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Sleep apnoea adversely affects the outcome in patients who undergo posterior lumbar fusion

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Abstract

Despite the increasing prevalence of sleep apnoea, little information is available regarding its impact on the peri-operative outcome of patients undergoing posterior lumbar fusion. Using a national database, patients who underwent lumbar fusion between 2006 and 2010 were identified,

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Supplementary material
A table detailing ICD-9-CM diagnosis codes for major complications is available alongside the electronic version of this article on our website www.bjj.boneandjoint.org.uk

sub-grouped by diagnosis of sleep apnoea and compared. The impact of sleep apnoea on various outcome measures was assessed by regression analysis. The records of 84 655 patients undergoing posterior lumbar fusion were identified and 7.28% also had a diagnostic code for sleep apnoea. Compared with patients without sleep apnoea, these patients were older, more frequently female, had a higher comorbidity burden and higher rates of peri-operative complications, post-operative mechanical ventilation, blood transfusion, and intensive care. Patients with sleep apnoea also had longer and more costly periods of hospitalisation.

In the regression analysis, sleep apnoea emerged as an independent risk factor for the development of peri-operative complications (Odds Ratio (OR) 1.50, Confidence Interval (CI) 1.38;1.62), blood transfusions (OR 1.12, CI 1.03;1.23), mechanical ventilation (OR 6.97, CI 5.90;8.23), critical care services (OR 1.86, CI 1.71;2.03), prolonged hospitalisation and increased cost (OR 1.28, CI 1.19;1.37; OR 1.10, CI 1.03;1.18). Patients with sleep apnoea who undergo posterior lumbar fusion pose significant challenges to clinicians.

Keywords

Sleep Apnoea Syndrome; Upper Airway Resistance Sleep Apnoea Syndrome; Outcomes Research; Spine Fusion; Complications

Although the mortality rate following posterior lumbar fusion has remained relatively consistent over the last decade, the rate of peri-operative complications has been rising.[[1–3]] Apart from age and medical comorbidities, sleep apnoea has emerged as a significant risk factor for the development of complications following posterior lumbar surgery.[[4]] In spite of the increasing number of patients suffering from sleep apnoea,[[5]] data on the prevalence of this condition and its impact on patients undergoing spinal fusion are limited, with the groups of patients studied often being very heterogeneous.[[6,7]] We hypothesised that sleep apnoea represents as an independent risk factor for an adverse outcome after posterior lumbar fusion.

Patients and Methods

Medical records were obtained from Premier Perspective, Inc. (Charlotte, North Carolina) covering the period between 2006 and 2010. This database contains discharge information from approximately 400 acute care hospitals located throughout the United States.[[8]] The authors' Institutional Review Board exempted this project from consent requirements. Rigorous quality assurance and data validation checks were performed by the provider before distribution in order to ensure accuracy of the entries. This database has previously been used to assess the incidence and risk factors for critical care service use among patients undergoing total hip (THR) and knee replacement (TKR),[[9]] and to determine comparative peri-operative outcomes associated with neuraxial *versus* general anaesthesia in patients undergoing simultaneous bilateral TKR.[[10]]

Using the International Classification of Diseases (9th revision) Clinical Modification (ICD-9-CM) codes, the authors sought entries for patients who had undergone a primary posterior lumbar fusion and divided them into two subgroups, according to whether there

was a concomitant diagnosis of sleep apnoea (group 1) or not (group 2). The groups were compared with regard to patient and healthcare related characteristics, including age, gender, race, type of admission, hospital size, location and teaching status; procedural characteristics including the number of vertebral levels operated on, the indication for undergoing spinal fusion, the presence of comorbidities including myocardial infarction, peripheral vascular disease, cerebrovascular disease, renal disease, chronic obstructive pulmonary disease (COPD), uncomplicated and complicated diabetes mellitus, obesity and the quantitative Deyo comorbidity burden.[[11]]

The incidence of sleep apnoea as a complication of surgery was computed using diagnosis codes for pulmonary compromise, pneumonia, cardiac complications (except non myocardial infarction), myocardial infarction, acute renal failure, gastrointestinal complications, infectious complications, pulmonary embolism, in-hospital and 30-day mortality. The rate of admission to intensive care, blood product transfusion and post-operative mechanical ventilation were recorded. The length of hospital stay and cost of hospitalisation were both compared as continuous variables and dichotomised at the 75th percentile. Entries exceeding this cut-off were defined as prolonged hospitalisation or increased hospital costs, respectively.

Statistical analysis

The primary aim was to detect differences in peri-operative outcomes of patients with a diagnosis of sleep apnoea, hypothesising that those suffering from this condition have a less favourable complication profile and higher length and cost of hospitalisation. All statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, North Carolina). In order to facilitate analysis of weighted data, SAS procedures SURVEYMEANS, SURVEYFREQ, SURVEYREG and SURVEYLOGISTIC were used for descriptive analyses and modelling efforts.

Means and percentages were described for continuous and categorical variables, respectively. For length and cost of hospitalisation, median and interquartile ranges were estimated to accommodate their skewed distributions. For continuous variables, 95% confidence intervals (CI) were shown as a measure of variability. The chi-square test was performed to evaluate the association of categorical variables. Two-sample *t*-test or Wilcoxon Ranked Sum tests were used to compare means or medians for a continuous variable between two groups.

Multivariate analysis was only performed for the group of patients undergoing lumbar fusion. Binary outcomes of major complications combined, mechanical ventilation, blood transfusion, intensive care requirement as well as prolonged stay and increased cost (each exceeding the 75th percentile) were defined as outcomes for a multivariate logistic regression analysis. In order to evaluate major complications a combined outcome variable was created including the complications listed above. For each outcome, logistic regression analysis was used to evaluate its association with the diagnosis of sleep apnoea, while controlling for age, gender, race, type of admission, hospital size, teaching status and location, vertebral levels operated and individual comorbidities. Adjusted odds ratios, 95% CI and p-values were reported. The conventional threshold of statistical significance (two-

sided p-value < 0.05) was used to determine significance of variables. In light of the potential undue effect a very large sample size might have on the p-values, 95% CIs of estimates were reported. The value inflation factor (VIF) for multicollinearity was evaluated. The conventional criterion of absence of multicollinearity, VIF < 10, was used. The final models were validated by a test of model discrimination using the c-statistic and a test of model calibration using the Hosmer–Lemeshow (H–L) test.[[12]] The c-statistic representing the area under the receiver-operating characteristic curve[[13]] was used to measure the level of discrimination between the observed data at different levels of the outcome. C-statistic values > 0.7 were considered indicative of acceptable discrimination. [[14]] In order to evaluate whether a logistic regression model was adequately calibrated, the H–L test was performed so that the predictions of probability from the model reflected the true occurrence of events in the data.

Results

We identified 84 655 entries for patients undergoing posterior lumbar fusion in the study period. Overall, 7.28% had a diagnosis code for sleep apnoea. The prevalence of sleep apnoea increased from 5.40% in 2006 to 9.91% in 2010. Compared with those without sleep apnoea, patients with the condition had a higher median age (59.7 (95% CI = (59.3 to 60.0)) *vs* 57.4 years (95% CI = (57.2 to 57.5), p < 0.001), were more frequently female (57.90% *vs* 42.72%, p < 0.0001), had a higher Deyo comorbidity burden (1.02 (95% CI = (0.99 to 1.06) *vs* 0.55 (95% CI = (0.54 to 0.56)), p < 0 001) and a higher prevalence of most comorbidities (Tables I and II). Amongst patients with sleep apnoea, 35.84% were diagnosed as obese, compared with only 11.85% in the group without sleep apnoea (p < 0.0001). Moreover, patients with sleep apnoea had higher rates of major complications including pulmonary compromise, pneumonia, cardiac complications (non-myocardial infarction), myocardial infarction, acute renal failure, gastrointestinal, and infectious complications (Table III).

Table IV shows the results of the multivariate logistic regression analysis. The diagnosis of sleep apnoea emerged as an independent risk factor for the development of major complications, use of mechanical ventilation, peri-operative blood transfusion, use of intensive care, as well as prolonged length and increased cost (i.e. > 75-percentile). Age, gender, race, type of admission, hospital size and three or more levels of vertebral fusion (odds ratio (OR) = 1.64 (CI 1.54 to 1.76), p < 0.0001) represent independent risk factors for combined complications. Furthermore, all comorbidities adjusted for yielded highly significant ORs for combined complications, except for renal disease: myocardial infarction: OR = 1.22 (confidence interval (CI) 1.09 to 1.36, p = 0.0005), peripheral vascular disease (OR=1.28 (CI 1.12 to 1.46), p = 0.0003), cerebrovascular disease (OR = 2.97 (CI 2.03 to 4.4), p < 0.0001), renal disease (OR = 1.84 (CI 0.70 to 4.78), p = 0.214), COPD (OR = 1.35 (CI 1.27 to 1.44), p < 0.0001), uncomplicated diabetes mellitus (OR = 1.30 (CI 1.23 to 1.38), p < 0.0001), complicated diabetes mellitus (OR = 2.46 (CI 2.11 to 2.86), p < 0.0001), obesity (OR = 1.45 (CI 1.36 to 1.55), p < 0.0001).

Multicollinearity was absent (value inflation factor < 2) from all regression models. The C-statistics were 0.7, 0.8, 0.7, 0.7, 0.7 and 0.6 for the outcomes of cumulative complications,

mechanical ventilation, transfusion, intensive care services, prolonged length of stay, and increased cost of hospitalisation, respectively.

Discussion

In patients undergoing posterior lumbar fusion, the authors found that sleep apnoea is associated with a higher risk of peri-operative complications, greater need for blood product transfusion, mechanical ventilation, use of intensive care, as well as increased length and cost of hospitalisation.

Sleep apnoea is defined as apnoeic events frequently occurring during sleep. It is invoked by partial or complete upper airway collapse or less frequently by pathology involving the central respiratory control.[[15]] The prevalence of obstructive sleep apnoea is estimated to be as high as 10% in females and 25% in the males.[[16]] The apnoeic events can occur hundreds of times during a night, are associated with brief periods of desaturation and terminated by arousal. Hypoxaemia as a consequence of apnoea, and with changes in intrathoracic pressure, pulmonary wedge pressure, ventricular preload and, ultimately, cardiac output are regarded as significant in the development of many acute and chronic cardio-respiratory disorders.[[17]] Marin et al[[18]] found that patients with untreated sleep apnoea had a considerably higher risk of incurring fatal (OR 2.87 CI 1.17 to 7.51) or non-fatal (OR 3.17, CI 1.12 to 7.51) cardiovascular events over a period of > ten years, compared with healthy controls.[[18]] Similarly, Yaggi et al found a significantly increased risk of stroke or death from other causes in patients with sleep apnoea (hazard ratio 1.97, CI 1.12 to 3.48, $p = 0.01$), compared with controls.[[19]]

We found that patients with sleep apnoea also had high rates of comorbid diseases. Most notably, one in three had diabetes or obesity. In addition to increased age and fusion involving more than three levels, all comorbid conditions studied in the regression analysis, with the exception of renal disease, constitute independent risk factors for the development of major peri-operative complications, cerebrovascular disease and complicated diabetes (a history of diabetes in conjunction with at least one related condition) exhibiting the highest adjusted odds ratios of 2.97 and 2.46, respectively. Patients suffering from a combination of sleep apnoea and one of those conditions are almost three times more likely to have major peri-operative complications than those who do not have these conditions. Patients suffering from conditions belonging to the metabolic syndrome complex are known to have worse outcomes after spinal surgery.[[20]] Although sleep apnoea and the metabolic syndrome share common mechanisms and similar phenotypes including obesity, a causal relationship between them is difficult to substantiate.[[21–23]] Hasan et al[[24]], found it was associated with obesity (mean BMI 36 (SD 6), 29.4 in controls, $p < 0.001$) and with hyperlipidaemia in 31%, diabetes in 59%, and arterial hypertension in 86% of patients with sleep apnoea.

Similarly, Robichaud-Hallé et al[[25]] reported correlations between the severity of sleep apnoea and morbidity indicating the coexistence of vascular disease ($r = 0.26$, $p = 0.01$) or metabolic syndrome ($r = 0.26$, $p = 0.01$), and a significant relationship between the presence of severe sleep apnoea and cardiovascular morbidity as defined by the score (OR = 7.33, CI 1.67–32.23, $p = 0.05$).[[26]] It has been suggested that patients with sleep apnoea should be

screened for diabetes regularly, and vice versa.[[26]] Moreover, in our study, almost one in three patients in the sleep apnoea group also had COPD. The co-existence of these conditions, referred to as ‘overlap syndrome’, exerts detrimental effects on the cardiopulmonary system and has disproportionally increased morbidity and mortality rates compared with sleep apnoea or COPD alone.[[27,28]]

Sleep apnoea has only recently been recognised and studied as a risk factor for adverse out comesperi-operatively.[[29]] The condition has been linked to frequent desaturation events, [[6]] hypoventilation in response to the administration of hypnotics or opioids, an increased risk of aspiration both during normal sleep[[30]] and post-operatively,[[7]] an increased need for mechanical ventilation and re-intubation,[[31]] which may be additionally complicated in these patients.[[32]] Moreover, an increased incidence of major ischaemic cardiovascular events,[[33]] as well as frequent occurrence of peri-operative arrhythmias and changes in blood pressure have been reported.

In the authors’ study, the risk of developing a major peri-operative complication in patients with sleep apnoea was about 50% higher than in those without the condition. An incident of pulmonary compromise similar to that found in the author’s study has recently been reported.[[6,34]] As also noted by Memtsoudis et al,[[20]] there was no increase in the rate of pulmonary embolism, and found that sleep apnoea is associated with an increased risk of admission to the intensive care unit and the need for transfusion and ventilation. While some patients with sleep apnoea might have received intensive care treatment, especially after high-risk procedures including upper airway surgery,[[35]] sleep apnoea is known as a risk factor for unplanned post-operative admission to the intensive care unit.[[36]] Hang et al[[37]] identified cardiovascular, respiratory and cerebrovascular events as the most common indications for intensive care admission in non-surgical patients with sleep apnoea.

This retrospective, database-driven analysis has a number of limitations. First, those patients who were allocated to the ‘no diagnosis of sleep apnoea’ group might have been misdiagnosed[[38]] and could have skewed the allocation of patients into this group to seem a ‘sicker’ group. However, this group is known to be subject to the highest risk for post-operative complications, rendering the results valid for patients with sleep apnoea diagnosed pre-operatively. It should also be noted that patients with a higher comorbidity index are likely to be more frequently exposed to medical services and increased diagnostic scrutiny, which might increase their chances of additional diagnoses (including sleep apnoea). This might result in conditional dependency in a subset of patients, known as Berkson’s bias. [[39]]

The database used does not have information beyond that reported by the participating institutions used within this analysis. We were thus unable to adjust for potential confounders such as severity of sleep apnoea. The individual peri-operative risk has previously been described both as a function of the severity of sleep apnoea and also the type of surgery.[[35]] This applies to smoking, which is a predisposing factor for sleep apnoea and a risk factor for cardiovascular disease.[[40]] Nor was there information on body mass index (BMI) of individual patients, thus the authors were unable to adjust for BMI as a continuous rather than a binary variable (‘morbid obesity’). Only one type of operation was

included, which controlled the level of invasiveness of the surgery, as well as accounting for the number of vertebral levels operated on as an effect variable in the regression. Owing to national differences in the prevalence of obesity, the data on the prevalence of sleep apnoea among the patients undergoing spinal surgery may not be applicable to other countries. However, the individual risk among patients suffering from sleep apnoea undergoing posterior lumbar fusion may be similar in most countries, as the diagnostic criteria are comparable.[[41]] Additionally, up to > 60% of patients with a definitive diagnosis of sleep apnoea have been reported to be non-obese.[[42]] Intra-operative events and preventive treatment measures including the application of continuous positive airway pressure (CPAP) used as a 'pneumatic airway splint', were not captured. Lack of this information makes it impossible to determine whether this form of treatment modifies the outcome. [[17]]However, it is well known that early CPAP for the treatment of hypoxia significantly reduces pulmonary morbidity and the incidence of infectious complications.[[44,45]] Events following discharge from hospital, except the 30-day mortality rate, were not captured due to the nature of the database. Finally, all comorbidities and complications were identified using ICD-9-CM or billing codes.

In conclusion, these results further suggest that patients with sleep apnoea represent a group at risk for adverse post-operative events. The early identification and triage of these patients might facilitate the appropriate stratification of risk. The subsequent introduction or optimisation of preventive treatment measures including, CPAP ventilation,[[18,43,44]] continuous pulse oximetry,[[45]] extended stay in the recovery room and the use of regional anaesthesia[[46]] might lead to improved outcomes in these patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table I

Patient and health care system related characteristics of groups.

Characteristics				
Variable	**Category**	**Diagnosed sleep apnoea**	**No diagnosed sleep apnoea**	**p-value**
N =		6163	78492	
% of Total		7.28%	92.72%	
Average comorbidity index		1.02 (0.99 to 1.06)	0.55 (0.54 to 0.56)	< 0.0001
Deyo comorbidity index categories	0	45.13	67.13	< 0.0001
	1	21.82	16.05	
	2	21.01	12.44	
	> / = 3	12.04	4.39	
Average age (years)		59.7 (59.3 to 60.0)	57.4 (57.2 to 57.5)	< 0.0001
Age group	< / = 44	10.8	20.35	< 0.0001
	45 to 54	20.63	20.94	
	55 to 64	32	23.24	
	65 to 74	26.86	22.34	
	> / = 75	9.7	13.12	
Gender	Female	57.9	42.72	< 0.0001
	Male	42.1	57.28	
Race	White	71.38	76.49	< 0.0001
	Black	6.77	6.98	
	Other	2.78	1.93	
	Missing	19.07	14.6	
Type of admission	Emergent	4.09	4.08	0.4166
	Urgent	3.3	3.67	
	Routine	92.16	91.65	
	Other	0.15	0.16	
	Missing	0.3	0.44	
Hospital size (bed number)	< / = 299	28.68	30.34	0.0396
	300 to 499	46.18	45.16	
	> / = 500	25.15	24.5	
Hospital teaching status	Non-Teaching	74.63	77.6	< 0.0001
	Teaching	25.37	22.4	
Hospital location	Rural	3.22	3.52	0.098
	Urban	96.78	96.48	
Levels operated	2 to 3	87.25	88.56	< 0.0001
	4 to 8	12.01	10.09	
	Unknown	0.75	1.36	

Characteristics				
Variable	**Category**	**Diagnosed sleep apnoea**	**No diagnosed sleep apnoea**	**p-value**
Indication for surgery	Degenerative Causes	56.45	56.43	< 0.0001
	Scoliosis	0.39	0.60	
	Trauma	0.26	1.25	
	Neoplastic	0.02	0.16	
	Combined diagnosis	39.92	37.40	
	Unknown	2.97	4.15	

Table II

Prevalences of pre-existing comorbidities among patients with or without a concomitant diagnosis of sleep apnoea. (COPD, chronic obstructive pulmonary disease)

Prevalence of pre-existing comorbidities					
	Diagnosed sleep apnoea		**No diagnosed sleep apnoea**		
	N	**%**	**N**	**%**	**p-value**
Myocardial infarction	378	6.15	2515	3.12	< 0.0001
Peripheral vascular disease	200	3.05	1615	1.97	< 0.0001
Cerebrovascular disease	19	0.35	143	0.19	0.0176
Renal disease	4	0.05	23	0.03	0.5684
COPD	1671	27.29	11206	13.91	< 0.0001
Diabetes	1768	28.51	11636	14.68	< 0.0001
Complicated diabetes	191	3.11	960	1.18	< 0.0001
Cancer	95	1.58	1350	1.72	0.4912
Obesity	2209	35.84	9301	11.85	< 0.0001

Table III

Incidence of complications, use of mechanical ventilation and blood product transfusion as well as median length of stay and cost of hospitalisation among patients with or without a concomitant diagnosis of sleep apnoea undergoing posterior lumbar spinal fusion.

Incidence of selected outcomes: posterior lumbar fusion					
	Diagnosed sleep apnoea		**No diagnosed sleep apnoea**		
	N	**%**	**N**	**%**	**p-value**
Pulmonary compromise	251	4.21	800	0.99	< 0.0001
Pneumonia	156	2.65	1108	1.44	< 0.0001
Cardiac complications (non-myocardial infarction)	404	6.69	2727	3.48	< 0.0001
Myocardial infarction	33	0.5	211	0.26	0.0018
Acute renal failure	186	3	1004	1.32	< 0.0001
Gastrointestinal complications	107	1.73	1114	1.42	0.0676
Infectious complications	387	6.39	3897	5	< 0.0001
Pulmonary embolism	15	0.25	189	0.26	0.9027
In-hospital death	10	0.19	92	0.11	0.1167
30-day mortality	10	0.19	120	0.14	0.4057
Mechanical ventilation	402	6.74	654	0.78	< 0.0001
Blood Product transfusion	915	14.41	10315	12.55	0.0001
Critical Care services	986	16.75	6624	8.2	< 0.0001
Length of stay *median (interquartiles)*	3.2 (2.2 to 4.6)		2.9 (2.0 to 4.1)		< 0.0001
Cost of hospitalisation *median (interquartiles)*	79 572 (55 096 to 110 969)		75 013 (52 556 to 104 172)		< 0.0001

Table IV

Results from six separate multivariate logistic regression analyses in patients undergoing posterior lumbar spinal fusion; odds ratios (sleep apnoea *vs.* no sleep apnoea (reference)) and 95% confidence intervals (CI) were adjusted for age, gender, race, type of admission, hospital size, status and location, vertebral levels fused and individual comorbidities.

Multivariate regression: Diagnosed sleep apnoea *vs* no Diagnosed Sleep Apnoea (Reference)		
Outcome	**Odds ratio (95% Confidence interval)**	**p-Value**
Combined complications	1.50 (1.38 to 1.62)	< 0.0001
Blood product transfusion	1.12 (1.03 to 1.23)	0.0092
Postoperative mechanical ventilation	6.97 (5.90 to 8.23)	< 0.0001
Critical care services	1.86 (1.71 to 2.03)	< 0.0001
Prolonged length of stay *	1.28 (1.19 to 1.37)	< 0.0001
Increased cost of hospitalisation *	1.10 (1.03 to 1.18)	0.0065

Note Combined complications comprise following events: pulmonary compromise, pneumonia, cardiac complications (non-myocardial infarction), myocardial infarction, acute renal failure, gastrointestinal complications, infectious complications, pulmonary embolism, in-hospital death, 30-day mortality.

* prolonged length of stay and increased cost of hospitalisation is defined as values exceeding the 75th percentile, respectively.