Henry Ford Health Henry Ford Health Scholarly Commons

Cardiology Articles

Cardiology/Cardiovascular Research

7-13-2022

Hospital procedural volume and outcomes with catheter-directed intervention for pulmonary embolism: a nationwide analysis

Ramy Sedhom

Ayman Elbadawi

Michael Megaly Henry Ford Health, mmegaly1@hfhs.org

Wissam A. Jaber

Scott J. Cameron

See next page for additional authors

Follow this and additional works at: https://scholarlycommons.henryford.com/cardiology_articles

Recommended Citation

Sedhom R, Elbadawi A, Megaly M, Jaber WA, Cameron SJ, Weinberg I, Mamas MA, and Elgendy IY. Hospital procedural volume and outcomes with catheter-directed intervention for pulmonary embolism: a nationwide analysis. Eur Heart J Acute Cardiovasc Care 2022.

This Article is brought to you for free and open access by the Cardiology/Cardiovascular Research at Henry Ford Health Scholarly Commons. It has been accepted for inclusion in Cardiology Articles by an authorized administrator of Henry Ford Health Scholarly Commons.

Authors

Ramy Sedhom, Ayman Elbadawi, Michael Megaly, Wissam A. Jaber, Scott J. Cameron, Ido Weinberg, Mamas A. Mamas, and Islam Y. Elgendy



Hospital procedural volume and outcomes with catheter-directed intervention for pulmonary embolism: a nationwide analysis

Ramy Sedhom (1)^{1†}, Ayman Elbadawi^{2†}, Michael Megaly³, Wissam A Jaber⁴, Scott J Cameron (1)⁵, Ido Weinberg⁶, Mamas A. Mamas^{7,8}, and Islam Y. Elgendy (1)⁹*

¹Department of Medicine, Albert Einstein Medical Center, Philadelphia, PA 19141, USA; ²Section of Cardiology, Baylor College of Medicine, Houston, TX 77030, USA; ³Division of Cardiology, Henry Ford Hospital, Detroit, MI 48202, USA; ⁴Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, GA 30322, USA; ⁵Section of Vascular Medicine, Department of Cardiovascular Medicine, Heart Vascular and Thoracic Institute, Cleveland Clinic Foundation, Cleveland, OH 44195, USA; ⁶Division of Cardiology, Massachusetts General Hospital, Boston, MA 02114, USA; ⁷Keele Cardiovascular Research Group, Centre for Prognosis Research, Keele University, Keele ST55BG, UK; ⁸Department of Cardiology, Royal Stoke University Hospital, Stoke-on-Trent ST46QG, UK; and ⁹Division of Cardiovascular Medicine, Gill Heart Institute, University of Kentucky, Lexington, KY 40536, USA

Received 30 April 2022; revised 20 June 2022; accepted 22 June 2022

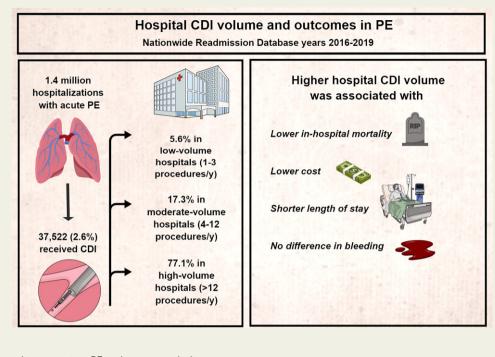
Aims	There is limited data on the association between hospital catheter-directed intervention (CDI) volume and outcomes among patients with acute pulmonary embolism (PE).
Methods and results	The Nationwide Readmissions Database years 2016–2019 was utilized to identify hospitalizations undergoing CDI for acute PE. Hospitals were divided into tertiles based on annual CDI volume; low-volume (1–3 procedures), moderate-volume (4–12 procedures) and high-volume (>12 procedures). The primary outcome was all-cause in-hospital mortality. Among 1 436 382 PE admissions, 2.6% underwent CDI; 5.6% were in low-volume, 17.3% in moderate-volume and 77.1% in high-volume hospitals. There was an inverse relationship between hospital CDI volume and in-hospital mortality (coefficient -0.344 , $P < 0.001$). On multivariable regression analysis, hospitals with high CDI volume were associated with lower in-hospital mortality compared with hospitals with low CDI volume (adjusted odds ratio [OR] 0.71; 95% confidence interval [CI] 0.53, 0.95). Additionally, there was an inverse association between CDI volume and length of stay (LOS) (regression coefficient -0.023 , 95% CI -0.027 , -0.019) and cost (regression coefficient -74.6 , 95% CI -98.8 , -50.3). There were no differences in major bleeding and 30-day unplanned readmission rates between the three groups.
Conclusion	In this contemporary observational analysis of PE admissions undergoing CDI, there was an inverse association between hospital CDI volume and in-hospital mortality, LOS, and cost. Major bleeding and 30-day unplanned readmission rates were similar between the three groups.

^{*} Corresponding author. Email: iyelgendy@gmail.com

[†] Both authors contributed equally to the study.

[©] The Author(s) 2022. Published by Oxford University Press on behalf of the European Society of Cardiology. All rights reserved. For permissions, please email: journals.permissions@oup.com.

Graphical Abstract



CDI, catheter-directed intervention; PE, pulmonary embolism.

Keywords

Pulmonary embolism • Catheter-directed intervention • Procedure volume

Introduction

Pulmonary embolism (PE) remains a leading cause of cardiovascular morbidity and mortality, with an estimated annual mortality rate of 4.1–4.5 deaths per 100 000 population in the United States (US) in 2017.¹ Traditionally, patients with low-risk [normotensive, no right ventricular (RV) strain] PE are treated with anticoagulation alone.² While, for those with high-risk PE (i.e. cardiac arrest or cardiogenic shock), reperfusion therapy, with systemic thrombolysis or surgical embolectomy, might be considered.^{2–4} Patients with intermediate-risk (RV strain, normotensive) are more challenging to treat, with care driven more by nuanced regional patterns, with anticoagulation, often with a catheter-directed intervention (CDI).⁵

In recent years, the utilization of CDI for the treatment of acute PE has increased reaching 2.5% of all PE cases.⁶ CDI is an alternative option in select patients with intermediate-high risk PE and may involve thrombus aspiration, thrombus maceration, targeted thrombolysis, or a combination of each. Two common types of CDI are catheter-directed thrombolysis (CDT) and catheter-directed embolectomy (CDE). CDT involves the administration of lower doses (around 1/20th of the systemic dose) of thrombolytic agents directly into the pulmonary arteries while CDE involves mechanical disruption or aspiration of the emboli. CDT can be combined with ultrasound (i.e. US-CDT) which disrupts fibrin strands allowing effective thrombolysis at lower doses.^{7–10} Studies have shown that CDT is associated with a lower risk of major and intracranial haemorrhage (ICH) compared with systemic thrombolysis.^{11–14} CDE has the advantage of

rapid mechanical extraction of the thrombus alongside avoidance of the use of thrombolytics¹⁵ and is most useful for proximal PE (i.e. main or lobar pulmonary arteries).^{16,17}

Prior studies have suggested that admission to high-volume hospitals was associated with lower 30-day and 1-year mortality, less readmission, lower cost, and shorter length of stay (LOS) among patients with acute PE.^{18,19} However, the data on the association between hospital CDI volume and outcomes in patients with acute PE are scarce. To better address these knowledge gaps, we aimed to examine the association between hospital CDI volume and shortterm outcomes from a contemporary nationally representative dataset.

Study design and methods

Data source

We used the Nationwide Readmissions Database (NRD) years 2016–2019. The NRD is sponsored by the Agency for Healthcare Research and Quality as a part of the Healthcare Cost and Utilization Project (HCUP).²⁰ The NRD contains discharge data from 30 geographically dispersed States, accounting for ~62% of the total US resident population and ~60% of all US hospitalizations. The NRD contains data from approximately 35 million weighted discharges. The NRD includes discharge records of patients treated at US community hospitals, excluding rehabilitation and long-term acute-care facilities. Patients with 1 or more inpatient

hospitalizations have verified patient linkage numbers that can be used to track individual patients across hospitals within a state. However, patient linkage numbers do not track hospitalizations across the calendar years.²⁰ We identified the cohort, procedures, and outcomes using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD 10-CM) and procedure (ICD 10-PCS) codes along. The codes used are summarized in Supplementary material online, *Table S1*.

Study population and exposure

The study cohort included hospitalized patients with acute PE who were \geq 18 years and underwent CDI defined as CDT or CDE. First, we identified hospitalizations with any diagnosis of acute PE using ICD 10-CM codes. Then, we identified those undergoing any form of CDI (i.e. CDT, CDE, or US-CDT) using the corresponding ICD 10-PCS codes (see Supplementary material online, Table S1). We excluded hospitalizations with acute limb ischaemia and acute ischaemic stroke, since these conditions might be treated with CDI as well as those with missing data on mortality. To examine 30-day readmission rates, we excluded those admitted in December of each calendar year (30-day readmissions for hospitalizations in December could not be obtained since the NRD does not cross the calendar year) and those who died during the index admission. We identified the proportion of urgent 30-readmissions due to PE recurrence using the ICD-10 codes of the first 3 recorded readmission diagnoses.

The main exposure was the annual hospital procedural volume for any CDI. Hospitals were divided into tertiles; low-volume (1–3 procedures/year), moderate-volume (4–12 procedures/year), and highvolume (>12 procedures/year).

Patient and hospital-level variables provided by HCUP NRD were used to identify demographics and baseline characteristics. The Elixhauser method was used to assess comorbidities.²¹ The other comorbidities were identified using appropriate ICD 10 CM codes (see Supplementary material online, *Table S1*). PE with critical illness was defined as PE with cardiogenic shock, mechanical ventilation, mechanical circulatory support [MCS], or vasopressors.^{22,23} The NRD is a publicly available database with de-identified hospitalization records; thus this study was exempt from institutional review board approval.

Outcomes

The primary outcome was the rate of all-cause in-hospital mortality. The secondary outcomes included (i) intracranial haemorrhage (ICH), (ii) non-ICH bleeding (i.e. respiratory tract haemorrhage, haemothorax, gastrointestinal haemorrhage, retroperitoneal bleeding, hematuria, hemarthrosis, hemopericardium, intraocular haemorrhage and unspecified post-procedural bleeding), (iii) 30-day unplanned readmissions, (iv) length of stay (LOS), and (v) cost.

Statistical analysis

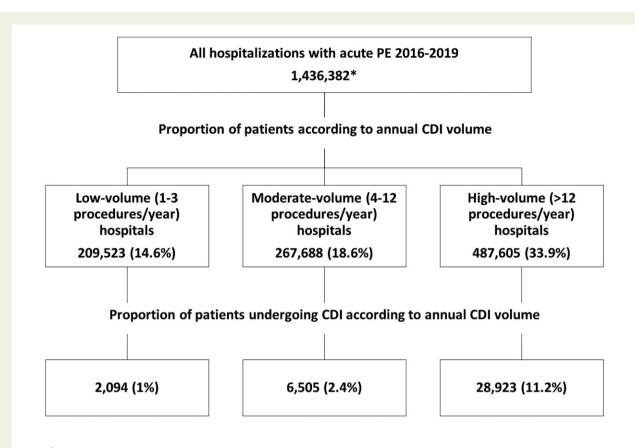
All analyses were conducted using multilevel complex analysis, to account for hospital clustering, weights, and stratification following the HCUP regulations. The hospital cost of an individual admission episode was calculated using total charge and cost-to-charge ratio data provided by the HCUP.^{20,24,} Continuous variables were summarized as medians and interquartile range (IQR) (25th and 75th percentiles) and compared with the Mann–Whitney U test. Categorical variables were displayed as frequencies and percentages and compared with Pearson's chi-square or Fisher's exact tests. All *P*-values are 2-sided with a significance threshold of <0.05. Statistical analyses were performed using STATA software for Windows (version 16.0. College Station, TX: StataCorp LLC) and IBM SPSS Statistics for Windows (version 27.0. Armonk, NY: IBM Corp).

Hospital CDI volume was analyzed both as a categorical and continuous variable. Curvilinear (quadratic) regression analysis was conducted to examine the association between hospital CDI volume as a continuous variable and the primary study outcome. Multivariable logistic regression analysis was conducted to account for the differences in patient- and hospital-related characteristics, PE severity and treatment modalities. We included the following variables in the regression model; age, sex, pregnancy, smoking history, morbid obesity, hypertension, diabetes mellitus, anemia, coagulopathy, pulmonary hypertension, chronic lung diseases, atrial fibrillation, heart failure, valvular heart disease, connective tissue disease, malignancy, chronic kidney disease, chronic liver disease, coronary artery disease, peripheral arterial disease, history of stroke, deep venous thrombosis (DVT), hospital size, hospital teaching status, hospital total PE volume, saddle PE, cor pulmonale, cardiogenic shock, vasopressors, MCS, mechanical ventilation, systemic thrombolysis, surgical embolectomy and CDE. We performed a sensitivity analysis for the primary outcome by excluding admissions who were transferred from another hospital. Additionally, multivariable linear regression analysis was conducted to examine the association between hospital CDI volume as a continuous variable and both LOS and cost. A falsification endpoint analysis was conducted to assess for residual confounders after the multivariable-adjusted analysis. For this analysis, we evaluated other outcomes that are not pathophysiologically related to acute PE or CDI, including sepsis, pressures ulcer and acute hepatitis.

Results

The total number of admissions with acute PE during the years 2016–2019 was 1 436 382 with 37 522 admissions (2.6%) who underwent CDI. Low-volume hospitals performed 1–3 (median 2, IQR 1–2), moderate-volume hospitals performed 4–12 (median 7, IQR 5–9) and high-volume hospitals performed 13–200 (median 23, IQR 17–37) procedures/year. Among all PE admissions, 209 523ad-missions (14.6%) were in low-volume, 267 688(18.6%) in moderate-volume and 487 605 (33.9%) in high-volume hospitals while the remainder of PE admissions were in hospitals which did not perform CDI. Among acute PE admissions in low-volume hospitals, 2094(1%) underwent CDI compared with 6505 (2.4%) in moderate-volume and 28 923 (5.9%) in high-volume hospitals. (*Figure 1*)

The baseline characteristics of the study cohort according to the CDI volume are shown in *Table 1*. Less than 1% of PE was associated with pregnancy. Admissions at low-volume hospitals had higher rates of anemia, coagulopathy, chronic pulmonary disease, atrial fibrillation, valvular heart disease, malignancy, and cardiogenic shock. Additionally, the utilization of systemic thrombolysis, CDE, inferior vena cava (IVC) filter, vasopressors and mechanical ventilation was



^{*}After excluding admissions with missing data on mortality (n=595) and admissions with ischemic stroke and acute limb ischemia (n= 29,008)

CDI: catheter-directed intervention, PE: pulmonary embolism

Figure 1 Study flowchart. CDI, catheter-directed intervention; PE, pulmonary embolism.

more common among admissions at low-volume hospitals. On the other hand, admissions at high-volume hospitals had higher rates of morbid obesity, hypertension, diabetes mellitus, pulmonary hypertension and acute cor pulmonale. The utilization of US-CDT was more common in high-volume hospitals.

Primary outcome

Among admissions receiving CDI, the unadjusted in-hospital mortality differed across the 3 groups. In-hospital mortality was 11% in lowvolume, 6.8% in moderate-volume and 5.1% in high-volume hospitals (P < 0.001) (*Table 2*). Among admissions who did not receive CDI, the unadjusted in-hospital mortality was 6.9% in low-volume, 7% in moderate- and 7.2% in high-volume centers (P = 0.13) (see Supplementary material online, *Table S2*).

Among admissions receiving CDI, curvilinear regression analysis revealed an inverse relationship between hospital CDI volume and in-hospital mortality (coefficient -0.344, P < 0.001). On multivariable regression analysis, in-hospital mortality was lower among high- vs. low-volume hospitals (adjusted odds ratio [OR] 0.71; 95% confidence interval [CI] 0.53, 0.95, P = 0.021) but no significant difference was observed among moderate- vs. low-volume hospitals

(adjusted OR 0.76; 95% CI: 0.58, 1.002, P = 0.051). (*Table 3*, *Figure 2*). Sensitivity analysis excluding admissions who were transferred from other hospitals showed that in-hospital mortality was lower among moderate- vs. low-volume hospitals (adjusted OR 0.72; 95% CI 0.54, 0.96, P = 0.02) and among high- vs. low-volume hospitals (adjusted OR 0.63; 95% CI 0.47, 0.85, P = 0.002).

When analyzing the hospital volume as a continuous variable, there was a significant reduction in in-hospital mortality with higher hospital CDI volume (for every increase in 10 procedures per year: adjusted OR 0.971; 95% CI 0.944, 0.999, P = 0.04) even after excluding admissions who were transferred from other hospitals (for every increase in 10 procedures per year: adjusted OR 0.969; 95% CI 0.942, 0.998, P = 0.04). (*Table 3*).

Secondary outcomes

In the unadjusted analysis, the rates of ICH were different while the rates of non-ICH bleeding events were similar among the 3 groups. The rates of ICH were 1.7% in low-volume, 1.3% in moderate-volume and 1% in high-volume hospitals (P = 0.04). Non-ICH was 12.8% in low-volume, 11.2% in moderate-volume and 10.8% in high-volume hospitals (P = 0.10) (*Table 2*). On multivariable logistic

	Low CDI volume (n = 2094)	Moderate CDI volume (n = 6505)	High CDI volume (n = 28 923)	P value
Percentage from all PE admissions	1% (2094/209 523)	2.4% (6505/267 688)	5.9% (28 923/487 605)	<0.001
Number of hospitals ^a				<0.001
Year 2016	168	200	193	
Year 2017	180	215	272	
Year 2018	146	227	341	
Year 2019	179	233	363	
Age, median (IQR)	63 (50–71)	63 (52–72)	62 (50–72)	0.02
Female	48.2%	47%	47.1%	0.75
Pregnancy	0.9%	0.2%	0.2%	<0.001
Smoking	22.5%	21%	23.2%	0.02
Comorbidities				
Morbid obesity	19.1%	19%	21.6%	0.001
Hypertension	61.9%	61.1%	63.3%	0.04
Diabetes mellitus	25.2%	25.3%	27.5%	0.01
Anemia	23.8%	18.6%	17.9%	<0.001
Coagulopathy	19.2%	17%	14.6%	<0.001
Pulmonary hypertension	15.1%	14.7%	17.4%	0.004
Chronic pulmonary disease	20.6%	18.5%	18.9%	0.31
Atrial fibrillation/flutter	14.6%	12%	11.8%	0.02
Heart failure	19.2%	18.3%	18.4%	0.78
Valvular heart disease	10.6%	7%	7.9%	0.002
Chronic kidney diease (stage 3 and above)	10.3%	8.9%	10.7%	0.002
Chronic liver disease	4.8%	4.8%	4.2%	0.18
Connective tissue diseases	2.9%	2.6%	3.1%	0.21
Malignancy	11.5%	9%	8.9%	0.01
CAD	13.2%	12.8%	14.4%	0.03
Prior MI	3.4%	2.7%	3.8%	0.002
Prior PCI	NR	0.3%	0.3%	0.80
Prior CABG	2.2%	1.9%	2.4%	0.28
Prior stroke	4.3%	4%	4.1%	0.88
PAD	3.3%	2.3%	2.4%	0.00
Presentation and severity	5.5%	2.576	2.7/0	0.15
Transfered from another hospital	9.9%	5.1%	6.2%	<0.001
Saddle PE	37.6%	38%	36.7%	0.39
Acute cor pulmonale	26.8%	31.4%	41.1%	< 0.001
I	8.5%	6.4%	5.1%	< 0.001
Cardiogenic shock				
Concomitant DVT PE with critical illness	57.1%	55.2%	57.5%	0.07
	22.9%	14.3%	11.3%	<0.001
Hospital characteristics	14 50/	10 (0)	(0.10)	0.001
Large hospital ^b	41.5%	48.6%	69.1%	< 0.001
Teaching hospital	59.3%	68.1%	79.2%	<0.001
Treatment modalities	4.404	1.00/	2.0%	<i>.</i>
Systemic thrombolysis	6.1%	4.8%	3.9%	0.001
Surgical embolectomy	NR	0.3%	0.3%	0.51
CDE	30.2% (633/2094)	26.7% (1734/6505)	20.1% (5810/28 923)	<0.001
CDT	76.5% (1602/2094)	78.9% (5133/6505)	82.9% (23 970/28 923)	<0.001

Table 1	Baseline patients' and hospitals' characteristics among adm	issions with acute PE undergoing CDI according
to the ar	annual hospital CDI volume	

Continued

Table 1 Continued

	Low CDI volume (<i>n</i> = 2094)	Moderate CDI volume (n = 6505)	High CDI volume (n = 28 923)	P value
US-facilitated CDT	12.5% (261/2094)	15.8% (1027/6505)	23.5% (6801/28 923)	<0.001
IVC filter	29%	23.1%	19.7%	<0.001
Circulatory and ventilatory support				
Vasopressors	2.8%	1.6%	1.3%	0.001
Mechanical ventillation	18.9%	11.2%	8.6%	<0.001
Mechanical circulatory support	1.7%	1.1%	1.2%	0.40
Impella	NR	0.2%	0.3%	0.65
ECMO	1.1%	0.8%	0.9%	0.67
IABP	NR	NR	0.1%	0.001

^aIndividual hospital cannot be tracked across different years as the NRD assigns a different number for each hospital each year.

^bLarge hospitals were defined based on HCUP definition which is based on hospital beds and are specific to the hospital's location and teaching status (https://www.hcup-us.ahrq.gov/ db/vars/hosp_bedsize/nisnote.jsp) as follows; Northeastern region: rural > 100, urban non-teaching > 200, urban teaching > 425 beds. Midwest region: rural > 50, urban non-teaching > 175, urban teaching > 375 beds. Southern region: rural > 75, urban non-teaching > 200, urban teaching > 450 beds. Western region: rural > 45, urban non-teaching > 175, urban teaching > 325 beds.

CAD, coronary artery disease; CDI, catheter-directed intervention; PE, pulmonary embolism; IQR, interquartile range; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, Coronary artery bypass grafting; DVT, deep venous thrombosis; CDT, catheter-directed thrombolysis; CDE, catheter-directed embolectomy; US, ultrasound; IVC, inferior vena cava; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; PAD, peripheral arterial disease; NR: not reportable.

	Low CDI volume (<i>n</i> = 2094)	Moderate CDI volume (n = 6505)	High CDI volume (n = 28 923)	P value
In-hospital mortality	11%	6.8%	5.1%	<0.001
Intracranial haemorrhage (ICH)	1.7%	1.3%	1%	0.04
Non-ICH	12.8%	11.2%	10.8%	0.10
Length of stay (days) median (IQR)	6 (4–10)	5 (3–8)	4 (3–7)	<0.001
Cost of stay (US Dollars) median (IQR)	30 189(20 556–48 459)	25 953(18 576-38 014)	23 833(18 059–32 909)	<0.001
30-day unplanned readmissions	8.5% (143/1685) ^a	8% (437/5457) ^a	7.3% (1825/25 102) ^a	0.19
- Due to PE recurrence	21.9%	15.4%	18.9%	0.30
- Due to DVT	12.9%	10.3%	11.1%	0.77

^aAfter excluding those who died during the index admissions and those who were admitted in December of each calendar year.

IQR, interquartile range; PE, pulmonary embolism; DVT, deep venous thrombosis; CDI, catheter-directed interventions

regression analysis, there was no difference in the rates of ICH and non-ICH bleeding events between high- vs. low-volume and moderate- vs. low-volume hospitals (*Table 3, Figure 2*).

The LOS and cost were lower among high- and moderate-volume hospitals compared with low-volume hospitals. Multivariable linear regression analysis revealed an inverse association between CDI volume and both LOS (regression coefficient -0.023, 95% CI -0.027, -0.019, P < 0.001) and cost (regression coefficient -74.6, 95% CI -98.8, -50.3, P < 0.001). There were no differences in the 30-day unplanned readmission rates between the three groups (*Table 2*).

Falsification endpoint analysis

There was no difference in the rate of sepsis among moderatevolume (adjusted OR 0.96; 95% CI 0.73, 1.26, P = 0.77) and highvolume (adjusted OR 0.88; 95% CI 0.67, 1.16, P = 0.39) hospitals compared with low-volume hospitals. There were no differences in the rates of pressure ulcers (moderate- vs. low-volume: adjusted OR 1.19; 95% CI 0.69, 2.04, P = 0.53; high- vs. low-volume: adjusted OR 1.03; 95% CI 0.62, 1.70, P = 0.91) and acute hepatitis (moderatevs. low-volume: adjusted OR 2.13; 95% CI 0.52, 8.69, P = 0.29; high- vs. low-volume: adjusted OR 1.37; 95% CI 0.47, 4.05, P = 0.56) between moderate- and high-volume hospitals compared with lowvolume hospitals.

of CDI				
	Moderate- vs. low-volume hospitals	High- vs. low-volume hospitals	Volume as a continuous variable ^a	
In-hospital mortality	0.76 (0.58–1.002)	0.71 (0.53–0.95)	0.971 (0.994–0.999)	
Intracranial haemorrhage (ICH)	0.79 (0.42–1.49)	0.60 (0.33–1.02)	0.960 (0.900-1.023)	
Non-ICH bleeding events	0.95 (0.78–1.16)	1.03 (0.85–1.24)	0.982 (0.964–1.001)	

Table 3 In-hospital mortality and bleeding events following CDI for PE according to the annual hospital volume of CDI

Values are adjusted odds ratio (95% confidence interval)

^aFor every increase in 10 procedures per year.

CDI, catheter-directed intervention; PE, pulmonary embolism

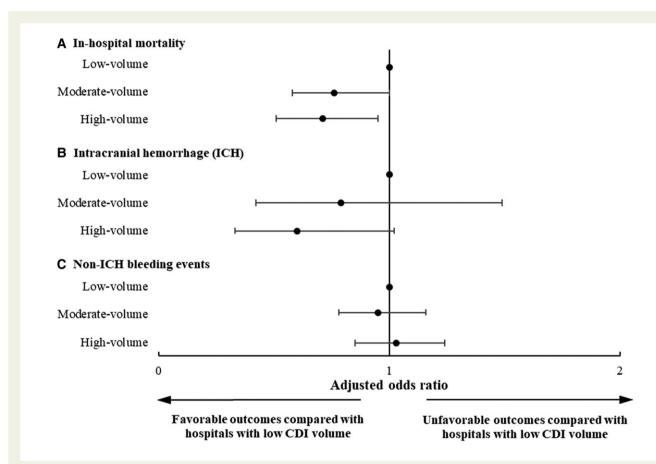


Figure 2 Forest plot showing the adjusted odds of in-hospital mortality, ICH and non-ICH bleeding events following CDI for PE according to the hospital annual volume of CDI. CDI, catheter-directed intervention; ICH, intracranial haemorrhage; PE, pulmonary embolism. Central Illustration. In-hospital mortality after CDI for acute PE according to the annual hospital CDI volume. (A) Forest plot for in-hospital mortality after CDI for acute PE according to the annual hospital CDI volume. (A) Forest plot for in-hospital mortality after CDI for acute PE according to the annual hospital CDI volume. (B) Scatter plot showing the relationship between annual hospital CDI volume and in-hospital mortality CDI, catheter-directed intervention; PE, pulmonary embolism.

Discussion

We investigated the association between hospital procedure volume and short-term outcomes among 37 522 hospitalizations with acute PE undergoing CDI. The main findings of this study were as follows: (1) there was an inverse association between in-hospital mortality following CDI for acute PE and annual hospital CDI volume. Compared with low-volume hospitals (1–3 procedures), high hospital CDI volume (>12 procedures) was independently associated with lower odds of in-hospital mortality. However, when the hospital volume was used as a continuous variable, the reduction in mortality was borderline significant; (2) hospitals with moderate or high CDI volumes were not associated with lower odds of ICH or non-ICH bleeding events compared with low-volume hospitals; (3) higher volume hospitals were associated with shorter LOS and lower cost; (4) there was no difference in the 30-day unplanned readmission rate according to the annual hospital CDI volume. Importantly, the falsification endpoint analysis showed no significant difference in the incidence of other outcomes, which are not influenced by acute PE and CDI, suggesting that the main findings from this analysis are unlikely driven by unmeasured confounding.

The current study demonstrated an inverse volume-outcome relationship among patients with acute PE undergoing CDI and inhospital all-cause mortality, cost, as well as LOS. Previous studies have shown that among all-comers with acute PE, admission to highvolume hospitals was associated with improved outcomes irrespective of the treatment modalities or severity of presentation.^{18,19} Additionally, improved clinical outcomes with higher procedural volume have been established with various catheter-based cardiovascular interventions including percutaneous coronary intervention,^{25,26} transcatheter aortic valve replacement,²⁷ transcatheter mitral valve repair,²⁸ CDT for acute DVT²⁹ and endovascular treatment for acute ischaemic stroke³⁰ and critical limb ischaemia.³¹

Several factors might explain the inverse association between in-hospital mortality and annual hospital CDI volume observed in the current study. These factors may be related to the patients, the procedure or other peri-procedural care factors. As with most interventional procedures, the learning curve and operator experience play an important role in procedural success and clinical outcomes. We found that higher CDI volume was not associated with lower odds of major bleeding thus, peri-procedural factors may play a larger role in the volume-outcome relationship. High-volume hospitals may have greater staff interventional experience, subspecialty support services, greater intensive care unit staffing and advanced infrastructure to ensure pre- and post-procedural care of patients undergoing CDI.¹⁹ Also, the development of multidisciplinary pulmonary embolism response teams (PERT) may contribute to the volume-outcome relationship. PERT help in rapid risk stratification of patients as well as choosing the most appropriate management strategy. Studies have shown that with the introduction of PERTs, there has been an increase in the utilization of advanced therapies for PE with a possible decrease in in-hospital mortality.^{32–35}

There was no difference in in-hospital mortality between low- and moderate-volume hospitals. However, when excluding admissions that were transferred from other hospitals, we found a significant reduction in mortality in moderate- vs. low-volume hospitals. This suggests that transferred patients may represent a cohort of patients who are 'sicker' and have worse outcomes. It has been previously shown that transferred PE patients had higher rates of right ventricular strain and oxygen requirements. They were more likely to have intermediate or high-risk PE and to receive advanced therapy. PE-related mortality was higher among transferred patients.^{36,37}

The current analysis showed that only a small proportion of patients admitted with acute PE to low- or moderate-volume hospitals receive CDI for PE (1 and 2.4%, respectively), whereas 5.9% of those admitted to high-volume hospitals receive CDI. Interestingly, admissions at low-volume centres had greater comorbidities and higher risk PE features. It is plausible that patients admitted to low-volume centres were sicker, hence, they were not offered CDI. Our results highlight the importance of the centers' experience in achieving better outcomes with CDI for acute PE. It has been suggested that an experienced interventionalist requires three to five cases to optimize CDE with FlowTriever Aspiration System (Inari Medical, Irvine, CA, USA).¹⁶ Additionally, the lower cost and shorter LOS seen with higher CDI volume suggest that adequate CDI volume can help in reducing healthcare costs, improving bed turnover, and preventing complications related to prolonged hospitalization (e.g. nosocomial infections).³⁸ Further analyses with longer follow-up periods are warranted to determine the CDI volume needed to achieve optimal outcomes.

Limitations

The findings of this study should be interpreted in the context of some limitations. First, this study is a retrospective observational study with the inherent limitation of selection bias. We attempted to mitigate that risk by performing multivariable regression analyses. Reassuringly, the falsification endpoint analysis suggested that the findings are unlikely driven by residual confounding. Second, given the administrative nature of the NRD, the study is subject to coding errors and data quality at the site of collection, without the ability to adjudicate accuracy. Additionally, the NRD uses discharge not admission diagnoses, so we could not ascertain if PE was present on admission or later during the course of hospitalization. Also, the NRD assigns a number for each hospital every year and an individual hospital cannot be followed across different years, so hospitals were classified based on their annual CDI procedural volume. Third, patients with multiple admissions could have been included more than once if they have received CDI for PE during each admission. Fourth, the temporal relationship of certain outcomes cannot be reliably established. Fifth, details about the CDI procedure including duration, thrombolytic dose, type of interventional device used as well as data on discharge medications are not available in the NRD. Sixth, long-term outcomes could not be assessed. Seventh, data regarding operators' volume and experience and the influence on the outcomes were also not available. Finally, the NRD also lacks data on imaging and cardiac biomarkers which could influence the outcomes.

Conclusions

In this nationwide contemporary analysis of patients admitted with PE and undergoing CDI, we found an inverse association between hospital CDI volume and in-hospital mortality, LOS, and cost. There were no differences in major bleeding and 30-day unplanned readmission rates among low-, moderate-, and high-volume hospitals. Future studies are needed to examine the effect of hospital CDI volume on long-term outcomes.

Supplementary material

Supplementary material is available at European Heart Journal: Acute Cardiovascular Care online.

Conflict of interest: None declared.

References

- Barco S, Valerio L, Ageno W, Cohen AT, Goldhaber SZ, Hunt BJ, Iorio A, Jimenez D, Klok FA, Kucher N, Mahmoudpour SH, Middeldorp S, Münzel T, Tagalakis V, Wendelboe AM, Konstantinides SV. Age-sex specific pulmonary embolism-related mortality in the USA and Canada, 2000–18: an analysis of the WHO mortality database and of the CDC multiple cause of death database. *Lancet Respir Med* 2021;**9**: 33–42. doi:10.1016/S2213-2600(20)30417-3
- 2. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, Huisman MV, Humbert M, Jennings CS, Jiménez D, Kucher N, Lang IM, Lankeit M, Lorusso R, Mazzolai L, Meneveau N, Ní Áinle F, Prandoni P, Pruszczyk P, Righini M, Torbicki A, Van Belle E, Zamorano JL, ESC Scientific Document Group. 2019 ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European respiratory society (ERS) the task force for the diagnosis and management of acute pulmonary embolism of the European society of cardiology (ESC). Eur Heart J 2020;41:543–603. doi:10.1093/eurheartj/ehz405
- Marti C, John G, Konstantinides S, Combescure C, Sanchez O, Lankeit M, Meyer G, Perrier A. Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis. *Eur Heart J* 2015;36:605–614. doi:10.1093/eurheartj/ ehu218
- Meneveau N, Seronde MF, Blonde MC, Legalery P, Didier-Petit K, Briand F, Caulfield F, Schiele F, Bernard Y, Bassand JP. Management of unsuccessful thrombolysis in acute massive pulmonary embolism. *Chest* 2006;**129**:1043–1050. doi:10.1378/ chest.129.4.1043
- Jaff MR, McMurtry MS, Archer SL, Cushman M, Goldenberg N, Goldhaber SZ, Jenkins JS, Kline JA, Michaels AD, Thistlethwaite P, Vedantham S, White RJ, Zierler BK. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension. *Circulation* 2011;**123**:1788–1830. doi:10.1161/CIR.0b013e318214914f
- Sedhom R, Megaly M, Elbadawi A, Elgendy IY, Witzke CF, Kalra S, George JC, Omer M, Banerjee S, Jaber WA, Shishehbor MH. Contemporary national trends and outcomes of pulmonary embolism in the United States. *Am J Cardiol* 2022;**176**: 132–138. doi: 10.1016/j.amjcard.2022.03.060
- Dudzinski DM, Giri J, Rosenfield K. Interventional treatment of pulmonary embolism. *Circ Cardiovasc Interv* 2017;**10**:e004345. doi:10.1161/CIRCINTERVENTIONS.116. 004345
- Chopard R, Ecarnot F, Meneveau N. Catheter-directed therapy for acute pulmonary embolism: navigating gaps in the evidence. *Eur Hear J Suppl* 2019;**21**:123–130. doi:10. 1093/eurheartj/suz224
- Pei DT, Liu J, Yaqoob M, Ahmad W, Bandeali SS, Hamzeh IR, Virani SS, Hira RS, Lakkis NM, Alam M. Meta-analysis of catheter directed ultrasound-assisted thrombolysis in pulmonary embolism. *Am J Cardiol* 2019;**124**:1470–1477. doi:10.1016/j.amjcard. 2019.07.040
- Nosher JL, Patel A, Jagpal S, Gribbin C, Gendel V. Endovascular treatment of pulmonary embolism: selective review of available techniques. World J Radiol 2017;9: 426–437. doi:10.4329/wjr.v9.i12.426
- 11. Patel N, Patel NJ, Agnihotri K, Panaich SS, Thakkar B, Patel A, Savani C, Patel N, Arora S, Deshmukh A, Bhatt P, Alfonso C, Cohen M, Tafur A, Elder M, Mohamed T, Attaran R, Schreiber T, Grines C, Badheka AO. Utilization of catheter-directed thrombolysis in pulmonary embolism and outcome difference between systemic thrombolysis and catheter-directed thrombolysis. *Catheter Cardiovasc Interv* 2015;**86**:1219–1227. doi: 10.1002/ccd.26108
- Beyer SE, Shanafelt C, Pinto DS, Weinstein JL, Aronow HD, Weinberg I, Yeh RW, Secemsky EA, Carroll BJ. Utilization and outcomes of thrombolytic therapy for acute pulmonary embolism: A nationwide cohort study. *Chest* 2020;**157**:645–653. doi:10. 1016/j.chest.2019.10.049
- Percy ED, Shah R, Hirji S, Tartarini RJ, Yazdchi F, Harloff M, Kaneko T, Pelletier MP. National outcomes of surgical embolectomy for acute pulmonary embolism. *Ann Thorac Surg* 2020;**110**:441–447. doi:10.1016/j.athoracsur.2020.02.024
- Gayou EL, Makary MS, Hughes DR, Hemingway J, Elliott ED, Spain JW, Prevedello LM. Nationwide trends in use of catheter-directed therapy for treatment of pulmonary embolism in medicare beneficiaries from 2004 to 2016. *J Vasc Interv Radiol* 2019; 30:801–806. doi:10.1016/j.jvir.2019.02.024
- Abou Ali AN, Saadeddin Z, Chaer RA, Avgerinos ED. Catheter directed interventions for pulmonary embolism: current status and future prospects. *Expert Rev Med Devices* 2020;17:103–110. doi:10.1080/17434440.2020.1714432
- 16. Tu T, Toma C, Tapson VF, Adams C, Jaber WA, Silver M, Khandhar S, Amin R, Weinberg M, Engelhardt T, Hunter M, Holmes D, Hoots G, Hamdalla H, Maholic RL, Lilly SM, Ouriel K, Rosenfield K. A prospective, single-arm, multicenter trial of catheter-directed mechanical thrombectomy for intermediate-risk acute pulmonary embolism: the FLARE study. J Am Coll Cardiol Intv 2019;**12**:859–869. doi:10.1016/j. jcin.2018.12.022
- Sista AK, Horowitz JM, Tapson VF, Rosenberg M, Elder MD, Schiro BJ, Dohad S, Amoroso NE, Dexter DJ, Loh CT, Leung DA, Bieneman BK, Perkowski PE, Chuang ML, Benenati JF, EXTRACT-PE Investigators. Indigo aspiration system for

treatment of pulmonary embolism: results of the EXTRACT-PE trial. J Am Coll Cardiol Intv 2021;**14**:319–329. doi: 10.1016/j.jcin.2020.09.053

- Jiménez D, Bikdeli B, Quezada A, Muriel A, Lobo JL, de Miguel-Diez J, Jara-Palomares L, Ruiz-Artacho P, Yusen RD, Monreal M, RIETE investigators. Hospital volume and outcomes for acute pulmonary embolism: multinational population based cohort study. *bmj* 2019;**366**:I4416. doi: 10.1136/bmj.I4416
- Finkelstein M, Cedillo MA, Kestenbaum DC, Shoaib OS, Fischman AM, Lookstein RA. Relationship of hospital volume on outcomes in patients with acute pulmonary embolism: analysis of a 70,000 patient database. *Vasc Med* 2021;**26**:38–46. doi:10.1177/ 1358863X20970263
- HCUP Nationwide Readmissions Database (NRD). Healthcare Cost and Utilization Project (HCUP). 2016 through 2019. Agency for Healthcare Research and Quality, Rockville, MD.
- Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care 1998;36:8–27. doi:10.1097/00005650-199801000-00004
- Elgendy IY, Gad MM, Mansoor H, Mahmoud AN, Elbadawi A, Saad A, Saad M, Elkaryoni A, Secemsky EA, Mamas MA, Monreal M, Weinberg I, Pepine CJ. Acute pulmonary embolism during pregnancy and puerperium: national trends and in-hospital outcomes. *Mayo Clinic Procr* 2021;**96**:2102–2113.
- Elbadawi A, Mentias A, Elgendy IY, Mohamed AH, Syed MH, Ogunbayo GO, Olorunfemi O, Gosev I, Prasad S, Cameron SJ. National trends and outcomes for extra-corporeal membrane oxygenation use in high-risk pulmonary embolism. Vasc Med 2019;24:230–233. doi:10.1177/1358863X18824650
- Khera R, Angraal S, Couch T, Welsh JW, Nallamothu BK, Girotra S, Chan PS, Krumholz HM. Adherence to methodological standards in research using the national inpatient sample. *Jama* 2017;**318**:2011–2018. doi:10.1001/jama.2017. 17653
- Srinivas VS, Hailpern SM, Elana K, Monrad ES, Alderman MH. Effect of physician volume on the relationship between hospital volume and mortality during primary angioplasty. J Am Coll Cardiol 2009;53:574–579. doi:10.1016/j.jacc.2008.09.056
- McGrath PD, Wennberg DE, Dickens J D Jr, Siewers AE, Lucas FL, Malenka DJ, Kellett MA Jr, Ryan TJ Jr. Relation between operator and hospital volume and outcomes following percutaneous coronary interventions in the era of the coronary stent. JAMA 2000;284:3139–3144. doi:10.1001/jama.284.24.3139
- Vemulapalli S, Carroll JD, Mack MJ, Li Z, Dai D, Kosinski AS, Kumbhani DJ, Ruiz CE, Thourani VH, Hanzel G, Gleason TG, Herrmann HC, Brindis RG, Bavaria JE. Procedural volume and outcomes for transcatheter aortic-valve replacement. N Engl | Med 2019;380:2541–2550. doi:10.1056/NEJMsa1901109
- Yeo I, Kim LK, Wong SC, Cheung JW, Itagaki S, Chikwe J, Egorova NN. Relation of hospital volume with in-hospital and 90-day outcomes after transcatheter mitral valve repair using MitraClip. Am J Cardiol 2019;**124**:63–69. doi:10.1016/j.amjcard. 2019.04.006
- Jarrett H, Zack CJ, Aggarwal V, Lakhter V, Alkhouli MA, Zhao H, Comerota A, Bove AA, Bashir R. Impact of institutional volume on outcomes of catheter directed thrombolysis in the treatment of acute proximal deep vein thrombosis: a 6-year US experience (2005–2010). *Circulation* 2015;**132**:1127–1135. doi:10.1161/ CIRCULATIONAHA.115.015555
- 30. Gupta R, Horev A, Nguyen T, Gandhi D, Wisco D, Glenn BA, Tayal AH, Ludwig B, Terry JB, Gershon RY, Jovin T, Clemmons PF, Frankel MR, Cronin CA, Anderson AM, Hussain MS, Sheth KN, Belagaje SR, Tian M, Nogueira RG. Higher volume endovascular stroke centers have faster times to treatment, higher reperfusion rates and higher rates of good clinical outcomes. J Neurointerv Surg 2013;5:294–297. doi:10. 1136/neurintsurg-2011-010245
- 31. Elbadawi A, Elgendy IY, Rai D, Mahtta D, Megaly M, Pershad A, Denktas A, Brilakis ES, Drachman DE, Banerjee S, Shishehbor MH, Jneid H. Impact of hospital procedural volume on outcomes after endovascular revascularization for critical limb ischemia. J Am Coll Cardiol Intv 2021;14:1926–1936. doi:10.1016/j.jcin.2021.06.032
- Chaudhury P, Gadre SK, Schneider E, Renapurkar RD, Gomes M, Haddadin I, Heresi GA, Tong MZ, Bartholomew JR. Impact of multidisciplinary pulmonary embolism response team availability on management and outcomes. *Am J Cardiol* 2019;**124**: 1465–1469. doi:10.1016/j.amjcard.2019.07.043
- Rosovsky R, Chang Y, Rosenfield K, Channick R, Jaff MR, Weinberg I, Sundt T, Witkin A, Rodriguez-Lopez J, Parry BA, Harshbarger S, Hariharan P, Kabrhel C. Changes in treatment and outcomes after creation of a pulmonary embolism response team (PERT), a 10-year analysis. J Thromb Thrombolysis 2019;47:31–40. doi:10.1007/ s11239-018-1737-8
- 34. Wright C, Goldenberg I, Schleede S, McNitt S, Gosev I, Elbadawi A, Pietropaoli A, Barrus B, Chen YL, Mazzillo J, Acquisto NM, Van Galen J, Hamer A, Marinescu M, Delehanty J, Cameron SJ. Effect of a multidisciplinary pulmonary embolism response team on patient mortality. *Am J Cardiol* 2021;**161**:102–107. doi:10.1016/j.amjcard. 2021.08.066
- 35. Wright C, Elbadawi A, Chen YL, Patel D, Mazzillo J, Acquisto N, Groth C, Van Galen J, Delehanty J, Pietropaoli A, Trawick D, James White R, Cameron P, Gosev I, Barrus B, Kumar NG, Cameron SJ. The impact of a pulmonary embolism response team on

the efficiency of patient care in the emergency department. J Thromb Thrombolysis 2019; 48:331-335. doi:10.1007/s11239-019-01875-0

- Elkaryoni A, Allen S, Newman J, Fareed J, Bechara C, Bunte M, Darki A. Trends and outcomes of acute pulmonary embolism transfers: a nationwide cohort sample 2008–2018. Eur Heart J 2021;42:ehab724.1905.
- Carroll BJ, Beyer SE, Shanafelt C, Kabrhel C, Rali P, Rivera-Lebron B, Rosovsky R, Ross CB, Pinto DS, Secemsky EA. Interhospital transfer for the management of acute

pulmonary embolism. *Am J Med* 2022;**135**:531–535. doi:10.1016/j.amjmed.2021.11. 015

 Siddique SM, Tipton K, Leas B, Greysen SR, Mull NK, Lane-Fall M, McShea K, Tsou AY. Interventions to reduce hospital length of stay in high-risk populations: A systematic review. JAMA Netw open 2021;4:e2125846–e2125846. doi:10.1001/ jamanetworkopen.2021.25846