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Short-term outcomes of pulmonary embolism: A National Perspective

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Background: Pulmonary embolism (PE) is associated with significant morbidity and mortality in hospitalized patients. Real time data on 90-day mortality, bleeding, and readmission is sparse.

Methods: The study cohort was derived from the National Readmission Data (NRD) 2013 to 2014. PE was identified using International Classification of Diseases, ninth Revision (ICD-9-CM) code 415.11/3/9 in the primary diagnosis field. Any admission within 90 days of primary admission was considered a 90-day readmission. Readmission etiologies were identified by ICD-9 code in the primary diagnosis field. Co-primary outcomes were 90-day readmission and 90-day mortality.

Results: We identified 260 614 patients with primary admission PE, 55 659 (21.36%) patients were readmitted within 90 days. Most of them were of old age (age ≥ 65 years: 49.04%) and females (52.78%). Among the etiologies of readmission pulmonary disorders (22.94%) (Including recurrent PE 7.33%), malignancies (8.31%), and bleeding disorders (6.75%) were the most important causes of 90-day readmissions. On multivariate analysis, higher readmission rates and 90 days mortality were seen in patients with heart failure, chronic pulmonary disease, Anemia, malignancy, and with higher Charlson score. Patients with longer length of stay during primary admission and who discharged to short/long-term facility were more likely get readmitted and die in 90 days. Paradoxically, obese patients showed an inverse relationship with co-primary outcomes.

Conclusions: Older female patients were more likely to have a pulmonary embolism. High-risk groups such as heart failure, chronic pulmonary disease, anemia, and malignancy need to be given extra attention to prevent worse outcomes.

KEYWORDS
comorbidities, mortality, outcomes, pulmonary embolism, readmission

1 | INTRODUCTION

Pulmonary embolism (PE) is associated with significant morbidity and mortality in hospitalized patients. The incidence of pulmonary embolism was nearly 69 cases per 100 000 persons in 1998.[1] With increased recognition of PE using the more sensitive computed tomography pulmonary angiogram in 1998, the incidence of PE has increased to 112.3 cases per 100 000 persons by year 2011.[2] Although the financial burden associated with PE alone is not known,

venous thromboembolism (VTE) has been known to cost the US healthcare system nearly $500 million dollars per year,[3] with an estimated mean cost for a PE hospitalization of $16 644 and mean cost of readmission of $14 722.[3,4]

The American College of Chest Physicians recommends anticoagulation for 3 months after a proximal DVT or PE that is provoked by a surgery or a transient non-surgical risk factor. For unprovoked DVT or PE, they recommend anticoagulation for 3 months if low risk of bleeding.[5] Treatment of PE with anticoagulation is also associated with the risk of bleeding. Limited real time data exist in the current

literature regarding the short-term outcomes of PE patients. We decided to analyze outcomes including readmission, mortality, and bleeding over 90 days.

2 | METHODS

2.1 | Data source

The study cohort was derived from the National Readmission Database (NRD) of 2013 and 2014, a subset of the Healthcare Cost and Utilization Project (HCUP) sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NRD is one of the largest publicly available all-payer inpatient care database in the United States. Unweighted, the NRD contains data from approximately 15 million discharges each year and weighted, it estimates roughly 35 million discharges in the United States. NRD represents 49.1% of total US hospitalizations. Patients were tracked using variable "NRD_visitlink" and time between two admissions was calculated by subtracting variable "NRD_DaysToEvent." Time to readmission was calculated by subtracting length of stay of index admissions to time between two admissions. The details regarding the NRD data are available online.[6]

2.2 | Data

Pulmonary embolism hospitalizations were classified as those with a principal discharge diagnosis of Pulmonary Embolism based on the International Classification of Diseases, ninth revision, Clinical Modification (ICD 9-CM) code 415.11/3/9. We only included first admission of the year and excluded patients with missing information on age, sex, mortality, and age ≤ 18. We also excluded October, November, and December admissions, as we did not have follow-up data on them. We identified total of 260 614 primary admissions. Patients who were readmitted to the hospital within 90 days during same calendar year were further evaluated (n = 55 659). (Figure S1, Supporting information).

2.3 | Outcomes

Co-primary outcomes were 90-day readmission and 90-day mortality. Secondary outcome was combination of 90-day mortality, gastrointestinal bleeding, and intracranial hemorrhage. The causes of readmissions were identified using ICD-9 codes in primary diagnosis field. We identified 2064 ICD 9 diagnosis codes and combined the ones with similar diagnoses to make clinically important groups, which were verified by two co-authors (Purav Shah and Varun Kumar) (**Table S1**). We also did subgroup analysis for surgical PEs. PE patients with surgical DRG codes in past 90 days (previous hospitalization) were identified as surgical PEs.

2.4 | Demographics, comorbidities, and other independent variables

NRD variables were used to identify patients' demographic characteristics including age; gender; hospital characteristics such as bed

size and teaching status; other patient specific characteristics including median household income category for patient's zip code, primary payer, admission type, admission day, and discharge disposition.[6] Comorbid variables provided by HCUP indicate different comorbidities by using *ICD-9-CM* diagnoses and the diagnosis-related group in effect on the discharge date.[7] These comorbidities are not directly related to the principal diagnosis or the main reason for admission and are likely to have originated before the hospital stay. Severity of comorbid conditions defined using Deyo modification of Charlson comorbidity index (CCI), which contains 17 comorbid conditions with differential weights. The score ranges from 0 to 33, with higher scores corresponding to greater burden of comorbid diseases[8] (Table S2).

2.5 | Statistical software and methods

SAS 9.4 (SAS Institute Inc., Cary, North Carolina) was utilized for analyses. Differences between categorical variables were tested using the χ^2 test and differences between continuous variables were tested using student's *t* test. We used cox proportional regression to adjust for confounder and consider timing in consideration too. We ran Kaplan Meyer curve for every outcome before running final multivariate models (Figures S2-S4). In multivariate models for readmission, 90 day mortality and 90 day mortality/ICH/GI bleed, we included patient level variables like age, sex, primary payer [Medicare/Medicaid as reference, private insurance including HMO, self-pay]; comorbidities like obesity, diabetes, peripheral vascular disease, renal failure, anemia; disposition during principal admission (facility vs home), median household income (0-25 percentile as reference, 26-50 percentile, 51-75 percentile, 76-100 percentile); length of stay (≤2 as reference, 3-4, 5-6, >6) and hospital characteristics such as hospital bed size(small as reference, medium, large), hospital teaching status (teaching vs non-teaching). Multivariate model for readmission was run only on patients who survived index admission. We also ran post hoc analysis of 30-day readmission for validation of our results (Table S3).

3 | RESULTS

We identified 260, 614 patients with primary admission of pulmonary embolism in year 2013-14, out of which 55, 659(21.36%) patients were readmitted within 90 days post discharge. Cohort consists of mainly old age (age ≥ 65 years) and female (52.78%) patients. Most common comorbidities were hypertension (58.02%), chronic pulmonary disease (24.79%), diabetes (21.97%), and obesity (21.75%). Majority of the patients were admitted to large hospitals (57.46%), teaching hospitals (53.03%), during weekdays (77.5%), and covered Medicaid/Medicare (61.79%). Average length of stay during primary admission was 5.09 days with 13.6% patients discharged to short/long term facility and 3.12% died during primary admission only (Table 1).

Pulmonary disorders (22.94%) were the most common causes of readmission. About 7.33% of these readmissions were secondary to recurrent PE. Malignancy contributed 8.31%, and bleeding was

TABLE 1 Baseline characteristics of overall pulmonary embolism and surgical pulmonary embolism

	Overall pulmonary embolism				Surgical pulmonary embolism			
	Readmission				Readmission			
Variables	No	Yes	Overall	P value	No	Yes	Overall	P value
Unweighted index admission	89 143(78.6%)	24 339(21.5%)	113 482		10 365(73.1%)	3819(26.9%)	14 184	
Weighted index admission	204 955(78.6%)	55 659(21.4%)	260 614		22 472 (72.9%)	8371 (27.4%)	30 844	
Patient level variables								
Age				<0.001				0.5321
18-34	7.57	5.55	7.14		4.93	5.07	4.97	
35-49	16.24	13.95	15.76		11.94	12.19	12.01	
50-64	28.06	28.06	28.06		29.44	30.17	29.64	
65-79	30.85	32.82	31.27		37.81	37.07	37.61	
≥80	17.28	19.61	17.77		15.89	15.5	15.78	
Gender				<0.001				0.7899
Male	47.73	45.35	47.22		46.01	46.18	46.06	
Female	52.27	54.65	52.78		53.99	53.82	53.94	
Deyo/Charlson score[a]				<0.001				<0.001
0	43.81	23.28	39.42		39.72	22.33	35	
1	24.13	22.76	23.84		22.75	20.83	22.23	
≥2	32.06	53.96	36.74		37.53	56.84	42.77	
Comorbidities								
Obesity[b]	22.16	20.26	21.75	<0.001	19.96	19.23	19.76	0.1499
History of hypertension[b]	56.77	62.59	58.02	<0.001	61.41	65.49	62.52	<0.001
History of diabetes[b]	20.6	27.02	21.97	<0.001	21.33	28.69	23.33	<0.001
Heart failure[f]	11.66	20.3	13.5	<0.001	11.39	18.96	13.44	<0.001
History of chronic pulmonary disease[b]	22.5	33.23	24.79	<0.001	21.3	28.59	23.28	<0.001
Peripheral vascular disease[b]	4.95	6.72	5.33	<0.001	6.06	9.3	6.94	<0.001
Renal failure	9.47	14.34	10.51	<0.001	9.54	15.29	11.1	<0.001
Neurological disorder or paralysis	8.81	11.94	9.48	<0.001	8.72	11.22	9.4	<0.001
Anemia[b]	16.6	25.97	18.6	<0.001	26	32.74	27.83	<0.001
Hematological or oncological malignancy[b]	11.55	23.41	14.08	<0.001	17.99	28.33	20.79	<0.001
Rheumatoid arthritis or another collagen vascular[b]	3.48	4.61	3.72	<0.001	3.06	4.69	3.5	<0.001
Depression, psychosis or substance abuse[b]	19.58	24.96	20.73	<0.001	16.45	21.13	17.72	<0.001
Median household income category for patient's zip code[c]				<0.001				<0.001
0-25th percentile	25.05	29.74	26.05		24.9	28.58	25.9	
26-50th percentile	27.25	27.27	27.25		26.55	26.64	26.58	
51-75th percentile	24.35	22.74	24.01		24.93	23.08	24.43	
76-100th percentile	21.72	18.84	21.1		22.11	20.65	21.72	
Primary payer				<0.001				<0.001
Medicare/Medicaid	59.02	72	61.79		63.06	70.75	65.14	
Private including HMO	32.36	20.92	29.92		31.03	25.03	29.4	
Self-pay/no charge/other	8.52	6.95	8.18		5.79	4.11	5.33	
Hospital characteristics								
Hospital bed size[d]				<0.001				<0.001
Small	16.21	13.78	15.69		15.44	12.54	14.65	
Medium	27.15	25.72	26.84		26.54	24.6	26.02	
Large	56.64	60.49	57.46		58.02	62.86	59.33	
Hospital teaching status[e]								<0.001
Non-teaching	47.74	44.09	46.97		41.05	37.22	40.01	
Teaching	52.26	55.91	53.03		58.95	62.78	59.99	

TABLE 1 (Continued)

Variables	Overall pulmonary embolism				Surgical pulmonary embolism			
	Readmission				Readmission			
	No	Yes	Overall	P value	No	Yes	Overall	P value
Admission day				0.6491				0.996
Weekdays	77.48	77.57	77.5		77.26	77.26	77.26	
Weekend	22.52	22.43	22.5		22.74	22.74	22.74	
Disposition								<0.001
Home	83.76	78.31	82.6		77.23	73.78	76.29	
Facility	11.75	20.39	13.6		18.08	25.32	20.05	
In hospital mortality	3.97	0	3.12		4.37	0	3.18	
Length of stay	4.82 ± 0.02	6.08 ± 0.04	5.09 ± 0.02	<0.001	5.04 ± 0.05	6.08 ± 0.09	5.35 ± 0.05	<0.001
Transfusion	3.96	7.38	4.69	<0.001	5.93	9.21	6.82	<0.001
Cardiac arrest	1.65	0.54	1.41	<0.001	1.73	0.6	1.43	<0.001
Cardiogenic shock	0.95	0.52	0.85	<0.001	1.23	0.64	1.07	<0.001
Use of vasopressor	0.45	0.29	0.41	<0.001	0.03	0.02	0.02	0.7672
Intracranial hemorrhage (ICH)	0.29	0.25	0.29	0.1096	0.55	0.7	0.59	0.142
Gastrointestinal bleed (GI bleed)	1.5	2.18	1.64	<0.001	1.51	2.51	1.78	<0.001
Other bleeding complications	0.47	0.64	0.51	<0.001	1.28	1.23	1.26	0.7306
Any bleed	2.23	2.99	2.39	<0.001	3.26	4.35	3.56	<0.001
Hemorrhage requiring transfusion	0.64	1.03	0.73	<0.001	0.98	1.5	1.12	<0.001

Abbreviation: HMO, Health Maintenance Organization.
[a] Charlson/Deyo comorbidity index (CCI) was calculated as per Deyo classification.
[b] Variables are AHRQ comorbidity measures.
[c] Represents a quartile classification of the estimated median household income of residents in the patients ZIP code, derived from ZIP code-demographic data obtained from Claritas. The quartiles are identified by values of 1 to 4, indicating the poorest to wealthiest populations. Because these estimates are updated annually, the value ranges vary by year. https://www.hcup-us.ahrq.gov/db/vars/zipinc_qrtl/nrdnote.jsp.
[d] The bed size cutoff points divided into small, medium, and large have been done so that approximately one-third of the hospitals in a given region, location, and teaching status combination would fall within each bed size category. https://www.hcup-us.ahrq.gov/db/vars/hosp_bedsize/nrdnote.jsp.
[e] A hospital is considered to be a teaching hospital if it has an AMA-approved residency program, is a member of the Council of Teaching Hospitals (COTH) or has a ratio of full-time equivalent interns and residents to beds of 0.25 or higher. https://www.hcup-us.ahrq.gov/db/vars/hosp_ur_teach/nrdnote.jsp.
[f] Comorbidity was identified by appropriate ICD 9 CM diagnosis codes in secondary diagnosis field.

associated with 6.75% of the 90-day readmissions. About 3.68% patients were readmitted due to a gastrointestinal bleeding and 0.82% patients had an intracranial bleed. About 2.25% patients were admitted due to a non-gastrointestinal or a non-intracranial bleed. Cardiovascular disorder (12.81%), non-respiratory tract infections (10.48%), and neurologic disorders (4%) were the other significant etiologies of readmissions (Table 2) (Figure 1).

In the multivariate analysis, malignancies were associated with the highest readmission rates (HR 1.63, CI 1.56-1.70, P < 0.001), followed by longer length of stay (LOS <2 days reference; LOS >6 days HR 1.47, CI 1.42-1.53, P < 0.001), higher Charlson/Deyo comorbidity score (score 1 HR 1.40, CI 1.34-1.46, P < 0.001; score ≥ 2 HR 1.78, CI 1.68-1.87, P < 0.001), heart failure (HR 1.30, CI 1.25-1.35, P < 0.001), anemia (HR 1.27, CI 1.23-1.31, P < 0.001), and neurologic disorders and paralysis (HR 1.17, CI 1.12-1.22, P < 0.001). Females had a slightly higher risk of readmission compared to males (HR 1.03, CI 1.01 1.06, P = 0.012), and obesity was associated with lower readmission rates (HR 0.86, CI 0.83-0.89, P < 0.001) (Table 3). Post hoc analysis of 30-day readmission showed similar results (Table S3).

The 90-day mortality rate was 4.92% (12 820 out of the 260 614 patients died) (Figure S2). Ninety-day mortality rates were highest in

patients with underlying malignancies (HR 3.29, CI 2.91-3.73, P < 0.001) and a Charlson/Deyo comorbidity index ≥2 (HR 3.38, CI 2.76-4.13, P < 0.001). Mortality rates were also higher in patients with heart failure (HR: 1.35, CI: 1.21-1.51, P < 0.001), chronic pulmonary disease (HR: 1.16, 1.05-1.28, p-0.003), and anemia (HR 1.30, CI 1.19-1.44, P < 0.001). Compared to Medicare/Medicaid, lower mortality rates were seen in patients with private insurance and HMOs (HR 0.94, CI 0.83-1.06, P = 0.311) and self-paid/other insurance (HR 0.77, CI 0.61-0.98, P = 0.03). Longer length of stay and discharge to short/long term facility were associated with higher 90-day mortality (Table 4). Similar results were observed for secondary outcomes (Table 4).

Among patients who underwent a surgical intervention in the preceding 90 days, the risk factors for readmission with PE were very similar to the overall PE cohort. We identified 30 844 patients with surgical intervention, of which 8371 (27.4%) were readmitted within 90 days. Over half of the patients were over the age of 65 and 46.18% were males. The comorbidities associated with PE related readmissions in the surgical PE subgroup were similar to the general PE population (Table 1).

The results of the multivariate analysis for patients readmitted for surgical PE were also similar to the general population. Malignancy

TABLE 2 Etiologies of readmissions among overall pulmonary embolism

Etiology	Value (%)
Pulmonary disorders	22.94
Asthma	0.76
COPD exacerbation and related disorders	2.60
Respiratory failure	2.43
Respiratory infections	5.12
Pulmonary embolism	7.33
Others	4.70
Infections	10.48
Neoplasms	8.31
Solid	7.49
Liquid	0.82
Hematological disorders	3.58
Endocrine disorders	1.10
Rheumatic/autoimmune/musculoskeletal	2.45
Kidney and urinary tract disorders	4.97
Electrolyte and Acid-Base disorders	1.47
Neurologic/psychiatric disorders	6.67
Neurological	4.00
Psychiatric	2.67
Cardiovascular disorders	12.81
Heart failure	5.08
CAD/IHD	1.61
Rhythm disorder	2.38
Valvular disorder	0.23
Hypertension and related complications	0.71
Others	2.80
Other vascular disorders	3.62
Gastrointestinal disorders	7.00
Trauma/fracture/poisoning	1.69
Others	3.58
Bleeding	6.75
Intracranial hemorrhage	0.82
GI bleed	3.68
Any bleed	2.25

Abbreviations: CAD, coronary artery disease; IHD, ischemic heart disease.

(HR 1.47, CI 1.33-1.67 $P < 0.0001$), heart failure (HR 1.34, CI 1.22 1.47, $P < 0.0001$). LOS >6 days (HR 1.38, CI 1.26-1.52, $P < 0.0001$) and higher Charlson/Deyo comorbidity score (Score 1 HR 1.33, CI 1.20-1.49, $P < 0.0001$ and score ≥ 2 HR 1.59, CI 1.40-1.82 $P < 0.0001$) were associated with the highest 90-day readmission rates. The multivariate for 30-day readmission also showed similar results (Table 3).

4 | DISCUSSION

Our primary outcome was to find the 90-day readmission rates and mortality in patients admitted with a primary diagnosis of PE. The 90-day readmission rate in our study was 21.36%, which was much lower than the 58.6% 90-readmission rates reported by Spyropoulos et al in 2007.[4] Although unclear, one of the major reasons could be better treatment options with the introduction of the direct factor Xa inhibitors in 2011, which have been shown to be non-inferior to vitamin K antagonists but with a lower bleeding risk.[9,10] With no need for weekly INR monitoring, patient compliance has also improved with direct factor Xa inhibitors.[11] The all-cause 90-day mortality rate following first admissions was 4.92% (12 820 of 260 614 patients admitted with PE initially died) whereas the mortality rate in readmitted patients was significantly higher at 23.03%. The 30-day all-cause mortality in the EMPEROR-trial was 5.4%, consistent with our analysis.[12]

Obesity was associated with a lower risk of 90-day readmission (HR 0.86, CI 0.83-0.89, $P < 0.001$) and mortality (HR 0.70, CI 0.61-0.80, $P < 0.001$). Although, several studies have shown obesity to be an independent predictor for pulmonary embolism, the mortality rate remains low.[13,14] This "obesity paradox" has been seen in several other diseases, especially heart failure.[15,16] The mechanism behind this is not clearly understood.

Malignancy increased the risk of 90-day readmission (HR 1.63, CI 1.56-1.70, $P < 0.001$). About 8.31% of the 90-day readmissions were related to malignancy with solid tumors contributing 7.49% of these readmissions. Malignancy itself is an independent risk factor for VTE with an odds ratio as high as 6%.[17] While the HR of 90-day mortality and bleeding was 1.81 in our study, older studies have showed a bleeding HR ranging from 0.9% to 4.5%.[18]

A study by Heit et al also showed limb paralysis to be an independent risk factor for VTE (OR 3, 95% CI 1.3-7.4).[17] We found that neurological disorders were associated with a higher risk of readmission, constituting 4% of the readmissions. Although likely, no relationship was established between immobilization and the increased risk of readmission for PE because of the small number of patients in this cohort.

A history of chronic pulmonary disease was also associated with a higher risk of 90-day readmission and mortality. They had a 16% higher risk of readmission compared to patients without pulmonary disease. A Canadian meta-analysis showed that up to 1 in 4 patients hospitalized for COPD could have a PE.[19] This was confirmed by another French study, which showed a 25% prevalence of PE in patients admitted with severe COPD.[20] Several other studies have shown COPD to be an independent risk factor for PE.[21] With such high prevalence of PE in COPD patients, clinicians should have a low threshold to screen for PE in the appropriate clinical setting. COPD exacerbations contributed to 2.60% of the 90-day readmissions. Respiratory infections have also been associated with an increased risk of PE.[22] Respiratory infections accounted for 2.43% of all 90-day readmissions in our analysis. Urinary tract infections have also been associated with a higher risk of PE. The risk reduced to baseline after 1 year.[22]

Ninety-day readmissions due to recurrence of PE were 7.33%. There are no recent data regarding PE recurrence rates after the use of NOACs. The 2-year recurrence rate of venous thromboembolism (DVT and PE) was 7.7% per year.[23] The 7, 30, and 180-day recurrence rates after an initial episode of VTE were 1.6%, 5.2%, and 10.1%.[17] The ICOPER study in 1999 showed a 7.9% recurrence rate of PE at
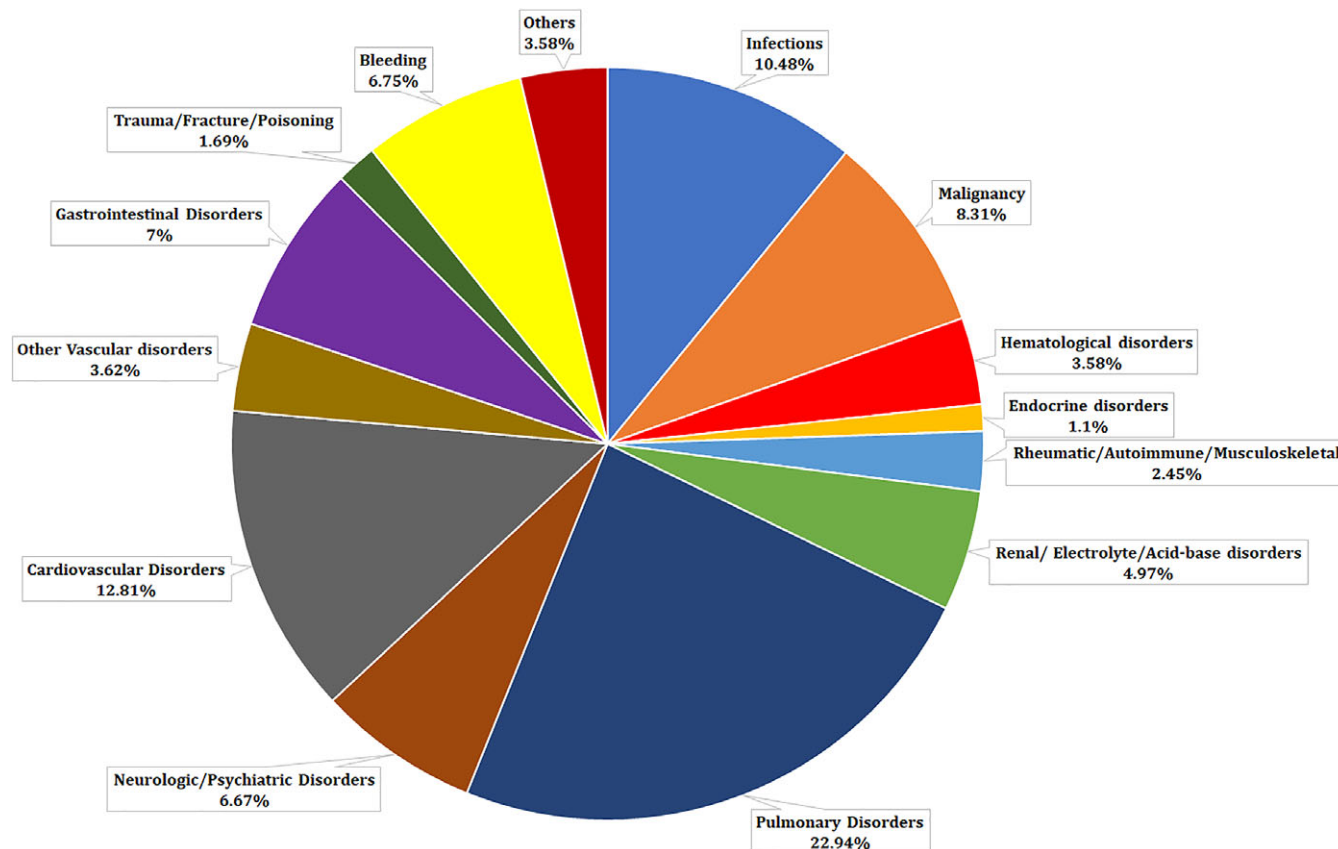
FIGURE 1 Etiologies of readmissions with overall pulmonary embolism

3 months. Our results were consistent with these findings (7.33% recurrence rate at 90-days).[21]

Bleeding is an important complication of anticoagulation treatment. We classified major bleeding as any intracranial bleed or gastrointestinal bleeding. All other bleeding complications were classified as "other bleeds." The incidence of intracranial bleeding in patients readmitted with PE was 0.25% and gastrointestinal bleeds was 2.18%. The incidence of patients readmitted with any bleed was 2.99%. Intracranial bleeds contributed 0.82% of readmissions; GI bleeding 3.68% and any bleeding contributed 2.25% of total 90-day readmissions. The 1996 ISCOAT trial showed an all-cause bleeding incidence due to of 6.8 per 3100 patient years. The study population was on warfarin or acenocoumarol.[24] With the introduction of direct factor Xa inhibitors, the incidence of major bleeding has decreased significantly compared with conventional vitamin K antagonist agents.[9,10] The oral direct thrombin inhibitor used in PE treatment also has a reversal agent now, thus improving the safety of these medications.[25] The 90-day mortality and major bleeding rates were significantly higher in patients with a higher Charlson/Deyo comorbidity score ≥ 2, anemia, hemato-oncologic malignancy, and patients discharged to a nursing facility. Obesity was associated with lower 90-day mortality and major bleeding rates.

The number of patients who died from PE in 2013 was 12 820, which translated into a mortality rate of 4.93%. In 1979, the number of people who died from PE was estimated at 35 754 falling to 24 947 in 1998.[26] The development of newer diagnostic techniques,

newer medications, lower bleeding rates, and risk stratification scores for PE treatment may be associated with this decrease in mortality from 1979 to 2013.[27] Our findings were also consistent with Kohn et al who showed similar 30- and 90-day mortality rates and 90-day readmissions using the Veterans Health Administration database.[28]

There are several limitations to this study. It is based on the National Readmission Database from the HCUP; although HCUP is well-designed, the data is limited by coding errors in the primary and readmission coding. Ninety-day readmission rates could not be calculated for patients hospitalized in the last 3 months of the calendar year, leaving approximately one quarter of admissions. Despite this, this is the largest population study for pulmonary embolism in the recent years incorporating data from 22 states accounting for 51.2% of total US population and 49.3% of all US hospitalizations.[29] Considering DRG code suggest either procedural status of admission or main diagnosis of admission, it would not be possible to identify primary cause of each readmission using DRG codes. We decided to use ICD-9 codes in primary diagnosis field to identify causes of readmission. Similar methodology was used by multiple researchers in multiple journals in past.

In conclusion, PE is a common cause of morbidity and mortality in hospitalized patients. With the recent advances in diagnosis and treatment, the morbidity and mortality has decreased significantly. The 90-day mortality and bleeding rates have decreased significantly in the recent years with use of newer anticoagulants and risk

TABLE 3 Multivariate analysis of 90-day and 30-day readmission of overall pulmonary embolism and surgical pulmonary embolism

Variables	Overall pulmonary embolism								Surgical pulmonary embolism							
	90-day readmission				30-day readmission				90-day readmission				30-day readmission			
	HR	LL	UL	P value	HR	LL	UL	P value	HR	LL	UL	P value	HR	LL	UL	P value
Age	0.99	0.99	0.99	<0.0001	0.99	0.99	0.99	<0.0001	0.99	0.99	0.99	<0.0001	0.99	0.99	0.99	<0.0001
Gender																
Male	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
Female	1.03	1.01	1.06	0.012	1.04	1.01	1.08	0.018	0.98	0.92	1.05	0.620	0.97	0.90	1.06	0.523
Deyo/Charlson score[a]																
0	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
1	1.40	1.34	1.46	<0.0001	1.40	1.32	1.48	<0.0001	1.33	1.20	1.49	<0.0001	1.31	1.14	1.50	0.000
≥2	1.78	1.68	1.87	<0.0001	1.79	1.67	1.92	<0.0001	1.59	1.40	1.82	<0.0001	1.51	1.27	1.78	<0.0001
Comorbidities																
Obesity[b]	0.86	0.83	0.89	<0.0001	0.85	0.81	0.88	<0.0001	0.89	0.81	0.97	0.006	0.89	0.80	0.99	0.039
History of hypertension[b]	1.05	1.02	1.08	0.001	1.04	1.00	1.08	0.029	1.06	0.98	1.14	0.160	1.06	0.96	1.16	0.248
History of diabetes[b]	1.05	1.02	1.09	0.004	1.08	1.03	1.13	0.001	1.14	1.05	1.24	0.002	1.13	1.02	1.25	0.025
Heart failure[f]	1.30	1.25	1.35	<0.0001	1.33	1.27	1.39	<0.0001	1.34	1.22	1.47	<0.0001	1.33	1.19	1.50	<0.0001
History of chronic pulmonary disease[b]	1.16	1.13	1.20	<0.0001	1.19	1.14	1.24	<0.0001	1.11	1.02	1.20	0.013	1.18	1.06	1.30	0.001
Peripheral vascular disease[b]	1.07	1.02	1.13	0.007	1.08	1.01	1.15	0.025	1.22	1.09	1.36	0.001	1.15	1.00	1.33	0.057
Renal failure	1.02	0.97	1.06	0.458	1.05	0.99	1.10	0.122	1.21	1.09	1.34	0.001	1.18	1.03	1.35	0.016
Neurological disorder or paralysis	1.17	1.12	1.22	<0.0001	1.17	1.11	1.23	<0.0001	1.09	0.98	1.21	0.120	1.10	0.96	1.25	0.186
Anemia[b]	1.27	1.23	1.31	<0.0001	1.31	1.26	1.36	<0.0001	1.12	1.04	1.20	0.002	1.14	1.05	1.25	0.003
Hematological or oncological malignancy[b]	1.63	1.56	1.70	<0.0001	1.76	1.66	1.85	<0.0001	1.47	1.33	1.64	<0.0001	1.60	1.40	1.82	<0.0001
Rheumatoid arthritis or another collagen vascular[b]	1.06	1.00	1.13	0.060	1.02	0.94	1.11	0.600	1.15	0.98	1.36	0.092	1.11	0.90	1.36	0.341
Depression, psychosis or substance abuse[b]	1.20	1.16	1.23	<0.0001	1.20	1.15	1.25	<0.0001	1.20	1.11	1.31	<0.0001	1.16	1.04	1.28	0.006
Median household income category for patient's zip code[c]																
0-25th percentile	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
26-50th percentile	0.94	0.91	0.98	0.001	0.94	0.90	0.98	0.006	0.94	0.86	1.02	0.155	0.93	0.83	1.04	0.210
51-75th percentile	0.94	0.90	0.97	<0.0001	0.94	0.90	0.98	0.006	0.93	0.85	1.02	0.118	0.91	0.81	1.02	0.109
76-100th percentile	0.90	0.87	0.94	<0.0001	0.92	0.88	0.97	0.001	0.94	0.85	1.03	0.185	0.99	0.88	1.11	0.801
Primary payer																
Medicare/Medicaid	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
Private including HMO	0.68	0.66	0.71	<0.0001	0.68	0.65	0.71	<0.0001	0.78	0.71	0.84	<0.0001	0.80	0.72	0.89	<0.0001
Self-pay/no charge/other	0.81	0.76	0.85	<0.0001	0.81	0.75	0.87	<0.0001	0.75	0.64	0.88	0.000	0.83	0.68	1.01	0.061
Hospital characteristics																
Hospital bed size[d]																

TABLE 3 (Continued)

| | Overall pulmonary embolism | | | | | | | | Surgical pulmonary embolism | | | | | | | |
| | 90-day readmission | | | | 30-day readmission | | | | 90-day readmission | | | | 30-day readmission | | | |
Variables	HR	LL	UL	P value	HR	LL	UL	P value	HR	LL	UL	P value	HR	LL	UL	P value
Small	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Medium	1.08	1.03	1.12	0.001	1.08	1.02	1.14	0.011	1.09	0.97	1.22	0.135	1.04	0.90	1.20	0.630
Large	1.11	1.07	1.16	<0.0001	1.12	1.06	1.18	<0.0001	1.17	1.06	1.30	0.003	1.12	0.98	1.27	0.092
Hospital teaching status[e]																
Non-teaching	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Teaching	1.08	1.05	1.11	<0.0001	1.09	1.06	1.13	<0.0001	1.05	0.98	1.12	0.151	1.03	0.95	1.12	0.494
Disposition																
Home	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Facility	1.24	1.19	1.28	<0.0001	1.24	1.19	1.30	<0.0001	1.16	1.07	1.25	0.001	1.08	0.97	1.20	0.159
Length of stay																
≤2	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
3-6	1.21	1.16	1.25	<0.0001	1.22	1.17	1.27	<0.0001	1.12	1.03	1.22	0.011	1.17	1.05	1.31	0.004
>6	1.47	1.42	1.53	<0.0001	1.53	1.46	1.61	<0.0001	1.38	1.26	1.52	<0.0001	1.44	1.27	1.62	<0.0001

Abbreviation: HMO, Health Maintenance Organization.

[a] Charlson/Deyo comorbidity index (CCI) was calculated as per Deyo classification.

[b] Variables are AHRQ comorbidity measures.

[c] Represents a quartile classification of the estimated median household income of residents in the patients ZIP code, derived from ZIP code-demographic data obtained from Claritas. The quartiles are identified by values of 1 to 4, indicating the poorest to wealthiest populations. Because these estimates are updated annually, the value ranges vary by year. https://www.hcup-us.ahrq.gov/db/vars/zipinc_qrtl/nrdnote.jsp.

[d] The bed size cutoff points divided into small, medium, and large have been done so that approximately one-third of the hospitals in a given region, location, and teaching status combination would fall within each bed size category. https://www.hcup-us.ahrq.gov/db/vars/hosp_bedsize/nrdnote.jsp.

[e] A hospital is considered to be a teaching hospital if it has an AMA-approved residency program, is a member of the Council of Teaching Hospitals (COTH) or has a ratio of full-time equivalent interns and residents to beds of 0.25 or higher. https://www.hcup-us.ahrq.gov/db/vars/hosp_ur_teach/nrdnote.jsp.

[f] Comorbidity was identified by appropriate ICD 9 CM diagnosis codes in secondary diagnosis field.

TABLE 4 Multivariate of 90-day mortality and 90-day mortality and bleeding among overall pulmonary embolism and surgical pulmonary embolism

| | Overall pulmonary embolism | | | | | | | | Surgical pulmonary embolism | | | | | | | |
| | 90-day mortality | | | | 90-day mortality/GI bleed/ICH | | | | 90-day mortality | | | | 90-day mortality/GI bleed/ICH | | | |
Variables	HR	LL	UL	P value	HR	LL	UL	P-value	HR	LL	UL	P-value	HR	LL	UL	P-value
Age	1.01	1.00	1.01	0.001	1.01	1.01	1.01	<0.0001	1.00	0.99	1.01	0.850	1.00	1.00	1.01	0.229
Gender																
Male	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
Female	0.96	0.88	1.05	0.388	0.92	0.87	0.97	0.001	1.10	0.88	1.38	0.408	0.93	0.81	1.06	0.280
Deyo/Charlson score[a]																
0	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
1	2.13	1.75	2.58	<0.0001	1.64	1.50	1.80	<0.0001	2.83	1.60	4.99	0.000	1.70	1.32	2.19	<0.0001
≥2	3.38	2.76	4.13	<0.0001	2.28	2.05	2.54	<0.0001	3.83	2.15	6.82	<0.0001	2.09	1.57	2.77	<0.0001
Comorbidities																
Obesity[b]	0.70	0.61	0.80	<0.0001	0.77	0.71	0.83	<0.0001	0.63	0.44	0.90	0.010	0.71	0.58	0.87	0.001
History of hypertension[b]	1.00	0.90	1.10	0.952	1.00	0.94	1.06	0.963	1.02	0.79	1.32	0.883	0.89	0.77	1.04	0.145
History of diabetes[b]	0.98	0.88	1.09	0.666	0.91	0.86	0.98	0.007	1.07	0.82	1.39	0.629	1.01	0.86	1.20	0.883
Heart failure[f]	1.35	1.21	1.51	<0.0001	1.08	1.01	1.16	0.034	1.39	1.04	1.87	0.028	1.11	0.92	1.34	0.290
History of chronic pulmonary disease[b]	1.16	1.05	1.28	0.003	0.96	0.90	1.02	0.175	1.01	0.78	1.31	0.918	0.87	0.74	1.02	0.092
Peripheral vascular disease[b]	1.12	0.96	1.31	0.154	1.13	1.03	1.24	0.013	1.75	1.25	2.47	0.001	1.34	1.07	1.68	0.010
Renal failure	1.00	0.88	1.14	0.983	0.91	0.84	0.99	0.027	1.38	0.99	1.91	0.054	1.20	0.97	1.49	0.098
Neurological disorder or paralysis	0.90	0.78	1.05	0.174	1.16	1.07	1.25	0.000	0.76	0.50	1.14	0.177	1.14	0.92	1.41	0.219
Anemia[b]	1.30	1.19	1.44	<0.0001	1.46	1.38	1.55	<0.0001	1.14	0.90	1.45	0.264	1.04	0.90	1.21	0.584
Hematological or oncological malignancy[b]	3.29	2.91	3.73	<0.0001	1.81	1.67	1.96	<0.0001	3.56	2.56	4.95	<0.0001	1.83	1.48	2.26	<0.0001
Rheumatoid arthritis or another collagen vascular[b]	1.17	0.95	1.44	0.130	1.05	0.92	1.19	0.484	0.92	0.48	1.74	0.788	1.13	0.80	1.60	0.495
Depression, psychosis, or substance abuse[b]	1.00	0.89	1.12	0.972	1.12	1.05	1.19	0.001	0.81	0.59	1.13	0.211	1.07	0.89	1.28	0.470
Median household income category for patient's zip code[c]																
0-25th percentile	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
26-50th percentile	0.89	0.79	1.01	0.066	0.94	0.88	1.01	0.098	0.87	0.64	1.19	0.382	0.93	0.77	1.11	0.416
51-75th percentile	0.90	0.80	1.02	0.096	0.92	0.86	0.99	0.027	0.86	0.62	1.17	0.333	0.89	0.74	1.08	0.236
76-100th percentile	1.03	0.91	1.17	0.601	0.91	0.84	0.98	0.015	0.97	0.71	1.33	0.859	0.84	0.69	1.03	0.093
Primary payer																
Medicare/Medicaid	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
Private including HMO	0.94	0.83	1.06	0.311	0.84	0.78	0.90	<0.0001	1.06	0.79	1.42	0.693	0.98	0.82	1.18	0.835
Self-pay/no charge/other	0.77	0.61	0.98	0.030	0.91	0.81	1.03	0.137	1.04	0.59	1.86	0.883	0.92	0.65	1.31	0.649
Hospital characteristics																
Hospital bed size[d]																
Small	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
Medium	0.98	0.85	1.14	0.795	1.10	1.01	1.21	0.036	0.98	0.65	1.47	0.918	1.19	0.92	1.54	0.193
Large	1.03	0.90	1.18	0.711	1.13	1.04	1.23	0.004	1.09	0.76	1.56	0.658	1.39	1.09	1.76	0.007

TABLE 4 (Continued)

| | Overall pulmonary embolism | | | | | | | | Surgical pulmonary embolism | | | | | | | |
| | 90-day mortality | | | | 90-day mortality/GI bleed/ICH | | | | 90-day mortality | | | | 90-day mortality/GI bleed/ICH | | | |
Variables	HR	LL	UL	P value	HR	LL	UL	P-value	HR	LL	UL	P-value	HR	LL	UL	P-value
Hospital teaching status[e]																
Non-teaching	Ref	Ref	Ref	Ref	Ref	Ref	Ref		Ref	Ref	Ref	Ref	Ref	Ref	Ref	
Teaching	1.17	1.07	1.28	0.001	1.18	1.12	1.24	<0.0001	1.20	0.95	1.52	0.134	1.11	0.96	1.28	0.156
Admission day																
Weekdays	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
Weekend	0.99	0.89	1.10	0.858	1.02	0.96	1.09	0.455	1.05	0.80	1.37	0.729	1.19	1.02	1.39	0.027
Disposition																
Home	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
Facility	1.60	1.45	1.78	<0.0001	1.46	1.37	1.56	<0.0001	1.43	1.10	1.85	0.008	1.34	1.14	1.57	<0.001
Length of stay																
≤2	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
3-6	1.47	1.28	1.68	<0.0001	1.41	1.31	1.53	<0.0001	1.30	0.93	1.82	0.128	1.32	1.07	1.61	0.008
>6	2.14	1.86	2.47	<0.0001	2.43	2.23	2.64	<0.0001	2.22	1.57	3.14	<0.0001	2.49	2.02	3.07	<0.0001

Abbreviation: HMO, Health Maintenance Organization; HR, Hazard Ratio; UL, Upper Limit; LL, Lower Limit.

[a] Charlson/Deyo comorbidity index (CCI) was calculated as per Deyo classification.

[b] Variables are AHRQ comorbidity measures.

[c] Represents a quartile classification of the estimated median household income of residents in the patients ZIP code, derived from ZIP code-demographic data obtained from Claritas. The quartiles are identified by values of 1 to 4, indicating the poorest to wealthiest populations. Because these estimates are updated annually, the value ranges vary by year. https://www.hcup-us.ahrq.gov/db/vars/zipinc_qrtl/nrdnote.jsp.

[d] The bed size cutoff points divided into small, medium, and large have been done so that approximately one-third of the hospitals in a given region, location, and teaching status combination would fall within each bed size category. https://www.hcup-us.ahrq.gov/db/vars/hosp_bedsize/nrdnote.jsp.

[e] A hospital is considered to be a teaching hospital if it has an AMA-approved residency program, is a member of the Council of Teaching Hospitals (COTH) or has a ratio of full-time equivalent interns and residents to beds of 0.25 or higher. https://www.hcup-us.ahrq.gov/db/vars/hosp_ur_teach/nrdnote.jsp.

[f] Comorbidity was identified by appropriate ICD 9 CM diagnosis codes in secondary diagnosis field.

stratification scores. Higher Charlson comorbidity index scores and women had a higher risk of readmission. Chronic pulmonary disease, malignancy, anemia, and longer length of stay during the primary admission also increased the risk of readmission. Malignancies, pulmonary diseases especially COPD, infections and bleeding disorders were the most common etiologies of readmission.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.