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ORIGINAL PAPER

Risk factors for pulmonary embolism after hip and knee arthroplasty: a population-based study

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Abstract Pulmonary embolism (PE) is a cause of death after total hip and knee arthroplasty (THA, TKA). We characterised the patient population suffering from in-hospital PE and identified perioperative risk factors associated with PE using nationally representative data. Data from the National Hospital Discharge Survey between 1990 and 2004 on patients who underwent primary or revision THA/TKA in the United States were analysed. Multivariate regression analysis was performed to determine if perioperative factors were associated with increased risk of in-hospital PE. An estimated 6,901,324 procedures were identified. The incidence of in-hospital PE was 0.36%. Factors associated with an increased risk for the diagnosis of PE included: revision THA, female gender, dementia, obesity, renal and cerebrovascular disease. An increased association with PE was found among patients with diagnosis of Adult Respiratory Distress Syndrome (ARDS), psychosis (confusion), and peripheral thrombotic events. Our findings may be useful in stratifying the individual patient's risk of PE after surgery.

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Résumé L'embolie pulmonaire (PE) est une cause de décès après prothèse totale de hanche ou du genou (THA, TKA). Nous avons essayé de déterminer quelle population pouvait présenter une telle complication et identifier les facteurs de risques pré-opératoires. Pour cela, nous avons analysé nos données hospitalières nationales entre 1990 et 2004 sur tous les patients ayant bénéficié d'une prothèse de hanche ou du genou primaire ou de révision aux Etats-Unis. Une analyse statistique a été réalisée afin de déterminer quels sont les facteurs de risque péri-opératoires associés. 6 901 324 procédures ont été identifiées. Le pourcentage d'embolie pulmonaire durant l'hospitalisation a été de 0,36%. Les facteurs associés sont la révision prothétique, le sexe féminin, la démence, l'obésité, les problèmes rénaux et les problèmes cérébraux vasculaires. Le taux le plus élevé d'embolie pulmonaire a été également trouvé chez les patients ayant un diagnostic d'ARDS et de troubles confusionnels ainsi que d'évènements thrombotiques périphériques. Ces données peuvent être utiles pour évaluer le risque d'embolie pulmonaire chez les patients après chirurgie arthroplastique.

Introduction

Pulmonary embolism (PE) is one of the most frequent causes of mortality following total hip and knee arthroplasty (THA, TKA) [19]. Much effort has been spent to decrease the prevalence of venous thrombosis and PE through the use of pharmacological and other perioperative interventions [25, 26]. Despite the efforts to lower the risk of venous thromboembolic events, the effectiveness of these interventions in reducing their incidence and all-cause mortality remains controversial [25, 26].

The current American College of Chest Physician Guidelines proposing routine use of powerful anticoagu-

lants [8] failed to prove a reduction in all-cause mortality [25, 26, 28], and their implementation in orthopaedic patients has led to high rates of local complications including bleeding, infection, and re-operation [5, 6, 20, 23]. Recently, the American Academy of Orthopaedic Surgeons released new guidelines for the pharmacological prophylaxis of venous thromboembolism following total joint arthroplasty. These guidelines limit the use of potent anticoagulation based on the preoperative stratification of the patient's individual risk for venous thromboembolism and bleeding [21].

The risk factors for venous thromboembolism that have been adopted by the orthopaedic community are based on large medical studies with little focus on specific surgical procedures [3]. Moreover, because of its relatively low incidence it is difficult to access a large enough sample of orthopaedic patients who developed postoperative PE in order to accurately assess the role of individual perioperative predisposing factors. Current studies, with large series but low number of patients suffering from venous thromboembolism, are available from single and specialised institutions where demographics and epidemiology are often unique [2, 4]. Thus, these studies are limited in their ability to provide nationally representative data for patient risk stratification.

To overcome this limitation we analysed data from a national database and attempted to answer the following questions. (1) What are the characteristics of patients who developed an in-hospital PE after total joint arthroplasty? (2) What are the perioperative risk factors associated with the development of in-hospital PE after THA and TKA?

Materials and methods

The National Hospital Discharge Survey (NHDS)

NHDS multi-year data files were obtained from the Centers of Disease Control and Prevention, Atlanta, GA. The plan and operation of the NHDS has been published in detail [24]. In summary, the NHDS includes medical information collected annually since 1965 by the National Center for Health Statistics with the purpose of compiling nationally representative data on inpatient use of short-stay hospitals. The hospital universe includes Medicare participating hospitals, non-institutional hospitals of various sizes, exclusive of military, Veterans Affairs, and federal facilities in the 50 states and the District of Columbia. Hospitals included in the survey are required to have an average length of stay of less than 30 days to be considered short-stay, or to be a general medical or surgical hospital, regardless of length of stay. Facilities are also required to have at least six beds for patient use. Periodic updates of the hospital universe are performed to account for changes.

The NHDS uses a battery of procedures to ensure accurate, nationally representative sampling. Information collected in the survey includes diagnosis and procedure codes (ICD-9-CM), as well as patient and hospital characteristics. Weighted data, with weights derived from census information, were provided by the NHDS to generate unbiased national estimates from the sample (1% of all hospital discharges in the US).

We and others have used the NHDS extensively to analyse data associated with a wide range of procedures across a variety of medical specialties [24]. Using similar methodology we have reported on the trends of total knee replacements in the United States [15], we have explored the safety of bilateral total knee replacement surgery [16], and we have reported on the predisposing factors for mortality after surgery.

Patient selection and analysis

Data collected for each year between 1990 and 2004 were obtained, read into a statistical software program (SAS version 8.2, SAS Institute, Cary, NC), and analysed. Discharges with a procedure code (ICD-9-CM) for primary or revision THA (81.51 and 81.53) and TKA (81.54 and 81.55) were identified and included in the analysis. Two study groups were created: (1) patients without a diagnosis of PE (pulmonary embolism; ICD-9-CM, 41.51) and (2) patients who had a diagnosis code for PE listed during their hospital stay. Patient demographics (age, gender, race, disposition status, length of hospital stay, and prevalence of comorbidities) were evaluated for each group. Frequencies of procedure-related complications were analysed by determining cases that listed ICD-9-CM diagnosis codes indicating complications of surgical care and medical care affecting specified body systems. In addition, the prevalence of selected adverse diagnoses, including peripheral thrombotic events, respiratory insufficiency after trauma or surgery/ARDS, and psychosis, using appropriate ICD-9-CM diagnosis codes were studied. Comorbidities were analysed by determining the prevalence of diabetes mellitus, cerebrovascular disease, pulmonary disease, renal disease, coronary artery disease, obesity, and dementia. ICD-9-CM diagnosis codes included for determining the presence of comorbidities and adverse diagnoses are listed in the Appendix. Differences in the incidence of in-hospital PE between procedure subtypes were also assessed. Subsequently, multivariate regression analysis was performed and odds ratios and 95% confidence intervals were calculated to determine if perioperative factors, including patient demographics, the presence of comorbidities, the occurrence of complications, and

the type of procedure were associated with increased risk of in-hospital PE.

Statistical analysis

The significance of differences between groups was assessed using Z-scores for categorical variables and a general linear model for continuous variables. In order to set stricter standards and account for the power introduced by the large weighted sample size in our analysis, we chose a p value of 0.001 to define significance. For multivariate logistic regression, variables included in the model were: procedure type, age, gender, comorbidities, and complications. Three five-year periods of interest (1990–1994, 1995–1999, and 2000–2004) were also included in the model to account for a potential temporal impact on the outcome.

Results

An estimated total of 6,901,324 primary and revision THA and TKA procedures were identified in the NHDS between 1990 and 2004 (primary THA 33.16% and revision THA 6.47%; primary TKA 55.50% and revision TKA 4.91%). The incidence of in-hospital PE was 0.36% (primary THA 0.33% and revision THA 0.39%, primary TKA 0.41% and revision TKA 0.17%). The incidence was 0.39% between 1990 and 1994; 0.30% between 1995 and 1999; and 0.40% between 2000 and 2004.

Patients with a PE were on average 1.2 years older and had an almost twice as long hospital stay compared to the total estimated patient sample. Women were over-proportionally affected by PE compared to men. While for a large number of patients an entry for the category race was not available, the incidence of PE among black patients was proportionally higher compared to their share of total procedures (Table 1).

Patients with the diagnosis of PE were more frequently discharged to a long- or short-term care facility versus their primary residence. Mortality was significantly higher among patients with the diagnosis of PE. The prevalence of obesity, cerebrovascular disease, pulmonary disease, renal disease, and dementia was higher among patients suffering from a PE (Fig. 1).

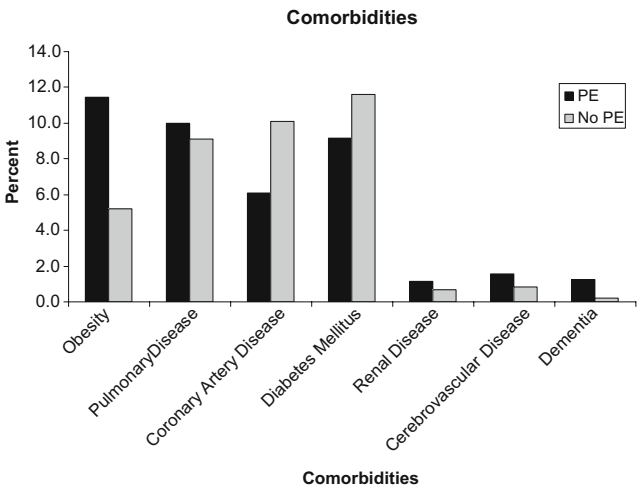
A higher incidence of procedure-related complications and peripheral thrombotic events, respiratory insufficiency after trauma or surgery/ARDS, and psychosis were associated with PE (Fig. 2).

In the multivariate regression analysis (Table 2), an increased risk for the diagnosis of PE was found for revision THA and primary TKA as compared to primary THA procedures. The age group with the highest risk for PE was 45–64 years. In addition, the odds for a diagnosis of PE were increased for females vs. males, and for black vs. white patients. Comorbidities associated with an increased risk for PE after THA and TKA were dementia, obesity, renal and cerebrovascular disease. The highest odds for PE

Table 1 Characteristics of patients without and with pulmonary embolism (PE)

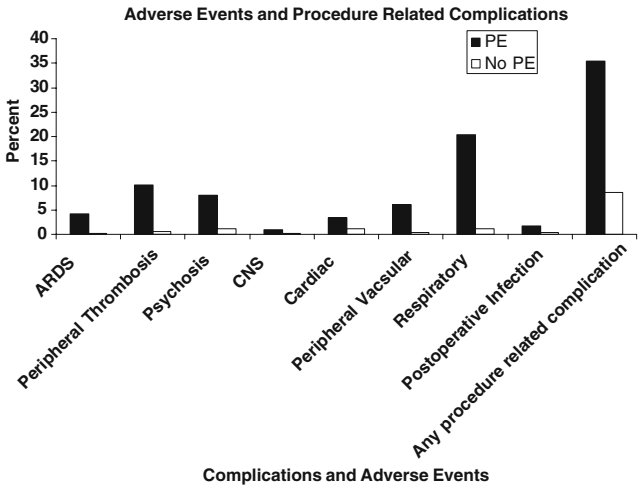
Group	No PE	PE
Total *N*	6,876,197	25,127
Age (years), mean (range)*	67.6 (3–99)	68.8 (35–89)
Age groups (years)		
<45**	4.4	1.6
45–64**	29.3	28.8
65–84**	61.8	65.2
85–99	4.5	4.5
Gender		
Male**	38.8	32.8
Female**	61.2	67.2
Race		
White**	69.3	64.2
Black**	5.0	6.1
Other**	1.7	1.0
Not stated**	24.0	28.8
Discharge status		
Routine discharge home**	50.6	35.9
Short-term facility**	9.0	13.0
Long-term facility**	21.1	25.9
Alive, disposition not stated**	16.9	14.8
Dead**	0.3	9.7
Not stated or reported**	2.0	0.7
Length of care (days), mean (range)*	5.6 (1–315)	10.2 (1–56)

Values given as percentages unless otherwise stated
* Significant difference ($p<0.001$) by general linear model
** Significant difference ($p<0.001$) by Z-scores



P<0.001 between groups for all comorbidities.

Fig. 1 Comorbidity profiles of patients with and without pulmonary embolism (PE)



P<0.001 between groups for all events and complications.

Fig. 2 Adverse events and procedure-related complications in patients with and without pulmonary embolism (PE)

however, were associated with complications and adverse events, including ARDS, psychosis (confusion), peripheral thrombotic events, procedure related infections, and respiratory complications. The odds for PE as a diagnosis during hospitalisation for lower extremity arthroplasty were slightly higher in the most recent time period studied as compared to the 1990s.

Discussion

Using a nationally representative patient sample containing data collected over 15 years, we were able to characterise the population with a diagnosis of PE during their hospital stay after THA and TKA, and compare them to those who had no such diagnosis. Further, we identified pre- and postoperative factors associated with the diagnosis of in-hospital PE.

Surgical procedure Revision THA and primary TKA were associated with a higher overall incidence and odds of in-hospital PE as compared to primary THA and revision TKA even when controlling for multiple covariates (Table 2). Similarly, Zhan et al. recently reported a postoperative venous thromboembolism (VTE) rate of 0.68% for primary THA versus 1.08% for revision THA [33]. Mahomed et al. suggested a lower PE rate after revision versus primary TKA

Table 2 Multivariate regression analysis using factors associated with pulmonary embolism after total hip and knee arthroplasty (THA, TKA)

Risk factor category	Risk factor	Odds ratio	Upper 95% CI	Lower 95% CI	*P* value
Procedure type	Revision THA	1.26	1.19	1.33	<0.0001
(referent: primary total hip arthroplasty)	Primary TKA	1.21	1.17	1.24	<0.0001
	Revision TKA	0.49	0.45	0.53	<0.0001
Time periods (referent: 1990–1994)	1995–1999	0.83	0.80	0.86	<0.0001
	2000–2004	1.16	1.12	1.20	<0.0001
Age group (referent: 45–64 years)	<44 years	0.44	0.40	0.49	<0.0001
	65–84 years	0.98	0.95	1.01	0.1372
	>85	0.77	0.72	0.83	<0.0001
Gender (referent: female)	Male	0.76	0.74	0.78	<0.0001
Race (referent: white)	Black	1.45	1.38	1.53	<0.0001
	Not stated	1.32	1.28	1.36	<0.0001
	Other	0.82	0.72	0.93	0.0017
Comorbidities	Diabetes mellitus	0.78	0.74	0.81	<0.0001
(referent: absence of comorbidity)	Cerebrovascular disease	2.05	1.84	2.28	<0.0001
	Pulmonary disease	0.96	0.92	1.00	0.0535
	Renal disease	1.71	1.51	1.92	<0.0001
	Coronary artery disease	0.58	0.55	0.61	<0.0001
	Dementia	6.40	5.66	7.22	<0.0001
	Obesity	2.70	2.59	2.81	<0.0001
Adverse diagnoses	ARDS	11.46	10.66	12.31	<0.0001
(Referent: absence of diagnosis)	Peripheral thrombosis	11.69	11.00	12.42	<0.0001
	Psychosis	9.43	8.98	9.91	<0.0001
Procedure related complications	Pulmonary	12.21	11.62	12.83	<0.0001
(referent: absence of complication)	Cardiac	1.02	0.94	1.11	0.6191
	CNS	2.36	2.04	2.73	<0.0001
	Peripheral vascular	2.55	2.34	2.77	<0.0001
	Postoperative infection	3.80	3.42	4.22	<0.0001
	Any procedure related complication	1.78	1.70	1.86	<0.0001

(0.5% vs. 0.8%) [13]. The reasons for these findings are not fully understood, but may be explained by the different volume of bone marrow entering the cardiovascular system and activating the coagulation cascade. In addition, revision THA often require prolonged fixed positioning of the limb in flexion and internal rotation during femoral work, resulting in prolonged venous stasis [18].

Age The average age of patients with a diagnosis of PE was 68.8 years. The age group distribution overall was similar among patients with and without the diagnosis of PE. While the incidence of PE was highest in the age group of 65–84 years (65.2% with PE; 61.8% without PE), multivariate regression suggested that the risk was highest among patients aged 45–64 years. However, age by itself has not been consistently identified as a risk factor for the development of PE after total joint arthroplasty [14, 31].

Gender Female gender was an independent risk factor for the development of PE, confirming reports by other authors [30, 32]. The reasons for this observation remain poorly understood, and further research is necessary.

Race We found an increased risk for the diagnosis of PE among black patients as compared to whites and a decrease in the risk among patients of other races. This is in concordance with previously published studies and population-based data [10, 29]. The lower incidence of PE among Asians and Pacific Islanders (which are categorised under "other" in our study), has been attributed to a lower prevalence of factor V Leiden and other genetic predisposing factors [22].

Comorbidities We observed that cerebrovascular and renal disease, obesity, and dementia were associated with increased risk of PE. The role of obesity as a risk factor in previous studies has been equivocal [12, 14]. Differences in the definition of obesity and patient populations in published studies have been suggested as reasons for these disparities [14]. Factors that have been suggested to increase the risk for obese patients to develop PE after lower extremity arthroplasty include slow mobilisation time, potential underdosing of anticoagulants, and the ineffectiveness of mechanical compression devices [31]. Interestingly, it has been suggested that obese patients may have a decreased risk of mortality from PE than their non-obese counterparts [1].

The impact of renal insufficiency on the risk for PE after hip and knee arthroplasty is less well studied. A recent study in the general population suggested that the rate of fatal PE is increased with progressive decrease in creatinine clearance [17]. Further, renal failure was identified as a risk factor for VTE in the general postsurgical patient population, including after orthopaedic surgery [7].

We identified dementia and cerebrovascular disease as independent risk factors for in-hospital PE. While this association remains poorly defined in the orthopaedic literature, research suggests that PE ranks among the top three reasons for mortality among demented patients [11]. While the reasons may seem obvious and may include the increased incidence of immobility associated with cerebrovascular disease and dementia as surrogate markers, further studies defining this relationship are warranted.

Interestingly, the presence of pulmonary disease did not increase the risk of in-hospital PE in our study, and coronary artery disease as well as diabetes mellitus were associated with a decrease in the odds for this outcome. While these findings may at first seem counterintuitive, previous studies have failed to identify diabetes mellitus as a risk factor for postoperative PE [7].

Further, when studying the risk of PE among hospital patients with pulmonary disease, Stein et al. found that the impact of chronic obstructive pulmonary disease (COPD) on the relative risk decreased dramatically with increasing age and was only 1.23 in the age group between 60 and 79 years, which represents the age group with the highest incidence in our study. The authors suggested that with the increase of the prevalence of other risk factors with increasing age, the contribution of COPD becomes less relevant [27].

The diagnosis of coronary artery disease was associated with a decreased risk for in-hospital PE. However, other authors using large databases found that many comorbidities, that on a clinical basis should be associated with increased risk of adverse outcomes, were linked with a lower risk of in-hospital death and complications [4, 9]. One explanation may be that coding bias against chronic diseases that often do not pose an active issue (and thus do not affect billing) may be omitted during a procedure-oriented hospital admission. Clinical reasons for such findings may be that patients with diagnosed cardiovascular disease are usually properly studied and optimised prior to surgery; they are also kept under stricter postoperative medical care and monitoring, and are frequently treated with antiplatelet agents, which may decrease the risk of PE [25, 26]. In contrast, patients who have undiagnosed disease (thus not coded in the database) may have worse outcomes.

Complications Peripheral venous thromboembolism, pulmonary complications, ARDS/pulmonary insufficiency after surgery, and psychosis were associated with the highest increase in the odds for in-hospital PE. While it is not possible to say with certainty if the complications studied predated the diagnosis of PE, this information is useful to the clinician in order to anticipate treatment of these associated complications. It becomes apparent that

many complications studied are associated with prolonged immobilisation and thus may increase the risk of PE.

Our study is limited by a number of factors associated with secondary data analysis of large administrative databases. Clinical information available in the NHDS is limited and our analysis has to be interpreted in this context. Because of the nature of the NHDS, only inpatient data are available and thus PE after discharge is not captured. Conclusions should be limited to the acute postoperative setting, with the notion that PE and other complications are likely underestimated. As mentioned previously, the inability to identify with certainty if a complication occurred, and thus contributed to PE or vice versa, poses an additional limitation. The bias associated with the retrospective nature of our study has to be mentioned.

Despite a number of limitations, our study of a large nationally representative patient sample undergoing THA and TKA allowed us to identify perioperative risk factors that are associated with an increased risk of in-hospital PE. Our findings may be useful for the allocation of resources and implementation of more aggressive measures to prevent PE in selected patients at risk.

Appendix

The following table is a list of ICD-9 diagnosis codes included to identify comorbidities, adverse diagnoses, and complications among discharges. (Four- and five-digit codes are included under the respective three- and four-digit codes.)

Diagnosis	ICD-9 diagnosis code
Comorbidities	
Diabetes mellitus	250
Cerebrovascular disease	433,434,437,438
Pulmonary disease	490, 491, 492, 493, 494, 496
Renal disease	582, 585, 403
Coronary artery disease	412, 413, 414, 4292
Dementia	290
Obesity	278
Procedure-related complications	
Central nervous system	9970
Cardiac	9971
Peripheral vascular	9972
Respiratory (aspiration pneumonia)	9973
Postoperative infection	9985
Any procedure-related complication	997–999
Other adverse events	
Pulmonary embolism	4151
Pulmonary insufficiency after trauma and surgery/ARDS	5185
Peripheral thrombosis events	4511, 4512, 4518, 4519, 4532, 4534, 4538, 4539

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