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Int J Spine Surg 2023, 17 (S2) S18-S25
doi: https://doi.org/10.14444/8510
https://www.ijssurgery.com/content/17/S2/S18

The International Journal of Spine Surgery
2397 Waterbury Circle, Suite 1,
Aurora, IL 60504, Phone: +1-630-375-1432

International Journal of Spine Surgery, Vol. 17, No. S2, 2023, pp. S18–S25
https://doi.org/10.14444/8510

Patient Optimization for the Prevention of Proximal Junctional Kyphosis

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ABSTRACT

Proximal junctional kyphosis (PJK) and proximal junctional failure (PJF) are well-recognized challenges of surgery for adult spinal deformity (ASD). Multiple risk factors have been identified for PJK/PJF, including osteoporosis, frailty, neurodegenerative disease, obesity, and smoking. Several surgical techniques to mitigate risk of PJK/PJF have been identified; however, patient optimization is also critical. This review summarizes the data behind these 5 risk factors (osteoporosis, frailty, neurodegenerative disease, obesity, and smoking) and details the related recommendations for patients undergoing surgery for ASD.

Focus Issue Article

Keywords: spine fusion, proximal junctional kyphosis, proximal junctional failure, spine deformity, pseudarthrosis

INTRODUCTION

Proximal junctional kyphosis (PJK) and proximal junctional failure (PJF) are well-recognized challenges of surgery for adult spinal deformity (ASD). PJK is broadly defined as radiographic evidence of kyphosis as the spine transitions from fused to mobile. A more specific and often-cited definition is an increase in the Cobb angle of >10° from the upper instrumented vertebrae (UIV) to 2 levels above the UIV (UIV +2).[1–4] PJF is the progression of PJK to the point of symptom onset, vertebral collapse, and/or instrumentation failure that requires revision surgery.[5] The reported prevalence of PJK has ranged from 17 to 47.9%.[1,2,6–11] In a systematic review conducted by Kim et al,[1] the following surgery-related risk factors for PJK were identified: combined anterior and posterior surgery, UIV at T1-T3, fusion extending to the sacrum, nonanatomic restoration of thoracic kyphosis, and thoracoplasty.

To prevent PJK, several surgical techniques have been developed, including ligament augmentation (using tethers), vertebroplasty, transverse process hooks, flexible rods, sublaminar tape, and multilevel stabilization screws.[3,12,13] These techniques have varying reports of success and have not been universally adopted. A recent systematic review concluded that vertebroplasty (which augments the anterior column) in addition to tethers and transverse process hooks (which both enhance the posterior column) shows potential; however, all techniques need higher quality studies.[12] The scope of this study is to address patient risk factors that may be optimized to prevent PJK. Specifically, this study addresses 5 key areas: osteoporosis, frailty, neurodegenerative disease, obesity, and smoking (Table).

OSTEOPOROSIS

Low bone mineral density (BMD) is a significant risk factor for PJF after surgical correction of ASD.[6,14–18] A study of 113 patients surgically treated for spinal deformity with propensity matching for age, upper and lower instrumented vertebrae, history of spine surgery, and Schwab-Scoliosis Research Society ASD classification found that the incidence of PJF was significantly higher in the patient group with significantly low BMD (average T score ≤ -1.5) when compared with patients with normal to mildly low BMD (average T score ≥ -1.5) (33% vs 8%, $P < 0.01$, OR 6.4, 95% CI: 1.2–32.3).[14] Multiple best practice guidelines for the assessment and management of osteoporosis in adult patients undergoing spine reconstruction have been proposed, including those with a focus on preventing pseudarthrosis and PJK.[18–20]

Regarding the age at which screening for osteoporosis prior to correction of spinal deformity should be initiated, a 2022 multidisciplinary panel of 18 experts, including orthopedic and neurological surgeons, endocrinologists, and rheumatologists, recommended screening of all patients older than 65 years, independent of risk factors, using BMD testing prior to surgery.[19] In patients aged 50 to 64 years, BMD testing is recommended if 1 or more of 12 risk factors are present: chronic glucocorticoid use defined as more than 3 months of prednisone use, minimum 5 mg/d,

Table. Recommendation summary for patient optimization to prevent PJK.

Osteoporosis
• Medications including bisphosphonates (antiresorptive), teriparatide (anabolic), denosumab (antiresorptive)
• Calcium + vitamin D supplementation
Frailty
• Triage patients using scoring system
• Prehabilitation
• Increase protein intake
Neurodegenerative disease
• Involve movement disorder specialist
• Treat Parkinson disease–associated osteoporosis
Obesity
• Body mass index <30 ideal, ≤35 realistic
• Offer assistance with diet, exercise, and weight loss plans
• Involve dietitian
Smoking
• Smoking cessation; most important postoperatively
• Nicotine replacement (eg, gum, patches)

Abbreviation: PJK, proximal junctional kyphosis.

personal history of previous low-energy fracture of the hip or spine, personal history of metabolic bone disease, chronic kidney disease ≥stage 3, high fracture risk as calculated by the fracture risk assessment tool, prior failed spine surgery, alcohol use of 3 or more units per day, vitamin D deficiency, current smoking, limited mobility, wheelchair based, on cancer treatment, and >10 years of diabetes mellitus with poor glycemic control.[19] In patients younger than 50 years, BMD testing is recommended if 1 or more of 5 risk factors are present: chronic glucocorticoid use, previous low-energy fracture, metabolic bone disease, cancer treatment, or chronic kidney disease, as defined above.[19] Screening recommendations proposed by Karikari et al were similar; however, a 5-year difference in age for asymptomatic patient screening was proposed in female vs male patients, recommending screening in women older than 65 years and men older than 70 years undergoing consideration for spinal fusion, citing practice parameters of the American College of Radiology.[18]

After identifying patients for whom screening is advised, the Congress of Neurological Surgeons (CNS) task force affirmed a grade B recommendation that preoperative assessment with either dual-energy x-ray absorptiometry images, computed tomography images, or serum vitamin D3 levels is appropriate. A dual-energy x-ray absorptiometry image with T score <−2.5, a CT image with Hounsfield units <97.9, and serum vitamin D3 level <20 ng/mL are associated with poor BMD and predict an increased risk of a postoperative adverse event in individuals undergoing spinal instrumentation.[20] However, a recent study of 63 ASD patients who underwent surgery found that a higher mean value, 120 Hounsfield units of the UIV and UIV +1, may be a superior cutoff for significant risk of PJK.[21]

Strategies for medical management of osteoporosis in preparation for correction of ASD can be categorized into the use of (1) bisphosphonates, (2) teriparatide, (3) denosumab, and (4) calcium and vitamin D3. While bisphosphonates are a first-line treatment of osteoporosis, the CNS task force affirmed 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.[20] A retrospective study by Kim et al of 44 patients undergoing posterior lumbar interbody fusion with osteoporosis-treated patients with either a bisphosphonate (alendronate) vs no bisphosphonate found that fusion rates were similar for the bisphosphonate group (66.7%) and the no bisphosphonate group (73.9%; $P = 0.599$).[22] A retrospective study by Kang et al of 97 postmenopausal women with osteoporosis undergoing posterior lumbar interbody fusion compared patients who were treated with bisphosphonates with those who had received no treatment and found that bisphosphonates may negatively delay fusion in the short term for the first 6 months but not at 2 years postoperatively with comparable overall fusion rates.[23]

Treatment with teriparatide, however, has been shown to increase BMD, induce earlier and more robust fusion, and may improve patient outcomes, including reducing the risk of PJF.[17,24] Yagi et al found that osteopenic patients, given immediate postoperative teriparatide after spinal deformity correction, had significantly lower rates of PJF when compared with control at 2-year follow-up (4.6% vs 15.2%; $P = 0.02$).[24] The CNS task force affirmed a grade B recommendation that preoperative osteoporosis treatment with teriparatide should be considered in patients with osteoporosis undergoing spinal instrumentation to decrease the risk of postoperative adverse events.[20] Denosumab was not included as a recommended agent for preventing postoperative adverse effects per CNS task force, citing lack of sufficient evidence at this time.[20]

Last, because oral calcium supplementation either alone or in combination with vitamin D has been shown to prevent bone loss and fragility fractures, supplementation is generally advised if deficiency is encountered.[25] Stoker et al found that among 313 patients undergoing spinal fusion, the rates of vitamin D inadequacy (<30 ng/mL) and deficiency were 57% and 27%, respectively.[26] Patients for whom a deficiency was identified were prescribed 50,000 IU of oral vitamin D_2 per week for 8 weeks—a regimen widely used.[27,28] This regimen

may be completed prior to surgery, and vitamin D toxicity due to supplementation is rare.[27,28]

FRAILTY

Frailty is defined as an aging-related syndrome of decline in physiological reserve and reduced resilience to stressors.[29,30] Higher frailty correlates with a higher risk of postoperative adverse events and increased health care utilization and costs in various types of surgeries.[31,32] These findings have been recently validated in the spine literature and are especially important to consider in patients undergoing surgery for spinal deformity given the invasiveness and complexity of the performed procedures.[32–36]

In 2022, Kitamura et al reported the results of their systematic review, evaluating the feasibility and quality of currently available frailty scales for patients undergoing spine surgery.[32] Of the 88 studies included, the authors identified 23 frailty scales with variable predictive values based on the indication and type of the index surgery, patients' age, and the outcomes of interest.[32] Because there was no ideal scale identified to be used in all the settings, the study recommended choosing an adequate scale based on the setting of interest (triage vs preoperative work-up).[32] The authors recommended using a simple scale for primary triage and a comprehensive scale for preoperative assessment. Candidate scales that can be used for primary triage include the modified 5-item frailty index (mFI-5); the FRAIL scale (fatigue, resistance, ambulation, illness, and loss of weight) scale (2 domains, 5 items); Fried's frailty phenotype (1 domain, 5 items); and the Clinical Frailty Scale (9 grades, from very fit to terminally ill). While the study found mFI-5 to be the most frequently reported among the 4 simple scales in the spine population, its validity in the elderly population remains unknown.[32] The authors recommended using the fatigue, resistance, ambulation, illness, and loss of weight scale for primary triage because its predictive value for morbidity and mortality has been further proven in prior studies.[32] Candidate scales that can be used for preoperative assessment include the mFI-11 (10 items for comorbidities and 1 item for physical function), ASD-Frailty Index (ASD-FI) (multidisciplinary with 40 items but its feasibility in clinical practice is questionable due to its length), and cervical deformity FI (4 domains, 40 items). The more simple forms, modfied ASD-FI (2 domains, 8 items), clinicial ASD-FI (2 domains 8 items), and modified cervical deformity frailty index (3 domains, 15 items), were developed to reach feasibility for use in clinical practice.[32] Moreover, the authors strongly recommended using the Risk Analysis Index, another multidisciplinary scale with 14 items, because it is the only scale in this study that has been used in an interventional prospective study and it has been implemented for preoperative assessment in other surgical domains.[32]

Sarcopenia, defined as decreased skeletal muscle mass leading to decreased muscle function, has also gained interest as a possible preoperative variable that can be used to predict surgical outcomes. However, there is conflicting evidence in the spine surgery literature about the role of sarcopenia in predicting postoperative outcomes, with some reports demonstrating that sarcopenia is associated with poor outcomes[37,38] and others demonstrating no association.[34,39,40] Akbik et al[34] performed a comparative analysis between sarcopenia (as measured by Psoas Muscle Index) and frailty (as measured by mF-11 and MF-5) in predicting outcomes in 235 patients undergoing ASD surgery. The authors found that frailty indices correlated with perioperative transfusion, longer hospital stay, and mortality, whereas sarcopenia was not associated with any of these outcome measures.[34] On the other hand, a study by Eleswarapu and colleagues that included 32 adult patients undergoing spinal deformity surgery with PJK and PJF occurring in 20 (62.5%) and 12 (37.5%) patients, respectively, identified psoas cross-sectional area to be an independent predictor of PJK ($P = 0.02$) and PJF ($P = 0.009$).[38] Additionally, the authors found that setting-specific psoas cross-sectional area thresholds of <12 cm^2 in men and <8 cm^2 in women resulted in a PJF rate of 69.2% for patients below these thresholds, relative to 15.8% for those above the thresholds.[38] In concordance, Babu et al[41] reported their experience with 73 patients and found that sarcopenia (measured by psoaslumbar vertebral index) is a risk factor for PJK and other 2-year complications following pedicle subtraction osteotomy. It is worth mentioning that variable definitions of sarcopenia and heterogenous populations included in previous studies necessitate further studies to validate these findings.

Identification of at-risk patients through frailty scores allows for patient optimization.[42] This can be via prehabilitation that can include respiratory muscular training to increase expiratory and inspiratory pressure, thereby lowering rates of pneumonia, exercise to increase cardiovascular reserve, as well as balance and strength training with a focus on strengthening the muscles that will be utilized the most during the recovery period. Optimization of nutritional status in frail patients can also be beneficial as surgical stress induces a catabolic state, which leads to protein breakdown

primarily from muscle.[42] Hence, adequate protein intake is necessary to prevent muscle loss or sarcopenia.[42] Of note, spine disease by itself is considered a contributing factor for developing frailty since there is an overlap between the clinical features of spine disease (reduced physical activity, slow walking speed, and poor endurance) and the clinical features of frailty (reduced gait speed, decreased muscle strength, and poor energy expenditure).[43] Therefore, timely spine surgery can improve frailty and reduce long-term morbidity and mortality.

NEURODEGENERATIVE DISEASE

Parkinson disease (PD) is the second most common neurodegenerative disease after Alzheimer disease and has the most well-recognized association with spinal deformity among neurodegenerative diseases.[44] PD is a movement disorder characterized by motor symptoms (eg, resting tremor, bradykinesia, rigidity, and postural and gait impairment) with 6.1 million people affected worldwide in 2016 and a rapid rise in prevalence over the past 2 decades for unknown reasons.[45] Patients with PD also have nonmotor symptoms (eg, cognitive decline, depression, pain, and cardiovascular dysfunction) and a notably higher rate of osteoporosis than non-PD patients.[46] The spinal deformity in PD (eg, kyphoscoliosis, Pisa syndrome, antecollis, camptocormia) is likely due to a combination of the previously listed motor and nonmotor symptoms in addition to osteoporosis.[47] Interestingly, the degree of spinal deformity in PD has been positively correlated with the severity of PD.[48]

Surgery for ASD in PD patients carries increased risk with an increased rate of inpatient complications in comparison with patients without PD.[49] A recent review of the literature from 2000 to 2013 in PD patients undergoing spinal fusion calculated a revision rate of 45% and a complication rate of 59%.[50] Despite the increased risk of complications,[49,51] successful outcomes after spine surgery are often achieved,[52] with 1 study reporting up to 78% of patients reporting favorable outcomes.[53] However, in their study of 23 patients with PD who underwent surgery for ASD, Koller et al[53] reported a 17.6% rate of PJK. In a retrospective review of 29 patients with PD who underwent revision for PJK at a single institution, 76% (22/29) were found to have neurologic comorbidities, although only one of these patients had PD.[54] In a retrospective review of 12 patients with PD who underwent T2-pelvis fixation and a mean follow-up of 33 months, 2 patients (16.7%) required revision for PJK.[55] In a cohort study of 13 PD patients undergoing ASD for degenerative sagittal imbalance matched to 26 non-PD patients, 8 PD patients (61%) underwent a revision for PJK in comparison with only 1 (3.8%) non-PD patient.[56] Analysis of risk factors for PJF demonstrated that decreased length of fusion and increased fatty changes in the paraspinal musculature were correlated with increased rate of PJF.[56]

To optimize surgical outcomes and prevent PJK in PD patients, several strategies have been discussed. Screening and treatment of osteoporosis in these patients are essential.[46] In their review, Ha et al[47] postulated that the majority of poor outcomes are likely due to poor patient selection and persistent coronal and sagittal imbalance. Involving a movement disorder specialist from the beginning is recommended for assistance with patient selection and to avoid perioperative complications involving medications.[57] It has been postulated that deep brain stimulation prior to spine surgery or even in replacement of spine surgery may benefit patient outcome due to the complexity of deformity surgery for PD patients.[58,59] In a 2015 systematic review, deep brain stimulation appeared to independently improve PD-related deformity without surgery.[59] Patients with higher preoperative function and high responsiveness to levodopa may be more likely to have successful outcomes.[47] Finally, analysis of preoperative spine measurements is paramount to formulate a surgical plan with sufficient length of fusion and osteotomies in order to improve spinal alignment and prevent PJK.

OBESITY

A high body mass index (BMI) has a significant adverse effect on the pain level and function of patients with ASD.[60] A study of 1004 ASD patients found an inverse relationship between BMI and functional scores, including the Core Outcome Measures Index back score and the Numerical Rating Scale back and leg scores, and a direct relationship between BMI and pain, even when accounting for patient age, gender, occupational status, smoking status, and the radiographic parameters known to relate to functional outcomes.[60] Furthermore, obesity negatively affects cost efficiency and outcomes following ASD surgery.[61] Patients with BMIs in the class I, class II, or class III range had more expensive total ASD surgery costs, with the 1-year cost being approximately 32% higher for obese patients than nonobese patients per quality-adjusted life year.[61] A recent meta-analysis of predictors of PJK did not identify obesity to be significantly associated with PJK;[62] however, at least 2 studies have identified obesity as a risk factor for the development of PJK and PJF in patients with adult lumbar scoliosis following long instrumented posterior spinal fusion.[63,64] Therefore, it is prudent to consider optimization of obesity prior to ASD surgery. Jain et al reported decreased length of stay, medical complications, and surgical site infections in patients who underwent preoperative bariatric surgery prior to undergoing elective posterior

lumbar fusion in comparison with a group of patients who did not have bariatric surgery.[65] In regard to specific BMI goals, there is likely a range that should be targeted, and it is both extremes of BMI that must be avoided. A recent study on obesity by Than et al in 106 patients undergoing minimally invasive deformity surgery[66] demonstrated worse postoperative quality-of-life outcomes and spinopelvic parameters for patients with BMI ≥30 mg/kg^2 in comparison with those patients with BMI ≤30 mg/kg^2. Their conclusion was that a BMI target of ≤30 mg/kg^2 for spine surgery is ideal; however, ≤35 mg/kg^2 is more realistic for elective clinical practice. Diet, nutrition, counseling, and exercise programs should be offered to patients in order to reach these BMI goals.

SMOKING

While the negative impact of smoking on overall health is universally agreed on, reports on its impact on the outcomes of spinal deformity surgery have not produced definitive conclusions. Two large retrospective analyses did not find significant differences in length of hospital stay, 30-day complications, or readmission rates between smokers and nonsmokers undergoing ASD surgery.[67,68] A prospectively collected, multicenter study by the International Spine Study Group on 346 patients reported that a history of smoking had no effect on early (<6 weeks) or late (up to 2 years) complication rates, but the study did not stratify the effect of smoking on specific complications.[69] In addition, a more recent meta-analysis included 14 studies and 1908 patients to determine risk factors for PJK in ASD surgery and did not identify smoking as one of the independent risk factors.[62] However, spine surgeons generally avoid performing ASD surgery on smokers, and therefore "selection bias" and insufficient active smokers enrolled may explain the negative findings of these studies. On the other hand, a more recent post hoc analysis on 272 patients from the Scoli-RISK-1 study (a prospective, multicenter international observational study of ASD surgery with neurological function as the primary outcome) accounted for the limitations of prior studies and found that a history of smoking significantly increased the risk of excessive intraoperative bleeding and nonsignificantly increased the rate of implant failure or surgery-related adverse events over 2 years.[70] In parallel, preclinical studies have demonstrated that smoking causes increased vertebral and endplate porosity and decreased trabecular thickness[71,72] and interferes with early and late processes in spinal fusion and bone healing.[73,74]

Current literature supports smoking cessation as a potentially effective tool in mitigating adverse events and improving the surgical outcomes following spine surgery.[72,74] While complete smoking cessation in both pre- and postoperative periods is ideally recommended for compliant patients, postoperative smoking cessation may have the greatest benefit in terms of improving fusion rates and decreasing perioperative complication rates, especially the first 4 weeks following surgery.[74] Moreover, it has been hypothesized that nicotine replacement therapy (nicotine patches and nicotine gum) may reduce the detrimental effects of smoking. The theory behind this hypothesis is supported by studies that have demonstrated that many of the components of smoking cigarettes are significantly more harmful than the nicotine component.[74] In addition, since one of the mechanisms behind smoking's interference with spinal fusion and bone healing is through its effect on pro-osteoblastic mediators such as cytokines, growth factors, and bone morphogenetic proteins, it is recommended to use osteoinductive proteins such as bone morphogenetic proteins in patients who smoke undergoing spine surgery to reduce the risk of pseudarthrosis.[74]

CONCLUSION

Diagnosis of ASD has become increasingly common, and surgery for ASD has become more prevalent over time.[75] In parallel, surgery has become increasingly successful in medically complex and elderly ASD patients, with complication rates reduced by 50% over the past decade.[75] As the population continues to live longer, it is imperative for spine surgeons to optimize patient-related factors prior to surgery. Patient-related risk factors that should be modified to avoid development of PJK include osteoporosis, frailty, neurodegenerative disease, obesity, and smoking. Several strategies are discussed to mitigate the negative effects of these factors.

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Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

Declaration of Conflicting Interests: Dr. Witham is a consultant for, investor in, and medical advisory board member for Augmedics. All other authors report no conflicts of interest in this work.

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Published 15 June 2023