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DEFORMITY

The Effect of Tobacco Smoking on Adverse Events Following Adult Complex Deformity Surgery

Analysis of 270 Patients From the Prospective, Multicenter Scoli-RISK-1 Study

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Study Design. *Post-hoc* analysis of a prospective, multicenter cohort study.

Objective. To analyze the impact of smoking on rates of postoperative adverse events (AEs) in patients undergoing high-risk adult spine deformity surgery.

Summary of Background Data. Smoking is a known predictor of medical complications after adult deformity surgery, but the effect on complications, implant failure and other AEs has not been adequately described in prospective studies.

Methods. Twenty-six patients with a history of current smoking were identified out of the 272 patients enrolled in the SCOLI-RISK-1 study who underwent complex adult spinal deformity surgery at 15 centers, with 2-year follow-up. The outcomes and incidence of AEs in these patients were compared to the nonsmoking cohort (n = 244) using univariate analysis, with additional multivariate regression to adjust for the effect of patient demographics, complexity of surgery, and other confounders.

Results. The number of levels and complexity of surgery in both cohorts were comparable. In the univariate analysis, the rates of implant failure were almost double (odds ratio 2.28 [0.75–6.18]) in smoking group (n = 7; 26.9%)) that observed in the nonsmoking group (n = 34; 13.9%), but this was not statistically significant ($P = 0.088$). Surgery-related excessive bleeding (>4 L) was significantly higher in the smoking group (n = 5 *vs.* n = 9; 19.2% *vs.* 3.7%; OR 6.22[1.48 – 22.75]; $P = 0.006$). Wound infection rates and respiratory complications were similar in both groups. In the multivariate analysis, the smoking group demonstrated a higher incidence of any surgery-related AEs over 2 years (n = 13 *vs.* n = 95; 50.0% *vs.* 38.9%; OR 2.12 [0.88–5.09]) ($P = 0.094$).

Conclusion. In this secondary analysis of patients from the SCOLI-RISK-1 study, a history of smoking significantly increased the risk of excessive intraoperative bleeding and nonsignificantly increased the rate of implant failure or surgery-related AEs over 2 years. The authors therefore advocate a smoking cessation program in patients undergoing complex adult spine deformity surgery.

Key words: adult complex spine deformity, adverse events, bleeding, complications, fusion, implant failure, infection, multicenter, smoking, surgery.

Level of Evidence: 2

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The management of adult spinal deformity (ASD) has been revolutionized by the application of new surgical techniques combined with more precise

approaches to achieve the goals of surgical correction, including the concepts of sagittal/coronal alignment and spinopelvic parameters. The Scoli-RISK-1 study was the first prospective, multicenter international observational study of ASD surgery with neurological function as the primary outcome.[1] While many previously published retrospective and registry-based studies of ASD surgery failed to reach consensus in regard to outcomes and complications,[2–10] subanalyses of the Scoli-RISK-1 study cohorts have provided important conclusions regarding the risk factors for neurological decline and outcomes of lower extremity motor function after complex ASD surgery.[11–13]

Over the years, the impact of smoking on overall health and postoperative complications has been extensively studied.[14–21] Based on evidence primarily derived from retrospective single-institution or multicenter registry studies, controversy still exists in the literature regarding the impact of tobacco on the rates of adverse events (AEs) after spine surgery.[14,15,17,18,20,22–26] In ASD surgery in particular, two large retrospective studies have suggested no difference between 30-day readmission or 30-day implant failure rates in smokers and nonsmokers.[16,27] A recent prospectively collected, multicenter study by the International Spine Study Group on 346 patients showed a history of smoking had no effect on the rates of early (<6 wk postoperatively) or late complications, but did not stratify the effect of smoking on specific complications.[28]

Recent evidence suggests the outcomes measured from retrospective, or registry-based, studies may be inadequate or under-reported.[29] The current study therefore aims to assess the impact of a history of smoking on rates of complications after complex ASD surgery in prospectively collected patient data from the Scoli-RISK-1 study.

MATERIALS AND METHODS

Patients

This analysis was based on data collected from the Scoli-RISK-1 study, a multicenter international study on the neurological outcomes of complex adult deformity surgery. Two hundred seventy-two consecutive patients were enrolled from September 2011 to October 2012, and all patients provided informed consent before enrolment. Forty-four surgeons recruited patients across nine centers in North America, three in Europe, and three in Asia. Patients included were between 18 and 80 years of age with a diagnosis of complex ASD and an apex of the major deformity between C7 and L2. The respective ethical committees or institutional review boards at all participating sites granted study approval. Surgical approach, instrumentation, corrective manoeuvres, and use of intraoperative neurological monitoring (motor-evoked potentials [MEP], somatosensory-evoked potentials, and/or electromyography) were left to the discretion of the operating surgeon. All patients had a minimum follow-up of 2 years.

For this study, the procedure met the definition of complex ASD surgery when one or more of the following criteria were met: corrective surgeries for curvatures with a major Cobb angle of 80° or more in the coronal and/or sagittal plane; corrective osteotomies for congenital spinal deformity; revision of a previous spinal deformity surgery requiring corrective osteotomies; three-column osteotomy (*i.e.*, pedicle subtraction osteotomy [PSO], vertebral column resection); reconstruction for myelopathy due to spinal deformity; or deformity reconstruction with concomitant spinal cord decompression for ossification of the ligamentum flavum or ossification of the posterior longitudinal ligament. Major exclusion criteria included patients with a history of substance dependency, psychosocial disturbance, active malignancy, active bacterial infection, recent history of significant spinal trauma/malignancy, complete long-term paraplegia, pregnancy, prisoners, and institutionalized individuals.

Outcomes

A history of current tobacco smoking was recorded at the time of patient enrolment. The outcomes and incidence of AEs of patients in the smoking group were compared to the nonsmoking cohort using univariable analysis with regards to early or late AEs, rate of wound infection, rate of implant failure, rate of respiratory AEs, loss of correction and surgery-related excessive bleeding. Multivariable regression analysis was used to adjust for the effect of patient demographics, complexity of surgery, and other confounders. For the purposes of this study, ex-smokers were included in the nonsmoking group.

Statistical Analysis

Descriptive statistics were presented by mean and standard deviation for continuous variables and count and percentage for categorical variables. The association of smoking status (exposure) with AEs (outcomes), specifically wound infection, implant failure, respiratory complication, loss of correction, and surgery-related excessive bleeding, was evaluated by univariable logistic regression to derive odds ratios (OR) and corresponding 95% confidence intervals (CI). Multiple logistic regression was used to adjust for the effects of key confounders, namely age, gender, BMI, three-column osteotomy, number of levels involved, and existence of a previous spine surgery.

RESULTS

Twenty-six patients were active smokers with a median pack-year history of 15.0 (inter quartile range: 7.5–33.0), compared to 244 nonsmokers, and 2 nonrespondents. No significant differences were observed between groups with respect to age, gender, BMI, number of comorbidities, surgical approach, and complexity of surgery (Tables 1 and 2). In the univariable analysis (Table 3), the incidence of excessive bleeding (defined by >4 L) was significantly higher in the smoking group compared to the nonsmoking group (n = 5 *vs.* n = 9; 19.2% *vs.* 3.7%; OR 6.22 [95% CI 1.48–22.75]; $P = 0.006$). Wound infection rates were higher in the smoking group when compared to the nonsmoking

TABLE 1. Patient Demographics in Smokers and Nonsmokers

	Smoker		
Variable	**No N = 244**	**Yes N = 26**	***P* Value**
Age (years)			0.597
n	244	26	
Mean (sd)	57.1 (15.4)	55.4 (14.0)	
Median (Q1; Q3)	61.0 (50.0; 69.0)	57.5 (53.0; 64.0)	
Min; max	18.0; 81.0	18.0; 79.0	
Sex, n (%)	244	26	0.132
Male	77 (31.6)	12 (46.2)	
Female	167 (68.4)	14 (53.8)	
Race, n (%)	243	26	
White or Caucasian	193 (79.4)	21 (80.8)	
Black or African-American	2 (0.8)	0 (0.0)	
Native American	1 (0.4)	0 (0.0)	
East Asian	44 (18.1)	5 (19.2)	
Other	3 (1.2)	0 (0.0)	
Race, n (%)	244	26	0.842
White or Caucasian	193 (79.1)	21 (80.8)	
Other	51 (20.9)	5 (19.2)	
Previous spine surgeries, n (%)	244	26	0.940
No	92 (37.7)	10 (38.5)	
Yes	152 (62.3)	16 (61.5)	
Body mass index (kg/m^2)			0.769
n	235	24	
Mean (sd)	27.0 (6.6)	26.6 (6.6)	
Median (Q1; Q3)	25.8 (22.7; 30.9)	25.2 (21.7; 30.8)	
Min; max	15.8; 70.1	17.0; 41.7	
BMI, n (%)	235	24	
<18.5	7 (3.0)	2 (8.3)	
18.5 –<25.0	99 (42.1)	9 (37.5)	
25.0 to <30.0	66 (28.1)	5 (20.8)	
>=30.0	63 (26.8)	8 (33.3)	

group (n = 3 *vs.* n = 17; 11.5% *vs.* 7.0%; OR 1.74 [0.30–6.70]; $P = 0.422$). The rate of implant failure was almost double that observed in the nonsmoking group (n = 7 *vs.* n = 34; 26.9% *vs.* 13.9%; OR 2.28 [0.75–6.18]). But this was not statistically significant ($P = 0.088$). The rates of respiratory-related AE were equivalent between groups (n = 1 *vs.* n = 13; 3.8% *vs.* 5.3%; OR 0.71 [0.02–5.13], $P = 1.000$), as was any loss of correction over the follow-up period (n = 1 *vs.* n = 17; 3.8% *vs.* 7.0%; OR 0.53 [0.01–3.72]; $P = 1.000$).

TABLE 2. Surgical Approach and Complexity Between Smokers and Nonsmokers

	Smoker		
Variable	**No N = 244**	**Yes N = 26**	***P* Value**
Levels involved in surgery			0.14
n	244	26	
Mean (sd)	11.8 (4.1)	10.7 (3.1)	
Median (Q1; Q3)	11.5 (9.0; 15.0)	10.0 (8.0; 13.0)	
Min; max	3.0; 23.0	6.0; 17.0	
Approach, n (%)	244	26	0.135
Anterior	0 (0.0)	0 (0.0)	
Posterior	184 (75.4)	23 (88.5)	
Both	60 (24.6)	3 (11.5)	
Three-column osteotomy, n (%)	244	26	0.757
No	59 (24.2)	7 (26.9)	
Yes	185 (75.8)	19 (73.1)	

TABLE 3. Univariable Analysis Comparing Wound Infection, Implant Failure, Respiratory Complications, Loss of Correction and Excessive Bleeding Between Smokers and Nonsmokers

	Smoker					
	No N = 244		Yes N = 26			
Adverse Events	n	% (95% CI)	n	% (95% CI)	Unadjusted Odds Ratio (95% CI)	Unadjusted *P* Value
Wound infection (deep, superficial, graft site)	17	7.0 (4.1; 10.9)	3	11.5 (2.4; 30.2)	1.74 (0.30;6.70)	0.422
Implant failure (onset <791 d after surgery)	34	13.9 (9.8; 18.9)	7	26.9 (11.6; 47.8)	2.28 (0.75;6.18)	0.088
Any respiratory AE (pneumonia, Atelectasis; onset <791 d after surgery)	13	5.3 (2.9; 8.9)	1	3.8 (0.1; 19.6)	0.71 (0.02;5.13)	1.000
Any loss of correction (onset <791 d after surgery)	17	7.0 (4.1; 10.9)	1	3.8 (0.1; 19.6)	0.53 (0.01;3.72)	1.000
Surgery related: excessive bleeding	9	3.7 (1.7; 6.9)	5	19.2 (6.6; 39.4)	6.22 (1.48;22.75)	0.006

In the multivariable analysis, the groups were compared with regards to AEs occurring within 30 days of the indexed surgery, between 30 days and 6 months, and between 30 days and 2 years postoperatively (Table 4). In the interval-based analysis, both groups demonstrated equivalent rates of AE ($P = 0.988$; $P = 0.872$; $P = 0.884$ respectively). However, pooled analysis over the 2-year follow-up post-surgery revealed a higher but not statistically significant rate of AEs in the smoking group (n = 13 *vs.* n = 95; 50.0% *vs.* 38.9%; OR 2.12 [0.88–5.09]; $P = 0.094$).

DISCUSSION

The Scoli-RISK-1 study was a landmark investigation into neurological outcomes after complex ASD surgery. Further subanalyses from this study have allowed other important insights to be obtained from this prospective cohort including risk factors for neurological decline, outcomes of lower extremity motor function after surgery, and outcomes following unilateral *versus* bilateral neurological decline.[11–13] To our knowledge, this is the first study to analyze the impact of smoking on the AE rates after complex ASD

TABLE 4. Multivariable Analysis of AEs at Multiple Time Intervals and Pooled 2-yr Results in Smokers and Nonsmokers

	Smoker							
	No N = 244		Yes N = 26					
Adverse Events	n	%(95% CI)	n	%(95% CI†)	Unadjusted Odds Ratio (95% CI)	Unadjusted *P* Value	Adjusted Odds Ratio (95% CI)	Adjusted *P* Value
Early AE (onset <=30 d after index surgery)	135	55.3 (48.9; 61.7)	13	50.0 (29.9; 70.1)	0.81 (0.36;1.81)	0.604	1.01 (0.42; 2.43)	0.988
Delayed AE (onset >30 up to 183 d after index surgery)	80	32.8 (26.9; 39.1)	10	38.5 (20.2; 59.4)	1.28 (0.56;2.95)	0.560	1.08 (0.42; 2.78)	0.872
Delayed AE (onset >30 up to 791 d (*i.e.*, upper visit window of 2-yrs visit) after index surgery)	127	52.0 (45.6; 58.5)	14	53.8 (33.4; 73.4)	1.07 (0.48;2.42)	0.862	0.94 (0.38; 2.30)	0.884
Any surgery related AE (onset <791 d after surgery)	95	38.9 (32.8; 45.4)	13	50.0 (29.9; 70.1)	1.57 (0.70;3.53)	0.274	2.12 (0.88; 5.09)	0.094

surgery based on prospectively collected data from a multicenter observational cohort study. Our analysis provided several important findings pertinent to the management and care of these patients. First, a history of current smoking significantly increased the incidence of excessive perioperative bleeding (>4 L) when compared with nonsmokers in univariable analysis. Therefore, raising the awareness intraoperative hemostasis can potentially reduce the blood loss and requirements for massive transfusions. Second, the rate of implant failure was seemingly double in the smoking group compared to the nonsmoking group; however, our results were just shy of statistical significance. Finally, the rate of all AEs over 2 years after surgery was higher in the smoking group compared to the nonsmoking group in the multivariable analysis.

Several recent retrospective institutional and national registry studies have assessed the potential impact of smoking on complication rates for spine surgery.[14,15,17–20,23,25,26] Although the negative impact on overall health caused by smoking is universally agreed, investigations into the effect of smoking on the rates of complication from adult deformity surgery have not produced reliable conclusions.[16,24,27] A recent prospective assessment of the complication rates of 346 adults undergoing ASD surgery over 2-year follow-up suggested smokers did not have an increased risk of early or delayed overall complications, but this study did not present a direct comparison of smokers *versus* nonsmokers with respect to specific complications.[28] The current study again presents results from prospectively collected, multicenter cohorts, but is the first to stratify rates of specific complications with regards to smokers compared to nonsmokers. The smoking cohort demonstrated an implant failure rate of 26.9%; almost double that of the nonsmoking group (13.9%). Although the results did not reach significance ($P = 0.088$), the authors feel this remains a pertinent finding. The same is true when comparing the 2-year rate of AEs for both groups; smokers had a higher rate of AEs (50.0%) compared to nonsmokers (38.9%; $P = 0.094$). The fact that both of these results do not achieve statistical significance could be a reflection of the limited sample size of the smoking group, and the fact that the study was not powered to represent differences between smokers and nonsmokers specifically. However, in our opinion, these results still carry important clinical relevance when managing these patients postoperatively.

The current study suggests smokers have significantly greater perioperative blood loss compared to the nonsmoking cohort ($P = 0.006$). Smoking is known to cause alterations in platelet membranes that lead to impairment in the clotting cascade, and this finding is consistent with previous studies on the effect of blood loss in smokers undergoing spine surgery.[20,30–32] Complex ASD surgery is often associated with blood loss in excess of 4 L, and given that transfusions in spine surgery are related to extended length of stay, increased risk of AEs, and nonhome discharge destination; this result also has important economical implications.[33,34]

The main limitation of the current study is that the results reflect a secondary analysis of an investigation that was not originally constructed to compare the complications and outcomes of smokers and nonsmokers. As such, the number of smokers is relatively low (n = 26, 9.6%) compared to the nonsmoking group (n = 244, 90.4%), which produces obvious effects on the power calculation within the univariate analysis. The implant failure rate in smokers (26.9%) compared to nonsmokers (13.9%) is borderline significant, but only has an observed power of 30%. Hypothetical power calculations (based on a smoker to nonsmokers ratio of 1:3 and a projected event rate of 30% and 10% of implant failure in each group) demonstrate that to achieve significance (alpha = 0.05) at an 80% power the sample size of the smoking cohort would need to be n = 45, with nonsmokers n = 135. The authors argue that despite these inherent discrepancies in sample size, the data is still able to demonstrate statistically significant differences with regards to perioperative blood loss, and important trends toward an increased rate of implant failure rate and AEs over 2 years.

We note that ex-smokers were included in the nonsmoking group, and since data on the time since cessation and total pack years was not collected, this could also have a potential confounding effect. In addition, the smoking behavior of the enrolled patients was not collected during the 2-year follow-up after surgery, and this may have produced additional bias. The event rate for each variable used in the multivariate regression model is low, and this may result in a slightly "over-fitted" model concerning the all-forms AEs. It is clear that further, prospective investigations with more balanced cohort sizes would be better powered to truly represent clinically relevant differences between smokers, nonsmokers, and ex-smokers. However, at present, the current study remains the only multicenter study into complex ASD surgery based on prospectively collected observational data, and therefore the conclusions of this secondary analysis provide important insights into the risks of smoking and further cement the authors' strong recommendations that smoking cessation should be persistently and actively encouraged in all patients undergoing elective spine surgery.

➢ Key Points

- ❑ Smoking significantly increases the risk of excessive perioperative bleeding in complex adult deformity surgery.
- ❑ The rate of implant failure in smokers was almost double that seen in the nonsmoking cohort, but this did not reach statistical significance.
- ❑ The rate of surgery-related adverse events up to 2 years postsurgery was higher but nonsignificantly increased in the smoking group compared to the nonsmokers.
- ❑ Smoking cessation should be actively encouraged in all elective patients undergoing complex adult spinal deformity surgery.

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