Alcoholism as a predictor for pseudarthrosis in primary spine fusion: An analysis of risk factors and 30-day outcomes for 52,402 patients from 2005 to 2013

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ABSTRACT

Introduction: This study assessed the incidence and risk factors for pseudarthrosis among primary spine fusion patients.

Methods: Retrospective review of ACS-NSQIP (2005–2013). Differences in comorbidities between spine fusion patients with and without pseudarthrosis (Pseud, N-Pseud) were assessed using chi-squared tests and Independent Samples *t*-tests. Binary logistic regression assessed patient-related and procedure-related predictors for pseudarthrosis.

Results: 52,402 patients (57yrs, 53%F, 0.4% w/pseudarthrosis). Alcohol consumption (OR:2.6[1.2–5.7]) and prior history of surgical revision (OR:1.6[1.4–1.8]) were risk factors for pseudarthrosis operation. Pseud patients at higher risk for deep incisional SSI (at 30-days:OR:6.6[2.0–21.8]). Pseud patients had more perioperative complications (avg:0.24 ± 0.43v0.18 ± 0.39,*p* = 0.026).

Conclusions: Alcoholism and surgical revision are major risk factors for pseudarthrosis in patients undergoing spine fusion.

1. Introduction

Pseudarthrosis is a well-known iatrogenic complication of spinal fusion surgery. Defined as failed solid bony fusion or *non-union*, pseudarthrosis can be associated with higher medical costs and lower quality of life for patients with adult spinal deformity (ASD).[1–3] The advent of new technologies and more advanced surgical techniques have led to an increase in the rate of fusion surgeries being performed.[4] Likewise, the rate of pseudarthrosis as a complication of ASD surgery has been reported as high as 24%, with more recent studies reporting lower rates of 9%–12% likely due to increased awareness and prevention.[5–7] Despite such promising trends, further investigation of preventable risk factors for pseudarthrosis is clinically important in order to reduce revisions and optimize surgical management.

A number of previous studies examining risk factors for non-union have identified smoking as a negative predictor.[8–10] Smoking is a leading cause of morbidity and mortality worldwide, and is a known risk factor for unfavorable surgical outcomes including but not limited to superficial and deep wound infections, delayed wound healing, and non-union.[11] Alcohol consumption is also strongly associated with adverse surgical outcomes, however its relationship to pseudarthrosis in patients undergoing spinal fusion has not been elucidated in the

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Table 1

Demographics and comorbidities of Pseud vs N-Pseud cohorts. Bolded cells represent statistical significance to p < 0.05. N-Pseud = Non-Pseudarthrosis, Pseud = pseudarthrosis.

	N-Pseud (N = 52,180)	Pseud (N = 222)	Univariate *p*-value	OR (95% CI)
Age (years)	57.31 ± 13.44	57.73 ± 16.45	0.641	0.99 (0.58–1.41)
BMI (kg/m^2)	29.99 ± 6.57	29.10 ± 6.00	0.99	1.00 (0.97–1.04)
Length of Stay (days)	3.97 ± 7.89	4.2 ± 3.70	0.664	1.00 (0.99–1.02)
Total Levels Fused	2.66 ± 2.22	2.54 ± 2.50	0.42	0.98 (0.92–1.04)
Mirza Surgical Invasiveness	4.08 ± 2.57	2.68 ± 2.23	< .001	0.65 (0.56–0.75)
EtOH (> 2drinks/day, 2 weeks pre-admission)	3.46%	91.4%	**0.023**	2.52 (1.13–5.64)
Diabetes mellitus	15.6%	26.2%	0.704	1.13 (0.61–2.10)
Current Smoker within 1 year	25.4%	24.3%	0.753	0.95 (0.56–1.60)

literature.

With the rising utility of spinal fusion in ASD treatment, it is more important than ever to identify predictors of adverse outcomes such as non-union. The current study aims to identify patient and procedure-related risk factors associated with higher rates of pseudarthrosis in spinal fusion patients.

2. Materials and methods

2.1. Data source

The American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP) database was used for analysis of pseudarthrosis patients. The US Department of Veterans Affairs developed NSQIP to track various risk-adjusted surgical outcomes in hospitals across the United States, including preop risk factors, intraoperative variables, 30-day postop complications, Current Procedural Terminology (CPT) codes, and International Classification of Disease 9th Edition (ICD-9) codes. Trained Surgical Clinical Reviewers collect and audit data from randomly assigned patients, ensuring the database's standardization and reliability.

2.2. Study design

This is a retrospective review of ACS-NSQIP data from the years 2005–2013. Inclusion criteria were patients over the age of 18 undergoing cervical or thoracolumbar arthrodesis. Patient groups were created: those undergoing primary spinal fusion, and those undergoing spinal fusion with a diagnosis of pseudarthrosis. ICD-9 codes were used to isolate for a diagnosis of pseudarthrosis, and CPT codes isolated for procedure type, including anterior lumbar interbody fusions (ALIF), posterior lumbar interbody fusions (PLIF), revision surgery, exploratory fusion, osteotomy, iliac fixation, and decompression.

2.3. Statistical analysis

Primary analysis compared patients diagnosed with pseudarthrosis undergoing spinal fusion (Pseud), and patients undergoing primary spinal fusion with no diagnosis of pseudarthrosis (N-Pseud). Univariate analysis of baseline demographics and comorbidities was conducted using independent samples *t*-tests for continuous variables and Chi-square tests for categorical variables. Multivariate analysis was performed using binary logistic regression, which assessed patient-related predictors for pseudarthrosis while controlling for age, sex, and BMI. Binary logistic regression also analyzed procedure-related predictors for pseudarthrosis, controlling for age, sex, BMI, surgical invasiveness index (Mirza), and comorbidities between Pseud and N-Pseud cohorts. All statistical analysis was performed using SPSS version 23.0 (Armonk, NY, USA). A *p* value of less than 0.05 was considered statistically significant.

3. Results

3.1. Demographics and comorbidity

This study analyzed a total of 52,402 patients (53.0% female, average age 57), 222 (0.4%) with pseudarthrosis. 41.1% of patients had an anterior approach, 51.5% had a posterior approach, 6.0% had a combined approach, and 1.4% unknown. Out of all fusion patients, 44.3% had one-level fusions, 1.7% had 2-level fusions, 23.4% had 2.5-level fusions, and 18% had 4.5-level fusions. N-Pseud patients underwent an average of 2.66 ± 2.22 levels of fusion and Pseudo patients underwent an average of 2.54 ± 2.50 levels of fusion (*p* = 0.42). Regionally, 41.6% of fusions were cervical, 3.9% were thoracic, 48.8% were lumbar, and 5.7% spanned multiple regions. 5.8% underwent revision, 3.8% underwent exploratory fusion, 1.2% underwent iliac fixation, 43.4% underwent decompression, and 2.8% underwent osteotomy (Table 2).

Table 2

Procedure-related risk factors. N-Pseud = Non-Pseudarthrosis, Pseud = pseudarthrosis, SSI = surgical site infection.

	N-Pseud (N = 52,180)	Pseud (N = 222)	*p*-value	OR (95% CI)
Revision	5.8%	18.9%	< 0.001	1.56 (1.40–1.75)
Surgical Approach				
Anterior	41.2%	18.9%	**< 0.001**	0.33 (0.24–0.45)
Posterior	51.4%	73.4%	**< 0.001**	2.61 (1.94–3.52)
Combined	6.0%	5.9%	0.920	0.97 (0.55–1.70)
Cervical	41.6%	51.4%	**0.003**	1.48 (1.14–1.93)
Thoracic	3.9%	5.9%	0.128	1.55 (0.88–2.71)
Lumbar	48.8%	40.1%	**0.010**	0.70 (0.54–0.92)
Deep Incisional SSI	0.6%	2.3%	**0.003**	3.80 (1.55–9.27)
Any Complication	18.1%	23.9%	**0.027**	1.42 (1.04–1.93)
Iliac Fixation	1.2%	2.7%	0.058	2.17 (0.976–4.80)
Osteotomy	2.8%	2.7%	0.925	0.962 (0.43–2.17)
Exploratory	3.8%	10.4%	**< 0.001**	2.96 (1.92–4.57)
Decompression (any level)	43.5%	17.1%	**< 0.001**	0.486 (0.39–0.61)

Bold values indicate statistical significance to p < 0.05.

Pseud patient had a lower mean surgical invasiveness index at baseline than N-Pseud (2.68 ± 2.23 and 4.08 ± 2.57, respectively, $p < 0.001$) (Table 1).

3.2. Patient-related predictors

Pseud patients had a significantly higher baseline consumption of alcohol than N-Pseud patients ($p = 0.023$), with alcohol consumption defined as greater than 2 drinks per day two weeks before admission (Table 1). There was a strong relationship between alcohol consumption and patients undergoing spinal fusion for pseudarthrosis, with alcohol significantly increasing the risk for non-union (OR: 2.64 CI: 1.21–5.75). A history of diabetes mellitus and smoking had no significant effect on pseudarthrosis risk.

3.3. Procedural predictors

Revision surgery was also identified as a strong predictor of non-union, with a history of previous revision surgery increasing the odds of undergoing spinal fusion for pseudarthrosis (OR: 1.56 CI: 1.40–1.75). Surgical approach was identified as a strong predictor for pseudarthrosis, with a posterior approach increasing odds of cervical non-union (OR: 12.9 CI: 5.7–29.2). A posterior approach, however, was also associated with lower odds of thoracolumbar non-union (OR: 0.35 CI: 0.17–0.71) (Table 2).

3.4. Complications

Compared to patients undergoing primary spinal fusion, Pseud patients had increased odds of developing deep incisional SSI (OR: 6.63 CI: 2.02–21.80) and perioperative complications within 30-days of fusion (OR: 1.42 CI: 1.04–1.93). On average, Pseud patients had higher rates of 30-day complications than N-Pseud patients (0.24 ± 0.43 and 0.18 ± 0.39, respectively, $p = 0.027$) (Table 2).

Compared to patients undergoing reoperation within 30 days of primary fusion (non-pseud-revision), Pseud patients had lower odds of deep incisional SSI (OR: 0.23 CI: 0.06–0.82), sepsis (OR:0.11 [0.03–0.92]), or periop blood transfusion(OR:0.11[0.03–0.33])

4. Discussion

The rising popularity and utilization of spinal fusion in the treatment of ASD demands a robust understanding of pseudarthrosis as a potential complication. Non-union is costly both in terms of hospital fees and patient quality of life, thus much research has been dedicated to identifying risk factors for its development.[1–3] As a number of studies have demonstrated an association between pseudarthrosis and decreased health-related quality of life, effective reduction in pseudarthrosis rates necessitates identification of predictors for non-union. This study identified alcoholism, previous revision surgery, and posterior approach in the cervical spine as strong predictors for pseudarthrosis. Additionally, Pseud patients had a significantly higher risk for deep incisional SSI and more perioperative complications than N-Pseud patients.

The demographic variables analyzed as predictors for pseudarthrosis included age, gender, BMI, diabetes, and smoking status – none of which were significant predictors for pseudarthrosis in the present study. The connection between obesity and postoperative surgical complications is well-documented, with obesity highly correlated to increased operative time, increased blood loss, and delayed hospital discharge.[12,13] Its effect, however, on pseudarthrosis rates has been somewhat less explored. In a study of adolescent idiopathic scoliosis, Upasani et al. showed there was no significant difference between overweight and healthy weight patients with regard to pseudarthrosis, surgical revision, or implant failure.[14] That being said, smoking has indeed been shown in previous studies to predict pseudarthrosis.[8–10]

Bydon et al. found that patients undergoing 2-level or greater PLF have pseudarthrosis rates as high as 30%, a significantly higher rate than nonsmokers.[15] Phan et al. suggested that perioperative smoking significantly increased odds of failed lumbar fusion in a retrospective study of patients who underwent anterior lumbar interbody fusion (ALIF).[16] Further investigation of smoking and pseudarthrosis is necessary to determine whether a direct correlation exists.

In this study, alcohol consumption was identified as a strong independent risk factor for pseudarthrosis in patients undergoing spinal fusion. We defined alcoholism as two or more alcoholic beverages per day within a two week period leading up to hospital admission. Though the literature surrounding alcohol's effects on non-union rates is somewhat lacking, its deleterious effects on fracture healing and remodeling is well documented.[17–19] Lauing et al. showed acute alcohol exposure resulted in significant impairment of fracture callus tissue formation through impairment of the beta-catenin pathway.[17] Nyquist et al. found impaired healing time in tibial fractures of alcohol abusers compared to non-abusers, however in another study of cervical hip fractures did not find a significant difference in pseudarthrosis rates between the two groups.[18,19] Our data supports previous conclusions of alcohol's deleterious effects on bone growth, with the odds of pseudarthrosis in drinkers increasing to 2.64 times the odds of pseudarthrosis in non-drinkers ($p = 0.015$).

Surgical approach was also analyzed as a risk factor for non-union in fusion surgery. Our study divided patients into cervical and thoracolumbar fusion procedures using ICD-9 codes to better localize pseudarthrosis development. A posterior approach increased odds of pseudarthrosis in the cervical spine, but decreased odds of pseudarthrosis in the thoracolumbar region. Outcomes for anterior, posterior, versus mixed approaches are currently areas of active investigation, and the literature has been equivocal in its findings. Previous studies have shown higher complications rates of posterior cervical fusion in terms of estimated blood loss (EBL) and length of stay (LOS) when compared to anterior approaches, but these same studies also suggest superior fusion rates and lower repeat revision rates in a posterior approach.[20–22] On the other hand, Dickson et al. found no significant effect of a posterior-only approach on pseudarthrosis rates in patients undergoing lumbar subtractionosteotomy.[23] The current study found a posterior approach decreases odds of thoracolumbar pseudarthrosis by 0.35 times compared to an anterior or mixed approach, possibly due to relative sparing of the vertebral vasculature and surrounding tissue resulting in greater bone formation.

A history of revision surgery significantly increased the risk of pseudarthrosis development. When compared to fusion patients who had no history of revision, revision patients were 1.56 times more likely to experience non-union. Likewise, Dickson et al. found pseudarthrosis developed significantly more often in patients with a history of prior lumbar decompressions (13/52 patients) or prior history of pseudarthrosis. Indeed, prior pseudarthrosis in any region of the spine, prior decompression in the lumbar spine, or prior inflammatory/neurological disorder were all found to be significant risk factors.[23] Such findings are clinically relevant, as patients with a history of revision may require special considerations in care planning and management.

Pseud patients had more post-operative complications than N-Pseud patients (0.23 vs 0.18, $p = 0.026$), where complications included superficial and deep wound infections, pulmonary embolism, UTI, reintubation, pneumonia, among others. Moreover, pseudarthrosis patients were 1.42 times more likely to develop any complication compared to non-pseudarthrosis patients, with the odds of deep incisional surgical site infection (SSI) being 3.8 times more likely. The interplay between surgical site infection and bony growth has been documented in previous studies with contradictory findings.[24–26] Some studies suggest infection actually mediates bony growth through biological inflammatory markers, supported by observations that anti-inflammatory medications like NSAIDs taken in the post-operative period inhibit osteogenesis and rates of bony fusion.[26–28] Conversely, other

studies such as Wang et al. found that post-operative infection, including deep incisional SSI, was correlated with higher rates of pseudarthrosis in patients who underwent lumbar fusion.[29]

This study is limited by its reliance on a large national database (NSQIP) for data collection, where patient data is inherently limited to the database design. NSQIP does not provide radiographic imaging or a comprehensive list of all medical comorbidities, rendering data analysis vulnerable to various confounds. In addition, the specific type of fusion surgery could not be controlled for in the present study, potentially leading to unknown confounding factors. In general, the NSQIP database is a validated, multi-centered, prospectively-collected patient sample whose data effectively reflects a representative national sample.

5. Conclusion

The present study utilizes NSQIP data from 2005 to 2013 to assess the incidence and risk factors for pseudarthrosis among primary spine fusion patients. Alcoholism and surgical revision were major risk factors for pseudarthrosis in patients undergoing fusion. Pseudarthrosis patients were at increased risk for deep incisional SSI following surgery, and had more complications than non-pseudarthrosis cohorts. Future studies should include a prospective longitudinal study model to assess the development of pseudarthrosis in patients undergoing primary spinal fusion.

Disclosure of funding related to current work

Ethical review committee statement

Each institution obtained approval from their local Institutional Review Board to enroll patients in the prospective database and informed consent was obtained from each patient.

Conflicts of interest outside submitted work

Peter G. Passias: Consultant to Zimmer Biomet; Consultant to Medicrea; Consultant to Spinewave.

Frank J. Schwab: Royalties from: K2M, MSD; Stock Ownership: Nemaris; Speaking/Teaching: Zimmer Biomet, Nuvasive, K2M, MSD, Medicrea; Board of Directors: Nemaris; Grants: SRS.

Virginie Lafage: Stock Ownership: Nemaris; Speaking/teaching: Depuy, Nuvasive, K2M, Medtronic; Board of Directors: Nemaris.

Appendix

CODES
ICD-9 Codes:
733.82 (pseudarthrosis)
CPT Codes:
Anterior Approach: 22548 22551 22552 22554 22556 22558 22585 22808 22845 22846 22808 22810 22812 22845 22846 22847
Posterior Approach: 22590 22595 22600 22610 22612 22614 22630 22632 22633 22800 22802 22804 22842 22843 22844
Anterior Lumbar Interbody Fusion (ALIF): 22548 22551 22552 22554 22556 22558 22585 22808 22845 22846 22532 22533 22534
Posterior Lumbar Interbody Fusion (PLIF): 22590 22595 22600 22610 22612 22614 22630 22632 22633
Revision Surgery: 22849 22855 22850 22852
Exploratory fusion: 22830
Anterior decompression: 63075 63076 63077 63078 63081 63082 63085 63086 63087 63088 63090 63091 22220 22222 22224 22226
Posterior decompression: 63030 63035 63003 63016 63005 63017 63047 63046 63048 63042 63044
Laminotomy: 63030 63035 63003 63016 63005 63017 63047 63046 63048 63042 63044
Osteotomy: 22206 22207 22208 22210 22212 22214 22216 22220 22222 22224 22226

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