Risk factors for reintubation after anterior cervical discectomy and fusion surgery: evaluation of three observational data sets

Facteurs de risque de réintubation après une chirurgie de discectomie cervicale antérieure avec fusion : évaluation de trois bases de données observationnelles

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Abstract

Purpose Postoperative loss of airway requiring reintubation is a rare but potentially catastrophic complication following anterior cervical discectomy and fusion (ACDF). We sought to identify risk factors associated with reintubation within one day following ACDF. Attention was focused on patient demographics, comorbidities, and factors potentially linked to soft tissue swelling and hematoma formation that could compromise the upper airway.

Methods We performed a retrospective cohort study of patients who underwent ACDF procedures at a high-volume institution from 2005 to 2014 ($n = 3,041$), participating hospitals in the National Surgical Quality Improvement Program (NSQIP) ($n = 47,425$), and Premier Healthcare ($n = 233,633$) databases from 2006 to 2016. Separate multivariable logistic regression models using the NSQIP and Premier samples were used to identify risk factors for reintubation within one day of ACDF. Odds ratios (OR) and 95% confidence intervals (CI) are reported.

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Results Incidence of reintubation within one day of ACDF was 0.19% in the institutional database and 0.21% in NSQIP and Premier databases. Risk factors for reintubation included older age, male sex, high comorbidity burden, procedures performed at large hospitals, non-elective procedures, Medicaid insurance, and use of heparin or more than one anticoagulant. Intravenous or oral steroid use (OR, 0.45; 95% CI, 0.36 to 0.56; $P < 0.001$) and delayed extubation (OR, 0.28 95% CI, 0.16 to 0.49; $P < 0.001$) were found to decrease risk of reintubation.

Conclusions Across three complementary data sets, incidence of reintubation within one day of ACDF was approximately 0.20%. Increased risk of reintubation associated with anticoagulant administration suggests upper airway hematoma as an underlying etiology. Steroid administration and delayed extubation may be useful in patients considered to be at higher risk for reintubation.

Résumé

Objectif La perte postopératoire du contrôle des voies aériennes nécessitant une réintubation est une complication rare mais potentiellement catastrophique après une discectomie cervicale antérieure avec fusion (DCAF). Nous avons cherché à identifier les facteurs de risque associés à la réintubation dans la journée suivant une DCAF. Nous avons examiné les données démographiques, les comorbidités et les facteurs liés aux patients et potentiellement associés à l'œdème des tissus mous et à la formation d'hématome qui pourraient mettre en péril les voies aériennes supérieures.

Méthode Nous avons réalisé une étude de cohorte rétrospective en nous fondant sur trois bases de données : les patients ayant subi des interventions de DCAF dans une institution à volume élevé entre 2005 et 2014 ($n = 3041$), ceux ayant été opérés dans les hôpitaux participant au Programme national d'amélioration de la qualité chirurgicale américain (National Surgical Quality Improvement Program (NSQIP)) ($n = 47\,425$), et ceux inscrits dans la base de données de Premier Healthcare ($n = 233\,633$) entre 2006 et 2016. Des modèles de régression logistique multivariée séparés utilisant les échantillons du NSQIP et de Premier ont été utilisés pour identifier les facteurs de risque de réintubation dans la journée suivant une DCAF. Les rapports de cotes (RC) et les intervalles de confiance (IC) à 95 % sont rapportés.

Résultats L'incidence de réintubation dans la journée suivant la DCAF était de 0,19 % dans la base de données institutionnelle et de 0,21 % dans les bases de données du NSQIP et de Premier. Les facteurs de risque de réintubation comprenaient un âge plus avancé, le sexe masculin, un fardeau de comorbidité élevé, les interventions réalisées dans des hôpitaux de grand volume, les interventions urgentes, l'assurance Medicaid, et l'utilisation d'héparine ou de plus d'un anticoagulant. Nous avons observé que l'utilisation de stéroïdes intraveineux ou oraux (RC, 0,45; IC 95 %, 0,36 à 0,56; $P < 0,001$) et une extubation retardée (RC, 0,28; IC 95 %, 0,16 à 0,49; $P < 0,001$) réduisaient le risque de réintubation.

Conclusion Selon trois bases de données complémentaires, l'incidence de réintubation dans la journée suivant une DCAF était d'environ 0,20 %. Le risque accru de réintubation associé à l'administration d'anticoagulant suggère une étiologie sous-jacente d'hématome au niveau des voies aériennes supérieures. L'administration de stéroïdes et l'extubation retardée pourraient être utiles chez les patients considérés comme courant un risque accru de réintubation.

Approximately 132,000 anterior cervical discectomy and fusion (ACDF) procedures are performed annually in the United States.¹ Although rare,² postoperative complications such as prevertebral soft tissue edema or hematoma formation have been reported.^{3–6} These complications can in turn lead to airway compromise requiring emergent reintubation.⁷ The latter may be associated with further complications requiring extended hospital stay, reoperation, and even death.⁸ Published estimates of the incidence of emergent reintubation following ACDF surgery range from 0.10% to 1.95%.^{4,6,9,10} Despite the serious nature of this complication, studies evaluating risk factors are rare or inconclusive.

Further emphasizing the importance of this evidence gap is the overall increasing annual volume of ACDF procedures¹ and the increasingly comorbid population undergoing these surgeries.¹¹ Moreover, with emerging reports encouraging outpatient ACDF,¹² it is important to identify subgroups at risk for perioperative emergent reintubation to mitigate catastrophic complications after discharge.

Because the incidence of reintubation is low in ACDF patients, much of the existing literature is limited to case reviews^{10,13} or cohort studies with questionable assumptions, including suboptimal distinction between

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emergency reintubation and (intentionally) prolonged intubation,¹⁴ non-homogenous cohorts,⁸ and broad outcome definitions, focusing on risk of reintubation at any point postoperatively.⁹ To help address these shortcomings, we utilized two comprehensive national data sets and a single hospital database that may provide additional insights into this matter. We analysed data from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) and the Premier Healthcare databases. The NSQIP database¹⁵ is a nationally validated, risk-adjusted database tracking surgical outcomes commonly used in spine research^{16–18} while the Premier Healthcare database is a national claims database containing comprehensive hospitalization information including both patient- and healthcare-related factors.¹⁹ In addition to this, Hospital for Special Surgery (HSS) is a high-volume surgical centre, making this institution's data uniquely suitable to retrospectively evaluate factors associated with reintubation. Therefore, using information from three distinct and complementary data sources, we sought to identify incidence and risk factors for reintubation, as a consequence of soft tissue swelling or bleeding, within one day following ACDF surgery. The one-day timeframe was chosen to minimize confounding by extraneous factors (e.g., respiratory infection, cardiac complications).¹⁰ Moreover, the majority of patients experiencing airway compromise do so within the first 24 hr after surgery. The use of multiple data sets for this study question is unique and allows for confirmation and the analysis of a wide range of potential risk factors beyond what is currently available in the literature.

We hypothesized that 1) the incidence of reintubation after ACDF would be low and consistent amongst data sets and 2) that factors associated with both increased and decreased risk for this complication could be identified.

Methods

Approval for this historical cohort study was obtained by the Institutional Review Boards of HSS (New York, NY, USA; #2012-050, #2016-436, and #2017-0716) and the Icahn School of Medicine (New York, NY, USA; #14-00647). Data on patients who underwent ACDF surgery were extracted (and analyzed) separately from three complementary data sources: institutional data, the NSQIP database, and the Premier Healthcare database (Premier Healthcare Solutions, Inc., Charlotte, NC, USA).¹⁹ General definitions of study sample (ACDF surgery), outcome (emergency reintubation), and database-specific covariates are described separately for each data set.

Risk factors of interest included those potentially associated with hematoma (perioperative coagulation profile: low platelets, international normalized ratio [INR], prothrombin time [PT], partial thromboplastin time [PTT], anticoagulant use), and swelling (tissue trauma associated with surgery, prolonged operation, number of vertebrae fused, and steroid use that may decrease swelling) as well as patient and hospital characteristics. A full overview of all covariates considered for each data set can be found in Appendix A; exact definitions can be found in Appendix B. In general, patients who were under 18 yr of age or with missing information on sex were excluded across all three data sets.

Institutional data

HSS is a high-volume orthopedic specialty hospital. Institutional data are made available for research by extraction from various sources (e.g., billing, pharmacy, and laboratory) and subsequent linkage. Patients who underwent ACDF surgery between 2005 and 2014 were identified by *International Classification of Diseases, Ninth Revision* (ICD-9) primary procedure code 81.02. Patients who were reintubated within one day after ACDF surgery were identified by either a current procedural terminology (CPT) of 31500 or ICD-9 procedure codes (96.04, 96.05) indicating postoperative intubation. Further chart review was conducted to determine timing of reintubation.

National Surgical Quality Improvement Program

The NSQIP is a risk-adjusted, outcomes-based program designed to evaluate and improve the quality of surgical care.²⁰ The NSQIP database utilizes a systematic sampling system to select surgical cases from each participating hospital and obtain an unbiased sample of the underlying risk-set. The program collects patient data on 273 variables with the most recent release containing information from 603 participating hospitals.²¹ Anterior cervical discectomy and fusion cases between 2006 and 2016 were identified based on primary CPT codes (22551, 22552, 22554, 22845, 22846, 63075). Additional exclusion criteria were emergency cases ($n = 644$) and unknown anesthesia type ($n = 1$).

Reintubation data are routinely collected in this data set; for this study this was defined as unplanned reintubation on postoperative day zero or one. Preoperative laboratory values for platelet count, PT, PTT, and INR were dichotomized based on clinically relevant cutoffs^{22–24} as a proxy for coagulation disorders. Obesity was defined as a body mass index $> 30 \text{ kg}\cdot\text{m}^{-2}$, and was calculated using the patient's height and weight.

Table 1 Summary of HSS ACDF patient characteristics, stratified by reintubation status on postoperative day 0 or 1

	Reintubation (<i>n</i> = 6) <i>n</i> (%)	No reintubation (<i>n</i> = 3,050) <i>n</i> (%)	Standardized difference
Patient demographics			
Age (median [IQR])	65.5 [53.75-69.75]	51 [44-61]	0.79
Sex			0.13
Male	3 (50.0)	1,721 (56.4)	
Procedure related			
Year of procedure			1.04
2005	-	207 (6.8)	
2006	-	228 (7.5)	
2007	-	225 (7.4)	
2008	1 (16.7)	247 (8.1)	
2009	1 (16.7)	266 (8.7)	
2010	1 (16.7)	325 (10.7)	
2011	1 (16.7)	347 (11.4)	
2012	1 (16.7)	372 (12.2)	
2013	-	377 (12.4)	
2014	1 (16.7)	456 (15.0)	
# of vertebrae fused			0.61
2-3	3 (50.0)	2,333 (76.5)	
4+	3 (50.0)	652 (21.4)	
Unknown	-	65 (2.1)	
Comorbidity related			
ASA class			0.40
1-2	6 (100.0)	2,821 (92.5)	
3+	-	221 (7.2)	
Unknown	-	8 (0.3)	
Sleep apnea			0.43
Present	-	258 (8.5)	
Absent	6 (100.0)	2,798 (91.5)	
Preoperative lab values [†]			
Platelet count			0.58
<150 × 10 ⁹ ·L ⁻¹	1 (16.7)	51 (1.7)	
>150 × 10 ⁹ ·L ⁻¹	4 (66.7)	2,173 (71.2)	
Unknown	1 (16.7)	826 (27.1)	
INR			0.28
<1.1	5 (83.3)	2,175 (71.3)	
>1.1	-	84 (2.8)	
Unknown	1 (16.7)	791 (24.6)	
PT			0.14
<13.5 sec	5 (83.3)	1,883 (61.7)	
>13.5 sec	-	18 (0.6)	
Unknown	1 (16.7)	1,149 (37.7)	
PTT			0.10
<35 sec	2 (33.3)	558 (18.3)	
>35 sec	-	3 (0.1)	
Unknown	4 (66.7)	2,489 (81.6)	
Intraoperative medications			
Ketorolac			0.22
Given	-	64 (2.1)	

Table 1 continued

	Reintubation (<i>n</i> = 6) <i>n</i> (%)	No reintubation (<i>n</i> = 3,050) <i>n</i> (%)	Standardized difference
Not given	5 (88.3)	2,595 (85.1)	0.62
Unknown	1 (16.7)	391 (12.8)	
Heparin			
Given	1 (16.7)	41 (1.3)	
Not given	4 (66.7)	2,618 (85.8)	
Unknown	1 (16.7)	391 (12.8)	

† Normal lab value ranges: platelet count ($150\text{--}450 \times 10^9\text{--L}^{-1}$) INR (> 1.1); PT (11–13.5 sec); PTT (25–35 sec). ACDF = anterior cervical discectomy and fusion; ASA = American Society of Anesthesiologists; HSS = Hospital for Special Surgery; INR = international normalized ratio; IQR = interquartile range; PT = prothrombin time; PTT = partial thromboplastin time

Premier

The Premier Healthcare database is a national claims-based database, representing approximately 25% of the nation's hospitalizations.¹⁹ Hospitals elect to participate in the database for benchmarking purposes. Participating hospitals are predominantly located in the South, while the rest are distributed equally across the country. Patients who underwent an inpatient ACDF procedure between 2006 and 2016, indicated by ICD-9 procedure code 81.02, were included. We excluded cases from hospitals that performed fewer than 30 procedures (to ensure sufficient sample size per cluster²⁵; $n = 946$), cases from three hospitals with coding errors in their billing files ($n = 1,934$), cases with unknown discharge status ($n = 1,976$), and those classified as emergencies ($n = 18,388$). Reintubation was identified based on billing descriptions for emergency intubation on the day of surgery or the day after.

Information regarding use of potential prophylactic interventions^{26–28} was uniquely available in the Premier database. Steroid use was defined based on billing codes for intravenous or oral administration of dexamethasone, hydrocortisone, or prednisone within one day of surgery. Delayed extubation was defined as cases billed for ICU and mechanical ventilation on the day of surgery where it is assumed that extubation did not take place immediately after surgery.

Statistical analysis

Analyses were performed separately for each data set. We first performed descriptive analyses of all study variables stratified by reintubation status. Categorical variables were reported as frequencies (%) and continuous variables as median [interquartile range] to account for non-normal distribution. In all descriptive analyses, standardized

differences were reported in lieu of *P* values, since group differences can easily achieve statistical significance with large sample sizes. Standardized differences, also referred to as effect sizes, reflect the difference between categories in units of standard deviation. A standardized difference of at least 0.1 (10%) generally indicates a meaningful difference in covariate distribution between groups.^{29,30}

Multivariable models estimated associations between study variables and emergency reintubation. Separate multivariable models were applied for the NSQIP and Premier databases: risk factors' odds ratios (OR) and 95% confidence intervals (CI) for reintubation within one day following ACDF are reported. Missing data were classified as “unknown” to retain all observations in the multivariable model. Because the number of patients experiencing the outcome was insufficient, it was not possible to run a multivariable regression model with the institutional data set. For the NSQIP sample, variables with a *P* value < 0.15 in univariable analyses³¹ were retained in the final multivariable logistic regression model while also applying the “minimum five outcome events per variable” rule as previously described.³² For the sample using Premier data, covariates were selected for inclusion in the multivariable model based on clinical significance and/or imbalance between reintubation groups. Given the large sample available in the Premier data, in practice this resulted in all available covariates included in the final model. A random intercept was used to account for within-hospital correlation, since patients treated at the same hospital are more likely to experience similar care. Procedure type was included as a covariate in both multivariable models, categorized as elective vs non-elective surgery, which consists of cases that were urgent, but not emergent. Additionally, the Deyo index was reported categorically in descriptive analyses, but treated as continuous in the multivariable model.

Table 2 Summary of NSQIP ACDF patient characteristics, stratified by reintubation status on postoperative day 0 or 1

	Reintubation (<i>n</i> = 100) <i>n</i> (%)	No reintubation (<i>n</i> = 47,325) <i>n</i> (%)	Standardized difference
Patient demographics			
Age (median [IQR])	60 [52-68]	53 [46-62]	0.60
Sex			0.27
Male	63 (63.0)	23,461 (49.6)	
Race			0.19
White	77 (77.0)	37,960 (80.2)	
Black	16 (16.0)	4,757 (10.1)	
Other	7 (7.0)	4,608 (9.7)	
Ethnicity			0.19
Hispanic	5 (5.0)	2,273 (4.8)	
Non-Hispanic/other	95 (95.0)	45,052 (95.2)	
Procedure related			
Year of procedure			0.39
2006	-	37 (0.1)	
2007	2 (2.0)	238 (0.5)	
2008	1 (1.0)	661 (1.4)	
2009	-	1,068 (2.3)	
2010	5 (5.0)	1,622 (3.4)	
2011	8 (8.0)	3,511 (7.4)	
2012	15 (15.0)	4,610 (9.7)	
2013	18 (18.0)	6,817 (14.4)	
2014	10 (10.0)	7,794 (16.5)	
2015	16 (16.0)	9,798 (20.7)	
2016	25 (25.0)	11,169 (23.6)	
Procedure type			0.38
Non-elective	17 (17.0)	2,453 (5.2)	
Elective	83 (83.0)	44,872 (94.8)	
Surgical diagnosis			0.30
Degenerative disease	64 (64.0)	36,333 (76.8)	
Trauma	3 (3.0)	394 (0.8)	
Other	33 (33.0)	10,598 (22.4)	
No. of vertebrae fused			0.24
2-3	58 (58.0)	27,461 (58.0)	
4+	15 (15.0)	3,617 (7.6)	
Unknown	27 (27.0)	16,247 (34.3)	
Operative duration (median [IQR])	121.5 [88-186]	112 [81-156]	0.19
Comorbidity related			
ASA class			0.66
1-2	28 (28.0)	27,809 (58.8)	
3+	72 (72.0)	19,454 (41.1)	
Unknown	-	62 (0.1)	
Functional status			0.27
Dependent	7 (7.0)	874 (1.8)	
Independent	88 (88.0)	46,184 (97.6)	
Unknown	5 (5.0)	267 (0.6)	
Diabetes	27 (27.0)	7,256 (15.3)	0.29
History of severe COPD	10 (10.0)	1,976 (4.2)	0.23
Current smoker	35 (35.0)	13,649 (28.8)	0.13

Table 2 continued

	Reintubation (<i>n</i> = 100) <i>n</i> (%)	No reintubation (<i>n</i> = 47,325) <i>n</i> (%)	Standardized difference
Obesity			0.05
BMI <30	55 (55.0)	25,689 (54.3)	
BMI ≥30	44 (44.0)	21,366 (45.1)	
Unknown	1 (1.0)	270 (0.6)	
Preoperative lab values [†]			
Platelet			0.32
< 150 × 10 ⁹ L ⁻¹	12 (12.0)	1,864 (3.9)	
> 150 × 10 ⁹ L ⁻¹	79 (79.0)	40,922 (86.5)	
Unknown	9 (9.0)	4,539 (9.6)	
PT			0.11
<13.5 sec	8 (8.0)	3,596 (7.6)	
>13.5 sec	1 (1.0)	313 (6.6)	
Unknown	91 (91.0)	43,416 (91.7)	
PTT			0.11
<35 sec	53 (53.0)	25,520 (53.9)	
>35 sec	5 (5.0)	1,577 (3.3)	
Unknown	42 (42.0)	20,228 (42.7)	
INR			0.25
<1.1	50 (50.0)	25,474 (53.8)	
>1.1	17 (17.0)	4,576 (9.7)	
Unknown	33 (33.0)	17,275 (36.5)	

[†] Normal lab value ranges: Platelet count (150–450 × 10⁹L⁻¹); INR (>1.1); PT (11–13.5 sec); PTT (25–35 sec).

ACDF = anterior cervical discectomy and fusion; ASA = American Society of Anesthesiologists; BMI = body mass index; COPD = chronic obstructive pulmonary disease; INR = international normalized ratio; IQR = interquartile range; NSQIP = National Surgical Quality Improvement Program; PT = prothrombin time; PTT = partial thromboplastin time

Model c-statistics are reported and are indicative of the model's predictive accuracy (i.e., its ability to distinguish patients by reintubation status [discrimination]). A c-statistic of 0.7 or greater typically indicates sufficient model discrimination. Given the inclusion of multiple variables and data sets, multivariable results with a $P < 0.005$ were considered statistically significant to account for the increased potential for type I (false positive) errors. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA), and modelling was done using PROC GLIMMIX, which calculates robust standard errors.

Results

There were 3,056 patients who underwent inpatient ACDF surgery at HSS from 2005 to 2014. Six (0.19%) patients were reintubated within 24 hr of surgery (Table 1). Of the 47,525 patients in the NSQIP database who underwent an ACDF procedure between 2006 and 2016, 100 (0.21%) experienced an unplanned reintubation within one day of

surgery. Incidence of reintubation did not follow any clear trend with some fluctuation annually (Table 2). There were 234,115 inpatient ACDF procedures identified in the Premier database. Of these, 482 (0.21%) were associated with an unplanned reintubation within one day of surgery. Incidence of reintubation increased over time, peaking at 0.42% in 2012 before declining again (Table 3).

Results of the multivariable regression models are presented in Table 4 for the NSQIP and Premier data sets. After adjusting for all other covariates, the NSQIP data identified older age (OR, 1.03; 95% CI, 1.02 to 1.05; $P < 0.001$) and American Society of Anesthesiologists (ASA) class of III or higher (OR, 2.18; 95% CI, 1.35 to 3.35; $P = 0.002$) as risk factors for emergency reintubation following ACDF surgery.

In the Premier database, male sex (OR, 1.79; 95% CI, 1.47 to 2.19; $P < 0.001$), Medicaid insurance (OR, 1.63; 95% CI, 1.2 to 2.21; $P = 0.002$), procedures performed at large hospitals (OR, 2.78; 95% CI, 1.37 to 5.64; $P = 0.005$), procedures performed in 2012 (OR, 2.81; 95% CI, 1.67 to 4.75; $P < 0.001$), non-elective (urgent) surgeries (OR, 6.02;

Table 3 Summary of Premier ACDF patient characteristics, stratified by reintubation status on postoperative day 0 or 1

	Reintubation (<i>n</i> = 482) <i>n</i> (%)	No reintubation (<i>n</i> = 233,633) <i>n</i> (%)	Standardized difference
Patient demographics			
Age (median [IQR])	56 [45-65]	54 [46-63]	0.04
Sex			0.37
Male	319 (66.2)	112,364 (48.1)	
Race/ethnicity			0.21
White	352 (73.0)	180,959 (77.5)	
Black	77 (16.0)	21,573 (9.2)	
Other	53 (11.0)	31,101 (13.3)	
Healthcare related			
Insurance type			0.36
Commercial	192 (39.8)	114,241 (48.9)	
Medicaid	71 (14.7)	16,153 (6.9)	
Medicare	177 (36.7)	71,342 (30.5)	
Uninsured	12 (2.5)	3,743 (1.6)	
Unknown	30 (6.2)	28,154 (12.1)	
Hospital location			0.09
Rural	25 (5.2)	17,036 (7.3)	
Urban	457 (94.8)	216,597 (92.7)	
Hospital size			0.51
Small (<300 beds)	82 (17.0)	59,570 (25.5)	
Medium (300-499 beds)	99 (20.5)	85,699 (36.7)	
Large (≥500 beds)	301 (62.4)	88,364 (37.8)	
Hospital teaching status			0.24
Non-teaching	202 (41.9)	125,739 (53.8)	
Teaching	280 (58.1)	107,894 (46.2)	
No. of Annual procedures per hospital (Median [IQR])	183 [93-310]	139 [84-222]	0.18
Procedure related			
Year of procedure			0.42
2006	21 (4.4)	17,683 (7.6)	
2007	18 (3.7)	17,855 (7.6)	
2008	27 (5.6)	17,313 (7.4)	
2009	25 (5.2)	19,904 (8.5)	
2010	35 (7.3)	21,315 (9.1)	
2011	55 (11.4)	22,447 (9.6)	
2012	100 (20.7)	23,896 (10.2)	
2013	72 (14.9)	24,026 (10.3)	
2014	44 (9.1)	23,721 (10.2)	
2015	42 (8.7)	24,329 (10.4)	
2016	43 (8.9)	21,144 (9.1)	
Procedure type			0.77
Non-elective	175 (36.3)	15,994 (6.8)	
Elective	307 (63.7)	217,639 (93.2)	
Surgeon specialty			0.32
Neurosurgeon	331 (68.7)	126,312 (54.1)	
Orthopedic surgeon	109 (22.6)	69,231 (29.6)	
Unknown	42 (8.7)	38,090 (16.3)	
Surgical diagnosis			0.50
Degenerative disease	310 (64.3)	199,394 (85.3)	

Table 3 continued

	Reintubation (<i>n</i> = 482) <i>n</i> (%)	No reintubation (<i>n</i> = 233,633) <i>n</i> (%)	Standardized difference
Trauma	5 (1.0)	216 (0.1)	
Other	167 (34.6)	34,023 (14.6)	
No. of vertebrae fused			0.21
2-3	365 (75.7)	196,980 (84.3)	
4+	90 (18.7)	26,947 (11.5)	
Unknown	27 (5.6)	9,706 (4.2)	
Drain use	88 (18.3)	51,270 (21.9)	0.09
Delayed extubation	16 (3.3)	2,276 (0.9)	0.16
Steroid use (3)	155 (32.2)	140,472 (60.1)	0.59
Comorbidity related			
Deyo index			0.71
0	173 (35.9)	149,302 (63.9)	
1	131 (27.2)	57,785 (24.7)	
2	77 (16.0)	17,100 (7.3)	
2+	101 (21.0)	9,446 (4.0)	
Obesity	89 (18.5)	27,472 (11.8)	0.19
Sleep apnea	58 (12.0)	20,543 (8.8)	0.11
Smoking	169 (35.1)	78,321 (33.5)	0.03
Anticoagulant use			0.46
Acetylsalicylic acid	18 (3.7)	7,213 (3.1)	
Other anti-platelet	2 (0.4)	524 (0.2)	
Heparin	95 (19.7)	17,931 (7.7)	
Warfarin	-	235 (0.1)	
Other anticoagulant	1 (0.2)	113 (0.0)	
>1 of above	21 (4.4)	1,606 (0.7)	
None	345 (71.6)	206,011 (88.2)	

ACDF = anterior cervical discectomy and fusion; IQR = interquartile range

95% CI, 4.68 to 7.75; $P < 0.001$), high comorbidity burden (OR, 1.32; 95% CI, 1.26 to 1.39; $P < 0.001$; per unit increase in Deyo index), and use of heparin (OR, 3.24; 95% CI, 2.46 to 4.25; $P < 0.001$) or multiple anticoagulants (OR, 5.34; 95% CI, 3.22 to 8.85; $P < 0.001$) were identified as risk factors for reintubation. Steroid use (OR, 0.45; 95%

CI, 0.36 to 0.56; $P < 0.001$) and delayed extubation (OR, 0.28; 95% CI, 0.16 to 0.49; $P < 0.001$) were associated with decreased odds of reintubation following ACDF. Model c-statistics were 0.74 and 0.94 for those using the NSQIP and Premier data sets, respectively.

Table 4 Results from multivariable logistic regression models predicting postoperative reintubation within one day of ACDF for NSQIP and Premier samples

Variable	NSQIP (<i>n</i> = 47,525)		Premier (<i>n</i> = 234,115)	
	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value
Age (yr)	1.03 (1.02 to 1.05)	<0.001	0.99 (0.99 to 1.00)	0.17
Sex (<i>reference</i> : female)	1.49 (0.99 to 2.25)	0.06	1.79 (1.47 to 2.19)	<0.001
Race (<i>reference</i> : white)				
Black	1.45 (0.83 to 2.51)	0.19	1.28 (0.97 to 1.68)	0.08
Other	0.75 (0.34 to 1.63)	0.46	1.14 (0.82 to 1.57)	0.48
Insurance type (<i>reference</i> : commercial)				
Medicaid	-	-	1.63 (1.20 to 2.21)	0.002
Medicare	-	-	1.21 (0.94 to 1.56)	0.15
Uninsured	-	-	0.58 (0.31 to 1.08)	0.09
Unknown	-	-	0.74 (0.50 to 1.10)	0.14
Hospital location (<i>reference</i> : urban)	-	-	1.31 (0.55 to 3.11)	0.54
Hospital size (<i>reference</i> : small)				
Large	-	-	2.78 (1.37 to 5.64)	0.005
Medium	-	-	1.05 (0.57 to 1.93)	0.89
Hospital teaching status (<i>reference</i> : teaching)	-	-	1.17 (0.70 to 1.97)	0.55
Provider volume			1.00 (1.00 to 1.00)	0.72
Year (<i>reference</i> : 2006)				
2007	-	-	0.89 (0.47 to 1.69)	0.73
2008	-	-	1.31 (0.74 to 2.35)	0.36
2009	-	-	0.75 (0.41 to 1.38)	0.36
2010	-	-	1.13 (0.63 to 2.01)	0.69
2011	-	-	1.42 (0.82 to 2.48)	0.21
2012	-	-	2.81 (1.67 to 4.75)	<0.001
2013	-	-	1.84 (1.07 to 3.16)	0.03
2014	-	-	1.02 (0.57 to 1.82)	0.95
2015	-	-	0.92 (0.51 to 1.65)	0.78
2016	-	-	1.03 (0.56 to 1.91)	0.92
Procedure type (<i>reference</i> : elective)	2.17 (1.21 to 3.87)	0.01	6.02 (4.68 to 7.75)	<0.001
Surgeon specialty (<i>reference</i> : neurosurgeon)				
Orthopedic surgeon	-	-	0.92 (0.71 to 1.18)	0.50
Unknown	-	-	0.48 (0.31 to 0.72)	0.001
Diagnosis (<i>reference</i> : degenerative disc disorder)				
Trauma	1.80 (0.52 to 6.20)	0.35	3.34 (1.19 to 9.36)	0.02
Other	1.48 (0.97 to 2.27)	0.07	1.96 (1.58 to 2.43)	<0.001
# vertebrae fused (<i>reference</i> : 2-3)				
4+	1.58 (0.87 to 2.86)	0.13	1.42 (1.10 to 1.83)	0.01
Unknown	0.76 (0.48 to 1.21)	0.25	1.60 (0.99 to 2.58)	0.06
Drains used	-	-	0.98 (0.74 to 1.29)	0.87
Delayed extubation	-	-	0.28 (0.16 to 0.49)	<0.001
Steroid use	-	-	0.45 (0.36 to 0.56)	<0.001
Operative duration	1.00 (1.00 to 1.00)	0.85	-	-
Deyo index	-	-	1.32 (1.26 to 1.39)	<0.001
Diabetes*	1.18 (0.74 to 1.87)	0.4	-	-
COPD*	147 (0.75 to 2.87)	0.262	-	-
Obesity	-	-	1.34 (1.03 to 1.73)	0.03
Sleep apnea	-	-	1.18 (0.88 to 1.60)	0.28

Table 4 continued

Variable	NSQIP (<i>n</i> = 47,525)		Premier (<i>n</i> = 234,115)	
	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value
Current smoker	-	-	1.03 (0.84 to 1.26)	0.7
Functional status (<i>reference</i> : independent)				
Dependent	1.75 (0.78 to 3.93)	0.17	-	-
Unknown	7.66 (3.04 to 19.3)	<0.001	-	-
ASA class (<i>reference</i> : 1-2)				
3+	2.18 (1.35 to 3.53)	0.01	-	-
Unknown	-	0.98	-	-
Platelet (<i>reference</i> : >150 × 10 ⁹ /liter)				
<150 × 10 ⁹ L ⁻¹	1.97 (1.05 to 3.70)	0.04	-	-
Unknown	1.34 (0.64 to 2.81)	0.45	-	-
INR (<i>reference</i> : <1.1)				
> 1.1	1.15 (0.65 to 2.04)	0.64	-	-
Unknown	1.04 (0.64 to 1.66)	0.89	-	-
Anticoagulant use (<i>reference</i> : None)				
Acetylsalicylic acid	-	-	1.58 (0.96 to 2.59)	0.071
Heparin	-	-	3.24 (2.46 to 4.25)	<0.001
Warfarin	-	-	0.37 (0.00 to 64.9)	0.71
Other anticoagulant [†]	-	-	4.29 (0.38 to 48.0)	0.24
> 1 anticoagulant	-	-	5.34 (3.22 to 8.85)	<0.001
Anti-platelet [‡]	-	-	1.53 (0.36 to 6.62)	0.57
c-statistic	0.744		0.941	

*Variables represented in Deyo Index variable in Premier sample.

[†] Includes any administered drug classified as an anticoagulant other than warfarin or heparin (identified based on billing codes).

[‡] Includes any administered drug classified as an anti-platelet other than acetylsalicylic acid (identified based on billing codes).

ACDF = anterior cervical discectomy and fusion; ASA = American Society of Anesthesiologists; CI = confidence interval; COPD = chronic obstructive pulmonary disease; INR = international normalized ratio; NSQIP = National Surgical Quality Improvement Program; PT = prothrombin time; PTT = partial thromboplastin time.

Discussion

Using institutional data as well as data from two observational data sets, we found a 0.2% incidence of unplanned reintubation within one day of ACDF surgery. In both the NSQIP and Premier databases, high comorbidity burden as indicated by ASA class or Deyo index was identified as a risk factor for emergent reintubation shortly after ACDF surgery. Older age was associated with increased risk of reintubation as shown in the NSQIP model. Within the Premier data, procedures performed in 2012, large hospitals, male sex, Medicaid insurance, non-elective procedures, and anticoagulant use were associated with an increased likelihood of reintubation. Potential preventive measures, including steroid use or delayed extubation, lowered the odds of reintubation following ACDF.

The observed incidence of reintubation (approximately 0.20%) is slightly lower than previous reports.^{4,6,9} This

could be because we uniquely restricted our outcome definition to reintubation within 24 hr of surgery, rather than at any point during the patient's postoperative stay. As we observed the same incidence across three different data sources, we are confident in the validity of our estimate.

Comorbidity burden was identified as a risk factor for reintubation in both the NSQIP and Premier databases. Additionally, male sex was a significant predictor of reintubation within the Premier database. These associations are consistent with prior studies.^{9,14}

We also found that administration of heparin or more than one anticoagulant increased the odds of reintubation within the first 24 hr following ACDF, likely a consequence of their association with increased risk of hematoma development.^{7,33,34} Though not significant based on our use of a *P* value threshold of 0.005 (Methods), the association of preoperative platelet count (NSQIP database) below 150 × 10⁹·L⁻¹ with reintubation may still warrant consideration. While adjusting for

multiple comparisons reduced the risk of a type I (false positive) error, it also increased the risk of a type II (false negative) error. Unfortunately, because of missing data from the NSQIP and Premier databases, we could not assess whether abnormal preoperative PT, PTT, and INR values were associated with increased risk for reintubation.

Within the Premier data, Medicaid was found to be a risk factor for reintubation following ACDF. Patients covered by Medicaid are more often of lower socioeconomic status, which is associated with worse overall health and higher comorbidity burden.³⁵

Of the potential preventive measures evaluated in the Premier database, delayed extubation and steroid use lowered the risk of reintubation, while drain use had no effect. Delayed extubation has previously been recommended in ACDF patients. For example, in a study examining the efficacy of a delayed extubation protocol, the incidence of emergency reintubation was decreased by maintaining intubation until a sufficient reduction in tracheal swelling was confirmed fibreoptically.²⁷ Our finding that steroid use decreased reintubation risk is consistent with a prior retrospective study which found that steroids reduce prevertebral soft tissue swelling, dysphagia, airway compromise, and subsequent reintubation in ACDF patients.²⁶ While it is anticipated that a cervical drain would also reduce upper airway compromise, secondary to hematoma, we did not observe any effect. This finding is consistent with a prior retrospective case-control study in ACDF patients that reported no effect of drains on postoperative respiratory complications.²⁸

This study is limited by its retrospective nature. In spite of using three data sets, each with distinct variables, residual confounding may persist. Because of the deidentified nature of the NSQIP and Premier databases, it was not possible to determine whether there was any patient overlap. We were restricted to the variables available in these data sets and some important laboratory and clinical information was missing, including preoperative coagulation tests (e.g., PT, PTT, INR) and the reason for reintubation. It would have been informative to assess the impact of *preoperative* anticoagulant use on reintubation, but this information was not available in any of the data sets; Premier only includes anticoagulant use *during* the index hospitalization. Identifying patients who were reintubated in the Premier database was dependent upon billing codes, which may be less robust as the methods used to define reintubation in the other two data sets. The NSQIP specifically denotes “reintubation” and instances of reintubation were

confirmed in the HSS data via chart review. Nevertheless, given that incidence estimates for reintubation were nearly identical across all three data sets, this supports the validity of using billing codes within Premier data. A number of our findings cannot be easily accounted for. For example, the incidence of reintubation was greater at large hospitals, and surgeries performed in 2012 were associated with an increase in the odds of reintubation.

In conclusion, we found a low incidence of reintubation following ACDF that was consistent throughout three separate data sets. The risk factors for reintubation included high comorbidity burden, older age, male sex, Medicaid insurance, surgery performed at large hospitals, non-elective surgery, and anticoagulant use. As prevertebral soft tissue swelling following ACDF continues to increase for two to three days after surgery,⁶ it seems prudent that patients with these risk factors be monitored especially closely following surgery. Such patients may also benefit from a period of prolonged ventilation and steroid administration.

Conflicts of interest Stavros G. Memtsoudis is a director on the boards of the American Society of Regional Anesthesia and Pain Medicine (ASRA) and the Society of Anesthesia and Sleep Medicine (SASM). He has consulted for Sandoz Inc. and Teikoku and is currently on the medical advisory board of HATH. He has a pending US Patent application for a Multicatheter Infusion System. US-2017-0361063. He is the owner of SGM Consulting, LLC and co-owner of FC Monmouth, LLC. None of the above relations influenced the conduct of the present study. All other authors declare no competing interests.

Editorial responsibility This submission was handled by Dr. Steven Backman, Associate Editor, *Canadian Journal of Anesthesia*.

Author contributions Lauren A. Wilson and Nicole Zubizarreta helped in study design/planning, data analysis, interpretation of results, and manuscript preparation and review. Janis Bekeris, Jiabin Liu, Megan Fiasconaro, Federico Girardi, and Nabil Elkassabany helped in study design/planning, interpretation of results, and manuscript review. Jashvant Poeran and Stavros G. Memtsoudis helped in study design/planning, interpretation of results, and manuscript preparation and review.

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Appendix A Variable composition of HSS institutional data, NSQIP and Premier Healthcare databases
Premier Healthcare databases

HSS institutional data	NSQIP	Premier
PATIENT DEMOGRAPHICS	PATIENT DEMOGRAPHICS	PATIENT DEMOGRAPHICS*
-Age	-Age*	-Age
-Sex	-Sex*	-Sex
PROCEDURE RELATED	-Race*	-Race/ethnicity
-Year of procedure	-Ethnicity	HEALTHCARE RELATED*
-# of vertebrae fused	PROCEDURE RELATED	-Insurance type
COMORBIDITY RELATED	-Year of procedure	-Hospital location
-ASA class	-# of vertebrae fused*	-Hospital size
-Sleep apnea	-Procedure type*	-Hospital teaching status
PREOPERATIVE LAB VALUES	-Surgeon specialty	-#Annual Procedures/hospital
-Platelet count	-Surgical diagnosis*	PROCEDURE RELATED*
-INR	-Operative duration*	-Year of procedure
-PT	COMORBIDITY RELATED	-# of vertebrae fused
-PTT	-ASA physical status*	-Procedure type
INTRAOPERATIVE MEDICATIONS	-Functional status*	-Surgeon specialty
-Ketorolac	-History of severe COPD*	-Surgical diagnosis
-Heparin	-Smoking	-Drain use
	-Diabetes*	-Delayed extubation
	-Obesity	-Steroid use
	PREOPERATIVE LAB VALUES	COMORBIDITY RELATED*
	-Platelet count*	-Deyo index†
	-INR*	-Sleep apnea
	-PT	-Obesity
	-PTT	-Smoking
		ANTICOAGULANT USE*
		-Acetylsalicylic acid
		-Other anti-platelet
		-Heparin
		-Warfarin
		-Other anticoagulant
		->1 of above

*Included in multivariable model.

ASA = American Society of Anesthesiologists; COPD = chronic obstructive pulmonary disease; HSS = Hospital for Special Surgery; INR = international normalized ratio; NSQIP = National Surgical Quality Improvement Program; PT = prothrombin time; PTT = partial thromboplastin time.

Appendix B Variable definitions for HSS, NSQIP, and Premier data sets

Variable	Data set	Type of code	Code	Description
Vertebrae fused	HSS & Premier	ICD-9 procedure	81.62	Fusion or refusion of 2-3 vertebrae
			81.63	Fusion or refusion of 4-8 vertebrae
	NSQIP	CPT	22845	Anterior instrumentation; 2-3 vertebral segments
			22846	Anterior instrumentation; 4-7 vertebral segments
Degenerative disc disease	NSQIP & Premier	ICD-9 diagnosis	721.XX	Spondylosis and allied disorders
			722.XX	Intervertebral disc disorders
	NSQIP	ICD-10 diagnosis	M47.XX	Spondylosis
			M48.1X	Ankylosing hyperostosis
			M48.2X	Kissing spine
			M48.3X	Traumatic spondylopathy
			M48.9X	Spondylopathy, unspecified
			M50.XX	Cervical disc disorders
			M51.XX	Thoracic, thoracolumbar, and lumbosacral intervertebral disc disorders
Trauma	NSQIP & Premier	ICD-9 diagnosis	805.XX	Fracture of vertebral column without mention of spinal cord injury
			806.XX	Fracture of vertebral column with spinal cord injury
	NSQIP	ICD-10 diagnosis	S12.XX	Fracture of cervical vertebra and other parts of neck
Sleep apnea	HSS & Premier	ICD-9 diagnosis	327.2X	Organic sleep apnea
			780.51	Insomnia with sleep apnea, unspecified
			780.53	Hypersomnia with sleep apnea, unspecified
			780.57	Unspecified sleep apnea
			786.03	Apnea
Smoking	Premier	ICD-9 diagnosis	305.1	Tobacco use disorder
			V15.82	History of tobacco use

† Charlson-Deyo comorbidity index is a weighted composite score of common comorbidities, with larger numbers reflecting greater comorbidity burden. COPD = chronic obstructive pulmonary disease; HSS = Hospital for Special Surgery; ICD = International Classification of Diseases; INR = international normalized ratio; NSQIP = National Surgical Quality Improvement Program; PT = prothrombin time; PTT = partial thromboplastin time.

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