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Brief Observation

Trends and Outcomes of Interhospital Transfer for High-Risk Acute Pulmonary Embolism: A Nationwide Analysis

Ramy Sedhom[a], Rafail Beshai[b], Ahmed Elkaryoni[c], Michael Megaly[d], Ayman Elbadawi[e], Ahmed Athar[f], Wissam Jaber[g], Aditya S. Bharadwaj[a], Vinoy Prasad[a], Liset Stoletniy[a], Islam Y. Elgendy[h,*]

[a] *Division of Cardiology, Loma Linda University Medical Center, Calif*
[b] *Division of Internal Medicine, Jefferson Health, Washington Township, NJ*
[c] *Division of Cardiovascular Disease, Loyola University Medical Center, Loyola Stritch School of Medicine, Maywood, Ill*
[d] *Division of Cardiology, Henry Ford Hospital, Detroit, Mich*
[e] *Division of Cardiology, University of Texas Southwestern Medical Center, Dallas*
[f] *Cardiology Section, Jerry L. Pettis Memorial Veteran's Hospital, Loma Linda, Calif*
[g] *Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, Ga*
[h] *Division of Cardiovascular Medicine, Gill Heart Institute, University of Kentucky, Lexington, KY*

ABSTRACT

Background: Data on outcomes of patients with high-risk acute pulmonary embolism (PE) transferred from other hospitals are scarce.
Methods: We queried the Nationwide Readmissions Database for admissions who were ≥18 years old, and with a primary discharge diagnosis of acute high-risk PE between the years 2016 and 2019. The main outcome of interest was the difference in all-cause in-hospital mortality between patients admitted directly to small/medium hospitals; patients admitted directly to large hospitals; and patients transferred to large hospitals.
Results: Among 11,341 weighted hospitalizations with high-risk PE, 631 (5.6%) patients were transferred to large hospitals. There was no significant change in the rates of transfer during the study period. Transferred patients were younger and had a higher prevalence of comorbidities. They were more likely to present with saddle PE and cor pulmonale and were more likely to receive advanced therapies. In-hospital mortality was not different between patients transferred to large hospitals and those admitted directly to large hospitals (adjusted odd ratio [OR] 1.11, 95% confidence interval [CI] 0.81, 1.54) as well as between patients transferred to large hospitals and those admitted directly to small/medium hospitals (aOR 1.28, 95% CI 0.92, 1.76). The rates of major bleeding and cardiac arrest were higher among transferred patients. Admissions for transferred patients were associated with higher cost and longer length of stay.
Conclusion: Transferred patients with high-risk PE were more likely to receive advanced therapies. There was no difference in-hospital mortality rates compared with patients admitted directly to the large or small/medium hospitals.

Clinical Significance

- Among patients with high-risk PE treated at large hospitals, 5.6% were transferred to large hospitals.
- Transferred patients were younger and had a higher prevalence of comorbidities. They were more likely to receive advanced therapies.
- Despite the higher rates of major bleeding and cardiac arrest among transferred patients, the rate of in-hospital mortality was not different between transferred and nontransferred patients.

Introduction

Patients presenting with high-risk pulmonary embolism (PE) have considerably high mortality rates (up to 40%).[1] Current guidelines recommend systemic thrombolysis as the main modality for pulmonary reperfusion in high-risk PE, while catheter-directed interventions (CDI) and surgical embolectomy can be considered as second-line therapies.[2] As such, CDI utilization has been rising and it has become the most widely used modality to restore pulmonary perfusion among all-comers with acute PE.[3] In addition, there has been an increase in the utilization of extracorporeal membrane oxygenation (ECMO) in refractory cases of high-risk PE.[4] Nevertheless, these advanced therapies are

Abbreviations: CDE, Catheter-directed embolectomy; CDI, Catheter-directed intervention; CDT, Catheter-directed thrombolysis; ICH, Intracranial hemorrhage; IQR, Interquartile range; MCS, Mechanical circulatory support; NRD, Nationwide Readmissions Database; OR, Odds ratio; PE, Pulmonary embolism.

* Corresponding author. Islam Y. Elgendy, Assistant Professor of Medicine, Gill Heart Institute, University of Kentucky, Lexington
E-mail address: iyelgendy@gmail.com (I.Y. Elgendy).
Social media: (I.Y. Elgendy).

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not available at every institution and there are no standardized protocols to guide the management and interhospital transfer of these high-risk patients.[5] Importantly, data on the outcomes of patients with acute PE transferred from other hospitals are scarce,[6,7] especially in the high-risk PE population. We aimed to examine the trends, differences in management, and outcomes of transferred patients with high-risk PE.

Study Design and Methods

We queried the Nationwide Readmissions Database (NRD)[8] for admissions who were ≥18 years old and had a primary discharge diagnosis of acute PE between the years 2016 and 2019. The NRD is sponsored by the Agency for Healthcare Research and Quality as a part of the Healthcare Cost and Utilization Project (HCUP). High-risk PE was defined as PE with cardiogenic shock, mechanical circulatory support (MCS), or vasopressors.[2] We excluded hospitalizations with missing data on mortality, other potential reasons for transfer, and pregnancy-associated PE (Figure 1). We used the International Classification of Diseases, Tenth Revision, Clinical Modification, and procedure codes (Table 1). According to HCUP regulations, the NRD is considered a limited data set (ie, deidentified); hence this study was exempted from institutional review board review.

We divided the study cohort into 3 groups: (1) patients presenting directly to small/medium hospitals, (2) patients presenting directly to large hospitals, and (3) patients transferred to large hospitals. Large hospitals were defined according to HCUP definition which is based on hospital beds, location, and teaching status as follows; Northeastern region: rural > 100, urban nonteaching > 200, and urban teaching > 425 beds; Midwest region: rural > 50, urban nonteaching > 175, urban teaching > 375 beds; Southern region: rural > 75, urban nonteaching > 200, urban teaching > 450 beds; Western region: rural > 45, urban nonteaching > 175, urban teaching > 325 beds.[9]

The main outcome of interest was the difference in all-cause in-hospital mortality between the 3 groups. The secondary outcomes were the trends of transfer and in-hospital mortality, the differences in cardiac arrest, discharge disposition, length of stay (LOS), cost, intracranial hemorrhage (ICH), and non-ICH bleeding events.

All analyses were conducted using the appropriate weighting, stratifying, and clustering samples following HCUP regulations.[8] A multivariable logistic regression analysis was conducted to determine the independent variables associated with the likelihood of transfer and another model for in-hospital mortality. Linear regression was used for trend analysis. All *P* values are 2-sided with a significance threshold of <0.05. Statistical analyses were performed using IBM SPSS Statistics for Windows (version 28.0; IBM Corp, Armonk, NY).

Results

Among 11,341 weighted hospitalizations with high-risk PE, 631 (5.6%) patients were transferred to large hospitals (Figure 1). There was no significant change in the trend of transfer during the study period (3.0% in Q1 2016 vs 5.0% in Q4 of 2019, P-trend = 0.53). Transferred patients to larger hospitals were younger and had a higher prevalence of comorbidities. They were more likely to have saddle PE (20.9% vs 22.9% vs 37.1%), cor pulmonale (26.6% vs 30.6% vs 43.2%), and deep venous thrombosis (DVT) (38.5% vs 39.2% vs 52.9%). Advanced therapies were more common among transferred patients to larger hospitals: surgical embolectomy (2.9% vs 5.8% vs 13.1%), catheter-directed embolectomy (4.5% vs 7.4% vs 14.1%), MCS (4.8% vs 11.8% vs 26.3%), and inferior vena cava (IVC) filter (15.6% vs 17.7% vs 29.1%) (Table 1).

In-hospital mortality was not different between patients transferred to large hospitals and those admitted directly to large hospitals (adjusted odd ratio [OR] 1.11, 95% confidence interval [CI] 0.81, 1.54) and between patients transferred to large hospitals and those admitted directly to small/medium hospitals (aOR 1.28, 95% CI 0.92, 1.76). The rate of in-hospital mortality did not change during the study years (Figure 2A). The rate of discharge to a rehabilitation facility was similar between the 3 groups. The rates of cardiac arrest and major bleeding were higher among transferred patients. Admissions for transferred patients were associated with higher cost and longer LOS (Table 2).

The factors associated with transfer are shown in Figure 2B. The need for MCS was the strongest predictor of transfer (aOR 2.42, 95% CI 1.74, 3.37). In contrast, older age was associated with lower odds of transfer (Figure 2B).

Discussion

In this nationwide analysis of 11,341 admissions with high-risk PE, we found that transferred patients to larger hospitals were younger and had a higher prevalence of comorbidities and risk factors for PE. Despite the higher rates of cardiac arrest and major bleeding among transferred patients, there was no difference in the in-hospital mortality rates between transferred patients and those presenting directly to the large or small/medium-sized hospitals. These findings suggest that rapid identification and transfer of select high-risk PE patients with multiple risk factors to large hospitals, which are capable of providing various forms of pulmonary reperfusion and circulatory support, might be beneficial.

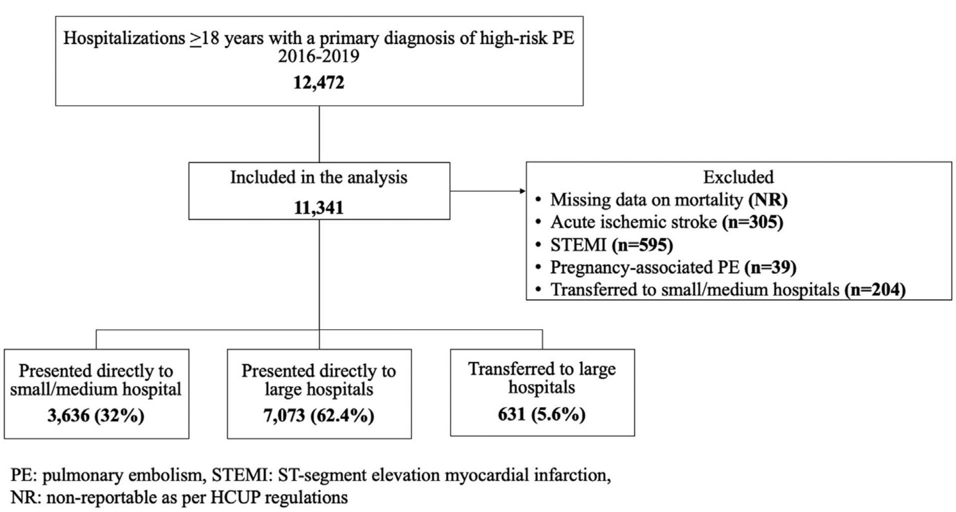
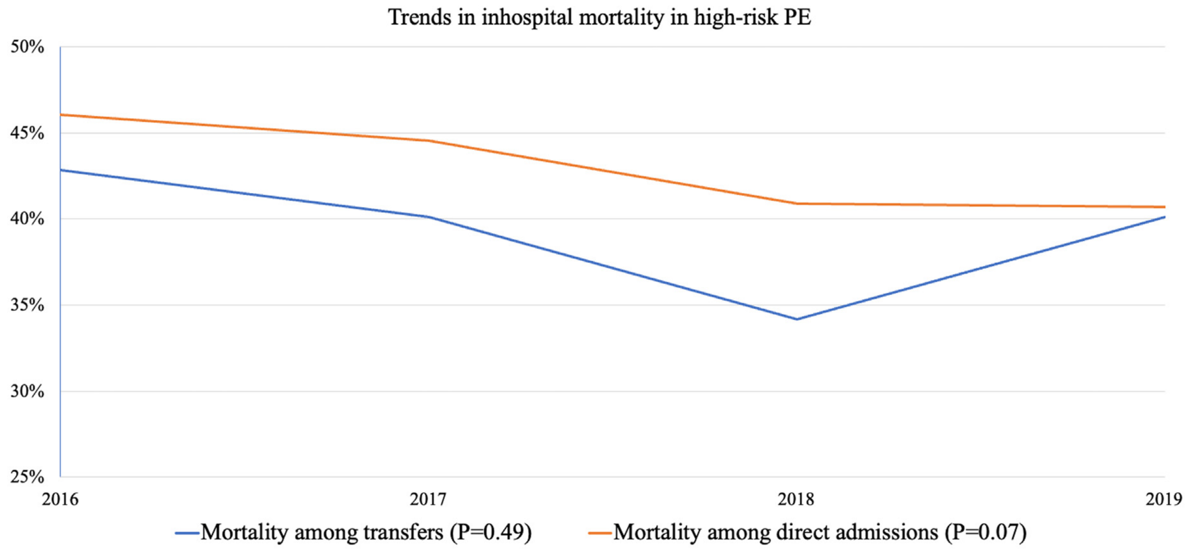
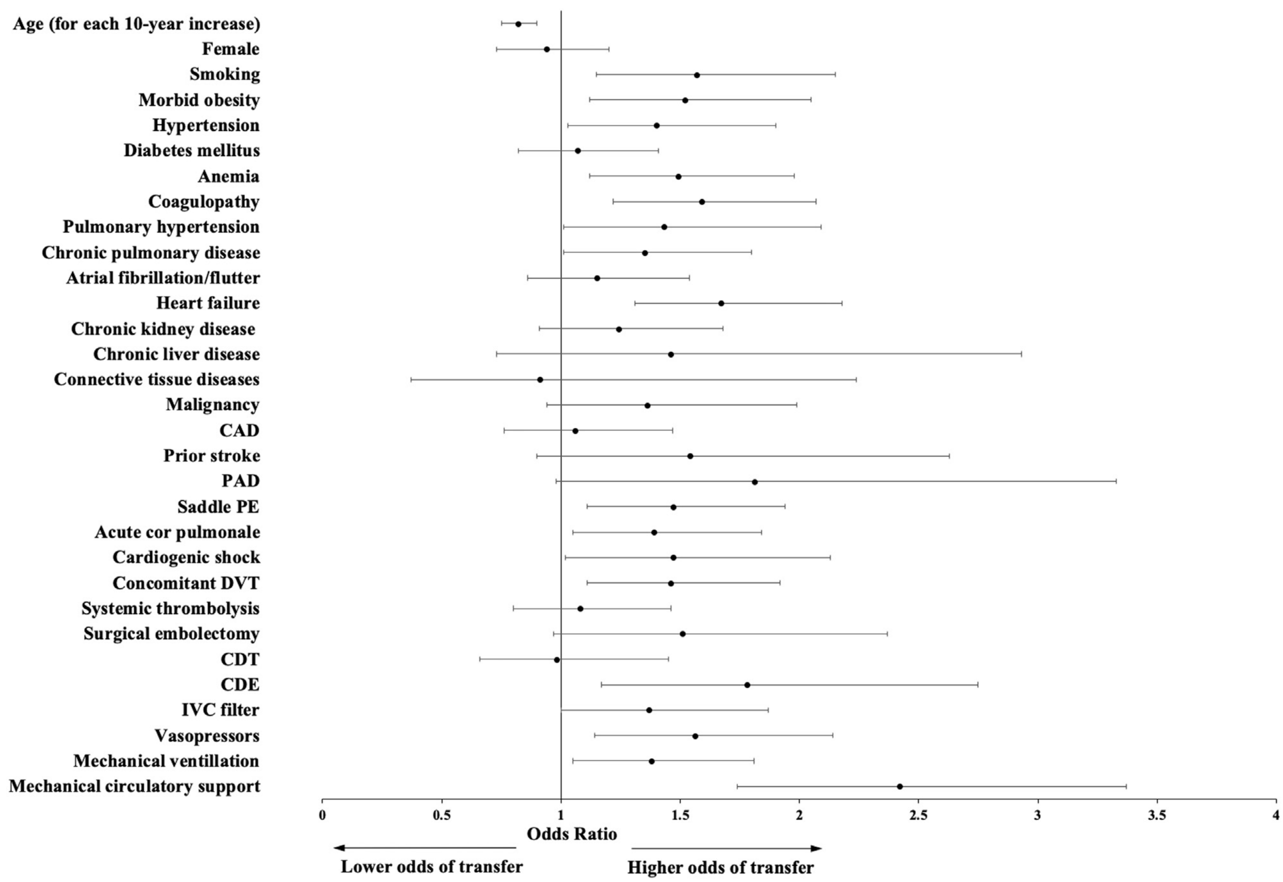


Figure 1. Flowchart of the study.



(A)



(B)

Figure 2. (**A**) Trends in high-risk PE mortality among transferred vs. nontransferred patients. (**B**) Forest plot showing factors associated with increased odds of transfer among patients with high-risk PE. CDE = catheter-directed embolectomy; CDT = catheter-directed thrombolysis; DVT = deep venous thrombosis; IVC = inferior vena cava; PAD = peripheral arterial disease; PE = pulmonary embolism.

Table 1
Characteristics of Admissions with High-Risk PE According to the Transfer Status.

	Presenting directly to small/medium hospitals (*n* = 3636)	Presenting directly to large hospitals (*n* = 7073)	Transferred to large hospitals (*n* = 631)	*P* value
Age, median (IQR%)	67 (56-76)	66 (54-75)	61 (47-70)	<.001
Female	1902 (52.3%)	3706 (52.4%)	300 (47.5%)	.24
Smoking	747 (20.5%)	1296 (18.3%)	157 (24.9%)	.01
Medicare	2152 (59.2%)	3919 (55.4%)	292 (46.4%)	<.001
Comorbidities				
Morbid obesity	517 (14.2%)	963 (13.6%)	148 (23.5%)	<.001
Hypertension	2287 (62.9%)	4256 (60.2%)	425 (67.4%)	.02
Diabetes mellitus	1133 (31.1%)	1969 (27.8%)	202 (32.1%)	.03
Anemia	884 (24.3%)	1610 (22.8%)	196 (31%)	.006
Coagulopathy	900 (24.7%)	1961 (27.7%)	281 (44.5%)	<.001
Pulmonary hypertension	423 (11.6%)	779 (11%)	119 (18.9%)	<.001
Chronic pulmonary disease	832 (22.9%)	1400 (19.8%)	156 (24.7%)	.01
Atrial fibrillation/flutter	1010 (27.8%)	1711 (24.2%)	176 (27.9%)	.01
Heart failure	1493 (41.1%)	2900 (41%)	370 (58.7%)	<.001
Chronic kidney disease	700 (19.3%)	1203 (17%)	142 (22.5%)	.01
Chronic liver disease	78 (2.1%)	108 (1.5%)	18 (2.8%)	.09
Connective tissue diseases	122 (3.4%)	189 (2.7%)	18 (2.8%)	.41
Malignancy	522 (14.3%)	1076 (15.2%)	93 (14.8%)	.73
CAD	727 (20%)	1282 (18.1%)	120 (19%)	.29
PAD	118 (3.2%)	221 (3.1%)	33 (5.2%)	.16
Prior stroke	172 (4.7%)	307 (4.3%)	38 (6%)	.41
Carotid stenosis	13 (0.4%)	21 (0.3%)	NR	.84
Presentation and severity				
Saddle PE	759 (20.9%)	1618 (22.9%)	234 (37.1%)	<.001
Acute cor pulmonale	969 (26.6%)	2163 (30.6%)	273 (43.2%)	<.001
Cardiogenic shock	2877 (79.1%)	5429 (76.8%)	508 (80.6%)	.16
Concomitant DVT	1400 (38.5%)	2770 (39.2%)	334 (52.9%)	<.001
Hospital characteristics				
Teaching hospital	2962 (81.5%)	5620 (79.4%)	576 (91.4%)	<.001
Treatment modalities				
Systemic thrombolysis	909 (25%)	1557 (22%)	138 (21.9%)	.07
Surgical embolectomy	106 (2.9%)	411 (5.8%)	83 (13.1%)	<.001
Catheter-directed thrombolysis	341 (9.4%)	825 (11.7%)	96 (15.2%)	.01
Catheter-directed embolectomy	164 (4.5%)	525 (7.4%)	89 (14.1%)	<.001
IVC filter	566 (15.6%)	1253 (17.7%)	184 (29.1%)	<.001
Circulatory and ventilatory support				
Vasopressors	981 (27%)	2057 (29.1%)	179 (28.4%)	.43
Mechanical ventilation	2029 (55.8%)	4000 (56.5%)	409 (64.9%)	.03
Mechanical circulatory support	173 (4.8%)	835 (11.8%)	166 (26.3%)	<.001
Impella	39 (1.1%)	100 (1.4%)	15 (2.4%)	.19
ECMO	108 (3%)	684 (9.7%)	148 (23.4%)	<.001
IABP	43 (1.2%)	85 (1.2%)	12 (1.9%)	.56

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.

Table 2
Unadjusted Outcomes Among High-Risk PE Admissions According to the Transfer Status.

	Presenting directly to small/medium hospitals (*n* = 3636)	Presenting directly to large hospitals (*n* = 7073)	Transferred to large hospitals (*n* = 631)	*P* value
In-hospital mortality	1520 (41.8%)	3057 (43.2%)	246 (39%)	.33
Cardiac arrest	927 (25.5%)	1808 (25.6%)	210 (33.3%)	.02
Discharge to a facility	769 (21.1%)	1531 (21.6%)	133 (21.1%)	.91
ICH	61 (1.7%)	177 (2.5%)	24 (3.9%)	.04
Non-ICH	966 (26.6%)	1911 (27%)	281 (44.6%)	<.001
Length of stay, days (IQR%)	5 (2-10)	6 (2-12)	13 (6-23)	<.001
Cost of stay, US dollars (IQR%)	24,387 (14,611-42,079)	28,278 (16,536-52,983)	57,410 (31,426-112,902)	<.001

ICH= intracranial hemorrhage; IQR = interquartile range.

Consistent with prior studies,[6,7] our analysis found that transferred patients with high-risk PE were sicker and required advanced therapies for PE other than systemic thrombolysis. However, in-hospital mortality was not different between transferred and nontransferred patients. The lack of other important clinical information in this dataset to better assess the severity of illness (such as cardiac biomarkers, right ventricular systolic function and pressure) might also partly explain the lack of difference in the rates of in-hospital mortality between the groups. Large, high-volume hospitals may have greater staff experience, subspecialty support services, and more advanced infrastructure. They offer other therapeutic options for patients with high-risk PE and those with cardiac arrest.[10,11] Indeed in our analysis, 1 in 4 transferred patients required MCS devices (especially ECMO) and they were more likely to require catheter or surgical embolectomy. Additionally, large tertiary hospitals are more likely to have pulmonary embolism response teams (PERTs) that help in the rapid risk stratification of patients as well as choosing the 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 and some studies showed that the incorporation of PERT was linked with better outcomes.[12]

This study has some limitations. This is a retrospective observational study with the inherent limitation of selection bias. Given the administrative nature of the NRD, the study is subject to coding errors and data quality at the site of collection. The exact reason for the transfer could not be determined. The temporal relationship of certain outcomes cannot be reliably established. The NRD lacks important clinical, laboratory, and imaging data that are needed for careful assessment of the illness severity (eg, vital signs, cardiac biomarkers, lactic acid, presence of right ventricular strain). Long-term outcomes could not be assessed. Finally, since the NRD lacks data on the hospital regions, we could not examine the association between regional variations and outcomes.

Conclusion

We found that transferred patients were more likely to receive advanced therapies. Although transferred patients had higher rates of major bleeding and cardiac arrest, there was no difference in-hospital mortality rates compared with patients admitted directly to large or small/medium-sized hospitals. Select high-risk PE patients with multiple risk factors might receive benefits from transfer to large hospitals.

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests. Aditya S. Bharadwaj reports a relationship with Abiomed Inc. that includes: consulting or advisory and speaking and lecture fees. Aditya S. Bharadwaj reports a relationship with Cardiovascular Solutions Inc. that includes: consulting or advisory and speaking and lecture fees. Aditya S. Bharadwaj reports a relationship with Shockwave Medical Inc. that includes: consulting or advisory and speaking and lecture fees.

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