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ORIGINAL ARTICLE

Saddle pulmonary embolism and in-hospital mortality in patients with cancer

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Abstract

Purpose Saddle pulmonary embolism (PE) has been associated with an increased risk of 1 year mortality when compared to non-saddle PE among patients with cancer. We sought to evaluate the association between saddle PE and in-hospital outcomes among patients with comorbid cancer.

Methods The 2013 and 2014 United States National Inpatient Sample was used to identify adult patients hospitalized for acute PE. Only patients with an International Classification Diseases, 9th Revision, Clinical Modification (ICD-9-CM) code indicating comorbid cancer were included. Identified admissions were stratified into the following 2 cohorts: saddle (defined as ICD-9-CM code = 415.13) and non-saddle PE. Multivariable logistic regression was performed to determine the association between saddle PE and the odds of in-hospital mortality after adjustment for age ≥ 80 years and sex.

Results A total of 10,660 admissions for acute PE in patients with comorbid cancer were identified. Of which, 4.5% ($n = 475$) had a saddle PE. Median age was 67 years (interquartile range = 58–76) and 48.9% were male. In-hospital mortality occurred in 6.1% of patients. Upon multivariable adjustment, the odds of in-hospital mortality were higher in saddle versus non-saddle PE (odds ratio = 1.51; 95% confidence interval 1.08–2.10).

Conclusion In this retrospective study of admissions for acute PE in patients with comorbid cancer, saddle PE was associated with a higher odds of in-hospital mortality.

Keywords Pulmonary embolism · Venous thrombosis · Venous thromboembolism · Neoplasms · Hospital mortality

Introduction

Patients with cancer are at a substantially higher risk of venous thromboembolism when compared to patients without cancer due to treatment (e.g., surgical interventions and chemotherapy) and disease related (e.g., hypercoagulable state) factors [1, 2]. When patients with cancer present with acute venous thromboembolism, assessing the risks and benefits of treatment strategies is difficult, as these patients have a higher occurrence of both recurrent venous thromboembolism and major bleeding versus those without cancer [3]. Identifying methods for optimal risk stratification in this population could aid clinicians making challenging treatment decisions.

Saddle pulmonary embolism (PE), or a thromboembolus straddling the bifurcation of the main pulmonary artery, is responsible for ~2 to 5% of PE cases [4]. A previous study of patients with cancer found that saddle PE was associated with increased mortality at 1 year and the authors concluded that the presence of saddle PE may be used for risk stratification in this population [5]. However, 30-day mortality did not differ in this study and in-hospital mortality was not compared between cohorts. We sought to evaluate the association between saddle PE and in-hospital outcomes among patients with comorbid cancer.

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Methods

This retrospective study used data from the 2013–2014 United States National Inpatient Sample (NIS), a database developed for the Healthcare Cost and Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality (AHRQ) [6, 7]. We identified all adult (≥ 18 years of age) admissions for acute PE (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] diagnostic code = 415.1X in the primary diagnostic position) who had an ICD-9-CM code for comorbid cancer (eTable1).

Identified admissions were stratified based on the presence or absence of an ICD-9-CM diagnostic code indicating saddle PE (415.13). Outcomes of interest included in-hospital mortality, hospital length-of-stay (LOS), and hospital costs in 2017 US dollars. Demographics and comorbidities for the cohorts are reported as percentages for categorical data and mean with standard deviations (SDs) or medians with interquartile ranges (IQR) for continuous data.

Using multivariable logistic regression, we determined the association between saddle PE and the odds of in-hospital mortality. Cost and LOS were compared between groups using a generalized linear regression model (gamma-distributed error and log-link). All analyses were adjusted for age ≥ 80 years and sex. Statistical analyses were performed using SPSSv23 (IBM Corp., Armonk, NY), with a p value < 0.05 considered statistically significant. This study was designated nonhuman research by the institutional review board at the Medical University of South Carolina.

Results

We identified 10,660 acute PE admissions in adults with comorbid cancer between January 1st, 2013 and December 31st, 2014 (Table 1). Of these, 4.5% (n = 475) had saddle PE. The overall median age was 67 (IQR = 58.0–76.0) and 48.9% (n = 5212) were male. In-hospital mortality occurred in 6.1% (n = 645) of patients; while mean LOS and hospital costs were 5.4 (SD = 5.3) days and $13,263 (SD=$15,471). Upon multivariate adjustment, saddle PE was associated with 51% higher odds of in-hospital mortality (p = 0.02; Table 2). LOS was ~ 1 day longer and cost were ~ $4500 higher among those with saddle PE (p < 0.001 for both).

Table 1 Demographics of patients with pulmonary embolism and comorbid cancer

	Total N = 10,660 n (%)	Saddle PE N = 475 n (%)	Non-saddle PE N = 10,185 n (%)
Patient characteristics			
Age, median (IQR)	67 (58–76)	65 (57–74)	67 (58–76)
Male	5212 (48.9)	238 (50.1)	4974 (48.8)
Race			
White	7647 (75.8)	369 (81.3)	7278 (75.5)
Black	1493 (14.8)	58 (12.8)	1435 (14.9)
Other	954 (9.5)	27 (5.9)	927 (9.6)
Hospital characteristics			
Size			
Small	1589 (14.9)	63 (13.3)	1526 (15.0)
Medium	2835 (26.6)	133 (28.0)	2702 (26.5)
Larger	6236 (58.5)	279 (58.7)	5957 (58.5)
Type of hospital			
Rural	995 (9.3)	34 (7.2)	961 (9.4)
Urban nonteaching	3259 (30.6)	133 (28.0)	3126 (30.7)
Urban teaching	6406 (60.1)	308 (64.8)	6098 (59.9)
Region			
Northeast	2295 (21.5)	91 (19.2)	2204 (21.6)
Midwest	2656 (24.9)	122 (25.7)	2534 (24.9)
South	3809 (35.7)	170 (35.8)	3639 (35.7)
West	1900 (17.8)	92 (19.4)	1808 (17.8)
Comorbidities			
Hypertension	5967 (56.0)	269 (56.6)	5698 (55.9)
Congestive heart failure	1124 (10.5)	41 (8.6)	1083 (10.6)
Diabetes	2057 (19.3)	96 (20.2)	1961 (19.3)
Obesity	1222 (11.5)	88 (18.5)	1134 (11.1)
Vascular disease	512 (4.8)	29 (6.1)	483 (4.7)
Renal failure	979 (9.2)	34 (7.2)	945 (9.3)
Number of comorbidities[a], median (IQR)	4 (2–5)	4 (2–5)	4 (2–5)
Solid tumor	9,302 (87.3)	414 (87.2)	8888 (87.3)
Hematologic malignancy	1358 (12.7)	61 (12.8)	1297 (12.7)
Metastatic disease	5225 (49.0)	225 (47.4)	5000 (49.1)

IQR interquartile range, *PE* pulmonary embolism

[a]Identified using Agency for Healthcare Research and Quality (AHRQ)-29 comorbidity coding

Discussion

In this study of ~ 11,000 acute PE admissions with comorbid cancer, saddle PE was associated with increased odds of in-hospital mortality. Furthermore, LOS was longer and costs were higher for admissions with saddle PE.

Table 2 Outcomes of admissions for patients with pulmonary embolism and comorbid cancer

Outcome	Saddle PE $N=475$	Non-saddle PE $N=10,185$	Effect size (95% CI)[a]	p value
Odds ratio				
In-hospital mortality, n (%)	41 (8.6)	604 (5.9)	1.51 (1.08–1.21)	0.02
Mean difference				
LOS, days (mean ± SD)	6.0 ± 4.8	5.3 ± 5.3	0.80 (0.35–1.21)	< 0.001
Cost, 2017US$ (mean ± SD)	$17,404±$16,621	$13,069±$15,390	$4469 ($3235–$5703)	< 0.001

CI confidence interval, *LOS* length-of-stay, *SD* standard deviation, *US$* United States dollars

[a]Analyses adjusted for age ≥ 80 years and sex

An analysis from the 2009–2011 NIS found no difference in the occurrence of unadjusted in-hospital mortality among admissions with saddle versus non-saddle PE (3.62% versus 3.19%, $p=0.73$) [4]. However, LOS was ~2 days longer in those with saddle PE ($p<0.001$). Although limited by small sample size, two additional studies evaluated mortality among patients with saddle PE; with one study reporting that that none of the 14 included patients died while hospitalized and the other reporting that only one of the 17 included patients experienced mortality at 2 weeks [8, 9]. In comparison, the occurrence of in-hospital mortality is ~4 to 7% among all patients with PE [4, 10, 11]. A notable difference between the aforementioned studies of saddle PE and our own was that we only included patients with comorbid cancer.

The association between saddle PE and mortality in patients with comorbid cancer has been assessed in several small, single center studies [5, 12]. Yusuf et al. evaluated 52 patients with PE and compared outcomes among those with saddle (defined as main pulmonary artery thrombus) versus non-saddle PE [5]. A total of 18 patients with saddle PE were included. Although there was no difference in mortality at 30 days (11.1% versus 8.8%, $p>0.99$), mortality at 1 year was higher among those with saddle versus non-saddle PE (83.2% versus 41.2%, $p=0.004$) [5]. Furthermore, Banala et al. identified 193 patients with cancer, including 7 patients with saddle PE, referred to an emergency department (ED) after being diagnosed with incidental PE (i.e., PE discovered during routine imaging for cancer treatment or screening) [12]. Thirty-day mortality was numerically higher in patients with saddle versus non-saddle PE (43% versus 7%). Moreover, the relative risk of 30-day mortality was 33.5 (95% CI 3.1–357.4) for those with saddle PE versus those with subsegmental PE. Interestingly, although 70% of patients in this study were discharged home from the ED, all patients with saddle PE were admitted to the hospital. We also observed increased utilization of healthcare resources among patients with saddle PE in our study, as LOS was longer and costs were higher in these patients. These studies taken with our own suggest PE location may be a prognostic factor among patients with cancer. If saddle PE is a risk factor for increased healthcare resource utilization and mortality, those with saddle PE may require more aggressive treatment upon presentation (e.g., treatment under the care of a multidisciplinary Pulmonary Embolism Response Team [PERT], [13]). However, the prognostic significance of saddle PE in patients with cancer should be confirmed in future studies that would ideally be prospective and identify additional predictors of mortality and healthcare resource utilization in these patients.

The ability of several PE clinical prediction rules to prognosticate 30-day mortality has been evaluated in patients with cancer [14, 15]. Most of these rules include factors such as bleeding risk, hemodynamic status, renal disease, and other comorbidities to prognosticate 30-day post-PE mortality [15]. In a meta-analysis, 9 of 10 rules demonstrated sensitivities of ≥ 88% for 30-day mortality. However, the meta-analysis only included 8 studies and half of the studies evaluated < 300 patients; thus, data on these rules in patients with active cancer are limited. Future research should focus on the development and validation of risk-stratification rules in patients with cancer and PE location may be a factor to consider as risk-stratification rules are developed for use in this population. These rules would ideally be developed using clinical data collected prospectively.

Our study has several limitations. Similar to other claims databases, the NIS does not contain vital sign data; thus, we could not account for hemodynamic instability upon PE presentation. We also could not restrict our analysis to only patients with active (as opposed to a history of) cancer or evaluate the impact of cancer type, stage, or treatment on outcomes. Moreover, misclassification bias could have been introduced by errors in coding, clinician misdiagnoses, and interference due to financial incentives, as data in the NIS are not specifically generated for research purposes [6, 7, 16]. For example, we were reliant on diagnostic coding to define our cohorts. While the coding used to identify all PE patients has been deemed appropriate for the identification of events in claims data, using coding to identify saddle PE has not been extensively validated [17]. When interpreting our results, it is important to remember that, like all analyses of claims data, our study was susceptible to misclassification bias.

Conclusion

In this retrospective study of admissions for acute PE in patients with comorbid cancer, saddle PE was associated with a higher odds of in-hospital mortality. PE location may be a factor to consider as risk-stratification rules are developed for use in patients with cancer.

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Compliance with ethical standards

Conflict of interest ERW has received research funding from Pfizer Inc. AP and IR have nothing to disclose.

Ethical standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required. This article does not contain any studies with animals performed by any of the authors. This study was designated nonhuman research by the institutional review board at our institution.

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