs. 0.13) mortality rates. Morbid obesity markedly contributed

to complications for both anterior cervical surgery and posterior lumbar fusions.

Summary: Although only 1,455 (1.72%) of 84,607 patients undergoing spinal fusions were morbidly obese, they accounted for 97% of in-hospital complications including; longer LOS (4.8 vs. 3.5 days), higher average hospital costs (\$108,604 vs. \$84,861), and higher (0.41 vs. 0.13) mortality rates.

Obesity risk with spinal surgery and indications for weight reduction including bariatric surgery

Obesity in general and morbid obesity in particular, pose increased risks to any spinal surgical procedure. Morbidly obese patients exhibit an increased risk of phlebitis (deep venous thrombosis (DVT)) and pulmonary embolism (PE). This is not only attributed to greater mechanical venous compression and immobility leading to venous stasis, but also to higher circulating levels of antiphospholipid activating Factor 1. Morbid obesity also offers other significant operative risks that include: difficulty positioning patients at surgery, trouble obtaining adequate localizing films (e.g., X-ray, fluoroscopy), an increased risk of wrong-level surgery, a greater likelihood of poorly executed operative procedures (e.g., technical limitations, including contraindication to lower anterior cervical arthroplasty), increased perioperative wound complications (seromas/hematomas), infection (largely related to a vascular fat pad), and increased estimated blood loss (EBL).

Increased estimated blood loss for morbidly obese patients undergoing spinal surgery

Han *et al.* documented that the higher body mass index (BMI) associated with morbid obesity leads to increased intra-abdominal pressure (IAP) and intraoperative blood loss (IBL) during spinal procedures performed in the prone position.^[26] They compared three groups of patients: Group 1 (BMI; 18.5–22.9 kg/m², Group 2 (BMI; 23–24.9 kg/m², and the morbidly obese Group 3 (BMI; 25.0–29.9 kg/m². IAPs increased disproportionately for the morbidly obese Group 3 patients, thereby increasing EBL: Group 1 (IAP-7.8 mmHg), Group 2 (IAP-8.2 mmHg), and Group 3 (IAP-10.4 mmHg).

For patients considering various weight reduction strategies (e.g. dieting under a physicians supervision, bariatric surgery) and achieving their goals, complications such as osteopenia/osteoporosis and poor nutritional status may also occur impacting surgical outcome. Alternatively, for those who fail to lose weight, surgery may not be viable.

Summary: Morbid obesity poses an increased risk of DVT/PE (increased levels of antiphospholipid activating Factor 1), wrong-level surgery, poorly executed procedures, wound seromas/hematomas, infection, and greater EBL.

Bariatric surgery increases osteopenia/osteoporosis

There has been an increase in candidates for spinal surgery who have previously undergone gastric bypasses, leaving them vitamin and nutritionally deficient, but more critically, osteopenic or osteoporotic. Fleischer *et al.* evaluated bone metabolism and bone mineral density (BMD) after Roux-en-Y gastric bypass surgery.^[21] In their 1-year prospective evaluation, 23 patients (mean BMI 47 kg/m, age range 20–64 years) underwent bariatric surgery. On average, patients lost 45 +/- 2 kg over 1 year, parathyroid hormone (PTH) increased (3 months, 43–50 pg/ml), but urinary calcium dropped (161–92 mg/24), despite doubling calcium intake (1318–2488 mg/d). The malabsorption of calcium and vitamin D resulted in decreased hip and bone densities.^[21] Scibora *et al.* also examined the potential increased risk for morbidly obese patients undergoing bariatric (malabsorption procedures) surgery to develop accelerated reductions in BMD (osteopenia/osteoporosis).^[60] Nevertheless, although they found that women exhibited decreased BMD of the hip and lumbar spine even with adequate calcium/vitamin D utilization (e.g., a 9–11% reduction in the femoral neck, and 8% reduction in the lumbar spine within the first year), the data did not conclusively support the greater frequency of osteoporosis or increased fracture risk in postbariatric patients.

Summary: Morbidly obese patients undergoing bariatric surgery experience malabsorption of calcium and vitamin D resulting in decreased hip and bone densities.

HEMATOLOGY/ONCOLOGY: COAGULATION SYNDROMES, MANAGEMENT OF PHLEBITIS/ PULMONARY EMBOLISM, AND DIAGNOSIS OF CARCINOMATOSIS

Hypocoagulation; genetic syndromes vs. Medication, food, vitamin, or supplement induced

Operative hematological complications may include hypocoagulation syndromes, (e.g., Von Willebrand's Disease (VWD), Hemophilia), or other factors contributing to poor platelet function; medications, vitamins, supplements, or foods; (e.g., myriad of medications including Aspirin, Asacol (for Crohn's disease contains equivalent of 1.5 aspirin/pill), Glucosamine/Chondroitin Sulfate, Vitamin E, multivitamins, (contains Vitamin E), nuts (Vitamin E), Fish/Fish Oils, Ginkgo biloba, and Omega-3 complexes among others. When marine-based n-3 fatty acids (Omega-3 Fish Oils) were evaluated in a rat model, plasma coagulation parameters resulted in strong hypocoagulation after only 1 week.^[41] Vitamin E, which may be taken separately or

as part of a multivitamin complex, or ingested in high concentrations in nuts-almonds are an increased source of Vitamin E.^[45] Vitamin E has not only an anti-platelet aggregant effect, but may also inhibit platelet procoagulant activity.^[33] In Kim *et al.* study, Vitamin E inhibited platelet phosphatidylserine (PS) and procoagulant activity both *in vitro* and *ex vivo* by increasing Aminophospholipid translocase (APLT) function.^[33]

When spine surgery is anticipated, it is optimal to discontinue specific vitamins, foods, or supplements up to 2–3 weeks prior to surgery. A minimum of 10 days is warranted to allow platelets to regenerate.

Summary: Hypocoagulation may be attributed to VWD, and Hemophilia, but it may also be due to multiple medications (aspirin-containing), vitamins (especially Vitamin E, Multivitamins), supplements (fish oils Glucosamine/Chondroitin Sulfate, Ginkgo biloba), or specific foods (fish, nuts, etc.).

Hypocoagulation with von willebrand's disease: A range of genetic disorders

VWD consists of a range of genetic disorders. "The molecular pathology of Type 2 and 3 VWD is now comprehensively documented and involves rare sequence variants at the Von Willebrand Factor (VWF) locus."^[29] Three clinical parameters are utilized to diagnose VWF: (1) excessive mucocutaneous hemorrhage, (2) laboratory studies consistent with VWF (VWF antigen/function), and (3) a family history of bleeding. Treatment includes, stimulating the release of intrinsic VWF with desmopressin (DDVAP) utilized preoperatively/intraoperatively/postoperatively, and/or infusing VWF concentrates.

Summary: VWD consists of a range of genetic disorders contributing to excessive bleeding, and may be treated pre-, intra-, and post-spinal surgery with desmopressin (DDVAP) and/or the infusion of VWF concentrates.

Hypocoagulation due to hemophilia: "on-demand" vs. "prophylaxis" with factor VIII may help reduce annual bleeding rates

Surgical prophylaxis for factor VIII (FVIII) deficiency is often considered the optimal treatment for managing patients about to undergo spinal surgery, as hemophilia poses an increased risk of intraoperative/postoperative hemorrhagic complications. However, even the chronic management of hemophilia without anticipated surgery, with either on-demand or continued prophylaxis, warrants further study.^[69] Valentino *et al.* compared two prophylaxis regimens for managing hemophilia in non-surgical patients. The first group received factor VIII "on-demand" (primary outcome) vs. "prophylactic" treatments with factor VIII (secondary outcome) to maintain FVIII trough levels at or above 1%. The annual

bleeding rates (ABR) for those utilizing “on-demand” therapy were greater than those utilizing continued “prophylaxis”. None of those treated “on-demand” was free of bleeding episodes, while the two prophylaxis regimens attained comparable reductions in ABR.^[69]

Summary: Hemophilic patients with Factor VIII deficiency exhibited fewer ABR if treated prophylactically (keeping FVIII trough levels at or above 1%) vs. those receiving “on demand therapy” (none were ABR free).

Other medications, vitamins, and foods promoting hypocoagulation should be stopped weeks prior to spine surgery

Multiple medications, vitamins, supplements, and foods contribute to hypocoagulation and should, therefore, be stopped prior to spine surgery. This specifically includes the most frequently utilized anti-platelet aggregants (e.g. aspirin, Clopidogrel Bisulfate, Dipyridamole, among others). Additionally, Vitamin E, contained in most multivitamins and present in high doses in nuts, is not only an antioxidant, but also directly inhibits platelet function as protein kinase C decreases platelet pseudopodia formation when stimulated by agonists, thereby reducing platelet adhesion.^[64] Vitamin E also potentiates bleeding when utilized along with other platelet aggregation inhibitors (e.g., aspirin, Clopidogrel Bisulfate, Dipyridamole). There are also anti-platelet aggregants contained in Glucosamine and Chondroitin Sulfate, Ginkgo biloba (in green teas), fish/fish oils, and Omega-3 Vitamins. Several weeks (preferably 3) prior to spine surgery, patients are cautioned to discontinue vitamins and/or other “supplements” or foods to reduce the perioperative bleeding risk.

Summary: Various medications (aspirin, Clopidogrel Bisulfate, Dipyridamole), Vitamin E containing compounds (multivitamins, nuts), Glucosamine Chondroitin Sulfate, Ginkgo biloba, fish/fish oils/Omega-3 supplements increase bleeding risk, and should be stopped several weeks (preferably 3) prior to spine surgery.

Hypercoagulation syndromes

There are many hypercoagulation syndromes that contribute to increased clumping of thrombocytes and fibrin, leading to arterial/venous thrombosis.^[68] Intrinsic disorders include deficiencies of anticoagulation proteins (antithrombin III, protein C, protein S), Factor V Leiden Mutation, Thrombophilia, or dysfibrinogenaemia, a deficiency of natural activators of fibrinolysis or increased activity of their inhibitors, and homocystinuria.^[68] Other acquired hypercoagulation syndromes include anticardiolipin antibodies (lupus anticoagulants), pregnancy, the use of oral contraceptives, malignancy, nephrotic syndrome, postoperative conditions, diabetes mellitus, and other diseases.

Summary: There are a multitude of both intrinsic and acquired hypercoagulation syndromes that contribute to arterial/venous thrombosis.

Various management strategies for preventing/managing phlebitis and pulmonary embolism in spine surgery

Over 2 million people in the United States develop DVT, and almost 100,000 have fatal PE.^[13] There are unique risks and benefits for differing regimens of prophylaxis against DVT/PE in neurosurgery due to the inherent risks of hemorrhage.^[13] These regimens included elastic stockings (ES), intermittent pneumatic compression stockings (CS), low-dose unfractionated heparin (LDH 5000 U q 8–12 h), and low molecular-weight heparin (LMWH e.g., enoxaparin and dalteparin). Although CS devices adequately reduced the incidence of DVT/PE in some series, the LDH/LMWH regimens further reduced the incidence of PE (not necessarily DVT). However, the LDH/LMWH regimens posed increased risks of hemorrhages; 2–4% of patients from a cranial series, 3.4% minor and 3.4% major hemorrhages in a combined cranial/spinal series, and 0.7% major/minor hemorrhages in a spinal series.^[13]

Summary: Intermittent CS adequately reduce the risk of DVT/PE in neurosurgical patients, avoiding the hemorrhagic complications of LDH/LMWH regimens: 2–4% (cranial), 3.4% minor and 3.4% major hemorrhages (cranial/spinal), and 0.7% major/minor hemorrhages (spinal series).

Efficacy of alternating compression stockings for deep venous thrombosis/pulmonary embolism prophylaxis for spine surgery

For complex lumbar spine surgery, including laminectomies with instrumented fusions, although LDH regimens reduce the frequency of DVT and PE, they still pose a risk of postoperative hematoma/neurological dysfunction, and/or wound dehiscence.^[14] In Epstein’s series, the utility of pneumatic CS as the sole mechanical prophylaxis against DVT/PE was evaluated in 139 patients undergoing average 3.8 level laminectomies with average 1.4 level instrumented fusions. All patients had CS stockings utilized intraoperatively and throughout their hospital stay. Pneumatic compression stocking prophylaxis was correlated with a 2.8% (4 patients) incidence of DVT vs. 0.7% (1 patient with Factor V Leiden deficiency) frequency of PE in 139 patients undergoing complex lumbar fusions. These rates were comparable to those reported in spinal series employing LDH or LMWH prophylaxis.^[14]

Summary: Pneumatic compression stocking prophylaxis resulted in a 2.8% incidence of DVT and 0.7% frequency of PE in 139 patients undergoing complex lumbar fusions; these results were comparable to those reported in other spine series utilizing LDH/LMWH.

Efficacy of low molecular weight heparin for prophylaxis against venous thromboembolism after lumbar surgery

Zhi-Jian *et al.* evaluated the efficacy and safety of LMWH prophylaxis for venous thromboembolism (VTE) following 78 lumbar decompressions.^[73] Their patients received a half dose of LMWH 6 h after surgery followed by a full dose LMWH once per day until discharge. They concluded that this regimen was safe and effective as none developed “symptomatic” DVT/PE, and other complications were minor; 1 wound ecchymosis, 1 wound bleeding, 4 with mild hepatic aminotransferase elevations, and 1 allergic reaction.^[73]

Summary: LMWH prophylaxis, beginning with a half dose administered 6 h postoperatively followed by full dose once a day, reduced DVT/PE to 0, while only 2 patients exhibited minor bleeding complications.

Indications and results of prophylactic inferior vena cava filter placement in high risks patients undergoing spine surgery

As the frequency of PE may reach 13% in high-risk patients undergoing spine surgery, McClendon *et al.* retrospectively analyzed the value of prophylactically placing preoperative inferior Vena Cava filters (IVCF).^[46] Criteria included “a (prior) history of DVT or PE, malignancy, hypercoagulability, prolonged immobilization, staged procedures >5 levels, combined anterior/posterior approaches, ilio caval manipulation during exposure, and anesthetic time >8 h.” Variables analyzed included: “age, sex, surgical approach, postoperative DVT, postoperative superficial thrombus, presence of PE or paradoxical embolus, mortality, and IVCF complications.” The complications observed in 219 patients averaging 58.8 years of age (range 17–86) included: 2 secondary to IVCF placement, an 8.7% incidence of DVT, and 3.7% frequency of PE. Fewer PE occurred with Greenfield as compared with retrievable filter placement.^[46]

Summary: Prophylactic IVCF were safely placed in high-risk patients undergoing spine surgery (history of DVT/PE, hypercoagulation, long (>5 levels), 360°, and/or staged operations over 8 h), resulting in an 8.7% incidence of DVT, and 3.7% frequency of PE.

Low threshold for ordering spinal computed tomography contrast angiography for diagnosing postoperative pulmonary embolism

Epstein *et al.* studied the incidence of positive CTA-PE protocols despite negative Doppler studies of the lower extremities performed in postoperative spinal patients.^[20] From 1 to 21 days postoperatively, 11 patients had negative lower extremity Doppler studies (routinely ordered postoperative day 2 and subsequently requested when indicated), but positive spinal computed tomography

contrast angiography (CTA) for PE. The frequency of positive CTA was 6.7% (5 patients) for 75 patients having cervical laminectomy/fusion, and 3.6% (6 patients) for 165 patients undergoing lumbar laminectomy/noninstrumented fusion. All patients immediately received IVCF (2 permanent, 9 retrievable), and 5 of 11 patients (45%) tested positive for hypercoagulation syndromes. Two patients required simultaneous full anticoagulation on postoperative days 3 and 21 due to saddle emboli (1 documented hypercoagulation syndrome), while for 7 patients (milder PE/mild residual seromas), anticoagulation was delayed for 6–12 weeks (4 documented hypercoagulation syndromes). Two patients over 70 years of age, at high risk for falls, were not anticoagulated (neither had a hypercoagulation syndrome). In order to avoid failure to diagnose PE after spinal surgery, one should have a “low threshold” (e.g., based even on minor symptoms) for requesting CTA-PE protocols.

Summary: Spine surgeons should have a “low threshold” for ordering CTA-PE protocols, as the incidence of positive CTA despite negative Doppler studies was 6.7% following cervical laminectomies/fusions, and 3.6% after lumbar laminectomies/noninstrumented fusions.

Transient cessation of warfarin in chronically anticoagulated patients: assessment of peri-procedural (operative) risks of thrombosis and bleeding

Tafur *et al.* looked at the 3-month risk for thrombosis (if anticoagulation was stopped) or bleeding (depending upon when anticoagulation was restarted) for patients whose chronic anticoagulation was transiently stopped for invasive procedures: (e.g. for DVT (38%), AFIB (30%), and mechanical heart valves (MVR) (27%)).^[66] Of the 2182 patients, 1496 (69%) received “bridging therapy” with LMWH. At 3-months, an overall 5.1% bleeding rate was observed; the cumulative major bleeding rate was 2.1%, and was more frequent with LMWH (3% vs. 1%). Factors increasing major bleeding risk included: a “mechanical MVR (2.2; 1.1–4.3), active cancer (1.8; 1.0–3.1), a prior bleeding history (2.6; 1.5–4.5), and re-initiation of heparin therapy within 24 h after the surgery (1.9; 1.1–3.4).”^[66]

Summary: For patients on chronic anticoagulation for AFIB, DVT, or MVR, transient cessation of anticoagulants, and the utilization of LMWH bridging therapy (69%) resulted in a 3-month 2.1% incidence of major bleeding, and an overall 5.1% bleeding rate.

When is it safe to anticoagulate high risk patients after spinal surgery?

When is it safe to anticoagulate patients who are at high risk for thromboembolic events following spinal surgery?^[9] The major risks of early postoperative anticoagulation include seroma/hematoma, wound breakdown, and the

potential for new neurological deficits. Cheng *et al.* evaluated 29 articles meeting stringent inclusion criteria (Recommendations Assessment, Development, Evaluation criteria from 1990 to 2008).^[9] They discovered; (1) PE in untreated patients (e.g., no prophylaxis) was somewhat greater following surgery addressing deformity (5.3%) vs. trauma (6.0%) vs. degenerative disease (2.3%), (2) fatal PE rarely occurred, (3) major bleeding was rare (0.0–4.3%), (4) and postoperative hematomas were rare (0.4% or 10 in 2507 patients). The authors concluded that the safe timing for the administration of anticoagulation agents (following spinal surgery) is not known.^[9]

Summary: Patients undergoing spinal surgery managed without prophylaxis developed PE in 5.3% of deformity, 6% of trauma, and 2.3% of degenerative disease cases. Fatal PE, major bleeding (0.0–4.3%), and hematomas (0.4%) were reportedly rare.

Cancer and hypercoagulation syndromes

Hypercoagulation syndromes, frequently observed in patients with cancer or paraneoplastic syndromes, are the second most prominent cause of death secondary to hemorrhages or thromboses.^[34] Kovacova *et al.* assessed 67 patients with gastric cancer; thrombophilia defined as the “activation of intravascular coagulation” was observed in 31.3% of patients, and 47.8% demonstrated disseminated intravascular coagulation (DIC).^[34] Causes for hypercoagulation included thrombocytosis (e.g., platelet hyper-aggregability), elevation of beta-thromboglobulin, and elevation of thrombomodulin (indicates vascular wall damage). They observed that lower antithrombin III levels, C-protein and S-protein in plasma indicated lower antithrombotic potential in patients in general, and specifically in patients with gastric cancer.^[34]

Summary: Hypercoagulation syndromes (thrombophilia, DIC, thrombocytosis), and lower antithrombin III, C-protein and S-protein plasma levels in patients with cancer or paraneoplastic syndromes, are the second most prominent cause of death secondary to hemorrhages or thromboses.

Oncology: Differentiation of leptomeningeal carcinomatosis from lumbar disease

Leptomeningeal disease, particularly carcinomatosis (carcinomas, lymphomas, among others), may mimic lumbar disc disease. In Reggars *et al.*, a 62-year-old male with a several day history of left-sided low back/leg pain with weakness was under treatment (e.g., chemotherapy) for low grade non-Hodgkin’s lymphoma.^[54] A lumbar CT/pelvis showed a mild disc bulge at the L4-L5 level, and he was initially treated with spinal traction. When he developed a left Bell’s palsy 2 days later, an MR of the brain and lumbar spine demonstrated pathological enhancement involving multiple cranial nerves, the cauda equina, and the L1 and L5 vertebrae,

consistent with the diagnosis of diffuse leptomeningeal carcinomatosis.^[54] He expired several weeks later. Despite its rarity, for patients with histories of carcinoma who develop new focal neurological deficits, leptomeningeal carcinomatosis remains an important differential diagnostic consideration.

Summary: Leptomeningeal disease, particularly carcinomatosis (carcinomas, lymphomas, other), may mimic lumbar disc disease, and should be a diagnostic consideration.

PULMONARY DISEASES

Patients with pulmonary disease/compromise attributed variously to asthma, chronic obstructive pulmonary disease (COPD), pulmonary conditions (e.g., sleep apnea), and lung cancer, may be optimized for spinal surgery, or may not be viable surgical candidates.

Value of asthma assessment and optimization prior to spine surgery

Select asthmatic patients (those with more severe disease) who undergo preventive preoperative pulmonary evaluations and treatment may avoid untoward intraoperative and postoperative events (e.g., bronchospasm). Liccardi *et al.* recommended assessing patients at least 1 week prior to surgical procedures involving general anesthesia.^[43] Obtaining a routine pulmonary function test (spirometry) was critical for detecting poorly controlled asthma which could then be “optimized” utilizing appropriate bronchodilators, inhaled steroids, Cromalyn Sodium, Montelukast, and other measures.

Summary: At least 1 week prior to spine surgery, patients with significant asthma should undergo preoperative pulmonary assessment (spirometry) to determine whether “optimization” with bronchodilators, inhaled steroids, Cromalyn Sodium, Montelukast, or other measures are warranted.

Chronic obstructive pulmonary disease

Patients with COPD need to be carefully screened to determine whether they are candidates for spinal surgery (inclusive of medications). Santus *et al.* characterized COPD as “neutrophilic airway inflammation and oxidative stress modulated via Leukotriene B (4) (LTB (4)), a potent proinflammatory mediator”, and recommended that clinically employing bronchodilators may optimize these patients for spine surgery.^[56]

Summary: Utilization of bronchodilators for patients with COPD may facilitate optimizing them for spinal surgery.

Cessation of smoking prior to spinal surgery: Duration of 4–8 weeks correlates with respiratory benefits

The negative musculoskeletal impacts of smoking on patients undergoing spinal surgery are well known.^[3,70]

These include impaired healing, more infections, delayed or impaired union/fusion, and inferior arthroplasty outcomes.^[3] When Wong *et al.* reviewed 25 studies regarding the timing for cessation of smoking prior to spine surgery they found: (1) respiratory complications were comparable for patients who did not stop smoking or who quit within <2–4 weeks preoperatively, (2) cessation of smoking at least 3–4 weeks before surgery improved wound healing, and (3) for those who quit smoking >4–8 weeks preoperatively, the risk of respiratory complications was reduced.^[71]

Summary: Cessation of smoking >4–8 weeks prior to surgery reduced respiratory complications, while the failure to quit smoking within <2–4 weeks of surgery did not. Additionally, cessation of smoking 3–4 weeks preoperatively improved wound healing.

Increased risks of sleep apnea and respiratory complications in diabetic patients undergoing spinal surgery

In Plantigna *et al.* series, sleep apnea positively correlated with the diagnosis of diabetes.^[53] In diabetic patients with undiagnosed sleep apnea, narcotic pain medication utilized following spinal surgery increased susceptibility to hypoventilation, aspiration, and pneumonia. They recommended that physicians be aware of sleep apnea as a diabetes-related risk factor/condition, and that appropriate treatment be instituted early to increase patients' safety and quality of life.

Summary: Sleep apnea is more prevalent in diabetic patients who, if undiagnosed prior to lumbar surgery, are susceptible to hypoventilation, aspiration, and pneumonia while utilizing routine narcotic pain medication.

ANESTHESIA FOR SPINAL SURGERY

There may be a role for spinal, epidural, combined spinal/epidural, and local anesthesia in spinal surgery

Some have found that spinal/local anesthetic techniques offer several advantages over general anesthesia for lumbar spinal surgery.^[12,30,31] Jellish and Shea observed multiple advantages of spinal anesthesia (e.g., combinations of subarachnoid and epidural dosing schemes) for lumbar spinal surgery. Intraoperatively, patients position themselves, mitigating neurological deficits associated with general anesthesia in the prone position, intraoperative blood loss (IBL) is reduced, and patients are more hemodynamically stable.^[31] Postoperatively, patients exhibit less pain (lower analgesia requirements), less nausea/vomiting, lower incidence of DVT, less urinary retention, shorter lengths of stay (LOS), and improved patient satisfaction.^[31]

Jellish *et al.* further documented better postlaminectomy and microdiscectomy outcomes utilizing spinal bupivacaine with epidural clonidine, and local infiltration of 0.5% bupivacaine at the lumbar incision sites in 120 patients.^[30] Pain scores were lower and analgesic requirements reduced for patients receiving both epidural clonidine and subcutaneous bupivacaine; together they improved pain relief so postoperative opioid dosages could be reduced along with their side effects.^[30]

Duger *et al.* also documented the efficacy (postoperative analgesia/sedation) and reduced side effects associated with utilizing epidural, or combined spinal/epidural anesthesia vs. spinal anesthesia alone (all with systemic morphine) for performing 64 lumbar laminectomies.^[12]

Summary: Some authors have documented a reduced perioperative morbidity associated with lumbar surgery performed under spinal (bupivacaine) and/or epidural (clonidine) anesthesia supplemented with local anesthetics (0.5% bupivacaine).

INFECTION

Risk of spinal infections and prophylaxis

The risk of postoperative spinal infections varies from 0.4% to 3.5%, but may be reduced utilizing multiple preoperative, intraoperative, and postoperative measures.^[17] Multiple preoperative prophylactic maneuvers, particularly aimed at preventing Methicillin-resistant *Staphylococcus aureus* (MRSA) include; (1) nasal cultures and nasally applied Bactroban ointment (mupirocin), (2) washing for several weeks with chlorhexidine gluconate (CHG) 4% (avoid ears, eyes, and groin), (3) the routine administration of a cephalosporin (not penicillin allergic) given within 60 minutes of surgery, (4) copious intraoperative irrigation [normal saline (NS) and/or NS with antibiotic (Polymyxin B Sulfate) applied every 15 minutes], (5) considering utilization of instrumentation coated/impregnated with antibiotics, and (6) potentially, the use of topical antibiotics. Other postoperative measures may include a silver (AgNo(3))-impregnated dressing (Silverlon dressing), and bed baths with CHG 4%.

Summary: The risk of postoperative spinal infections varies from 0.4% to 3.5%, but may be reduced utilizing multiple preoperative, intraoperative, and postoperative preventative measures.

Avoiding nosocomial surgical site infections

Harrop *et al.* observed that the majority of surgical site infections (SSI) were nosocomial (e.g., hospital-acquired contaminant/infections), and that these led to revision surgery, delayed wound healing, increased use of antibiotics, and increased LOS.^[27] Measures required to avoid SSI included; proper skin preparation, vigilant

sterile technique, shorter operative procedures, and fewer personnel walking in and out of the operating room.^[27] These factors proved more important than patient-related comorbidities (e.g., diabetes mellitus, obesity, and preexisting colonization with MRSA).

Sound levels including talking in the operating room and at the operating room table contribute to surgical site infections

Kurmann *et al.* documented what many of us already know; that talking in the operating room and/or at the operating room table may increase the risk of SSI.^[35] The authors performed a study evaluating the “noise level in an operating theatre as a possible surrogate marker for intraoperative behavior, and to detect any correlation between sound level and subsequent SSI.”^[35] Sound levels and surgical team behavior were correlated with a 17% 30-day postoperative SSI rate. Sound levels were 2-fold higher for patients with SSI, and discussions were typically unrelated to the surgery. They attributed the latter to a “lack of concentration, or a stressful environment, and may therefore represent a surrogate parameter by which to assess the behavior of a surgical team.”^[35]

Summary: Measures required to avoid SSI, especially nosocomial, include; proper skin preparation, vigilant sterile technique, shorter operative procedures, fewer personnel walking in and out of the operating room, and limiting noise levels/talking.

Comparative efficacy of two skin preparation solutions (chloraprep and duraprep) utilized for spine surgery

The relative efficacy of different skin preparation solutions utilized prior to spine surgery has been thoroughly investigated. Savage *et al.*, in a prospective randomized study, evaluated two commonly used skin preparation solutions for 100 consecutive patients undergoing lumbar spinal surgery.^[58] The two Food and Drug Administration (FDA) approved solutions included; Chloraprep (2% CHG and 70% isopropyl alcohol) or Duraprep (0.7% iodine and 74% isopropyl alcohol). Cultures were obtained (aerobic/anaerobic) before and after skin preparation, and following wound closure. Prior to skin preparation, an 82% positive culture rate was observed for Coagulase-negative Staphylococcus, Propionibacterium acnes, and Corynebacterium. Positive cultures following skin preparation were 0% for Chloraprep (0/50) and 6% (3/50) for Duraprep. After wound closure, comparable increases in positive skin cultures were observed for both the Chloraprep group (34%) and Duraprep group (32%). The two skin preparation solutions provided comparable prophylaxis against SSI.

Summary: Two commonly utilized skin preparation solutions (Chloraprep and Duraprep) provided comparable skin prophylaxis for spinal surgery.

Hibiclens (chlorhexidine) bathing may reduce central venous catheter infections

Montecalvo *et al.* observed that prophylaxis with Hibiclens (CHG 2%) vs. soap and water significantly reduced the incidence of infection/sepsis following the placement of central venous catheters; 2.6/1000 central venous catheter days (Chlorhexidine) vs. 6.4/1000 central venous catheter days (soap and water).^[47] The results were “sustained postintervention when chlorhexidine bathing was unmonitored”. These authors concluded that Chlorhexidine bathing reduced central venous catheter-associated bloodstream infection.^[47]

Efficacy of daily bathing with chlorhexidine for reducing healthcare-associated blood stream infections

O'Horo *et al.* studied the beneficial impact of daily bathing with Chlorhexidine (CHG) for avoiding blood stream infections (BSI) in various hospital (including intensive care unit (ICU)) settings.^[50] They found that 291 (0.0043) CHG patients developed a BSI over 67,775 patient-days vs. 557 (0.008) control patients over 69,617 catheter-days. They concluded that daily baths utilizing CHG decreased the frequency of BSI, including central line-associated BSI, for medical ICU patients.^[50] They recommended that other studies be performed to address issues like the optimal frequency of CHG application, the method, the concentration, and indications (e.g., ICU and non-ICU populations) for its use.^[50]

Bathing prior to and following spinal surgery with hibiclens (chlorhexidine gluconate)

In many institutions, a routine measure utilized to avoid spinal SSI is to bathe with Hibiclens the night before and the morning of spinal surgery. Hibiclens operative sponges may be dispensed at same day testing. Epstein also recommended that patients bathe with Hibiclens for up to 2 weeks prior to surgery, and receive Hibiclens baths twice a day while hospitalized postoperatively.^[17] Prior to surgery, patients may apply Hibiclens with a washcloth after showers/baths. This may be applied to all areas except the eyes, ears, and groin, with concentration on the proposed surgical site. After application, Hibiclens should be washed off. Postoperatively, Hibiclens cloth baths may continue, with the same restrictions, assisted by the nursing staff.^[17]

Summary: Daily bathing with Chlorhexidine (CHG) avoids BSI. Many hospitals provide CHG brushes for bathing the night before and the morning of surgery to reduce SSI. Others promote even longer preoperative utilization of CHG baths (e.g., for up to 2 weeks preoperatively, during the hospital stay, and postoperatively).

Antibiotic prophylaxis for spinal surgery utilizing a cephalosporin

There is an ongoing debate as to which antibiotic prophylaxis regimens are better/best for avoiding SSI. Petignat *et al.* in a double-blind, placebo-controlled, randomized clinical trial, established the efficacy of a single dose of 1.5 g cefuroxime in preventing lumbar disc SSI (up to 6 months postoperatively).^[52] SSI occurred in only 1.3% of patients receiving cefuroxime vs. 2.8% in the placebo group. No patient in the cefuroxime vs. 9 in the placebo group developed spondylodiscitis or epidural abscesses.

Efficacy of cefuroxime and gentamicin as prophylaxis against Methicillin-resistant *Staphylococcus aureus*

Hammond *et al.* evaluated the prevalence of MRSA in 175 patients transferred to neurosurgery units; screening occurred in 61% of patients, 15% of whom were MRSA positive.^[25] They concluded that Gentamicin was active against >95% of MRSA strains in the institution overall, and against 87% of MRSA strains documented for the neurosurgery unit.^[25] They further determined cefuroxime plus gentamicin administered together on induction could prevent one MRSA infection/421 treated patients vs. those only treated with cefuroxime. They ultimately reserved Vancomycin for those clearly colonized with MRSA.

Epstein recommended that the optimal antibiotic prophylactic regimen to prevent SSI should include utilizing 2 gm of a cephalosporin (e.g., Cefazolin) administered within 1 h of surgery (others prefer 15 minutes), and one preoperative dose of Gentamicin (dose tailored to the patient) as additional prophylaxis against MRSA.^[17] There is disagreement regarding the continuation of postoperative antibiotic prophylaxis. However, Epstein utilizes 2 g of Cefazolin every 8 h for 48 h, and then 1 g Cefazolin every 8 h until the drains are removed.

Summary: Cefuroxime and Gentamicin provide increased prophylaxis against MRSA at the time of induction of anesthesia for patients undergoing spine surgery.

Silver impregnated dressings may limit postoperative wound infections

Biffi *et al.* evaluated in a randomized, double-blind trial, the value of silver impregnated antimicrobial dressings (Aquacel (R) Ag Hydrofiber) in preventing SSI (over 30 postoperative days) for patients undergoing elective surgery for colorectal cancer.^[7] Although the SSI rate was less than the control population, overall 15.5% vs. 20.4%, differences were not considered statistically significant.^[7]

Barnea *et al.* also reviewed the utility of Aquacel Ag (R) that contained soft nonwoven sodium carboxymethylcellulose fibers integrated with ionic silver; they found it to be both safe and effective in reducing various types of wound infections.^[6] The dressing retained moisture, and on contact formed a gel that contained

ionic silver with resultant antimicrobial effects. Their study evaluated both the *in vitro* and *in vivo* efficacy, and the clinical applications of the dressing. Dressing provided antimicrobial efficacy, and the ionic silver proved cytotoxic to keratinocytes/fibroblasts either of which may delay in-wound re-epithelialization.^[6] Other advantages included: reduced local pain, fewer dressing changes, and broad-spectrum antimicrobial properties that did not negatively impact wound healing.

The incidence of SSI was lowered by utilizing silver impregnated dressings in 106 of Epstein's patients undergoing lumbar spinal surgery.^[15] The incidence of postoperative spinal infection was assessed in a prospective cohort of 106 patients undergoing instrumented lumbar fusions utilizing postoperative silver-impregnated dressing (SD; Silverlon, Argentum Medical, LLC, Lakefront, GA). Postoperative infection rates were compared to those observed in 128 comparable patients who previously underwent instrumented lumbar fusions utilizing routine dressings (RD): iodine- or alcohol-based swab and dry 4 × 4 gauze.^[15] For those receiving SD, no postoperative deep or superficial wound infections/irritation were observed, while 3 with RD developed deep postoperative wound infections (culture confirmed and managed with 6 weeks of postoperative antibiotics), and 11 acquired superficial infections. Although the numbers were small (0/106 with SD vs. 14/128 with RD), SD appeared to limit/reduce the incidence of both postoperative deep and superficial wound infections following lumbar-instrumented fusions.

Summary: Silver impregnated dressings did not significantly limit/reduce the incidence of wound infections in a series of patients undergoing elective colon surgery, however, it did appear to reduce postoperative deep and superficial wound infections following lumbar-instrumented fusions.

GASTROINTESTINAL DISORDERS

Rare esophageal perforation following anterior cervical surgery and thoracic fractures

Esophageal injuries/perforations are infrequently encountered following anterior cervical surgery or spinal trauma. Patients with continued drainage, fever, infection, and dysphagia 1 week following an anterior cervical procedure, must be suspected of having sustained an esophageal tear.^[23] Unrecognized esophageal perforation following spinal trauma, may lead to mediastinitis and sepsis. In Lee *et al.* case report, a "missed" esophageal perforation following a T2 compression fracture led to osteomyelitis involving adjacent vertebrae 5 months later.^[38] The original CT/MR studies failed to document periesophageal-free gas, and contrast esophagography

showed no leakage from the esophagus. Although the subsequent MR demonstrated a T1-T2 lesion that could not be differentiated from esophageal cancer with local tumor infiltration vs. infection, it was presumptively and successfully treated with 4 months of antibiotic therapy; the “lesion” did not recur (2-year follow-up).^[23]

Summary: Esophageal injuries/perforations are infrequently encountered following anterior cervical surgery or spinal trauma. Continued drainage, fever, infection, and dysphagia 1 week following anterior cervical surgery should prompt one to suspect an esophageal tear. The surgical approach, and the potential for a major esophageal complication with anterior cervical procedures, should prompt careful consideration of the alternative, posterior cervical surgery, when feasible.

NEUROLOGICAL DISEASES

Diagnosis of multiple sclerosis

Multiple Sclerosis (MS), a chronic demyelinating disease involving the central nervous system, often presents with variable manifestations; atypical motor deficits, sensory findings, and spasticity (hyper-reflexic symptoms/signs).^[42] Due to its variability, MS is often misdiagnosed. This was demonstrated by Levin *et al.* in a series of 29 patients (58%) who were initially given 41 incorrect diagnoses. The majority were women diagnosed with “mental/psychiatric problems”, while the males were typically assigned “orthopedic” diagnoses. Patients were referred to an average of 2.2 +/- 1.3 specialists prior to being sent to a neurologist, and MS was ultimately diagnosed an average of 3.5 years following the initial onset of symptoms.^[42]

Summary: Establishing the diagnosis of MS is often delayed. In one series, it took an average of 2.2 years before patients were referred to a neurologist, and an average of 3.5 years (following the initial onset of symptoms) before MS was correctly diagnosed.

Differentiating multiple sclerosis from cervical spondylotic myeloradiculopathy, and recognizing MS-related deficits and types

It is often difficult to differentiate the symptoms and signs of MS from cervical spondylotic myeloradiculopathy (CSM).^[4] Although the two entities can coexist in select (rare) patients, more typically MS predominates. In Arias *et al.* series, 18 MS patients presented at the average age of 50 years (12 females and 6 males), and their most frequent initial symptoms included; motor deficits (33%), multisystem deficits (33%), and cerebellar disorders (16%).^[4] The clinical course (minimum 5-year follow-up) included: primary progressive-MS (62%), secondary progressive-MS (22%), or relapsing-remitting-MS (16%).

Summary: The symptoms and signs of MS that may “mimic” cervical CSM, typically include; motor (33%), multisystem (33%), and cerebellar disorders (16%). The three major types of MS are primary progressive-MS (62%), secondary progressive-MS (22%), or relapsing-remitting-MS (16%).

Barkhof criteria seen on magnetic resonance scans in multiple sclerosis patients

The Barkhof Criteria as observed on MR scans of MS patients include: “(a) at least 1 gadolinium-enhancing lesion or at least 9 lesions on T2-weighted images, (b) at least 3 periventricular lesions, (c) at least 1 juxtacortical lesion, and (d) at least 1 infratentorial lesion”.^[4,57] In Arias *et al.* series, abnormal hyperintense signals seen on cranial MR studies indicative of MS were observed in all patients, and 12 of 18 cases (67%) fulfilled the Barkhof criteria.^[4] The majority of MS patients exhibited positive oligoclonal IgG bands in the CSF (64%), and abnormal visual evoked potentials (VEPs) (73%).^[4] The most frequent incorrect differential diagnoses included: cerebrovascular disorders and cervical spondyloarthritic/spondylotic myelopathy (CSM).

Summary: The Barkhof Criteria observed on MR scans of MS patients include: “(a) at least 1 gadolinium-enhancing lesion or at least 9 lesions on T2-weighted images, (b) at least 3 periventricular lesions, (c) at least 1 juxtacortical lesion, and (d) at least 1 infratentorial lesion.”

Intramedullary cervical plaque (C4-C7) consistent with adolescent multiple sclerosis

Selviardis *et al.* reported a 15-year-old female who presented with progressive spastic quadriplegia, attributed to an MR-documented, hyperintense (on T2 weighted images) intramedullary spinal lesion extending from C3-C7.^[61] The etiology of her lesion was uncertain; differential diagnoses included an intramedullary tumor vs. MS. As the brain MR and other studies were negative for MS, a surgical biopsy was performed; the pathology was consistent with an MS plaque.^[61]

Summary: Intramedullary spinal MS lesions may mimic intrinsic spinal cord tumors. In order to avoid inadvertent biopsy of these lesions, additional preoperative studies (e.g., evoked response testing, other tests) to rule out MS are warranted.

Differentiation of cervical spondylotic myeloradiculopathy from neuromyelitis optica (Neuromyelitis optica or Devic syndrome)

It is important to differentiate spinal pathology from Devic Syndrome (Neuromyelitis optica (NMO)).^[49] While NMO is a disabling inflammatory process that targets astrocytes in the optic nerves and spinal cord, unlike MS, only 50% of patients originally present with isolated unilateral optic neuritis. These episodes may occur many months/years prior to further demyelinating events,

and/or may present in a typical MS-related progressive fashion. NMO is characterized by the serum antibody aquaporin-4 called NMO-IgG (e.g., 75% sensitivity). Acute NMO attacks are typically managed with high-dose intravenous steroids, and less often plasma exchange. Preventive measures may include broad-spectrum or selective B-lymphocyte immune suppression.^[49]

Summary: NMO (Devic Syndrome) is a disabling inflammatory process that targets astrocytes in the optic nerves and spinal cord, but unlike MS, only 50% of patients experience isolated unilateral optic neuritis. Preventive measures include broad-spectrum or selective B-lymphocyte immune suppression, and acute attacks can be managed with high-dose intravenous steroids, and occasional plasma exchange.

Differentiating amyotrophic lateral sclerosis from spinal disease

Amyotrophic lateral sclerosis (ALS) is a progressive neurological disorder. Differentiating ALS from other treatable/untreatable disorders (e.g., multifocal motor neuropathy, CSM, or MS) early in the clinical course may avert unnecessary spinal surgery, and other therapeutic interventions.^[8] Cellura *et al.* retrospective analysis revealed an average diagnostic delay of 11 months for 260 ALS patients (e.g. average of 10 months with predominant bulbar-symptoms (65 patients), and 12 months with spinal complaints (195 patients)), and discovered that 31.1% of patients initially received incorrect diagnoses.^[8]

Summary: The diagnosis of ALS is often delayed for up to 11 months, and 31.1% of patients initially receive incorrect diagnoses.

PSYCHIATRIC DISORDERS

Psychiatric disorders and spine disease

It is critical to recognize when concurrent, significant psychiatric disease is present in patients with spinal complaints, especially when considering them for spinal surgery. Patients with psychiatric disorders and pain alone, without focal neurological deficits, and/or positive radiographic findings, should be treated conservatively (without surgery) by neurologists and psychiatrists. However, for patients with significant psychiatric pathology, with pain and critical neurological and/or radiographic findings, the decision to treat conservatively (without surgery) vs. surgically becomes far more complex. Studies focusing on psychiatric comorbidities in patients with spinal complaints (pain alone vs. pain with significant neurological deficits/radiographic pathology) differ in terms of their recommendations for or against surgical intervention.^[5,37]

Summary: Studies focusing on psychiatric comorbidities in patients with spinal complaints (pain alone vs. pain with significant neurological deficits/radiographic

pathology) differ in terms of their recommendations for or against surgical intervention.

Microdiscectomy (Surgery) was effective and improved depression

Even with significant underlying depression, in carefully selected cases where spinal pathology is clear and focal, as with microdiscectomy, surgery may be effective. Lebow *et al.* evaluated 100 patients who underwent microdiscectomy, and followed them for depression, somatization, and mental well-being postoperatively for 6 weeks, and 3, 6, and 12 months.^[37] Patients improved on postoperative outcome measures leading the authors to conclude, “microdiscectomy significantly improves pain-associated depression, somatic anxiety, and mental well-being in patients with herniated lumbar disc”.^[37]

Summary: Microdiscectomy significantly improve pain-associated depression, somatic anxiety, and mental well-being in patients with herniated lumbar disc.

Depression and anxiety negatively impact outcomes of instrumented fusion for failed back surgery

Despite the best intentions, the documented need for spinal surgery (e.g. positive radiographic and physical examination findings), and correctly performed surgery, some patients with significant psychiatric pathology will still exhibit poor outcomes. In Arts *et al.*, 82 patients with failed back syndromes were evaluated prior to secondary spinal instrumented fusions on multiple outcome scales (including psychiatric scales); VAS, functional disability (Roland Disability Questionnaire for Sciatica (RDQ), ODI, and The Hospital Anxiety and Depression Scale (HADS)).^[5] Underlying depression/anxiety disorders contributed to poor outcomes; at 15 postoperative months, 35% reported good outcomes, while 65% of outcomes were unsatisfactory. The HADS score documented “a possible anxiety disorder in 28% of patients, and in 30%, possible underlying depression.”^[5] The authors concluded that “conservative management is probably more beneficial and, therefore, more selective and careful assessment should be done in order to prevent unnecessary surgery.”

Summary: In a series of patients with failed back syndromes, secondary spinal fusions resulted in a high failure rate (65%), with nearly one-third of patients exhibiting anxiety/depression disorders. Conservative management may be more beneficial and selective and careful assessment should be performed to prevent unnecessary surgery.

CONCLUSION

As spine surgeons, expanding our medical knowledge, particularly regarding major comorbidity risk factors, should help us improve patient selection and more

effectively treat patients with spine disease. After all, we along with our medical colleagues, share a common goal; promoting the best care and outcomes for our patients.

ACKNOWLEDGEMENT

I would like to thank Ms. Sherry Lynn Grimm, Office Administrator of Long Island Neurosurgical Associates for encouraging me to write and helping to edit this article. I also thank Dr. James Ausman for his astute comments.

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Disclaimer: No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. No funds were received in support of this article.