Perioperative Management & Optimization of Spine Patient

ARTICLES see below
Full Program TBD

Co-Chairs:
Professor Michael Fehlings (Host)
Professor Albert Yee
Co-Directors, U of T Spine Program

Info: Nadia Jaber at uoft.spine@utoronto.ca

This is an accredited group learning activity as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada.
BACKGROUND: Opioid use disorders in the United States have rapidly increased, yet little is known about the relationship between preoperative opioid duration and dose and patient outcomes after spine surgery. Likewise, the utility of preoperative opioid weaning is poorly understood.

OBJECTIVE: The purpose of this evidence-based clinical practice guideline is to determine if duration and dose of preoperative opioids or preoperative opioid weaning is associated with patient-reported outcomes or adverse events after elective spine surgery for degenerative conditions.

METHODS: A systematic review of the literature was performed using the National Library of Medicine/PubMed database and Embase for studies relevant to opioid use among adult patients undergoing spine surgery. Clinical studies evaluating preoperative duration, dose, and opioid weaning and outcomes were selected for review.

RESULTS: A total of 41 of 845 studies met the inclusion criteria and none were Level I evidence. The use of any opioids before surgery was associated with longer postoperative opioid use, and longer duration of opioid use was associated with worse outcomes, such as higher complications, longer length of stay, higher costs, and increased utilization of resources. There is insufficient evidence to support the efficacy of opioid weaning on postoperative opioid use, improving outcome, or reducing adverse events after spine surgery.

CONCLUSION: This evidence-based clinical guideline provides Grade B recommendations that preoperative opioid use and longer duration of preoperative opioid use are associated with chronic postoperative opioid use and worse outcome after spine surgery. Insufficient evidence supports the efficacy of an opioid wean before spine surgery (Grade I).

The full guidelines can be accessed at https://www.cns.org/guidelines/browse-guidelines-detail/1-preoperative-opioid-evaluation.

KEY WORDS: Opioids, Elective spine surgery, Degenerative spine conditions, Outcomes, Adverse events

RECOMMENDATIONS

Question
1. Does duration of preoperative opioid use impact postoperative opioid use (duration, morphine milligram equivalents), patient-reported outcomes, or adverse events after spine surgery?

Recommendations

Longer duration of opioid use before spine surgery is associated with worse outcomes (chronic postoperative opioid use, higher complications, increased length of stay, and higher costs and utilization of resources).

Strength of Recommendation: Grade B

© Congress of Neurological Surgeons 2021. All rights reserved.
For permissions, please e-mail: journals.permissions@oup.com

Neurosurgery 01–8, 2021
https://doi.org/10.1093/neuros/nyab315 www.neurosurgery-online.com

Neurosurgery Speaks! Audio abstracts available for this article at www.neurosurgery-online.com.
Supplemental digital content is available for this article at www.neurosurgery-online.com.

ABBREVIATIONS: ACD, anterior cervical disectomy and fusion; MME, morphine milligram equivalents; NASS, North American Spine Society; NDI, Neck Disability Index; ODI, Oswestry Disability Index; PDMP, Prescription Drug Monitoring Program; SRS, Scoliosis Research Society
Question

2. Does preoperative morphine milligram equivalents impact postoperative opioid use (duration, morphine milligram equivalents), patient-reported outcomes, or adverse events after spine surgery?

Recommendations

Preoperative opioid use of any dose (yes/no) is associated with risk of longer duration of postoperative opioid use and worse clinical and patient-reported outcomes.

Strength of Recommendation: Grade B

Question

3. Does preoperative weaning of opioids impact postoperative opioid use (duration, morphine milligram equivalents), patient-reported outcomes, or adverse events after spine surgery?

Recommendations

There is insufficient evidence to support the efficacy of opioid weaning on postoperative opioid use, improving outcomes, or reducing adverse events after spine surgery.

Strength of Recommendation: Grade Insufficient

INTRODUCTION

Goals and Rationale

This clinical guideline was created to improve patient care by outlining the appropriate information gathering and decision-making processes involved in the treatment of patients with perioperative spinal disease. Spinal surgical care is provided in many different settings by many different providers. This guideline was created as an educational tool to guide qualified physicians through a series of diagnostic and treatment decisions to improve the quality and efficiency of care.

This guideline should not be construed as including all proper methods of care or excluding methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment must be made in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution.

Spine surgeries are often performed to treat painful spinal conditions and rates of spine surgery have increased over time. From 2005 to 2014, opioid use disorders increased 6.47% annually in the United States and were reported 25% more often between 2010 and 2014 compared with 2005 to 2009 among patients hospitalized for treatment of spinal conditions. In the current opioid crisis, provider prescribing practices and the effects of perioperative opioid use are under intense scrutiny. Despite increasing attention to opioid use, evidence to support best practice regarding preoperative opioid dose and duration in the management of patients with surgical degenerative spine disease is not well known. Likewise, the efficacy of preoperative opioid weaning is poorly understood, although this has been suggested as a potential intervention.

The purpose of this work is to systematically review the literature to form evidence-based guidelines regarding the relationship between duration and dose of preoperative opioids and patient-reported outcomes and adverse events after elective spine surgery for degenerative conditions. We also review the literature regarding the association between preoperative opioid weaning and these outcomes.

METHODS

The guidelines task force initiated a systematic review of the literature and evidence-based guideline relevant to the preoperative treatment of patients with spinal disorders. Through objective evaluation of the evidence and transparency in the process of making recommendations, this evidence-based clinical practice guideline was developed for the diagnosis and treatment of adult patients with various spinal conditions. These guidelines are developed for educational purposes to assist practitioners in their clinical decision-making processes. Additional information about the methods used in this systematic review is provided below.

Literature Search

Task force members identified search terms/parameters and a medical librarian implemented the literature search, consistent with the literature search protocol (see Supplemental Digital Content 1), using the National Library of Medicine/PubMed database and Embase for the period from 1946 to September 20, 2019 using the search strategies provided in Supplemental Digital Content 1.

Inclusion/Exclusion Criteria

Articles were retrieved and included only if they met specific inclusion/exclusion criteria (Supplemental Digital Content 2). These criteria were also applied to articles provided by guideline task force members who supplemented the electronic database searches with articles from their own files. To reduce bias, these criteria were specified before conducting the literature searches.

Rating Quality of Diagnostic Evidence

The guideline task force used a modified version of the North American Spine Society’s (NASS) evidence-based guideline development methodology. The NASS methodology uses standardized levels of evidence (Supplemental Digital Content 3) and grades of recommendation (Supplemental Digital Content 4) to assist practitioners in easily understanding the strength of the evidence and recommendations within the guidelines. The levels of evidence range from Level I (high-quality randomized controlled trial) to Level IV (case series). Grades of
recommendation indicate the strength of the recommendations made in the guideline based on the quality of the literature. Levels of evidence have specific criteria and are assigned to studies before developing recommendations. Recommendations are then graded based upon the level of evidence. To better understand how levels of evidence inform the grades of recommendation and the standard nomenclature used within the recommendations, see Supplemental Digital Content 4.

Guideline recommendations were written using a standard language that indicates the strength of the recommendation. “A” recommendations indicate a test or intervention is “recommended”; “B” recommendations “suggest” a test or intervention; and “C” recommendations indicate a test or intervention or “is an option.” “I” or “Insufficient Evidence” statements clearly indicate that “there is insufficient evidence to make a recommendation for or against” a test or intervention. Task force consensus statements clearly state that “in the absence of reliable evidence, it is the task force’s opinion that” a test or intervention may be appropriate.

In evaluating studies as to levels of evidence for this guideline, the study design was interpreted as establishing only a potential level of evidence. For example, a therapeutic study designed as a randomized controlled trial would be considered a potential Level I study. The study would then be further analyzed as to how well the study design was implemented and significant shortcomings in the execution of the study would be used to downgrade the levels of evidence for the study’s conclusions (see Supplemental Digital Content 5 for additional information and criteria).

Revision Plans

In accordance with the Institute of Medicine’s standards for developing clinical practice guidelines, the task force will monitor related publications after the release of this document and will revise the entire document and/or specific sections “if new evidence shows that a recommended intervention causes previously unknown substantial harm; that a new intervention is significantly superior to a previously recommended intervention from an efficacy or harms perspective; or that a recommendation can be applied to new populations.” In addition, the task force will confirm within 5 yr from the date of publication that the content reflects current clinical practice and the available technologies for the evaluation and treatment for patients with perioperative spinal disease.

RESULTS

The literature search encompassed terms relevant to all chapters in this guideline series and yielded 6812 abstracts (5689 after duplicates were deleted). After a double-blind review, 845 abstracts were identified as relevant to the PICO (patient/population, intervention, comparison, and outcomes) question(s). Task force members reviewed all abstracts yielded from the literature search and identified the literature for full text review and extraction, addressing the clinical questions, in accordance with the literature search protocol (Supplemental Digital Content 1). Task force members identified the best research evidence available to answer the targeted clinical questions. When Level I, II, and/or III literature was available to answer specific questions, the task force did not review Level IV studies.

The task force selected 78 full-text articles for full text review. Of these, 37 were rejected for not meeting the inclusion criteria or for being off-topic. A total of 41 articles were selected for systematic review (Supplemental Digital Content 6).

DISCUSSION

Question

Does duration of preoperative opioid use impact postoperative opioid use (duration, morphine milligram equivalents), patient-reported outcomes or adverse events after spine surgery?

Recommendation

Longer duration of opioid use before spine surgery is associated with worse outcomes (chronic postoperative opioid use, higher complications, increased length of stay, and higher costs and utilization of resources). Strength of Recommendation: Grade B

Most studies met the criteria for Level II evidence and no studies met the criteria for Level I evidence. Preoperative opioid use was associated with postoperative opioid use after cervical fusion surgery, lumbar discectomy, and lumbar fusion surgery. While the literature varied on the definition of chronic opioid use, studies were similar in finding a significant association between duration of pre- and postoperative opioid use.

Level II Evidence

Cervical Fusion Surgery

In patients undergoing cervical spine surgery, chronic opioid use before surgery was associated with chronic opioid use after surgery, although definitions of “chronic opioid use” varied by study. Harris et al defined chronic postoperative opioid use as >120 d of filled opioid prescriptions or >10 opioid prescriptions filled between 3 and 12 mo after surgery. Among patients undergoing elective 1 or 2 level anterior cervical disectomy and fusion (ACDF) for degenerative diagnoses, they found that preoperative opioid use was strongly associated with chronic postoperative opioid use (odds ratio [OR] 5.7 [95% CI 5.3-6.2], P < .001). A history of drug abuse, depression, anxiety, and surgery in the western United States was also associated with chronic postoperative opioid use. Likewise, Karhade et al performed a chart review among patients undergoing ACDF at 2 academic medical centers and found that duration of preoperative opioid use of >180 d, antidepressant use, tobacco use, and Medicaid insurance were significant predictors of prolonged postoperative opioid use for at least 90 to 180 d after surgery. In the Humana database, Pugely et al also found that nearly half of preoperative opioid users continued to fill opioid prescriptions 1 yr after anterior or posterior cervical fusions. Duration of preoperative opioid use was also associated with lower rates of return to work status, disability, and higher costs in a workers’ compensation population undergoing single-level cervical fusions. Short-term opioid users,
defined as patients who received opioids for <3 mo, were more likely to return to work in the first year after surgery compared with intermediate (3-6 mo) and long-term (>6 mo) preoperative opioid users. Finally, Jain et al used the Humana commercial insurance database to study patients with opioid prescriptions for >6 mo before cervical fusion surgery and outcomes. They found higher risk of 90-d wound complications, emergency department visits, and pain-related emergency department visits among patients with chronic preoperative opioid use. They also noted that patients with preoperative chronic use were more likely to have chronic longer-term opioid use (defined as opioid use ≤1 yr after surgery), repeat cervical fusion surgery, and epidural or facet joint injections within the year after surgery.

Lumbar Surgery

In patients undergoing lumbar spine surgery, chronic opioid use before surgery was associated with chronic opioid use after surgery. Again, definitions of “chronic opioid use” were not standardized across studies. Karhade et al performed a chart review among patients undergoing surgery for lumbar disc herniation at 5 medical centers. The predictors of sustained postoperative opioids for 90 to 180 d after surgery included use of instrumentation, duration of preoperative opioid prescription of >180 d, and diagnosis of depression. Qureshi et al reported similar findings using the PearlDiver database. Preoperative opioid prescriptions were associated with long-term postoperative opioid prescriptions, defined as >3 mo after lumbar discectomy (OR 3.4). Comorbidities, such as fibromyalgia, migraine disorder, depression, and smoking, were also associated with increased odds of postoperative long-term opioid prescriptions. In a retrospective single-center study, Hockley et al compared minimally invasive and open transforaminal lumbar interbody fusion patients and found those undergoing minimally invasive surgery were less likely to report postoperative opioid use at the 3-mo follow-up. Anderson et al studied chronic opioid therapy after lumbar fusion surgery among patients with Workman’s Compensation claims. In this Ohio claims database study, they found that chronic opioid use before surgery, defined as opioids analgesics supplied for >120 d during the year before lumbar fusion, was associated with chronic opioid use. Chronic postoperative use was defined as opioid prescriptions supplied for >1 yr after the immediate 6 wk after surgery.

Tank et al used the Nationwide Inpatient Sample to study patients with a diagnosis of opioid dependence (International Classification of Diseases, 9th revision, Clinical Modification codes 304.0 for opioid-type dependence and 304.7 for combinations of opioid-type drug with any other) and duration of stay, costs, and surgical complications after elective primary or revision 1- or 2-level lumbar fusions. Opioid dependence was associated with higher odds of prolonged duration of stay of ≥5 d, surgical complications, and higher costs. Kalakoti et al in the Humana claims database between 2007 and 2015, found that duration of preoperative opioid prescriptions within 3 mo before surgery was significantly associated with opioid use 1 yr after anterior or posterior lumbar fusions. Jain et al used the Humana claims database from 2007 to 2016 and found that patients with a preoperative opioid prescription of >6 mo had a higher risk of 90-d emergency department visits and readmissions, wound dehiscence and infection, and revision surgery within 1 yr after posterior lumbar fusions. Finally, Connolly et al using an Optum commercial health insurance claims database, also found that duration of preoperative opioid use, indication for refusion, and diagnosis of depression were associated with increased risks of long-term opioid use after lumbar fusion, defined as postoperative long-term use for ≥365 d after surgery. The preoperative use of opioids for ≥250 d before surgery was associated with an increased odds of postoperative long-term opioid use (OR 220 [95% CI 149-326], P < .001).

Level III Evidence

Two Level III studies reported an association between duration of preoperative opioid use and postoperative outcomes. Rosenthal et al found that patients with opioid prescriptions 3 and 6 mo before spine surgery had a significantly increased risk of continued opioid use compared with patients with opioid prescriptions at 3 mo before surgery or with no opioid prescriptions before surgery. Oleisky et al studied chronic opioid use in a degenerative cervical and lumbar elective spine surgery population and found that the Edlund and the Schoenfeld definitions of chronic opioid use had the highest predictive ability for postoperative opioid use. The Edlund definition accounts for duration and usage of opioids and the Schoenfeld definition accounts for duration; both were associated with postoperative opioid use, patient satisfaction, and patient-reported disability and pain.

Question

Does preoperative morphine milligram equivalents impact postoperative opioid use (duration, morphine milligram equivalents), patient-reported outcomes, or adverse events after spine surgery?

Recommendations

Preoperative opioid use of any dose (yes/no) is associated with risk of longer duration of postoperative opioid use and worse clinical and patient-reported outcomes.

Strength of Recommendation: Grade B

The overall goal of this section was to evaluate the association between preoperative opioid dose and postoperative opioid use, patient-reported outcomes, or adverse events after spine surgery. However, most studies evaluated the relationship between clinical outcome and any preoperative opioid use vs none, did not delineate by preoperative morphine milligram equivalents (MME), or used nonstandardized dosing descriptions such as “weak” and “strong” opioids.

Most studies met the criteria for Level II evidence and no studies met the criteria for Level I evidence. The association...
between higher preoperative MME or weak vs strong opioid use before surgery and postoperative opioid use was inconsistent. In a Level II analysis of lumbar fusion surgery patients, Deyo et al20 linked the Oregon Prescription Drug Monitoring Program (PDMP) and the statewide hospital discharge registry and studied long-term postoperative opioid use. The cumulative opioid dose in the 7 mo before surgery was the strongest predictor of long-term postoperative use, defined as ≥4 opioid fills in the 7 mo after the index hospitalization with at least 3 of those more than 30 d after hospitalization. Long-term preoperative use was associated with long-term postoperative use (OR 10.8 [95% CI 8.2-13.2]). The odds of long-term opioid use also increased with increasing preoperative dose, with an OR of 15.47 (95% CI 8.53-28.06) for a preoperative mean daily dose of >39 MMEs. In a Level II subanalysis of the control ACDF group for 2 randomized studies of cervical arthrodesis, Anderson et al21 found weak opioid use was significantly associated with lower odds of achieving a composite success score including Neck Disability Index (NDI) at 24 mo after surgery (presumably compared with no opioid use, although this was not directly stated). However, in a later and larger study by Kelly et al,22 no significant association was found between preoperative opioid strength and outcomes. Opioid use was self-reported on a patient questionnaire. “Weak” opioid use was defined as codeine, propoxyphene, and hydrocodone. “Strong” opioid use was defined as oxycodone, morphine, and meperidine.

In a Level III analysis of patients undergoing cervical or lumbar surgery, Ahn et al23 reported no persistent postoperative opioid use difference between patients with any preoperative opioid use (yes/no) at either the first or second postoperative visits, 4 to 6 wk or 8 to 12 wk, after cervical or lumbar surgeries. However, patients with any preoperative opioid use reported significantly higher inpatient opioid consumption. All other studies consistently showed a significant association between any preoperative opioid use (yes/no) and postoperative opioid use and outcomes and are presented in the following sections.

**Level II Evidence**

**Cervical Fusion Surgery**

Reid et al24 studied 1- to 3-level patients undergoing ACDF and found that opioid-tolerant patients, defined as patients who filled an opioid prescription within the 30-d preoperative period, were more likely to have chronic postoperative opioid use >90 d after surgery (OR 4.42 [95% CI 2.02-9.63], P < .001). Lawrence et al25 reported a similar association between chronic preoperative opioid use (yes/no) and 2-yr poor outcome as assessed using a modification of the Robinson criteria. Chronic preoperative opioid use was defined as patients using daily opioid pain medication for 6 mo before surgery. Preoperative opioid use was also associated with increased iliac crest donor site pain at 1 and 2 wk after ACDF.26

Among a workers’ compensation population in Ohio who underwent single level anterior or posterior fusion surgeries, Faour et al11 reported an association between prolonged preoperative opioid use and a lower likelihood of return to work. Kalakoti et al27 used the Humana dataset to study preoperative chronic opioid use, defined as an active opioid prescription within 3 mo of surgery, among patients undergoing anterior cervical, posterior cervical or CI-2 fusions. Preoperative chronic opioid use (yes/no) was significantly associated with 2-yr reoperations, ED visits, epidural steroid and facet joint injections, and adverse events, including constipation, venous thromboembolism, acute renal failure, wound complications, infections, and neurological complications. Preoperative chronic opioid use was also associated with prolonged postoperative opioid use at 2 yr after surgery (OR 5.75 [95% CI 5.21-6.36], P < .001).

**Cervical and Lumbar Surgery**

Amraghani et al28 found patients reporting any preoperative opioid use had lower odds of being independent from self-reported opioid use at 12 mo after cervical or lumbar spine surgery compared with patients with no preoperative opioid use.

**Lumbar Surgery**

Six Level II studies focused on lumbar surgery and outcome. Any preoperative opioid use was consistently associated with higher risk of long-term opioid use after lumbar surgery. Lall et al29 and Adogwa et al30 similarly reported that preoperative opioid use (dichotomized yes/no preoperative use) significantly predicted weeks to opioid cessation after lumbar fusion. Adogwa et al31 also reported any preoperative prescription for opioids in the 6 mo before lumbar decompression and fusion surgery was associated with prolonged opioid use for > 1 yr after surgery.

Villavicencio et al32 found patients with any preoperative opioid use before undergoing transfarominal lumbar interbody fusion surgery for degenerative conditions were significantly more likely than nonusers to report higher pain scores (visual analog scale [VAS]) for low back, greater disability, and lower Medical Outcomes Study Survey Short Form 36 physical component summary scores 1 yr after surgery. O’Donnell et al33 also reported preoperative opioid use was a significant predictor of lower return to work rates after lumbar discectomies among Ohio workers’ compensation patients.

In the single study evaluating tramadol use, Hassan et al34 evaluated patients undergoing lumbar discectomy and found that preoperative tramadol abuse (meeting ≥1 Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria for substance use disorders within a 12-mo period) was associated with worse postoperative VAS scores for the low back and lower limb, worse Prolo functional rating scale, and higher complications during the follow-period than the nonuser control group. The tramadol group had a longer length of stay and was more likely to be using tramadol up to a year after surgery.

**Level III Evidence**

**Cervical and Lumbar Surgery**

Any preoperative opioid use was associated with higher early postoperative patient-controlled analgesia morphine
consumption in the first 3 d after lumbar spine surgery for degenerative changes. Five other Level III studies evaluated patients after cervical or lumbar spine surgeries. Armaghani et al. reported that any preoperative opioid use was associated with worse 2-yr outcomes (higher Oswestry Disability Index [ODI] or NDI scores, lower Medical Outcomes Study Survey Short Form 12 and EuroQol 5D health-related quality of life survey scores, and higher Numeric Rating Scale scores) compared with no use. Dunn et al. reported that preoperative opioid use was associated with chronic postoperative opioid use 1 yr after spine surgery.

Hills et al. used their institutional spine registry and the state’s PDMP data to study patient-reported outcomes after elective spine surgery. Preoperative chronic opioid use was defined as having an active prescription for opioids for >50% of the month for 3 consecutive months before surgery. Patients with any preoperative chronic opioid use had worse outcome at 1 yr after surgery, with higher odds of not achieving meaningful improvements in pain, function, and quality of life; higher odds of dissatisfaction with surgery; continued opioid use; and 90-d complications compared with patients without preoperative chronic opioid use. High preoperative opioid dosage >30 MMEs was significantly associated with postoperative chronic opioid use. Wick et al. also evaluated registry data for patients undergoing cervical or lumbar spine surgery in a single spine center. The odds of achieving a minimum clinically important difference in outcome decreased significantly as morphine equianalgesic dose increased from 47.8 to 90 mg per day (95% CI 29.0-60.0 mg/day).

Lumbar Surgery

Level III studies were also congruent with Level II studies in reporting a significant association between any preoperative opioid use (yes/no) and long-term postoperative opioid use. Compared with patients without preoperative opioid use, Kanaan et al. reported that patients with preoperative opioid use were associated with increased postoperative leg pain intensity 2 wk after lumbar spine surgery. Wright et al. defined chronic postoperative opioid use as a consecutive opioid prescription for >90 d within the first year after the lumbar discectomy or laminectomy surgery at a single center and found a significant association between preoperative and chronic postoperative opioid use. Albert et al. noted that preoperative opioid use was associated with postoperative use among 37 patients with lumbar pseudoarthrosis. O’Connell et al. reported a significant association between preoperative and postoperative opioid use among patients undergoing lumbar fusion surgery.

Deformity Surgery

Two Level III studies evaluated any preoperative opioid use (yes/no) and outcome after deformity surgery. Elsamadicy et al. found that preoperative opioid users reported greater first postoperative pain scores but that the reduction in pain score from baseline to discharge was greater in the preoperative opioid users than nonusers. The preoperative opioid use group also had a greater number of first ambulatory steps compared with the nonuser group (103.8 ± 144.4 vs 46.4 ± 84.0, P = .034). Mesfin et al. reported that preoperative opioid users had worse baseline ODI and Scoliosis Research Society (SRS) scores, but the mean improvement in ODI was similar between groups at 24 mo of follow-up. In contrast, the mean improvement in SRS pain scores was significantly higher for the preoperative opioid user group at 24 mo compared with the nonopioid user group. Overall mean change in SRS scores, however, was not significantly different between groups.

Question

Does preoperative weaning of opioids decrease postoperative opioids use (duration, morphine milligram equivalents), patient-reported outcomes, or adverse events after spine surgery?

Recommendations

There is insufficient evidence to support the efficacy of opioid weaning on postoperative opioid use, improving outcome, or reducing adverse events after spine surgery.

Strength of Recommendation: Grade Insufficient

There was a single Level II study that met the inclusion criteria for this question, without any additional supporting studies. Patients in this study were taken off opioids for a 3- to 489-mo prescription-free “drug holiday” before 1 or 2-level posterior lumbar fusion surgery and had risks of adverse outcomes, defined as emergency department visits, readmissions, and wound dehiscence and infection, that were similar to opioid-naïve patients, and lower than patients who had preoperative opioid prescriptions sustained for >6 mo.

Future Research

This systematic review of the literature highlighted areas that need further research. The relationship between differences in preoperative opioid dose and clinical outcome should be clarified. Only 1 study evaluated tramadol, and the relationship between MMEs and outcome remains unclear. More research is needed regarding interventions to reduce postoperative adverse events. The impact of preoperative opioid weaning and a preoperative opioid-free period on clinical outcome and postoperative opioid requirement should also be studied.

CONCLUSIONS

Overall, the literature is consistent in reporting an association between preoperative opioid use and duration with chronic postoperative use of opioids and outcome. The definition of pre- and postoperative use and outcome, however, differed between studies. The literature supports higher complications, worse outcome, and lower return to work among patients who use preoperative opioids, and patients who use preoperative opioids for a prolonged period before surgery. In addition, there are
limited data to support the efficacy of an opioid wean before spine surgery.

Funding

These evidence-based clinical practice guidelines were funded exclusively by the Congress of Neurological Surgeons and the AANS/CNS Joint Section on Disorders of the Spine and Peripheral Nerves (through a donation to the CNS Foundation), which received no funding from outside commercial sources to support the development of this document.

Disclosures

All Guideline Task Force members were required to disclose all potential conflicts of interest (COIs) before beginning work on the guideline, using the COI disclosure form of the AANS/CNS Joint Guidelines Review Committee. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination and participation on the task force. The CNS Guidelines Committee and Guideline Task Force Chair may approve nominations of task force members with possible conflicts and restrict the writing, reviewing, and/or voting privileges of that person to topics that are unrelated to the possible COIs. See below for a complete list of disclosures.

Table: Author Disclosure

<table>
<thead>
<tr>
<th>Author</th>
<th>Disclosure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marjorie C. Wang, MD, MPH</td>
<td>Zimmer Biomet, Medtronic, Abbott, ABNS, AANS, JNS Spine Editorial Board</td>
</tr>
<tr>
<td>James S. Harrop, MD, MSHQS</td>
<td>Depuy Synthesis, Ethicon, Globus, Stryker</td>
</tr>
<tr>
<td>Erica F. Bisson, MD, MPH</td>
<td>PCORI, NREF, MiRs, nView, Stryker, Medtronic, AO Spine, NREF, ISSS, Depuy, Globus, Stryker, Spinicity, ISD, Depuy, Thieme Publishers, Springer Publishers, CNS/NPA</td>
</tr>
<tr>
<td>Praveen V. Mummaneni, MD, MBA</td>
<td>Medtronic, Depuy, Stryker, Johnson &amp; Johnson, Pfizer, Glaxo-Smith Kline, Eli Lilly, Abbot, Hoffman La Roche, Abbie, Pfizer, Norton Hospital, Medtronic, Stryker, SRS &amp; FOSA (2020), JAAOS, Spine, Spinal Deformity, GSJ (Reviewer)</td>
</tr>
<tr>
<td>John Dimar, MD</td>
<td>Medtronic, Depuy, Stryker, Johnson &amp; Johnson, Pfizer, Hoffman La Roche, Abbie, Pfizer, Norton Hospital, Medtronic, Stryker, SRS &amp; FOSA (2020), JAAOS, Spine, Spinal Deformity, GSJ (Reviewer)</td>
</tr>
<tr>
<td>Sanjay Dhall, MD</td>
<td>Depuy Synthes, Globus Medical Great Circle Technologies</td>
</tr>
<tr>
<td>Daniel J. Hoh, MD</td>
<td>The Spine Journal Editorial Board, CNS Officer, CNS Foundation Board, JNS Spine Editorial Board, The Spine Journal Editorial Board</td>
</tr>
</tbody>
</table>

Disclaimer of Liability

This clinical, systematic, evidence-based clinical practice guideline was developed by a multidisciplinary physician volunteer taskforce and is provided as an educational tool based on an assessment of the current scientific and clinical information regarding this guideline topic. These guidelines are disseminated as an educational tool based on an assessment of the current scientific and clinical evidence and are not intended to be used as a substitute for the medical advice of an individual provider. The development of these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

REFERENCES


Acknowledgments

The guidelines task force would like to acknowledge the CNS Guidelines Committee for their contributions throughout the development of the guideline, the AANS/CNS Joint Guidelines Review Committee, the AANS/CNS Joint Section on Disorders of the Spine and Peripheral Nerves for their donation to the CNS Foundation to support this project, as well as the contributions of Kirsten Aquinto, contracted project manager for the CNS, Trish Rheing, MPH, Associate Director for Evidence-Based Practice Initiatives for the CNS, Janet Waters, MLS, BSN, RN, for assistance with the literature searches, and Kenneth Probst for the cover illustrations. Throughout the review process, the reviewers and authors were blinded from one another. At this time, the guidelines task force would like to acknowledge the following individual peer reviewers for their contributions: Patricia Raksin, MD, Jason Stacy, MD, Neil Majmunder, MD, Yi Lu, MD, Alex Beier, MD, Andrew Carlson, MD, Brandon Rocque, MD, Robert Whitmore, MD, Jay Turner, MD, and Owoicho Adogwa, MD.

Neurosurgery Speaks! Audio abstracts available for this article at www.neurosurgery-online.com.

Supplemental digital content is available for this article at www.neurosurgery-online.com.

Supplemental Digital Content 1. Literature searches.

Supplemental Digital Content 2. Inclusion criteria.

Supplemental Digital Content 3. Criteria grading the evidence.

Supplemental Digital Content 4. Linking levels of evidence to grades of recommendation.

Supplemental Digital Content 5. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart.

BACKGROUND: Patient factors (increased body mass index [BMI], smoking, and diabetes) may impact outcomes after spine surgery. There is a lack of consensus regarding which factors should be screened for and potentially modified preoperatively to optimize outcome. 

OBJECTIVE: The purpose of this evidence-based clinical practice guideline is to determine if preoperative patient factors of diabetes, smoking, and increased BMI impact surgical outcomes. 

METHODS: A systematic review of the literature for studies relevant to spine surgery was performed using the National Library of Medicine PubMed database and the Cochrane Library. Clinical studies evaluating the impact of diabetes or increased BMI with reoperation and/or surgical site infection (SSI) were selected for review. In addition, the impact of preoperative smoking on patients undergoing spinal fusion was reviewed. 

RESULTS: A total of 699 articles met inclusion criteria and 64 were included in the systematic review. In patients with diabetes, a preoperative hemoglobin A1c (HbA1c) > 7.5 mg/dL is associated with an increased risk of reoperation or infection after spine surgery. The review noted conflicting studies regarding the relationship between increased BMI and SSI or reoperation. Preoperative smoking is associated with increased risk of reoperation (Grade B). There is insufficient evidence that cessation of smoking before spine surgery decreases the risk of reoperation. 

CONCLUSION: This evidence-based guideline provides a Grade B recommendation that diabetic individuals undergoing spine surgery should have a preoperative HbA1c test before surgery and should be counseled regarding the increased risk of reoperation or infection if the level is > 7.5 mg/dL. There is conflicting evidence that BMI correlates with greater SSI rate or reoperation rate (Grade I). Smoking is associated with increased risk of reoperation (Grade B) in patients undergoing spinal fusion. The full guidelines can be accessed at https://www.cns.org/guidelines/browse-guidelines-detail/2-preoperative-surgical-risk-assessment 

KEY WORDS: Spine, Preoperative evaluation, Diabetes, Tobacco, HbA1c, Body mass index
**RECOMMENDATIONS**

**Question**
1. In patients with diabetes undergoing spine surgery, what preoperative diagnostic studies predict increased risk for reoperation or postoperative infection?

**Recommendations**

Diabetic individuals undergoing spine surgery should have a preoperative hemoglobin A1C (HbA1c) test before surgery and be counseled regarding the increased risk of reoperation or infection if the level is >7.5 mg/dL.

*Strength of Recommendation: Grade B*

There was insufficient evidence to support other preoperative diagnostic studies for predicting the risk for reoperation or postoperative infection in patients with diabetes undergoing spine surgery (eg, preoperative blood glucose levels).

*Strength of Recommendation: Grade Insufficient*

**Question**
2. Is increased body mass index (BMI) associated with increased risk for reoperation or postoperative infection in patients undergoing spine surgery?

**Recommendations**

There is conflicting evidence that increased BMI is associated with a greater risk of surgical site infection (SSI) in patients undergoing spinal surgery. Given the number of studies demonstrating a correlation between a BMI >30 kg/m² and SSI, particularly with lumbar surgery, the task force recommends that clinicians counsel patients with elevated BMI regarding this possible risk.

*Strength of Recommendation: Grade Insufficient*

There is conflicting evidence that increased BMI is correlated with an increased risk of reoperation after spinal surgery.

*Strength of Recommendation: Grade Insufficient*

**Question**
3. Is preoperative smoking associated with increased risk of reoperation in patients undergoing spinal fusion surgery? Does preoperative smoking cessation decreases risk of reoperation?

(Continued from previous page)

**Recommendations**

Individuals undergoing spinal fusion surgery who are active smokers should be counseled regarding the increased risk of reoperation.

*Strength of Recommendation: Grade B*

There is insufficient evidence that cessation of smoking before spine surgery decreases risk of reoperation, but it is suggested that patients be counseled to abstain from smoking before and after spinal fusion surgery.

*Strength of Recommendation: Grade Insufficient*

**INTRODUCTION**

**Goals and Rationale**

This clinical guideline was created to improve patient care by outlining the appropriate information gathering and decision-making processes involved in the treatment of patients with perioperative spinal disease. Spinal surgical care is provided in many different settings by many different providers. This guideline has been created as an educational tool to guide qualified physicians through a series of diagnostic and treatment decisions in an effort to improve the quality and efficiency of care.

This guideline should not be construed as including all proper methods of care or excluding methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment must be made in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution.

**Objectives**

Most spine surgeries are performed electively. This affords the surgeon and the preoperative team the opportunity to evaluate an individual patient for risk factors and to potentially optimize these factors before surgery. Diabetes, obesity, and smoking are 3 prevalent comorbidities that negatively impact health status, increase healthcare costs, and have been implicated in worse outcomes after spine surgery. There is a lack of consensus regarding appropriate screening for these factors and if preoperative modification improves outcome.

One objective of this review is to determine preoperative diagnostic studies that predict increased risk of reoperation or SSI in patients with diabetes. In addition, the published literature was assessed to determine if an increased BMI correlates with an increased risk of reoperation or SSI. Finally, the impact of preoperative smoking and risk of reoperation after spinal fusion was evaluated and if smoking cessation decreases risk.

**METHODS**

The guidelines task force initiated a systematic review of the literature and evidence-based guideline relevant to the preoperative treatment of patients with spinal disorders. Through objective evaluation of the
evidence and transparency in the process of making recommendations, this evidence-based clinical practice guideline was developed for the diagnosis and treatment of adult patients with various spinal conditions. These guidelines are developed for educational purposes to assist practitioners in their clinical decision-making processes. Additional information about the methods used in this systematic review is provided below.

**Literature Search**

The task force members identified search terms/parameter and a medical librarian implemented the literature search, consistent with the literature search protocol (see Supplemental Digital Content 1), using the National Library of Medicine/PubMed database and Embase for the period from 1946 to September 20, 2019, using the search strategies provided in Supplemental Digital Content 1.

**Inclusion/Exclusion Criteria**

Articles were retrieved and included only if they met specific inclusion/exclusion criteria (Supplemental Digital Content 2). These criteria were also applied to articles provided by guideline task force members who supplemented the electronic database searches with articles from their own files. To reduce bias, these criteria were specified before conducting the literature searches.

**Rating Quality of Diagnostic Evidence**

The guideline task force used a modified version of the North American Spine Society's (NASS) evidence-based guideline development methodology. The NASS methodology uses standardized levels of evidence (Supplemental Digital Content 3) and grades of recommendation (Supplemental Digital Content 4) to assist practitioners in easily understanding the strength of the evidence and recommendations within the guidelines. The levels of evidence range from Level I (high-quality randomized controlled trial) to Level IV (case series). Grades of recommendation indicate the strength of the recommendations made in the guideline based on the quality of the literature. Levels of evidence have specific criteria and are assigned to studies before developing recommendations. Recommendations are then graded based upon the level of evidence. To better understand how levels of evidence inform the recommendations, see the standard nomenclature used within the recommendations, see Supplemental Digital Content 4.

Guideline recommendations were written using a standard language that indicates the strength of the recommendation. "A" recommendations indicate a test or intervention is "recommended"; "B" recommendations "suggest" a test or intervention; and "C" recommendations indicate a test or intervention or "is an option." "I" or "Insufficient Evidence" statements clearly indicate that "there is insufficient evidence to make a recommendation for or against" a test or intervention. Task force consensus statements clearly state that "in the absence of reliable evidence, it is the task force's opinion that" a test or intervention may be appropriate.

When evaluating studies as to levels of evidence for this guideline, the study design was interpreted as establishing only a potential level of evidence. For example, a therapeutic study designed as a randomized controlled trial would be considered a potential Level I study. The study would then be further analyzed as to how well the study design was implemented and significant shortcomings in the execution of the study would be used to downgrade the levels of evidence for the study's conclusions (see Supplemental Digital Content 5 for additional information and criteria).

**Revision Plans**

In accordance with the Institute of Medicine's standards for developing clinical practice guidelines, the task force will monitor related publications after the release of this document and will revise the entire document and/or specific sections "if new evidence shows that a recommended intervention causes previously unknown substantial harm; that a new intervention is significantly superior to a previously recommended intervention from an efficacy or harms perspective; or that a recommendation can be applied to new populations." In addition, the task force will confirm within 5 yr from the date of publication that the content reflects current clinical practice and the available technologies for the evaluation and treatment for patients with perioperative spinal disease.

**RESULTS**

The initial literature search encompassed terms relevant to all chapters in this guideline series and yielded 6812 abstracts (5689 after duplicates were deleted). After a double-blind review, the literature search yielded 699 abstracts for this question. Task force members reviewed all abstracts yielded by the initial literature search. They identified the literature for full text review and extraction that addressed the clinical questions, in accordance with the literature search protocol (Supplemental Digital Content 1). Task force members identified the best research evidence available to answer the targeted clinical questions. When Level I, II, and/or III literature was available to answer specific questions, the task force did not review Level IV studies.

The task force selected 192 full text articles for full text review. Of these, 128 were rejected for not meeting inclusion criteria or for being off-topic. Sixty-four were included in the systematic review (Supplemental Digital Content 6). There were 5 articles selected for question 1 concerning diabetic preoperative diagnostic tests, and all of these were graded Level II. Question 2 had 54 articles selected where 41 focused on increased BMI and SSI. Thirty were graded Level II and 11 were graded Level III. Sixteen were selected on reoperation with 14 graded Level II and 2 graded Level III. Lastly, 8 articles were chosen for question 3 concerning reoperation risk factors with 6 graded Level II and 2 graded Level III.

**DISCUSSION**

**Question**

In patients with diabetes undergoing spine surgery, what preoperative diagnostic studies predict increased risk for reoperation or postoperative infection?
Recommendations

Diabetic individuals undergoing spine surgery should have a preoperative HbA1c test before surgery and be counseled regarding an increased risk of reoperation or infection if the level is >7.5 mg/dL.

Strength of Recommendation: Grade B

There was insufficient evidence to support other preoperative diagnostic studies for predicting the risk for reoperation or postoperative infection in patients with diabetes undergoing spine surgery (eg, preoperative glucose levels).

Strength of Recommendation: Grade Insufficient

There were 5 articles (Level II studies) demonstrating the relationship between increased HbA1c and risk of reoperation or infection after spinal surgery. Cancienne et al8 used preoperative HbA1c levels in patients with diabetes in 3341 anterior cervical discectomy and fusion patients requiring reoperation. In the series, a significant relationship was observed between increased HbA1c level and reoperation rate (P = .005), where a subanalysis determined the inflection point in the area under the curve of 7.5 mg/dL with a sensitivity of 46% and specificity of 68%. Hikata et al10 performed a retrospective review of 36 patients with diabetes (19 males and 17 females; median age 64.3 yr) who underwent thoracic and lumbar spinal fusion over a 6-yr period (2005-2011). Diabetics had an overall higher rate of infection (9/36 vs 10/309). There was no difference in infection based on preoperative serum glucose level, but preoperative HbA1c values were significantly higher in patients who developed SSI (7.6 mg/dL) than in those who did not (6.9 mg/dL). The authors defined controlled diabetes as a HbA1c < 7.0 mg/dL and there were no infections in that population compared with 35.3% in patients with HbA1c > 7.0 mg/dL.

In a separate analysis, Cancienne et al8 reviewed the effect of HbA1c on 5194 single-level lumbar decompressions and patients with diabetes. The infection point for infection by HbA1c level was >7.5 mg/dL (P = .01; specificity 70%, sensitivity 53%). In a subanalysis controlled for patient demographics and medical comorbidities, the authors reported that HbA1c > 7.5 mg/dL correlated with a higher risk for deep SSI (odds ratio [OR] 2.9 [95% confidence interval [CI] 1.8–4.9, P < .0001]. Caputo et al9 analyzed 3138 patients (2005-2010) and found that patients with diabetes had an increased risk for SSI (6.4% vs 3.2%). Perioperative blood glucose levels >140 mg/dL doubled the risk of an SSI (P = .0091). These authors did not identify a correlation with HbA1c measurements preoperatively; however, they used a higher threshold for HbA1c than the other studies (8.0%). Koutsoumbelis et al10 analyzed 3218 patients with posterior lumbar instrumented fusion over 6 yr (2000-2006) and reported a postoperative infection rate of 2.6%. Multiple regression analysis noted that diabetes mellitus was a predictor for SSI. Preoperative serum glucose levels did not correlate with SSIs, but there was a significant relationship with higher postoperative glucose levels and the infected group (P < .001).

Question

Is increased BMI associated with an increased risk for reoperation or postoperative infection in patients undergoing spine surgery?

Recommendations

There is conflicting evidence that increased BMI is associated with greater risk of SSI in patients undergoing spinal surgery. Given the number of studies demonstrating a correlation between BMI >30 kg/m² and SSI, particularly with lumbar surgery, the task force recommends that clinicians counsel patients with elevated BMI regarding this possible risk.

Strength of Recommendation: Grade Insufficient

There is conflicting evidence that increased BMI is correlated with an increased risk of reoperation after spinal surgery

Strength of Recommendation: Grade Insufficient

Lumbar

There were 42 lumbar surgery articles identified assessing increased BMI and SSI. Of the articles, 31 (25 Level II and 6 Level III articles) noted a direct correlation between increased BMI and SSI, while 10 articles (6 Level II and 5 Level III articles) showed no significant difference.

Lumbar Surgery: Studies Showing a Correlation Between Increased BMI and SSI

Most of the lumbar surgery studies were Level II and noted a positive correlation with increased BMI and a higher risk of SSI. Mehta et al11 reported 298 lumbar patients treated at a single institution (2006-2008) where 24 (8%) had postoperative infections. They reported that increased BMI (≥30 kg/m²) correlated with SSI (P = .025). Jain et al12 reviewed 36 440 patients (28 813 patients [79.07%] undergoing lumbar spine surgery) using the American College Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database. The overall rate of SSI was 0.72% (n = 264). They reported a significant correlation with increased BMI and infection (P < .001) that persisted in multivariate analysis. Wang et al13 reported a posterior lumbar SSI rate of 3.0% (267/8879 cases) and a significant correlation between increased BMI and SSI (P < .0001). De la Garza-Ramos et al14 retrospectively reviewed 732 lumbar fusion patients, 662 (90.44%) nonobese and 70 (9.56%) obese, and showed that increased BMI was associated with increased risk of postoperative SSI (relative risk 3.11 [CI 1.48-6.52]). Li et al15 further reviewed 448 patients undergoing transforaminal lumbar interbody fusion (TLIF) and compared SSI risk factors. In univariate analysis, there was a significant correlation with increased BMI (P < .001). Kurtz et al16 reviewed Medicare data with 15 069 primary fusion procedures and 605 revision procedures and noted an SSI rate of 8.5% in primary and 12.2% in revision procedures. Increased BMI was a significant predictor of 10-yr infection risk (P < .001). Puvanesarajah et al17 reviewed 48 210 patients ≥ 65 yr of age using Medicare...
Three Level III studies did not show an association between SSI and increased BMI. Pereira et al, reviewed 118 lumbar surgeries performed in 100 patients and noted no correlation between increased BMI and SSI. The 2 additional studies involved minimally invasive surgery approaches, which overall have a low incidence of infections. Goldin and Alander reviewed 82 patients who underwent lumbar surgery via various minimally invasive techniques with no significant difference in SSI rate (3 infections in the obese group and none in the control population). Fakouri et al reported a smaller series of patients undergoing minimally invasive surgery lumbar disectomy (34 obese and 30 nonobese patients) performed over 3 yr and noted that obese patients had 2 superficial infections, but this was not significant.

### Multilevel Lumbar or Thoracolumbar Surgery: Studies Showing a Correlation Between Increased BMI and SSI

There were 8 studies with multilevel lumbar or thoracolumbar surgery demonstrating a correlation between increased BMI and SSI (4 Level II studies and 4 Level III studies). Soroceanu et al reviewed 175 nonobese and 66 obese patients with adult spinal deformity (ASD). Their regression model noted that obese patients had a higher overall incidence of wound infection (OR 4.88, P = .02). In a retrospective study by Zhang et al, 153 patients with adult degenerative scoliosis with multilevel spinal fusion and 2 yr of follow-up reported an association between an increased risk of infection and elevated BMI (OR 1.11, P = .008). Sing et al identified 2536 patients in the ACS NSQIP database undergoing revision spine surgery and evaluated early (30-d) complications. They found that revision spine surgery and obesity correlated with increased wound complications on multivariate analysis (P = .028). Elsamadicy et al reviewed 500 patients (281 nonobese and 219 obese patients) undergoing elective spine surgery and reported an association between increased BMI and an increased risk for deep SSI (P = .04).

A study using the National Inpatient Sample database evaluated 244,170 thoracolumbar or lumbar spine fusion patients treated for degenerative disease (1988-2004). The authors reported that patients with morbid obesity (BMI ≥ 40 kg/m²) were 70% more likely to have an SSI (P < .01). Chin et al further reported on 1010 patients, 642 in a hospital setting and 368 in an outpatient setting, where increased BMI > 30 kg/m² was associated with a significant increase in SSI (relative risk (RR) 9.3, P = .005). Pull ter Gunne et al performed a retrospective review of 830 adult patients undergoing spinal deformity surgery for kyphosis or scoliosis. SSI occurred in 29 patients (3.5%) and increased BMI was found to be an independent risk factor (P = .014). In a case-control study of 55 patients with SSI after spinal surgery and 179 control spine surgery patients, increased BMI was noted as a risk factor for SSI in 32 of 47 (68%) vs 72 of 167 (43%) (OR 2.81 [95% CI 1.41-5.59], P < .003).

Four studies did not note a correlation between SSI and increased BMI performed in multilevel lumbar or thoracolumbar spine surgery. Two Level II articles both featured cohorts of

---

**Lumbar Surgery: Studies Showing No Correlation Between Increased BMI and SSI**

Two Level II studies reported no correlation between increased BMI and SSI. Both studies had smaller subject populations and involved anterior surgery, which is associated with an overall lower rate of SSIs than posterior surgery. Adogwa et al reported 63 patients (29 obese and 34 nonobese patients) undergoing lateral lumbar interbody fusion for degenerative spine disease (2010-2012). There was no correlation between increased BMI and SSI. Rodgers et al performed a retrospective study of lateral lumbar interbody fusion for lumbar degenerative disease in 313 patients (156 obese and 157 nonobese patients) and noted no association between increased BMI and SSI.
patients with deformities; 1 included 532 patients where 20 (4%) experienced SSIs. The second case-control study by Boston et al also reported no correlation in 55 patients who developed SSIs after spinal surgery and 179 control subjects with high BMI. An additional Level III article by Savetti et al reported no association between obesity and SSI in 387 spine surgery patients. The fourth article, a Level III article by Elsamadicy et al, reviewed 112 ASD patients (BMI > 30 kg/m²) undergoing elective complex spinal fusion (>7 levels) for deformity correction and found no correlation with increased BMI and SSI.

Cervical

Three studies demonstrated a correlation (all Level II) between BMI and SSI and 2 did not (both Level II). Jalai et al reviewed 3057 patients undergoing surgery for cervical spondylotic myelopathy with an overall infection rate of 1.15% (35/3057). Logistic regression analysis revealed that SSI correlated with increased BMI (OR 1.162 [95% CI 1.269-1.064], P = .001). In a review of patients undergoing posterior cervical spine surgery, 9 of 483 (1.86%) patients had an acute postoperative deep SSI. A significantly higher rate of infection was noted in patients with BMI > 30 kg/m² (OR 4.1 [95% CI 1.5-7.7], P = .005). In a study of 5441 posterior cervical surgery patients, 160 patients with SSI (2.94%), a multivariate analysis noted that a BMI > 35 kg/m² (OR 1.78, P = .003) independently correlated with SSI.

Buerba et al used the ACS NSQIP database from 2005 to 2010 to examine cervical anterior or posterior fusion and did not identify an association with increased BMI and SSI. In addition, Srinivasan et al evaluated a smaller series of 69 anterior cervical fusion patients and noted no significant correlation between BMI and SSI, but it should be noted that this study was underpowered to detect a difference because of the rare occurrence of anterior cervical infections.

Increased BMI and Risk of Reoperation

There is conflicting evidence regarding the association between increased BMI and reoperation rate, with most studies failing to demonstrate a correlation. There were 12 studies (11 Level II and 1 Level III) that showed no correlation. Specifically, cervical surgery studies (4 Grade II) and thoracolumbar (2 Level II) reported no association of increased BMI and reoperation. Four studies (3 Level II and 1 Level III) did report a correlation between increased BMI and reoperation, with all studies restricted to lumbar surgery.

Lumbar: Increased BMI Does Not Correlate With Increased Risk of Reoperation

Narain et al examined 274 patients who had undergone lumbar minimally invasive TLIF with multivariate Cox proportional hazards survival analysis to evaluate the risk of increased BMI and reoperation. Increased BMI was not associated with undergoing reoperation within 2 yr after minimally invasive TLIF (P = .599). Gerling et al performed a multivariate regression analysis of the 8-yr postoperative follow-up from the Spine Patient Outcomes Research Trial (SPORT) for spondylolisthesis (406 patients, 72% instrumented, 21% noninstrumented fusion, and 7% decompression alone) and reported no correlation between increased BMI and reoperation. In addition, Leven et al analyzed the 8-yr postoperative follow-up from a multicenter randomized controlled lumbar discectomy trial and noted a reoperation rate of 15% (691 no reoperation, 119 reoperation) with no correlation between increased BMI and reoperation. Kahn et al evaluated 569 patients who had undergone open posterior lumbar spine fusion with 290 (50.97%) patients with BMI < 30 kg/m² (nonobese) and 279 (49.03%) patients with BMI ≥ 30 kg/m² (obese). There was no difference in reoperation rates between the 2 groups. Owens et al reviewed 164 patients in a case-control study (Level III) with 5-yr reoperation rate by BMI. There was no correlation between reoperation rate and BMI, stratified into 3 tiers: BMI 20-25 kg/m² (normal), BMI 25-30 kg/m² (overweight), and BMI 30-40 kg/m² (obese). Wadhwa et al reviewed the National Neurosurgery Quality and Outcomes Database lumbar spine registry and identified 9853 lumbar degenerative surgery patients. They reported a 2% 30-d reoperation rate that did not correlate with increased BMI. Kara et al retrospectively reviewed 80 lumbar discectomy patients. The authors noted no association between increased BMI and reoperation rates in the 46 patients that had a single operation and the 34 that required a reoperation.

Lumbar Article: BMI Correlates to Increased Reoperation

Rihn et al analyzed the 4-yr postoperative follow-up from the SPORT degenerative spondylolisthesis trial and observed twice the reoperation rate at 4 yr for patients with BMI ≥ 30 kg/m² compared with those with BMI < 30 kg/m² (20% vs 11%, P = .01). Obesity, however, did not negatively impact the overall clinical outcome. Bohl et al reviewed 226 single-level minimally invasive lumbar discectomy patients and 23 (10.2%) underwent reoperation. The 2-yr risk of reoperation was 1.8% for nonobese patients, 12.5% for overweight patients, 9.1% for obese patients, and 25.0% for morbidly obese patients. In the multivariate-adjusted analysis model, increased BMI was independently associated with undergoing reoperation (P = .038). Beack et al examined 160 patients undergoing primary lumbar discectomy with 24 reoperations (15%) for recurrent disc herniation and noted that a BMI > 30 kg/m² was significantly associated with reoperation (P < .05). A final Level III article by Gaudelli et al reported patients with BMI > 35 kg/m² who underwent elective lumbar spine surgery had an increased risk of postsurgical complications, as evidenced by reoperation within 3 mo postoperatively (RR 1.73 [95% CI 1.03-2.90]).

Multilevel Lumbar or Thoracolumbar Surgery: Increased BMI Does Not Correlate With Increased Reoperation

Puvanesarajah et al appraised 2293 patients with ASD with ≥ 8 fusion levels. At the 5-yr follow-up, 424 (18.5%) patients required reoperation. Multivariate analysis did not identify an
association between increased BMI and reoperation. Hofler et al assessed 148 081 thoracic or lumbar fusion patients. A total of 2665 (1.8%) patients developed pseudarthrosis and there was no correlation between reoperation and increased BMI. Narain et al retrospectively reviewed primary this group, there was no correlation between reoperation and increased BMI. In this group, there was no correlation between reoperation and increased BMI. Narain et al retrospectively reviewed primary anterior cervical decompression and fusion, reporting an incidence of 0.40% for hematoma requiring reoperation. In the thoracic group, there was no correlation between reoperation and increased BMI.59 Overall, there were no cervical articles that noted a positive correlation between increased BMI and reoperation.

**Cervical: Increased BMI Does Not Correlate With an Increased Risk of Reoperation**

Bovonratwet et al evaluated 37 261 patients who had undergone anterior cervical decompression and fusion, reporting an incidence of 0.40% for hematoma requiring reoperation. In this group, there was no correlation between reoperation and increased BMI. Narain et al retrospectively reviewed primary 1- to 2-level anterior cervical decompression and fusion for degenerative cervical disease. Patients were stratified by BMI: normal weight (<25.0 kg/m²), overweight (25.0-29.9 kg/m²), obese I (30.0-34.9 kg/m²), or obese II-III (≥35.0 kg/m²). No association with reoperation was identified. Hofler et al further assessed 107 420 cervical fusion patients with 1295 (1.2%) patients undergoing reoperation for pseudarthrosis. There was no correlation between reoperation and increased BMI. Overall, there were no cervical articles that noted a positive correlation between increased BMI and reoperation.

**Question**

Is preoperative smoking associated with increased risk of reoperation in patients undergoing spinal fusion surgery? Does preoperative smoking cessation decrease risk of reoperation?

**Recommendations**

Individuals undergoing spinal fusion surgery who are active smokers should be counseled regarding the increased risk of reoperation.

**Strength of Recommendation: Grade B**

There is insufficient evidence that cessation of smoking before spine surgery decreases the risk of reoperation, but it is suggested that patients be counseled to abstain from smoking before and after spinal fusion surgery.

**Strength of Recommendation: Grade Insufficient**

In total, there are 8 studies included in the analysis of the effect of smoking on reoperation for patients undergoing spinal fusion surgery. Six studies showed a positive correlation between smoking and reoperation with all 6 being Class II evidence. The literature for cervical spinal fusion demonstrated a consistent association between smoking and reoperation (4 Class II articles). 43,39,62,63

Hofler et al reviewed the Healthcare Cost and Utilization Project State Inpatient Databases in New York, California, Florida, and Washington for adult patients who had undergone new spinal fusion from 2009 to 2011 to define factors that correlated with pseudarthrosis. Of 107 420 cervical surgery patients, 1295 (1.2%) developed pseudarthrosis. In cervical spine surgery patients, smoking had a significant relationship with the development of a pseudarthrosis (P = .01). Lee et al performed a retrospective analysis of 1358 cervical spine patients and 94 had a reoperation for adjacent segment pathology. Smoking was associated with an increased risk of reoperation by a factor of 1.75 times (95% CI 1.15-2.67). An additional cervical analysis of 1038 primary surgeries noted higher rates of adjacent level pathology in tobacco users. Lee et al reviewed 1038 anterior cervical disectomy fusion patients that developed adjacent level disease and noted that smoking was an independent risk factors for reoperation.

Gerling et al performed a subanalysis of patients undergoing lumbar fusion from a multicenter randomized controlled trial for lumbar spondylolisthesis. Multivariate analysis identified no correlation between smoking and reoperation at 8 yr of follow-up. Hofler et al analyzed 148 081 thoracic and lumbar surgeries of which 2665 (1.8%) developed pseudarthrosis. In the thoracolumbar group (P < .001), smoking history demonstrated a significant relationship with pseudarthrosis. Macki et al reviewed 110 instrumented lumbar fusions and bone morphogenetic protein usage and noted that the tobacco users had a 32% risk of reoperation for pseudarthrosis, which was significantly greater than nonsmokers (P = .027). However, this effect on reoperation also extended to the nonfusion population. Bydon et al reported 500 patients who had undergone primary laminectomy and noted on a multiple logistic regression analysis that tobacco was an independent predictor for reoperation in single level (OR 11.3, P = .02) and multilevel laminectomy (OR 1.98, P = .05).

There were 2 studies that assessed the relationship between smoking and reoperation in patients with ASD. Puvanesarajah et al reported in a multivariate analysis of 2293 patients an association between history of smoking and increased risk of reoperation (OR 1.37). De la Garza Ramos et al, in a series of 1368 patients with ASD, also noted a higher reoperation rate among smokers, but this was not statistically significant as well as Grade III.

One study analyzed patients requiring reoperation for SSI after spine surgery. Macki et al reviewed 209 instrumented lumbar fusions and tobacco use was the highest predictor of reoperation for SSI (OR 5.75, P = .007). The literature search did not identify any studies that specifically addressed the question of preoperative smoking cessation and risk of reoperation and that met inclusion and exclusion criteria.

**Future Research**

This review shows that there are numerous gaps in our knowledge about perioperative spine care. Future research should be focused on how to optimize patients for pending spinal surgical treatments. Specifically, optimal preoperative goals to maximize postoperative outcomes in terms of preoperative weight loss, smoking cessation, and diabetic blood sugar control are needed.
In addition, an analysis of timing to initiate these strategies and duration of optimization would enhance patient care.

CONCLUSIONS

There remains significant work for preoperative optimization of spine patients. Particularly, defining target goals that patients should meet to reduce perioperative risk and timing of these interventions are needed. There is evidence, however, that patients with preoperative HbA1c level >7.5 mg/dL have an increased risk of postoperative infection and reoperation after spine surgery. Therefore, individuals with diabetes who are undergoing elective degenerative spine surgery should undergo preoperative HbA1c testing before surgery and be counseled regarding the increased risk of reoperation or infection if the level is > 7.5 mg/dL (Grade B). There is conflicting evidence regarding increased BMI and risk of postoperative infection and reoperation after spine surgery. Particularly, defining target goals that patients under spin surgery should meet to reduce perioperative risk and timing of these interventions are needed. There is evidence, however, that patients with elevated BMI should be appropriately preoperatively risk assessed. Finally, preoperative smoking correlates with an increased risk of reoperation in patients undergoing spinal fusion surgery. Preoperative counseling will benefit patients to understand these associated risk factors and care should be directed toward reducing these variables.

Funding

These evidence-based clinical practice guidelines were funded exclusively by the Congress of Neurological Surgeons and the AANS/CNS Joint Section on Disorders of the Spine and Peripheral Nerves (through a donation to the CNS Foundation), which received no funding from outside commercial sources to support the development of this document.

Disclosures

All Guideline Task Force members were required to disclose all potential conflicts of interest (COIs) before beginning work on the guideline, using the COI disclosure form of the AANS/CNS Joint Guidelines Review Committee. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination and participation on the task force. The CNS Guidelines Committee and Guideline Task Force Chair may approve nominations of task force members with possible conflicts and restrict the writing, reviewing, and/or voting privileges of that person to topics that are unrelated to the possible COIs. See below for a complete list of disclosures.

Disclaimer of Liability

This clinical, systematic, evidence-based clinical practice guideline was developed by a multidisciplinary physician volunteer task force and is provided as an educational tool based on an assessment of the current scientific and clinical information regarding this guideline topic. These guidelines are disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not meant to replace the individualized care and treatment advice from a patient’s physician(s). If medical advice or assistance is required, the services of a physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

REFERENCES

Acknowledgments

The guidelines task force would like to acknowledge the CNS Guidelines Committee for their contributions throughout the development of the guideline, the AANS/CNS Joint Guidelines Review Committee, the AANS/CNS Joint Section on Disorders of the Spine and Peripheral Nerves for their donation to the CNS Foundation to support this project, as well as the contributions of Kirsten Aquino, contracted project manager for the CNS, Trish Rehring, MPH, Associate Director for Evidence-Based Practice Initiatives for the CNS, and Janet Waters, MLS, BSN, RN, for assistance with the literature searches and Kenneth Probst for the cover illustrations. Throughout the review process, the reviewers and authors were blinded from one another. At this time, the guidelines task force would like to acknowledge the following individual peer reviewers for their contributions: Patricia Raksin, MD, Jason Stacy, MD, Neil Majmunder, MD, Yi Lu, MD, Alex Beier, MD, Andrew Carlson, MD, Brandon Rocque, MD, Robert Whitmore, MD, Jay Turner, MD, and Owoicho Adogwa, MD.

Supplemental digital content is available for this article at www.neurosurgery-online.com.

Supplemental Digital Content 1. Literature searches.
Supplemental Digital Content 2. Inclusion criteria.
Supplemental Digital Content 3. Criteria grading the evidence.
Supplemental Digital Content 4. Linking levels of evidence to grades of recommendation.
Supplemental Digital Content 5. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart.
BACKGROUND: Osteoporosis is a metabolic bone disease that commonly affects the elderly. Degenerative spinal disease that may require surgical intervention is also prevalent in this susceptible population. If undiagnosed or untreated before spine surgery, osteoporosis may result in an increased risk of postoperative adverse events. Nontreatment of osteoporosis preoperatively may be related to a poor understanding of bone physiology, a lack of standardized treatment algorithms, limited cost-effective interventions, and reluctance by spine surgeons to be the primary provider of osteoporosis management.

OBJECTIVE: The objective of this evidence-based review is to develop guidelines for the preoperative assessment and treatment of osteoporosis in patients undergoing spine surgery.

METHODS: A systematic review of the literature was performed using the National Library of Medicine/PubMed database and Embase for studies relevant to preoperative diagnostic studies that predict increased risk of osteoporosis-related postoperative adverse events and whether the preoperative treatment of low bone mineral density (BMD) in patients with osteoporosis improves outcome.

RESULTS: Out of 281 studies, 17 met the inclusion criteria and were included for systematic review. The task force affirmed a Grade B recommendation that preoperative osteoporosis testing with a dual-energy X-ray absorptiometry scan (T-score $\leq -2.5$), a computed tomography scan (Hounsfield units $< 97.9$), and serum vitamin D3 level ($\leq 20$ ng/mL) predict an increased risk of osteoporosis-related adverse events after spine surgery. The task force determined a Grade B recommendation that preoperative osteoporosis treatment with teriparatide increases BMD, induces earlier and more robust fusion, and may improve select patient outcomes. There is insufficient evidence regarding preoperative treatment with bisphosphonates alone and postoperative outcome.

CONCLUSION: This evidence-based clinical guideline provides a recommendation that patients with suspected osteoporosis undergo preoperative assessment and be appropriately counseled about the risk of postoperative adverse events if osteoporosis is confirmed. In addition, preoperative optimization of BMD with select treatments improves certain patient outcomes. The full guidelines can be accessed at https://www.cns.org/guidelines/browse-guidelines-detail/3-preoperative-osteoporosis-assessment

KEY WORDS: Osteoporosis, Vitamin D3, Calcium, Teriparatides, Bisphosphonates, Denosamab, Bone mineral density

© Congress of Neurological Surgeons 2021. All rights reserved.

Supplemental digital content is available for this article at www.neurosurgery-online.com.
RECOMMENDATIONS

Question
1. What preoperative diagnostic studies predict the risk of osteoporosis-related adverse events after spine surgery?

Recommendations
Preoperative testing with a dual-energy X-ray absorptiometry (DEXA) scan T-score < −2.5, a computed tomography (CT) scan (Hounsfield units [HUs] < 97.9), or serum vitamin D3 level <20 ng/mL is associated with poor bone mineral density and predicts an increased risk of a postoperative adverse event in individuals undergoing spinal instrumentation. Preoperative assessment with one of these tests (DEXA scan, CT, or serum vitamin D3 level) should be performed in patients with suspected osteoporosis. Patients with confirmed osteoporosis should be counseled regarding the potential increased risk of postoperative adverse events.

Strength of Recommendation: Grade B

Question
2. Does preoperative treatment of low bone mineral density decrease the risk of postoperative adverse event after spine surgery?

Recommendations
Clinicians should consider preoperative teriparatide in patients with osteoporosis undergoing spinal instrumentation to decrease the risk of postoperative adverse events, including screw loosening and a delayed or lower rate of fusion.

Strength of Recommendation: Grade B

There is insufficient evidence to support the use of bisphosphonates alone in patients with osteoporosis undergoing spinal instrumentation to decrease postoperative adverse events after spinal instrumentation.

Strength of Recommendation: Grade Insufficient

INTRODUCTION

Goals and Rationale
This clinical guideline has been created to improve patient care by outlining the appropriate information gathering and decision-making processes involved in the treatment of patients with preoperative osteoporosis, specifically if preoperative identification and treatment of this metabolic bone disorder decreases the risk of postoperative adverse events after spine surgery. Spinal surgical care is provided in many different settings by many different providers. This guideline has been created as an educational tool to guide qualified physicians through a series of diagnostic and treatment decisions in an effort to improve the quality and efficiency of care.

This guideline should not be construed as including all proper methods of care or excluding methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment must be made in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution.

Osteoporotic fragility fractures have become a major healthcare epidemic with the aging population, occurring in 2.1 million patients yearly.1 The spine is affected in 245,000 patients annually, and mortality after a vertebral fracture is 22.4%, 32.7%, and 49.4% at 1, 2, and 4 yr, respectively.2 Suboptimal diagnosis and management of bone health before spine surgery can contribute to increased osteoporosis-related postoperative adverse events and unsatisfactory surgical outcomes in the elderly. These include pseudarthrosis, instrumentation complications (particularly loss of fixation at the screw–bone interface), and proximal junctional failure (PJF), with potentially catastrophic spinal fracture with or without neurological injury.3 The cause of these postoperative complications may be multifactorial; however, poor bone density is often a major contributor that is potentially modifiable with appropriate preoperative diagnosis and management.

Osteoporosis can result from aging, genetic and environmental factors, certain comorbidities, and abnormal homeostasis of calcium and vitamin D metabolism. Despite the relative prevalence of osteoporosis and vitamin D3 deficiency4,5 and various available diagnostic6 and treatment modalities, there is a lack of consensus regarding the management of osteoporosis before spine surgery.7 This deficiency may be related to poor understanding by many spine surgeons of bone physiology, limited cost-effective interventions, and the reluctance of spine surgeons to be the primary provider of treatment or to consult an endocrinologist. The objective of this evidence-based review is to develop guidelines for the preoperative assessment and treatment of osteoporosis in patients who are undergoing spine surgery.

METHODS
The guidelines task force initiated a systematic review of the literature and evidence-based guideline relevant to the preoperative treatment of patients with spinal disorders with osteoporosis. Through objective evaluation of the evidence and transparency in the process of making recommendations, this evidence-based clinical practice guideline was developed for the diagnosis and treatment of adult patients with various spinal conditions. These guidelines are developed for educational purposes to assist practitioners in their clinical decision-making processes. Additional information about the methods used in this systematic review is provided below.
**Literature Search**

The task force members identified search terms/parameters and a medical librarian implemented the literature search, consistent with the literature search protocol (see Supplemental Digital Content 1), using the National Library of Medicine/PubMed database and Embase for the period from 1946 to September 20, 2019, using the search strategies provided in Supplemental Digital Content 1.

**Inclusion/Exclusion Criteria**

Articles were retrieved and included only if they met specific inclusion/exclusion criteria (Supplemental Digital Content 2). These criteria were also applied to articles provided by guideline task force members who supplemented the electronic database searches with articles from their own files. To reduce bias, these criteria were specified before conducting the literature searches.

**Rating Quality of Diagnostic Evidence**

The guideline task force used a modified version of the North American Spine Society’s (NASS) evidence-based guideline development methodology. The NASS methodology uses standardized levels of evidence (Supplemental Digital Content 3) and grades of recommendation (Supplemental Digital Content 4) to assist practitioners in easily understanding the strength of the evidence and recommendations within the guidelines. The levels of evidence range from Level I (high-quality randomized controlled trial) to Level IV (case series). Grades of recommendation indicate the strength of the recommendations made in the guideline based on the quality of the literature. Levels of evidence have specific criteria and are assigned to studies before developing recommendations. Recommendations are then graded based upon the level of evidence. To better understand how levels of evidence inform the grades of recommendation and the standard nomenclature used within the recommendations, see Supplemental Digital Content 4.

Guideline recommendations were written using a standard language that indicates the strength of the recommendation. “A” recommendations indicate a test or intervention is “recommended”; “B” recommendations “suggest” a test or intervention; and “C” recommendations indicate a test or intervention or “is an option.” “I” or “Insufficient Evidence” statements clearly indicate that “there is insufficient evidence to make a recommendation for or against” a test or intervention. Task force consensus statements clearly state that “in the absence of reliable evidence, it is the task force’s opinion that” a test or intervention may be appropriate.

In evaluating studies as to levels of evidence for this guideline, the study design was interpreted as establishing only a potential level of evidence. As an example, a therapeutic study designed as a randomized controlled trial would be considered a potential Level I study. The study would then be further analyzed as to how well the study design was implemented and significant shortcomings in the execution of the study would be used to downgrade the levels of evidence for the study’s conclusions (see Supplemental Digital Content 4 for additional information and criteria).

**Revision Plans**

In accordance with the Institute of Medicine’s standards for developing clinical practice guidelines, the task force will monitor related publications after the release of this document and will revise the entire document and/or specific sections “if new evidence shows that a recommended intervention causes previously unknown substantial harm; that a new intervention is significantly superior to a previously recommended intervention from an efficacy or harms perspective; or that a recommendation can be applied to new populations.” In addition, the task force will confirm within 5 yr from the date of publication that the content reflects current clinical practice and the available technologies for the evaluation and treatment for patients with perioperative spinal disease.

**RESULTS**

The initial literature search encompassed terms relevant to all chapters in this guideline series and yielded 6812 abstracts (5689 after duplicates were deleted). After a double-blind review, the literature review search yielded 281 abstracts for this question. Task force members reviewed all abstracts distilled from the literature search and identified the relevant literature for full text review and extraction in accordance with the Literature Search Protocol that addressed the 2 clinical PICO (patient/population, intervention, comparison, and outcomes) questions (Supplemental Digital Content 5). Two members of the task force initially screened all the abstracts culled from the literature followed by all members of the entire task force who graded the best research articles that answered the 2 research questions. The task force graded the articles from Level I to Level IV. The task force reviewed 281 articles, collected data on 78, and finally selected 17 articles for use in developing the chapter guidelines (Supplemental Digital Content 6).

**DISCUSSION**

**Question**

1. What preoperative diagnostic studies predict risk of osteoporosis-related adverse events after spine surgery?

**Recommendations**

Preoperative testing with a DEXA scan T-score $<-2.5$, a CT scan (HUs $<97.9$), or serum vitamin D3 level $<20$ ng/mL is associated with poor bone mineral density and predicts an increased risk of a postoperative adverse event in individuals undergoing spinal instrumentation. Preoperative assessment with one of these tests (DEXA scan, CT, or serum vitamin D3 level) should be performed in patients with suspected osteoporosis. Patients with confirmed osteoporosis should be counseled regarding the potential increased risk of postoperative adverse events.

**Strength of Recommendation: Grade B**

There were 11 articles that specifically addressed this question and met the inclusion and exclusion criteria. These studies primarily evaluated the predictive effect of preoperative serum vitamin D3 levels (1 study) on time to fusion and nonunion and CT and DEXA scan (10 studies) on cage subsidence, pedicle screw loosening, proximal junctional kyphosis (PJK), and outcome measures. There were no Level I studies. There were 4 Level II studies and 7 Level III studies. There were no Level IV studies included in the recommendation.
**Level II Evidence**

There is significant Level II evidence demonstrating the relationship of osteoporosis to adverse events after spinal fusion surgery. Cho et al\(^9\) retrospectively reviewed a 2-yr series of 268 patients who underwent posterolateral fusion (182 patients) or 1 level posterior lumbar interbody fusion (PLIF = 86 patients) to evaluate the effect of osteoporosis on patient-related outcomes, fusion success, instrumentation failure, and cage subsidence. Two groups were evaluated based on their T-scores: group A (nonosteoporotic: T-score > −1.0 consisting of 55 patients) and group B (osteoporotic: T-score < −2.5 consisting of 31 patients). The authors found that low body mass index (BMI) was associated with both cage subsidence (65.4% vs 17.6%, \(P < .001\)) and screw loosening rates (32.3% vs 12.7%, \(P < .029\)). Other than osteoporosis, the groups had similar demographics except that group A had a higher BMI, and group B had an expected higher rate of osteoporosis treatment of 48% vs 4% (\(P < .001\)). Although patient-related clinical outcomes did not differ between the osteoporotic patients (group B) who had cage subsidence or screw loosening and the normal BMD patients (group A), the fusion rate was lower in those that had screw loosening compared with those that did not (71.4% vs 93.9%, \(P = .029\)). The authors suggest that surgeons should continue to monitor screw loosening to detect a potential nonunion.

Sakai et al\(^10\) retrospectively evaluated the mean value of the HUs inside a rectangle within the pedicle, which was defined as the HU of screw trajectory. The authors used a CT scanning model superimposing preoperative images on the postoperative CT using 3-dimensional image analysis software. They found that the mean HU values of the screw trajectory were significantly less in the osteoporotic patient group compared with the nonosteoporotic group (147 ± 94 vs 208 ± 91, \(P < .001\)). The osteoporotic group was associated with increased screw loosening and was particularly a risk factor in women. The authors recommended additional augmentation with cement, hooks, or lamina taping in females with low bone density to prevent pedicle screw loosening.\(^10\) Yagi et al\(^11\) performed a retrospective propensity-matched study with 2 yr postoperative follow-up of patients with preoperative DEXA scans. Two cohorts were compared: a moderate osteoporosis group (M group; T > −1.5) vs a severe osteoporosis group (S group; T < −1.5). They observed that BMD was a risk factor for PJF, and the incidence of PJF was significantly higher in the severe group (33% vs 8%, odds ratio [OR] 6.4 [95% confidence interval (CI) 1.2-32.3], \(P < .01\)). They concluded that surgeons should consider prophylactic measures against PJF when correcting adult spinal deformity in patients with low BMD.

One study included for review was not supportive of the effect of osteoporosis on spine surgery’s adverse events. Yagi et al\(^12\) in an earlier article reviewing patients with adult spinal deformity found no correlation between DEXA scan T-scores of the hip and spine, and curve magnitude, fusion, and complication rates.

**Level III Evidence**

Ravindra et al\(^13\) retrospectively reviewed a series of prospectively enrolled patients to evaluate the relationship between vitamin D3 deficiency (<20 ng/mL) and fusion rate. They found that nonunion at 12 mo was associated with vitamin D deficiency (20% of patients with adequate serum vitamin D3 level vs 38% of vitamin D3-deficient patients, \(P = .063\)). In addition, multivariate analysis showed that vitamin D3 deficiency was an independent predictor of nonunion (OR 3.449, \(P = .045\)) when adjusted for age, sex, obesity, fusion length, location, graft type, smoking, and bone morphogenetic protein use. Finally, when the authors analyzed the vitamin D3-deficient group (<20 ng/mL) vs the insufficient group (20-30 ng/mL) vs the nondeficient group (>20 ng/mL), there was a significantly longer estimated median time to fusion in the vitamin D3-deficient group (12 vs 8.6 vs 6 mo, \(P = .001\)). They concluded that serum vitamin D3 levels may affect nonunion rate and time to fusion.\(^13\)

Schreiber et al\(^14\) retrospectively reviewed postoperative CT scans at a minimum of 12 mo measuring the HUs and found that the successful fusion levels had higher CT HUs than nonunion levels. The authors reported that successful lumbar fusion was associated with higher bone density both globally and within the fusion construct levels compared with patients with CT evidence of nonunion.\(^14\) Kim et al\(^15\) showed in a retrospectively reviewed consecutive series that patients with osteoporosis trended toward increased posterior spinous process fractures after an interspinous process device placement. There was a trend toward lower BMD in the fractures group as measured by DEXA and CT HU scans, but the association was weak.\(^15\) Oh et al\(^16\) performed a retrospective review of PLIF and found that BMD had a significant but weak correlation with cage subsidence (\(r = 0.285, P < .001\)). Severe osteoporotic segments (T-score < −3.0) had greater risk of severe subsidence (>3 mm), but that subsidence did not cause a deterioration in clinical outcomes.\(^16\) Kim et al\(^17\) retrospectively reviewed a prospectively collected database of 364 patients after adult deformity surgery with 2-yr postoperative follow-up. All patients underwent preoperative DEXA scans and osteoporosis was defined as a T-score < −2.5. Osteoporosis was present in 20.4% of patients who ultimately developed PJK vs only 9.8% of patients who did not develop PJK (\(P = .016\)). This observation suggests that a T-score < −2.5 is associated with higher likelihood of PJK in patients undergoing adult deformity surgery.\(^17\) Puvanesarajah et al\(^18\) performed a multivariate analysis of patients with 5 yr of postoperative follow-up and found that osteoporosis increases the risk of revision surgery (OR 1.98 [95% CI 1.60-2.46], \(P < .0001\)). More than one-third (44.9%) of patients who ultimately developed PJK had osteoporosis.

Finally, Salzmann et al\(^19\) retrospectively evaluated 21 patients who had long segment spinal fusion surgery (mean 5.6 levels) that included the sacrum and found a weak association between BMD as measured by a standard qualitative CT scan of the L1/L2 vertebral body. They unexpectedly found no association between...
sacral fractures and BMD. The study did find, however, that obese patients had a 52.4% (11/21) incidence of sacral fractures ($P = .002$) (univariate analysis showed the OR 5.99, $P = .030$).

**Question**

2. Does preoperative treatment of low BMD decrease the risk of postoperative adverse event after spine surgery?

**Recommendations**

Clinicians should consider preoperative teriparatide in patients with osteoporosis who are undergoing spinal instrumentation to decrease the risk of postoperative adverse events, including screw loosening and delayed or lower rate of fusion.

*Strength of Recommendation: Grade B*

There is insufficient evidence to support the use of bisphosphonates alone in patients with osteoporosis undergoing spinal instrumentation to decrease postoperative adverse events after spinal instrumentation.

*Strength of Recommendation: Grade Insufficient*

There were 6 articles that specifically addressed this question and met inclusion and exclusion criteria. The task force identified 3 Level II studies, 2 Level III studies, and 1 Level IV study.

**Level II Evidence**

Ohtori et al$^{20}$ performed a prospective, nonrandomized sequential study of osteoporotic postmenopausal women with equal BMD undergoing instrumented decompression and fusion (local autograft) for symptomatic degenerative spondylolisthesis. There were 57 females divided into 2 groups: the first 28 patients received a weekly dose of a bisphosphonate (risedronate). The next 29 patients received daily teriparatide injections. All patients were followed for 1 yr and evaluated with CT scanning preoperatively and at 3, 6, and 12 mo postoperatively for fusion. The rate of bone fusion in the teriparatide group was significantly higher (82% fusion rate at 8 mo) than that in the risedronate group (68% fusion rate at 10 mo; $P < .05$). The teriparatide group also demonstrated earlier fusion. Although teriparatide was superior to bisphosphonate regarding fusion rate and time to fusion, both groups had similar clinical outcomes. Ohtori et al$^{21}$ evaluated 62 patients divided into 3 groups: 22 patients received no osteoporotic treatment (control), 20 received a bisphosphonate (risedronate), and 20 received teriparatide. They demonstrated that the incidence of pedicle screw loosening was significantly lower in the teriparatide group (7%) compared with the bisphosphonate (risedronate) group (13%), which was similar to the control group (15%; $P < .05$). Teriparatide was also associated with increased bone mass compared with bisphosphonate.

Cho et al$^{22}$ evaluated a prospective cohort of 47 patients undergoing PLIF with pedicle screws that were divided into 2 groups: the first group (23 patients) received daily teriparatide injections for 3 mo, which was alternated with a bisphosphonate for 3 mo; the second group (24 patients) received oral bisphosphonate. Both groups underwent their respective osteoporosis treatment protocol for 1 yr postoperatively. In addition to clinical outcome, postoperative T-scores (DEXA scan), fusion rate, and duration to fusion (CT) were assessed. The cyclical teriparatide plus bisphosphonate group showed a significantly higher fusion rate at 6 mo after surgery vs the bisphosphonate alone group (77.8% vs 53.6%), while fusion rates were equal at 2 yr postoperatively (92.6% vs 96.4%). CT follow-up at 12 mo postoperatively demonstrated bridging bone in 88.9% of the bisphosphonate group and 87.5% of the teriparatide group. Screw loosening was 10.7% in the bisphosphonate group and 11.1% in the teriparatide group. Cage subsidence was 14.3% in the bisphosphonate group and 14.8% in the teriparatide group. None of these CT outcomes were significantly different between the 2 groups ($P = .374$, $P = .648$, and $P = .626$, respectively). There was no significant difference in T-score between the 2 groups at 12 and 24 mo postoperatively, although the teriparatide group trended toward a higher BMD (DEXA T-score $−3.0$ vs $−3.4$) and earlier improvement in T-scores ($0.7 ± 1.4$ vs $0.1 ± 0.5$, $P = .013$). There was no significant difference between cohorts with respect to clinical outcomes. The authors concluded that there was no significant benefit in fusion rate and clinical outcome when adding teriparatide with bisphosphonate compared with bisphosphonate alone, but the addition of a teriparatide resulted in faster bony union and a higher BMD recovery rate.$^{22}$

**Level III**

Wang et al$^{23}$ performed a retrospective comparative cohort study of 59 patients undergoing anterior cervical discectomy and fusion. Group A (31 patients) was treated for osteoporosis with calcium, vitamin D, and diphosphonate. Group B received no treatment. All patients underwent DEXA scan with osteoporosis defined as a T-score $< −2.5$ with no baseline difference between groups ($P = .584$). The authors found that group A (osteoporosis treatment) exhibited significantly better BMD (g/cm$^2$) than group B (no treatment) at 8.3 mo postoperatively, as well as improved sagittal alignment ($P = .03$), interbody disc height ($P = .03$), and visual analog scale ($P = .03$) for upper limb pain. Kang et al$^{24}$ retrospectively reviewed 97 postmenopausal women undergoing PLIF and compared 63 patients who were treated with bisphosphonates vs 34 who had received no treatment. All subjects had osteoporosis as measured by preoperative DEXA scan (bisphosphonate group T $< −2.7$ vs no treatment T $< −2.3$, $P < .001$). The authors found that bisphosphonates may negatively delay fusion in the short term for the first 6 mo but not at 2 yr postoperatively. Regardless, overall fusion rate in those treated with bisphosphonate was $>80$% and clinical outcomes were comparable to those who were not treated with bisphosphonate.

**Level IV**

Kim et al$^{25}$ retrospectively evaluated 44 patients undergoing PLIF with osteoporosis diagnosed by CT. Patients were treated with either bisphosphonate (alendronate) vs no bisphosphonate. The fusion rate was similar for the bisphosphonate group (66.7%) vs the no bisphosphonate group (73.9%; $P = .599$). Subjects
who developed nonunion appeared to have more endplate degeneration compared with those who did not (91.3% vs 52.4%, \( P = .004 \)). The authors concluded that alendronate does not negatively affect fusion rates in osteoporotic patients.25

Future Research
The lack of Level I evidence is an area for improvement that would also benefit future guidelines. Future research should include randomized controlled studies to compare the efficacy of preoperative osteoporosis treatment protocols (single or multiagent), such as vitamin D3, teriparatide, bisphosphonates, and denosumab, in improving bone health and clinical outcome after spine surgery.

CONCLUSIONS
Undiagnosed and/or untreated osteoporosis can lead to potentially significant postoperative adverse events in patients undergoing spine surgery. A systematic review of the literature identified that preoperative assessment with DEXA scan (T-score < -2.5), CT (HU < 97.9), and serum vitamin D3 level (<20 ng/mL) predicted a risk of adverse events, including lower fusion rate, instrumentation failure (cage subsidence and screw loosening), and PJF. Preoperative treatment with teriparatide was associated with a higher fusion rate, earlier fusion, and lower screw loosening rates, whereas there was conflicting evidence regarding the potential benefit of preoperative bisphosphonates alone. Spine surgeons should consider preoperative assessment and treatment with these modalities in patients with suspected osteoporosis who are undergoing spine surgery and counsel patients regarding the potential risks when indicated.

Funding
These evidence-based clinical practice guidelines were funded exclusively by the Congress of Neurological Surgeons and the AANS/CNS Joint Section on Disorders of the Spine and Peripheral Nerves (through a donation to the CNS Foundation), which received no funding from outside commercial sources to support the development of this document.

Disclosures
All Guideline Task Force members were required to disclose all potential conflicts of interest (COIs) before beginning work on the guideline, using the COI disclosure form of the AANS/CNS Joint Guidelines Review Committee. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination and participation on the task force. The CNS Guidelines Committee and Guideline Task Force Chair may approve nominations of task force members with possible conflicts and restrict the writing, reviewing, and/or voting privileges of that person to topics that are unrelated to the possible COIs. See below for a complete list of disclosures.

Disclaimer of Liability
This clinical, systematic, evidence-based clinical practice guideline was developed by a multidisciplinary physician volunteer task force and is provided as an educational tool based on an assessment of the current scientific and clinical information regarding this guideline topic. These guidelines are disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not meant to replace the individualized care and treatment advice from a patient’s physician(s). If medical advice or assistance is required, the services of a physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

REFERENCES


Acknowledgments

The guidelines task force would like to acknowledge the CNS Guidelines Committee for their contributions throughout the development of the guideline, the AANS/CNS Joint Guidelines Review Committee, the AANS/CNS Joint Section on Disorders of the Spine and Peripheral Nerves for their donation to the CNS Foundation to support this project, as well as the contributions of Kirsten Aquino, contracted project manager for the CNS, Trish Rehring, MPH, Associate Director for Evidence-Based Practice Initiatives for the CNS, and Janet Waters, MLS, BSN, RN, for assistance with the literature searches, and Kenneth Probst for the cover illustrations. Throughout the review process, the reviewers and authors were blinded from one another. At this time, the guidelines task force would like to acknowledge the following individual peer reviewers for their contributions: Patricia Raksin, MD, Jason Stacy, MD, Neil Majmunder, MD, Yi Lu, MD, Alex Beier, MD, Andrew Carlson, MD, Brandon Rocque, MD, Robert Whitmore, MD, Jay Turner, MD, and Owoicho Adogwa, MD.

Supplemental digital content is available for this article at www.neurosurgery-online.com.
CNS Guidelines for Perioperative Spine: Preoperative Nutritional Assessment

Erica F. Bisson, MD, MPH*  
John Dimar, MD†  
James S. Harrop, MD, MSHQ§  
Daniel J. Hoh, MD*  
Basma Mohamed, MBChB‖  
Praveen V. Mummaneni, MD, MBA‡  
Marjorie C. Wang, MD, MPH**  
Sanjay Dhall, MD#  

*Clinical Neurosciences Center, University of Utah Health, Salt Lake City, Utah, USA;  
†Department of Orthopedics, University of Louisville, Pediatric Orthopedics, Norton Children’s Hospital, Norton Leatherman Spine Center, Louisville, Kentucky, USA;  
‡Department of Orthopedics, University of Kentucky, USA;  
§Norton Children’s Hospital, Norton Leatherman Spine Center, Louisville, Kentucky, USA;  
(Continued on next page)  

Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines for Perioperative Spine: Preoperative Nutritional Assessment

BACKGROUND: Preoperative malnutrition has been implicated in adverse events after elective surgery, potentially impacting patient outcomes.

OBJECTIVE: As a potentially modifiable risk factor, we sought to determine which assessments of nutritional status were associated with specific adverse events after spine surgery. In addition, we explored if a preoperative nutritional improvement intervention may be beneficial in lowering the rates of these adverse events.

METHODS: The literature search yielded 115 abstracts relevant to the PICO (patient/population, intervention, comparison, and outcomes) questions included in this chapter. The task force selected 105 articles for full text review, and 13 met criteria for inclusion in this systematic review.

RESULTS: Malnutrition, assessed preoperatively by a serum albumin <3.5 g/dL or a serum prealbumin <20 mg/dL, is associated with a higher rate of surgical site infections (SSIs), other wound complications, nonunions, hospital readmissions, and other medical complications after spine surgery. A multimodal nutrition management protocol decreases albumin and electrolyte deficiencies in patients with normal preoperative nutritional status. It also improves overall complication rates but does not specifically impact SSIs.

CONCLUSION: It is recommended to assess nutritional status using either serum albumin or prealbumin preoperatively in patients undergoing spine surgery. The full guidelines can be accessed at https://www.cns.org/guidelines/browse-guidelines-detail/4-preoperative-nutritional-assessment.

KEY WORDS: Preoperative nutrition, Albumin, Prealbumin, Nutritional deficiency

RECOMMENDATIONS

Question
1. What preoperative serological studies of nutritional status (and timing of these studies) are predictive of adverse event after spine surgery?

Recommendations
Serum markers of malnutrition including low preoperative albumin, prealbumin, total protein, and albumin/globulin are associated with multiple adverse events after spine surgery. In at-risk individuals, clinicians should assess nutritional status preoperatively and counsel patients on the potential for adverse events.

Strength of Recommendation: Grade B

Question
2. What preoperative nonserological assessments of nutritional status (and timing of these assessments) are predictive of adverse event after spine surgery?

Recommendations
There is insufficient evidence to make a recommendation on the impact of preoperative use of nonserological assessments of nutrition status on adverse outcomes in patients undergoing spine surgery.

Strength of Recommendation: Grade Insufficient

ABBREVIATIONS: CRP, C-reactive protein; MNM, multimodal nutrition management; NASS, North American Spine Society; SSI, surgical site infection; TLIF, transformaminal lumbar interbody fusion

Supplemental digital content is available for this article at www.neurosurgery-online.com.
Question

3. In patients with poor nutrition, does preoperative treatment (and type of treatment) decrease the risk of postoperative adverse events?

Recommendations

In patients with malnutrition undergoing spine surgery, there is insufficient evidence to support the use of a perioperative multimodal nutrition management (MNM) protocol to decrease the risk of postoperative adverse events.

Strength of Recommendation: Grade I

INTRODUCTION

Goals and Rationale

This clinical guideline has been created to improve patient care by outlining the appropriate information gathering and decision-making processes involved in the treatment of patients with perioperative spinal disease. This guideline has been created as an educational tool to guide physicians through a series of diagnostic and treatment decisions in an effort to improve the quality and efficiency of care.

This guideline should not be construed as including all proper methods of care or excluding methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment must be made in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution.

Adverse events after surgery are significant drivers of both cost and quality of life, impacting the overall value of these interventions. Studies have shown that spine surgery for degenerative conditions can result in significant improvements in pain, disability, and quality of life. However, postoperative complications, including surgical site infection (SSI), readmission to the hospital, and nonunion, may add substantial morbidity and ultimately result in poor overall outcomes and satisfaction.

There has been increased attention on identifying potentially modifiable risk factors for adverse outcomes after surgical intervention. Across surgical specialties, age, body mass index, diabetes, smoking, and nutrition have been shown to predict adverse outcomes. Among these, few are modifiable. This chapter will provide a systematic review of the relationship of nutritional status and adverse outcomes after spine surgery to guide preoperative evaluation and intervention.

METHODS

The guidelines task force initiated a systematic review of the literature and evidence-based guideline relevant to the preoperative treatment of patients with spinal disorders. Through objective evaluation of the evidence and transparency in the process of making recommendations, this evidence-based clinical practice guideline was developed for the diagnosis and treatment of adult patients with various spinal conditions. These guidelines are developed for educational purposes to assist practitioners in their clinical decision-making processes. Additional information about the methods used in this systematic review is provided below.

Literature Search

The task force members identified search terms/parameters and a medical librarian implemented the literature search, consistent with the literature search protocol (see Supplemental Digital Content 1), using the National Library of Medicine/PubMed database and Embase for the period from 1946 to September 20, 2019 using the search strategies provided in Supplemental Digital Content 1.

Inclusion/Exclusion Criteria

Articles were retrieved and included only if they met specific inclusion/exclusion criteria (Supplemental Digital Content 2). These criteria were also applied to articles provided by guideline task force members who supplemented the electronic database searches with articles from their own files. To reduce bias, these criteria were specified before conducting the literature searches.

Rating Quality of Diagnostic Evidence

The guideline task force used a modified version of the North American Spine Society’s (NASS) evidence-based guideline development methodology. The NASS methodology uses standardized levels of evidence (Supplemental Digital Content 3) and grades of recommendation (Supplemental Digital Content 4) to assist practitioners in easily understanding the strength of the evidence and recommendations within the guidelines. The levels of evidence range from Level I (high-quality randomized controlled trial) to Level IV (case series). Grades of recommendation indicate the strength of the recommendations made in the guideline based on the quality of the literature. Levels of evidence have specific criteria and are assigned to studies before developing recommendations. Recommendations are then graded based upon the level of evidence. To better understand how levels of evidence inform the grades of recommendation and the standard nomenclature used within the recommendations, see Supplemental Digital Content 4.

Guideline recommendations were written using a standard language that indicates the strength of the recommendation. “A” recommendations indicate a test or intervention is “recommended”; “B” recommendations “suggest” a test or intervention; and “C” recommendations indicate a test or intervention or “is an option.” “I” or “Insufficient Evidence” statements clearly indicate that “there is insufficient evidence to make a recommendation for or against” a test or intervention. Task force consensus statements clearly state that “in the absence of reliable evidence, it is the task force’s opinion that” a test or intervention may be appropriate.

In evaluating studies as to levels of evidence for this guideline, the study design was interpreted as establishing only a potential level of evidence. As an example, a therapeutic study designed as a randomized...
controlled trial would be considered a potential Level I study. The study would then be further analyzed to determine whether the study design was implemented and whether there were any significant shortcomings in the execution of the study that would be used to downgrade the levels of evidence for the study’s conclusions (see Supplemental Digital Content 4 for additional information and criteria).

Revision Plans

In accordance with the Institute of Medicine’s standards for developing clinical practice guidelines, the task force will monitor related publications after the release of this document and will arrange for the entire document and/or specific sections “if new evidence shows that a recommended intervention causes previously unknown substantial harm; that a new intervention is significantly superior to a previously recommended intervention from an efficacy or harms perspective; or that a recommendation can be applied to new populations.”7 In addition, the task force will confirm within 5 yr from the date of publication that the content reflects current clinical practice and the available technologies for the evaluation and treatment for patients with perioperative spinal disease.

RESULTS

The literature search encompassed terms relevant to all chapters in this guideline series and yielded 6812 abstracts (5689 after duplicates were deleted). After a double-blind review, 845 abstracts were identified as relevant to the PICO (patient/population, intervention, comparison, and outcomes) question(s). The review yielded 115 abstracts relevant to this chapter. Task force members reviewed all abstracts yielded from the literature search and identified the literature for full text review and extraction, addressing the clinical questions, in accordance with the literature search protocol (Supplemental Digital Content 1). Task force members identified the best research evidence available to answer the targeted clinical questions. When Level I, II, or III literature was available to answer specific questions, the task force did not review Level IV studies.

The task force selected 105 articles for full text review. Of these, 92 were rejected for not meeting inclusion criteria or for being off topic. Thirteen were selected for systematic review (Supplemental Digital Content 5-6).

DISCUSSION

Question

1. What preoperative serological studies of nutritional status (and timing of these studies) are predictive of adverse event after spine surgery?

Recommendations

Serum markers of malnutrition including low preoperative albumin, prealbumin, total protein, and albumin/globulin are associated with multiple adverse events after spine surgery. In at-risk individuals, clinicians should assess nutritional status preoperatively and counsel patients on the potential for adverse events.

Strength of Recommendation: Grade B

SSI and Other Wound Complications

Up to 1 in 6 patients having spine surgery will develop an SSI,9-18 potentially resulting in a prolongation of their hospital stay, an increased likelihood of readmission, and revision surgery. This added morbidity comes at an increased cost to both the individual and society with lost productivity and increased cost of care.11,12

Known risk factors for wound complications include age, sex, diabetes, body mass index, immunosuppression, and tobacco use.4,13,14 More recently, nutritional status has been investigated as a potential risk factor for these outcomes.

Malnutrition, defined by low levels of albumin, prealbumin, and other serum rapid turnover proteins (transferrin and retinol-binding protein), is a potentially modifiable risk factor for wound complications. Four studies specifically evaluated the role of these markers.

Salvetti et al15,16 reported on the impact of a low preoperative prealbumin level for spine surgery patients. In 2015, this group performed a case-control series, identifying 292 patients over a 3-yr period who underwent surgical wound washouts. Preoperative prealbumin levels were available for 32 patients. A control cohort of 74 patients who underwent open posterior spine surgery during the same time interval were selected. There were no differences between the groups except for the presence of nutritional deficiency (P = .04). Both univariate and multivariate analysis found both diabetes and preoperative prealbumin <20 mg/dL to be independent risk factors for SSI (odds ratio [OR] 2.26 [95% confidence interval [CI] 1.05-4.84], P = .037 and OR 2.15 [95% CI 1.05-4.44], P = .037)16 (Level II). In a follow-up study,15 this group evaluated patients undergoing posterior spinal decompression and/or fusions. For this study, the authors evaluated the impact of nutritional sufficiency on deep wound infections (according to the U.S. Centers for Disease Control and Prevention definition). Of the 387 patients included, 19% were considered nutritionally insufficient (prealbumin <20 mg/dL). After adjusting for baseline differences, those with prealbumin <20 mg/dL were 3 times as likely to experience a deep SSI (OR 3.28 [95% CI 1.19-9.09], P = .02) (Level II).

To investigate serum markers of possible early wound infection (SSI), Kudo, et al17 measured total lymphocyte count, serum albumin, transferrin, prealbumin, retinol binding protein, C-reactive protein (CRP), and white blood cell count in patients undergoing spine surgery at a single institution. They defined possible SSI by an increase in CRP or lymphopenia after postoperative day 3 or 4. While a lower prealbumin was identified as significantly associated with possible SSI on univariate analysis, only operative duration was a predictor on multivariable analysis.

Focusing on revision surgeries for septic and aseptic reasons, Khanna et al18 used the American College of Surgeons National Surgical Quality Improvement Program registry to evaluate the relationship between hypoalbuminemia and reason for revision surgery and subsequent postoperative infectious complications. More than 3000 patients undergoing revision spinal surgery were included, 11% of whom had preoperative hypoalbuminemia.
Hypoalbuminemia was significantly more common in those undergoing septic revision compared with aseptic revision surgery (49.1% vs 8.5%, \(P < .001\)). In the patients undergoing aseptic revision, low albumin increased the risk of having an acute postoperative infection (OR 2.53, [1.17, 5.49], \(P = .019\) (Level II).

In addition to studies focusing on malnutrition as an independent risk factor for wound complications, several studies have sought to identify all major risk factors for these adverse events in spinal surgery. Two independent groups in China, using large cohorts of patients undergoing spine surgery, sought to identify major risk factors for SSI. Wang et al\(^{19}\) retrospectively evaluated all patients from 3 major medical centers undergoing posterior lumbar surgery. With >8000 patients included, they found a prevalence of SSI in their population of 3%. In addition to multiple other factors, low preoperative total protein and albumin were independently predictive of an increase in SSI (\(P = .003\) and \(P = .009\), respectively) (Level III). Li et al\(^{20}\) investigated patients undergoing open transforaminal lumbar interbody fusion (TLIF) procedures and found an overall incidence of SSI of 4.5%, with 55% of those patients having superficial wound infection. Independent risk factors for any SSI were thicker subcutaneous fat (OR 1.383 [95% CI 1.178-1.623], \(P < .001\)), higher preoperative American Society of Anesthesiologists score (OR 3.164 [95% CI 1.302-7.692], \(P = .011\)), lower preoperative albumin (OR 0.802 [95% CI 0.708-0.907], \(P < .001\)), and longer postoperative wound drainage (OR 3.745 [95% CI 1.464-9.580], \(P = .006\)) (Level II). These studies, while demonstrating hypoalbuminemia as an independent risk factor for SSI, are limited by their retrospective nature and their low SSI rate.

Nonunion

Nonunion or pseudarthrosis is a well-known complication of spinal fusion surgery, occurring in \(\leq 56\%\) of patients.\(^{21,22}\) This complication is impacted by patient factors, including age, smoking status, diabetes, and surgical factors. Surgical factors include levels of surgery, surgical approach/technique, use of adjuncts, and grafts. While nonunion may be clinically asymptomatic, it may result in \(\geq 1\) readmissions or revision surgeries with resultant individual and societal costs.\(^{23}\) Therefore, avoiding this complication is paramount.

In an effort to discern preoperative modifiable risk factors associated with nonunion, Inose et al\(^{24}\) studied 74 consecutive patients undergoing lumbar decompression and instrumented fusion surgery (either posterior lumbar fusion, TLIF, or both) for degenerative disease. Serum bone turnover markers, procollagen type 1 amino-terminal peptide, tartrate-resistant acid phosphatase 5b, and a nutritional status marker serum albumin were assessed. Computed tomography was performed at 1 yr to evaluate bony union. Preoperative albumin and bone turnover markers were independently predictive of nonunion (OR 0.028 [95% CI 0.001-0.379], \(P = .015\)) (Level II).

Hospital Readmissions

Adverse events often require additional interventions, prolonging hospital stays or resulting in unplanned readmissions after surgery.\(^{25,26}\) Two recent articles suggest malnutrition as an independent risk factor for 30-d hospital readmission.\(^{27,28}\)

Adogwa et al\(^{27}\) used an institutional database to identify 145 patients undergoing elective spine surgery. All patients had preoperative albumin levels drawn with 27% having levels <3.5 g/dL. The malnourished cohort had a 3 times higher rate of unplanned readmission (27.5% vs 9.5%, \(P = .02\)). In addition to number of levels fused and length of surgery, measures of surgical invasiveness, preoperative albumin level was an independent predictor of 30-d readmission (\(P = .01\)) (Level III). In a large registry cohort, Phan et al\(^{28}\) found hypoalbuminemia to confer a 2.7 times risk for unplanned readmission (OR 2.7 [95% CI 1.1-6.3], \(P = .023\)) (Level II).

Specific Patient Populations

With the growing elderly global population and increase in spine surgery in this potentially at-risk group, Puvanesarajah et al\(^{29}\) sought to quantify the impact of poor nutritional status in the elderly on postoperative medical risk and quantify differences in length of stay and readmission rates. Using an administrative database, the authors identified patients aged 65 to 84 yr undergoing elective spine surgery. Poor nutrition was defined by International Classification of Diseases, 9th revision codes and outcomes included major medical complications, revision surgeries, wound complications, and mortality. While <1% of the cohort were malnourished, these patients had a significantly increased odds of 90-d major medical complications (OR 4.24 [95% CI 3.64-4.94], \(P < .001\)), 1-yr mortality (OR 6.16 [95% CI 3.70-10.25], \(P < .001\)), postoperative infections (OR 2.27 [95% CI 1.70-3.04], \(P < .001\)), and wound dehiscence (OR 2.52 [95% CI 1.64-3.88], \(P < .001\)) (Level II).

Invasiveness of surgery has been demonstrated to be a predictor of multiple adverse events. Adult spinal deformity is often characterized by an increase in invasiveness, spanning multiple levels, combining varied surgical approaches, and involving osteotomy procedures. Phan et al\(^{30}\) analyzed 2236 patients in the American College of Surgeons National Surgical Quality Improvement Program registry who were undergoing surgery for adult spinal deformity to determine the impact of nutritional insufficiency, defined by a preoperative albumin level of <3.5 g/dL, on adverse outcomes. Nutritional insufficiency, present in 8.6% of this population, was found to be an independent risk factor for multiple adverse events. It most significantly impacts mortality, with malnourished patients having a 15 times risk of mortality (Level II).

Takemoto et al\(^{31}\) examined 274 patients undergoing elective thoracolumbar or lumbar surgeries and found that only 1.8% of these patients were malnourished (defined by prealbumin <15 mg/dL and transferrin <170 mg/dL). In this study, there was no association with malnutrition and postoperative...
complication, including wound complications. While this finding is contradictory, the chosen cutoff values for malnutrition may have been overly selective, and the potentially heterogenous patient population (did not clearly exclude tumor and trauma) may lead to bias in this study (Level III).

Question
2. What preoperative nonserological assessments of nutrition status (and timing of these assessments) are predictive of adverse events after spine surgery?

Recommendations
There is insufficient evidence to make a recommendation on the impact of preoperative use of nonserological assessments of nutrition status on adverse outcomes in patients undergoing spine surgery.

Strength of Recommendation: Grade Insufficient

The literature search did not identify any studies that specifically addressed this question and met the inclusion and exclusion criteria.

Question
3. In patients with poor nutrition, does preoperative treatment (and type of treatment) decrease the risk of postoperative adverse events?

Recommendations
In patients with malnutrition undergoing spine surgery, there is insufficient evidence to support the use of a perioperative MNM protocol to decrease the risk of postoperative adverse events.

Strength of Recommendation: Grade Insufficient

Nutritional status, a modifiable risk factor for adverse events, may be impacted by altering the diet of patients in the perioperative period. Strategies to improve the nutritional status of patients may range from the introduction of protein and carbohydrate supplements immediately preoperatively to the timed administration of enteral or parental nutrition. While this has been studied in other surgical populations, there is a paucity of literature evaluating the impact of nutrition-based interventions in spine surgery patients.

To date, there are few studies describing specific protocols to boost nutrition in this patient population. While excluded from this systematic review because of population characteristics, Hu et al.\(^{32}\) studied the impact of administration of total parenteral nutrition between stages of 2-stage surgery. They found that receiving total parenteral nutrition was associated with a lower risk of postoperative infectious complications. Belthur et al.\(^{33}\) studied the surgeon practice related to preoperative optimization for patients with cerebral palsy undergoing corrective spine surgery and found that 97% of responders identified nutrition status as a risk factor that should be optimized, yet the timing and strategy of optimization varied.

Specific to the investigated population for this systematic review, Xu et al.\(^{34}\) evaluated a multimodal nutritional management plan in patients undergoing lumbar instrumented fusion surgery. Patients who were not malnourished preoperatively, as defined by a preoperative albumin level \( \geq 35 \) g/L, were randomized to the MNM protocol (MNM group) or a control group. The MNM group received protein powder and carbohydrate powder at intervals both before and immediately after surgery as well as an early feeding protocol. Outcomes measured were the use of albumin in the immediate postoperative period, incidence of electrolyte disturbance, transfusion rate, length of stay, medical complications, wound drainage, and wound infection. A total of 187 patients were randomized. Compared with the control group, those receiving the MNM received a significantly lower volume and number of transfused albumin \((P = .009\) and \(P = .017\), respectively\), had a lower incidence of postoperative hypokalemia \((P = .006\)\), hyponatremia \((P = .001\)\), and hypocalcemia \((P = .026\)\), and a shorter length of stay \((P < .001\)\). The groups had a similar incidence of superficial infection, 2% in the MNM group and 5% in the control group, and neither group had any patients with deep wound infections. There was a significant difference in the number of patients with wound drainage, with more than double the number of patients in the control group with this outcome \((P = .008\)\) (Level II).

It is important to note that the patients in this study had normal nutrition before surgery, and as such may not be representative of the patients for which we would advocate intervention. In addition, while this was a randomized controlled trial, it lacked blinding for the patients and the surgeons, introducing potential bias, particularly in the assessment of wound drainage. Overall, this study demonstrates the utility of nutritional supplementation in patients with normal nutritional status undergoing spine surgery.

Future Research
This systematic review provides evidence that malnutrition, defined by a serum albumin level <3.5 g/dL or prealbumin level <20 mg/dL, is an independent risk factor for adverse events after elective spine surgery.

Future directions include (1) ascertaining which cutoff values for preoperative albumin and prealbumin are most indicative as predictors of adverse outcomes in spine patients; (2) the investigation of nonserological assessments of nutritional status (eg, anthropometric measurement [arm or calf circumference, hip-waist ratio] or questionnaires [Mini Nutritional Assessment]) and their impact on outcomes after spine surgery; and (3) the development of specific nutrition protocols and the evaluation of these protocol to (a) improve malnutrition and (b) avoid adverse events after spine surgery.

CONCLUSIONS
In conclusion, malnutrition, as evidenced by low albumin and prealbumin, has been shown to predict SSI, nonunion, readmission rates, and overall mortality.
Disclosures

All Guideline Task Force members were required to disclose all potential conflicts of interest (COIs) before beginning work on the guideline, using the COI disclosure form of the AANS/CNS Joint Guidelines Review Committee. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination and participation on the task force. The CNS Guidelines Committee and Guideline Task Force Chair may approve nominations of task force members with possible conflicts and restrict the writing, reviewing, and/or voting privileges of that person to topics that are unrelated to the possible COIs. See below for a complete list of disclosures.

Author Disclosure

<table>
<thead>
<tr>
<th>Author</th>
<th>Disclosure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marjorie C. Wang, MD, MPH</td>
<td>Zimmer Biomet, Medtronic Abbott ABNS, AANS JNS Spine Editorial Board</td>
</tr>
<tr>
<td>James S. Harrop, MD, MSHQS</td>
<td>Depuy Synthesis, Ethicon Globus, Stryker</td>
</tr>
<tr>
<td>Erica F. Bisson, MD, MPH</td>
<td>PCORI, NREF MiRs, nView, Stryker, Medtronic</td>
</tr>
<tr>
<td>John Dimar, MD</td>
<td>Medtronic, Depuy, Stryker Johnson &amp; Johnson, Pfizer, Glaxo-Smith Kline, Eli Lilly, Abbott, Hoffman La Roche, Abbvie Pfizer, Norton Hospital Medtronic, Stryker SRS &amp; FOSA (2020) JAAOS, Spine, Spinal Deformity, GSJ (Reviewer)</td>
</tr>
<tr>
<td>Sanjay Dhall, MD</td>
<td>Depuy Synthes, Globus Medical Great Circle Technologies</td>
</tr>
<tr>
<td>Daniel J. Hoh, MD</td>
<td>The Spine Journal Editorial Board CNS Officer, CNS Foundation Board, JNS Spine Editorial Board, The Spine Journal Editorial Board</td>
</tr>
</tbody>
</table>

Disclaimer of Liability

This clinical, systematic, evidence-based clinical practice guideline was developed by a multidisciplinary physician volunteer task force and is provided as an educational tool based on an assessment of the current scientific and clinical information regarding this guideline topic. These guidelines are disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not meant to replace the individualized care and treatment advice from a patient’s physician(s). If medical advice or assistance is required, the services of a physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

REFERENCES

7. Raaschou DF, Pignone M, Sox HC. How to decide whether a clinical practice guideline is trustworthy. JAMA. 2013;309(2):139-140.

Acknowledgments
The guidelines task force would like to acknowledge the CNS Guidelines Committee for their contributions throughout the development of the guideline, the AANS/CNS Joint Guidelines Review Committee, the AANS/CNS Joint Section on Disorders of the Spine and Peripheral Nerves for their donation to the CNS Foundation to support this project, as well as the contributions of Kirsten Aquino, contracted project manager for the CNS, Trish Rehring, MPH, Associate Director for Evidence-Based Practice Initiatives for the CNS, and Janet Waters, MLS, BSN, RN, for assistance with the literature searches and Kenneth Probst for the cover illustrations. Throughout the review process, the reviewers and authors were blinded from one another. At this time, the guidelines task force would like to acknowledge the following individual peer reviewers for their contributions: Patricia Raksin, MD, Jason Stacy, MD, Neil Majmunder, MD, Yi Lu, MD, Alex Beier, MD, Andrew Carlson, MD, Brandon Rocque, MD, Robert Whitmore, MD, Jay Turner, MD, and Owoicho Adogwa, MD.

Supplemental digital content is available for this article at www.neurosurgery-online.com.

Supplemental Digital Content 1. Literature searches
Supplemental Digital Content 2. Inclusion criteria
Supplemental Digital Content 3. Criteria grading the evidence
Supplemental Digital Content 4. Linking levels of evidence to grades of recommendation
Supplemental Digital Content 5. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart
Supplemental Digital Content 6. Evidence table