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ORIGINAL RESEARCH

Trends in Treatment Patterns and Outcomes of Patients With Pulmonary Embolism in Japan, 2010 to 2020: A Nationwide Inpatient Database Study

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BACKGROUND: The impact of major changes in the treatment practice of pulmonary embolism (PE), such as limited indications for systemic thrombolysis and the introduction of direct oral anticoagulants, is not well documented. This study aimed to describe annual trends in the treatment patterns and outcomes in patients with PE.

METHODS AND RESULTS: Using the Japanese Diagnosis Procedure Combination inpatient database from April 2010 to March 2021, we identified hospitalized patients with PE. Patients with high-risk PE were defined as those admitted for out-of-hospital cardiac arrest or who received cardiopulmonary resuscitation, extracorporeal membrane oxygenation, vasopressors, or invasive mechanical ventilation on the day of admission. The remaining patients were defined as patients with non–high-risk PE. The patient characteristics and outcomes were reported with fiscal year trend analyses. Of 88 966 eligible patients, 8116 (9.1%) had high-risk PE, and the remaining 80 850 (90.9%) had non–high-risk PE. Between 2010 and 2020, in patients with high-risk PE, the annual proportion of extracorporeal membrane oxygenation use significantly increased from 11.0% to 21.3%, whereas that of thrombolysis use significantly decreased from 22.5% to 15.5% (*P* for trend <0.001 for both). In-hospital mortality significantly decreased from 51.0% to 43.7% (*P* for trend=0.04). In patients with non–high-risk PE, the annual proportion of direct oral anticoagulant use increased from 0.0% to 38.3%, whereas that of thrombolysis use significantly decreased from 13.7% to 3.4% (*P* for trend <0.001 for both). In-hospital mortality significantly decreased from 7.9% to 5.4% (*P* for trend <0.001).

CONCLUSIONS: Substantial changes in the PE practice and outcomes occurred in patients with high-risk and non–high-risk PE.

Key Words: epidemiology ■ extracorporeal membrane oxygenation ■ factor Xa inhibitors ■ mortality ■ pulmonary embolism ■ thrombolytic therapy

Venous thromboembolism contributes to a major global burden of disease, and the incidence of venous thromboembolism increases with increasing age.[1] Acute pulmonary embolism (PE) is the most serious clinical manifestation of venous thromboembolism.[2] In addition, acute PE has a wide range of clinical presentations and is classified into low, intermediate, or high risk of early death, depending on the hemodynamic instability, right ventricular dysfunction, and comorbidities.[3] High-risk PE presents an immediate life-threatening situation defined by hemodynamic instability, including cardiac arrest, obstructive shock, or persistent hypotension.[3]

The guidelines consistently have placed systemic thrombolysis as the first-line reperfusion treatment for

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CLINICAL PERSPECTIVE

What Is New?

- To the best of our knowledge, this is the first nationwide study on the annual trends in the treatment patterns and outcomes in patients with high-risk and non–high-risk pulmonary embolism (PE) in Japan between 2010 and 2020.
- In the patients with high-risk PE, the annual proportions showed an increasing trend in extracorporeal membrane oxygenation use and a decreasing trend in thrombolysis use and in-hospital mortality.
- In the patients with non–high-risk PE, the annual proportions showed a remarkably increasing trend in direct oral anticoagulant use and decreasing trends in thrombolysis use and in-hospital mortality.

What Are the Clinical Implications?

- Given that more than half of the patients with high-risk PE who received extracorporeal membrane oxygenation had extracorporeal membrane oxygenation alone, an aggressive additional surgical embolectomy or catheter-directed therapy in combination with extracorporeal membrane oxygenation might be warranted to reduce high in-hospital mortality in those patients.
- In Japan, where there are no dedicated devices for catheter-directed thrombolysis or embolectomy, surgical embolectomy should be further considered for patients with high-risk PE who have bleeding concerns.

Nonstandard Abbreviations and Acronyms

DOAC	direct oral anticoagulant
OHCA	out-of-hospital cardiac arrest

patients with high-risk PE but have limited the indications for systemic thrombolysis for a rescue reperfusion treatment in patients with intermediate-risk PE in the United States, Europe, and Japan since 2012, 2014, and 2017, respectively.[4,5] Direct oral anticoagulants (DOACs) have become commonly used in patients with low- and intermediate-risk PE in Japan since their approval for venous thromboembolism; edoxaban was approved in September 2014, rivaroxaban in September 2015, and apixaban in December in 2015.[6] At present, it is unclear whether these major changes in the PE practice have affected the treatment patterns and clinical outcomes.

Capturing the trends in the treatment practice resulting from changes in the guideline recommendations and the introduction of new anticoagulants is important for understanding the current state of PE practice and to establish evidence-based medicine in the future. The present study therefore aimed to describe the annual proportions of treatment patterns and outcomes, and their trends in patients with PE, using a nationwide inpatient database in Japan.

METHODS

Data Availability

The data sets analyzed during the current study are not publicly available due to contracts with the hospitals providing the data to the database.

Design and Ethical Statements

This was a retrospective cohort study using an inpatient administrative database, and the study conformed to the REporting of studies Conducted using Observational Routinely-collected health Data statement reporting guidelines.[7] This study was conducted in accordance with the amended Declaration of Helsinki and was approved by the institutional review board of the University of Tokyo (approval number, 3501-[5]; May 19, 2021). Because the data were anonymous, the institutional review board waived the requirement for informed consent. No information about individual patients, hospitals, or treating physicians was available.

Data Source

We used the Japanese Diagnosis Procedure Combination inpatient database, which contained administrative claims data and discharge abstracts from >1500 acute care hospitals and covers ≈90% of all tertiary emergency hospitals in Japan.[8] The database includes the following patient-level data for all hospitalizations: age, sex, diagnoses (main diagnosis, admission-precipitating diagnosis, most resource-consuming diagnosis, second-most resource-consuming diagnosis, comorbidities present on admission, and complications arising after admission) recorded with the *International Classification of Diseases, Tenth Revision* (*ICD-10*) codes, daily procedures recorded using Japanese medical procedure codes, daily drug administration, and discharge status.[8] A previous validation study showed that the specificity of the recorded diagnoses in the database exceeded 96%, the sensitivity of the diagnoses ranged from 50% to 80%, and the specificity and sensitivity of procedures both exceeded 90%.[9]

Study Population

Using the database from July 2010 to March 2021, which was the maximum period available at that time,

we identified hospitalized patients with the primary diagnosis of PE (*ICD-10* code, I26). We did not include patients with a suspected PE diagnosis and patients who developed PE as a complication after hospitalization. Patients who were admitted for out-of-hospital cardiac arrest (OHCA) (*ICD-10* code, I46) or who received cardiopulmonary resuscitation, extracorporeal membrane oxygenation (ECMO), vasopressors (adrenaline, noradrenaline, dopamine, or vasopressin), or invasive mechanical ventilation on the day of admission were defined as patients with high-risk PE in accordance with the guidelines,[3] and the remaining patients were defined as patients with non–high-risk PE in this study.

Variables and Outcomes

The variables included the age, sex, body mass index at admission, Japan Coma Scale at admission,[10] OHCA, comorbidities (coronary artery disease, heart failure, chronic lung disease, hypertension, diabetes, chronic kidney disease, cancer, and sepsis), ambulance use, weekend admissions, intensive care unit admissions, high-dependency care unit admissions, procedures on the day of admission (cardiopulmonary resuscitation, ECMO, surgical embolectomy, thrombolysis, inferior vena cava filter, and invasive mechanical ventilation), resuscitative drugs on the day of admission (vasopressors or dobutamine), and anticoagulant agents on the day of admission (DOACs [rivaroxaban, apixaban, or edoxaban], warfarin, or heparin).

The primary outcome was in-hospital mortality. The secondary outcomes were the length of hospital stay, total hospitalization cost, major bleeding, and total blood transfusion volume during the hospitalization. Major bleeding was defined as the presence of intracranial bleeding (*ICD-10* code, I61), intraspinal bleeding (G951), pericardial hematomas (I312), intra-abdominal or retroperitoneal hematomas (K661), intra-articular bleeding (M250), intraocular bleeding (H448), and compartment syndrome (M622), which was in accordance with the International Society of Thrombosis and Hemostasis definitions.[11]

Statistical Analysis

Continuous variables are presented as the mean and SD and categorical variables as the number and percentage. Continuous variables were compared using the Student *t* test, and categorical variables were compared using the χ^2 test. To evaluate the trends by the fiscal year, we performed Cochran-Armitage tests for the binary variables and Jonckheere-Terpstra tests for the continuous variables. The trends in the incidence, patient characteristics, and outcomes were separately assessed among the patients with high-risk and non–high-risk PE. Patients with high-risk PE were categorized into the following 8 treatment categories on the day of admission: (1) none, (2) thrombolysis alone, (3) ECMO alone, (4) surgical embolectomy alone, (5) thrombolysis+ECMO, (6) ECMO+surgical embolectomy, (7) thrombolysis+surgical embolectomy, and (8) thrombolysis+ECMO+surgical embolectomy. We then presented the age, sex, and outcomes stratified by the treatment categories among the patients with high-risk PE. We presented the trends in the patient characteristics and outcomes stratified by the age category in the overall patients with PE. Finally, we separately assessed the trends in in-hospital mortality stratified by the age category in the overall patients and the patients with high-risk and non–high-risk PE. The body mass index and total hospitalization cost had missing values as shown in Table S1–S6. We considered all reported *P* values as 2-sided and a $P<0.05$ as statistically significant. All analyses were performed using Stata/SE 17.0 software (StataCorp).

RESULTS

During the study period, we identified 88 966 patients with a primary diagnosis of PE. Of those, 8116 (9.1%) were identified as having high-risk PE and the remaining 80 850 (90.9%) as having non–high-risk PE. The annual incidence of overall PE per 100 000 hospitalizations significantly increased from 100.9 in 2010 to 124.2 in 2020 (*P* for trend <0.001) (Figure S1 and Table S2). The annual incidence of high-risk and non–high-risk PE per 100 000 hospitalizations also significantly increased from 9.6 and 91.3 in 2010 to 11.0 and 113.2 in 2020, respectively.

The patient characteristics differed widely between the patients with high-risk and non–high-risk PE (Table 1). The patients with high-risk PE were more likely to be women, have poor consciousness, and receive thrombolysis on the day of admission and less likely to have comorbidities or receive DOACs on the day of admission. In patients with high-risk PE, 33.2% had OHCA, and 36.7%, 16.3%, and 78.2% received cardiopulmonary resuscitation, ECMO, and vasopressors on the day of admission, respectively.

In the patients with high-risk PE, the annual proportion of OHCA significantly increased from 26.2% in 2010 to 38.2% in 2020 (*P* for trend <0.001) (Table S3). The annual proportion of ECMO use significantly increased from 11.0% in 2010 to 21.3% in 2020 (*P* for trend <0.001). However, the annual proportion of thrombolysis use significantly decreased from 22.5% in 2010 to 15.5% in 2020 (*P* for trend <0.001) (Figure 1). In-hospital mortality significantly decreased from 51.0% in 2010 to 43.7% in 2020 (*P* for trend=0.04).

In the patients with non–high-risk PE, the annual proportion of DOAC use increased from 0.0% in 2010

Table 1. Patient Characteristics

Characteristic	Overall (n=88 966)	High-risk PE (n=8116)	Non–high-risk PE (n=80 850)	*P* value
Age, y, mean (SD)	68.7 (15.7)	69.3 (16.3)	68.6 (15.7)	<0.001
Men, n (%)	36 546 (41.1)	3088 (38.0)	33 458 (41.4)	<0.001
Body mass index on the day of admission, kg/m^2, mean (SD)	23.8 (4.6)	23.7 (5.1)	23.8 (4.6)	0.006
Japan Coma Scale on the day of admission, n (%)				
0, alert	74 078 (83.3)	2927 (36.1)	71 151 (88.0)	<0.001
1–3, dizzy	8889 (10.0)	1109 (13.7)	7780 (9.6)	
10–30, somnolent	1877 (2.1)	574 (7.1)	1303 (1.6)	
100–300, coma	4119 (4.6)	3505 (43.2)	614 (0.8)	
Out-of-hospital cardiac arrest, n (%)	2698 (3.0)	2698 (33.2)	0 (0.0)	<0.001
Comorbidities, n (%)				
Coronary artery disease	5482 (6.2)	418 (5.2)	5064 (6.3)	<0.001
Heart failure	17 155 (19.3)	1527 (18.8)	15 628 (19.3)	0.26
Chronic lung disease	5249 (5.9)	336 (4.1)	4913 (6.1)	<0.001
Hypertension	25 497 (28.7)	1440 (17.7)	24 057 (29.8)	<0.001
Diabetes	11 430 (12.8)	767 (9.5)	10 663 (13.2)	<0.001
Chronic kidney disease	2234 (2.5)	231 (2.8)	2003 (2.5)	0.04
Cancer	16 663 (18.7)	740 (9.1)	15 923 (19.7)	<0.001
Sepsis	43 340 (48.7)	2678 (33.0)	40 662 (50.3)	<0.001
Ambulance use, n (%)	34 393 (38.7)	6733 (83.0)	27 660 (34.2)	<0.001
Weekend admission, n (%)	13 687 (15.4)	1949 (24.0)	11 738 (14.5)	<0.001
Intensive care unit admission, n (%)	13 733 (15.4)	4073 (50.2)	9660 (11.9)	<0.001
High-dependency care unit admission, n (%)	13 978 (15.7)	1875 (23.1)	12 103 (15.0)	<0.001
Procedures on the day of admission, n (%)				
Cardiopulmonary resuscitation	2977 (3.3)	2977 (36.7)	0 (0.0)	<0.001
Extracorporeal membrane oxygenation	1326 (1.5)	1326 (16.3)	0 (0.0)	<0.001
Surgical embolectomy	500 (0.6)	452 (5.6)	48 (0.1)	<0.001
Thrombolysis	7868 (8.8)	1602 (19.7)	6266 (7.8)	<0.001
Inferior vena cava filter	7703 (8.7)	479 (5.9)	7224 (8.9)	<0.001
Invasive mechanical ventilation	4974 (5.6)	4974 (61.3)	0 (0.0)	<0.001
Resuscitative drugs on the day of admission, n (%)				
Vasopressors	6346 (7.1)	6346 (78.2)	0 (0.0)	<0.001
Dobutamine	1882 (2.1)	1376 (17.0)	506 (0.6)	<0.001
Anticoagulant agents on the day of admission, n (%)				
Rivaroxaban	5308 (6.0)	123 (1.5)	5185 (6.4)	<0.001
Apixaban	5943 (6.7)	121 (1.5)	5822 (7.2)	<0.001
Edoxaban	3537 (4.0)	68 (0.8)	3469 (4.3)	<0.001
Warfarin	11 339 (12.7)	323 (4.0)	11 016 (13.6)	<0.001
Heparin	55 202 (62.0)	5943 (73.2)	49 259 (60.9)	<0.001

PE indicates pulmonary embolism.

to 38.3% in 2020 (*P* for trend <0.001). However, the annual proportion of warfarin use decreased from 27.4% in 2010 to 2.1% in 2020 (*P* for trend <0.001) (Table S4). The annual proportion of thrombolysis use significantly decreased from 13.7% in 2010 to 3.4% in 2020 (*P* for trend <0.001) (Figure 2). In-hospital mortality significantly decreased from 7.9% in 2010 to 5.4% in 2020 (*P* for trend <0.001). Both the length of hospital stay and total hospitalization cost significantly decreased (*P* for trend <0.001) (Table S4).

The patient characteristics and outcomes across treatment categories in patients with high-risk PE are shown in Table 2. In-hospital mortality was the lowest in patients who underwent surgical embolectomy and the highest in those who received ECMO alone (17.8% and 58.7%, respectively). Major bleeding occurred

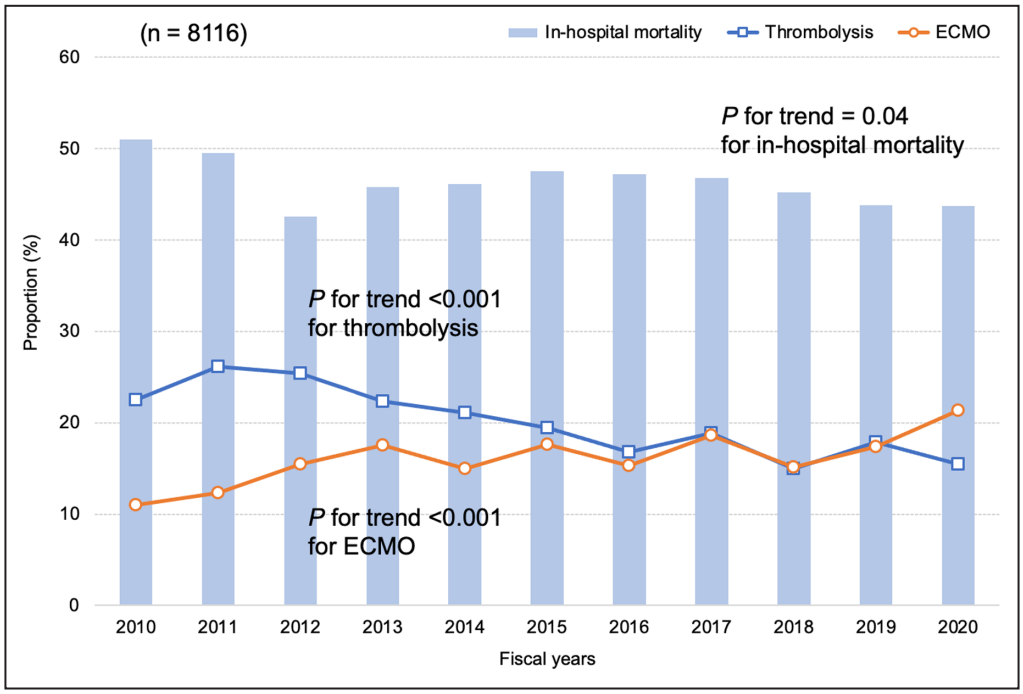

Figure 1. Annual proportions of in-hospital mortality, thrombolysis use, and ECMO use in patients with high-risk pulmonary embolism.
Each fiscal year started on April 1 and ended on March 31. ECMO indicates extracorporeal membrane oxygenation.

most frequently in patients who received thrombolysis and surgical embolectomy (5.0%) but not in those who received ECMO and surgical embolectomy.

In the overall patients with PE, the proportions of thrombolysis and ECMO use decreased with increasing age from 13.4% and 3.1% in patients aged 0 to 39 years to 3.3% and 0.2% in patients aged ≥90 years, respectively (Figure 3). On the other hand, in-hospital mortality increased with increasing age from 5.5% in patients aged 0 to 39 years to 21.9% in patients aged ≥90 years. The detailed patient characteristics and outcomes across age categories are shown in Table S5. There were no specific trends by the age category in patients who received ECMO, thrombolysis, and DOACs (Table S6).

DISCUSSION

To the best of our knowledge, this is the first nationwide study on the annual trends in the treatment patterns and outcomes in patients with high-risk and non–high-risk PE in Japan. In the patients with high-risk PE, the annual proportions showed an increasing trend in ECMO use and decreasing trend in thrombolysis use and in-hospital mortality between 2010 and 2020. In the patients with non–high-risk PE, the annual proportions showed a remarkably increasing trend in DOAC use and decreasing trends in thrombolysis use and in-hospital mortality between 2010 and 2020.

In the patients with high-risk PE, the annual proportion of ECMO use exhibited an increasing trend, which was consistent with that in the previous reports from the United States and Germany.[12,13] The proportion of ECMO use in the patients with high-risk PE in Japan (between 2010 and 2020) reached 19.2%, which was remarkably high as compared with 2.8% in Germany (between 2005 and 2018) and 0.3% in the United States (between 2005 and 2013).[12,13] In addition, the patients with high-risk PE with ECMO in Japan (mean age of 60 years) were older than those with a mean age of 42 years in the United States and those with a median age of 55 years in Germany.[12,13] In the present study, among all the ECMO users, the percentage of patients with high-risk PE aged ≥70 years was >30%. These results may indicate a high resource availability and low threshold for ECMO implementation in Japan. In-hospital mortality in patients with high-risk PE with ECMO was similar across Japan, the United States, and Germany (58.7%, 61.6%, and 61.8%, respectively). Given that previous reports showed the potential benefit of ECMO for patients with high-risk PE aged ≤60 years,[14] careful selection in older patients for ECMO may be needed to reduce the high in-hospital mortality. Furthermore, in the present study, more than half (65%) of patients who received ECMO had ECMO alone. Based on a concept that ECMO is a bridge to reperfusion therapy,[13,15,16] aggressive additional

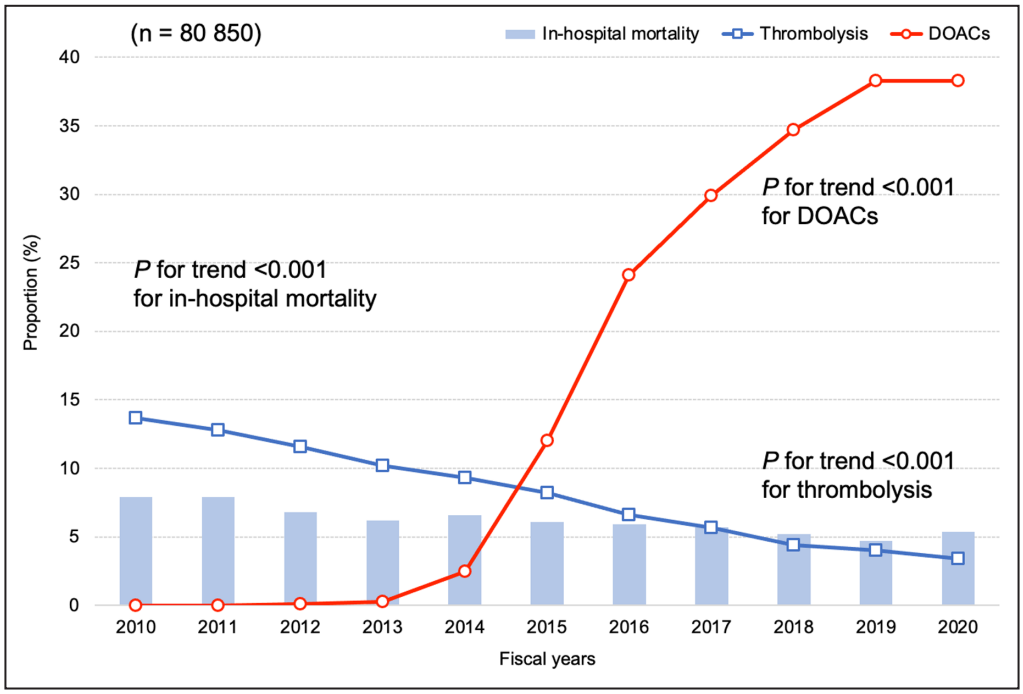

Figure 2. Annual proportions of in-hospital mortality, thrombolysis use, and DOAC use in patients with non–high-risk pulmonary embolism.
Each fiscal year started on April 1 and ended on March 31. DOAC indicates direct oral anticoagulant.

surgical embolectomy or catheter-based therapy in combination with ECMO might be warranted.[17]

Although the guidelines recommend systemic thrombolysis as the first-line reperfusion treatment for patients with high-risk PE,[3,18] the present study showed a decreasing trend in the annual proportion of thrombolysis use. Systemic thrombolysis promotes resolution of PE and a rapid hemodynamic improvement[19,20] but increases major bleeding events.[21] Concern about the bleeding risk and poor prognosis after bleeding events[22] may have led to a decreasing trend in thrombolysis use in Japan, a super-aging society. The proportion of thrombolysis use was lower in the older patients, and the finding was consistent with that in a previous report from Germany.[23] In regard to surgical embolectomy, the annual proportion remained low. In particular, the proportion of surgical embolectomy in combination with ECMO was 1.4%. This figure was considerably low as compared with 20.4% in the United States and 17.1% in Germany,[12,13] even considering that the proportion in the present study was based only on the day of admission. Given the effectiveness of surgical embolectomy for patients with high-risk PE with ECMO,[24] there is a need to encourage a setup with multidisciplinary PE response teams[25] and perform surgical embolectomy for appropriately selected patients with high-risk PE in Japan.

The present study had several strengths. First, the present study was based on one of the largest databases, which covered ≈90% of all tertiary emergency hospitals in Japan. Second, our database included data before and after the change in the indications for systemic thrombolysis and the introduction of DOACs.

The present study had several limitations. First, our definition of high-risk PE depended on the diagnosis of PE and OHCA using the *ICD-10* codes or procedures such as cardiopulmonary resuscitation, ECMO, or vasopressors on the day of admission, because the database did not contain detailed clinical information such as the vital signs. Therefore, misclassifications may have led to a bias in our study. Second, we could not classify non–high-risk PE into intermediate- and low-risk PE due to a lack of data such as the vital signs, laboratory tests, and imaging examinations. Third, the outcomes may be overestimated by rehospitalization for the primary diagnosis of PE. Fourth, the proportion of major bleeding events in the present study was considerably lower than that in the previous studies.[13,15,16] Given that the sensitivity of the diagnosis might have been low in our database,[9] there was a possibility of having underreported the major bleeding events. Finally, dedicated devices for catheter-based thrombolysis or embolectomy are not available in Japan, suggesting caution should be taken when applying our results to those in other countries where dedicated devices for catheter-based thrombolysis or embolectomy are available.

Table 2. Patient Characteristics and Outcomes Across the Treatment Categories in Patients With High-Risk Pulmonary Embolism

Characteristics and outcomes	Total	Treatment category								*P* value
		None	Thrombolysis alone	ECMO alone	Surgical embolectomy alone	Thrombolysis+ ECMO	ECMO+surgical embolectomy	Thrombolysis+ surgical embolectomy	Thrombolysis+ ECMO+surgical embolectomy	
	(n=8116)	(n=5259)	(n=1191)	(n=857)	(n=320)	(n=357)	(n=78)	(n=20)	(n=34)	
Age, y, mean (SD)	69 (16)	73 (16)	69 (15)	60 (15)	62 (16)	59 (16)	59 (16)	64 (13)	52 (17)	<0.001
Men, n (%)	3088 (38.0)	1960 (37.3)	416 (34.9)	344 (40.1)	156 (48.8)	142 (39.8)	39 (50.0)	12 (60.0)	19 (55.9)	<0.001
Outcomes										
In-hospital mortality, n (%)	3737 (46.0)	2595 (49.3)	342 (28.7)	503 (58.7)	57 (17.8)	186 (52.1)	31 (39.7)	5 (25.0)	18 (52.9)	<0.001
Length of hospital stay, d, mean (SD)	22.5 (36.9)	20.6 (34.5)	25.1 (35.4)	23.8 (33.2)	29.5 (25.1)	28.3 (72.4)	28.6 (26.7)	27.5 (26.2)	36.9 (73.3)	<0.001
Total hospitalization cost, $\times 10^3$ dollars, mean (SD)	16.1 (20.1)	11.3 (16.3)	14.2 (13.9)	27.9 (22.2)	45.3 (25.7)	29.2 (24.6)	47.8 (30.4)	25.0 (11.5)	43.7 (39.3)	<0.001
Major bleeding in a critical area or organ, n (%)	79 (1.0)	24 (0.5)	10 (0.8)	26 (3.0)	4 (1.3)	13 (3.6)	0 (0.0)	1 (5.0)	1 (2.9)	<0.001
Intracranial bleeding, n (%)	40 (0.5)	14 (0.3)	6 (0.5)	11 (1.3)	4 (1.3)	3 (0.8)	0 (0.0)	1 (5.0)	1 (2.9)	<0.001
Blood transfusions, mL, mean (SD)										
Red blood cells	949 (5885)	425 (7150)	313 (1239)	2675 (2785)	2901 (3795)	2758 (2653)	4319 (4597)	966 (1513)	3426 (3151)	<0.001
Fresh-frozen plasma	491 (1619)	171 (1226)	117 (826)	1460 (2007)	2078 (2811)	1377 (2128)	2845 (3150)	384 (844)	1813 (3035)	<0.001
Platelet concentrate	107 (1006)	50 (1223)	21 (170)	300 (533)	400 (650)	247 (535)	637 (1088)	23 (70)	319 (559)	<0.001

ECMO indicates extracorporeal membrane oxygenation.

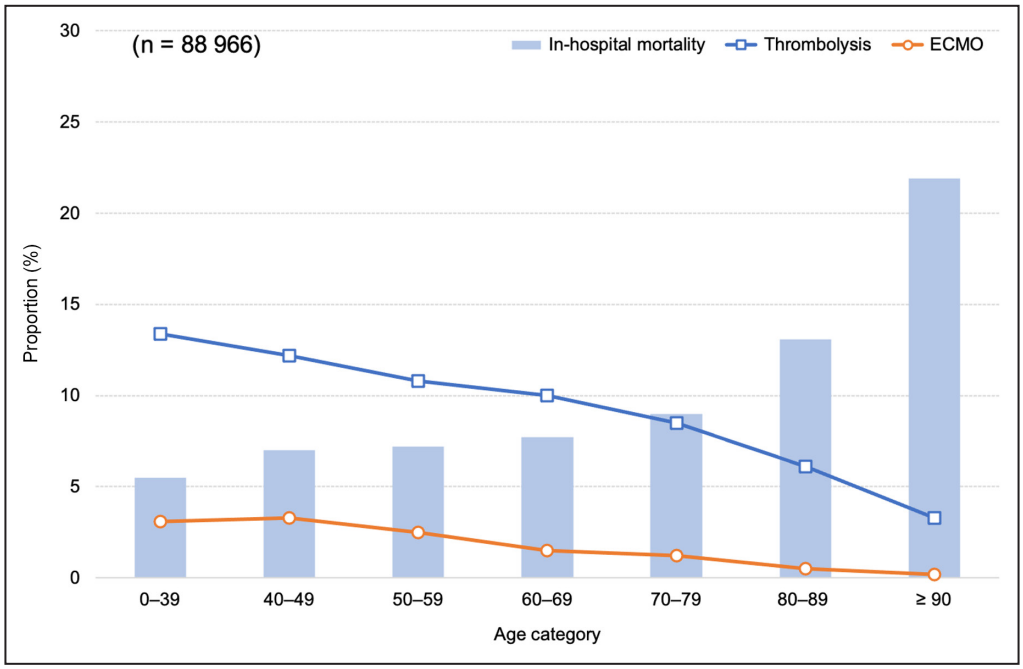

Figure 3. Proportions of in-hospital mortality, thrombolysis use, and ECMO use according to the age category in the overall patients with pulmonary embolism.
ECMO indicates extracorporeal membrane oxygenation.

CONCLUSIONS

The present study using a nationwide inpatient administrative database showed substantial changes in the clinical practice and outcomes in patients with high-risk and non–high-risk PE. In the patients with high-risk PE, the annual proportion of ECMO use increased, that of thrombolysis use decreased, and that of in-hospital mortality remained high over time. In patients with non–high-risk PE, the annual proportion of DOAC use remarkably increased, and that of thrombolysis use and in-hospital mortality decreased over time.

ARTICLE INFORMATION

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Disclosures

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Supplemental Material

Tables S1–S6
Figure S1

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Supplemental Material

Table S1. The number of missing values.

	Overall (*n* = 88,966)	High-risk PE (*n* = 8,116)	Non-high-risk PE (*n* = 80,850)
Body mass index on the day of admission, *n* (%)	8,846 (9.9)	2,129 (26.2)	6,717 (8.3)
Outcomes			
Total hospitalization cost, *n* (%)	691 (0.8)	46 (0.6)	645 (0.8)

PE, pulmonary embolism

Table S2. Annual incidence of overall, high-risk, and non-high-risk PE.

	Fiscal year											*P* for trend
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	
Incidence per 100,000 hospitalizations												
Overall PE	100.9	104.5	111.2	107.5	109.1	103.1	108.3	106.6	108.5	110.9	124.2	<0.001
High-risk PE	9.6	9.1	10.5	10.2	9.3	8.9	10.1	10.3	9.8	10.5	11.0	0.003
Non-high-risk PE	91.3	95.3	100.7	97.4	99.8	94.3	98.2	96.4	98.7	100.4	113.2	<0.001

Each fiscal year started on 01 April and ended on 31 March. PE, pulmonary embolism

Table S3. Patient characteristics and outcomes on an annual basis in high-risk pulmonary embolism patients.

	Fiscal year											*P* for trend
	2010 (*n* = 435)	2011 (*n* = 618)	2012 (*n* = 749)	2013 (*n* = 722)	2014 (*n* = 748)	2015 (*n* = 728)	2016 (*n* = 864)	2017 (*n* = 848)	2018 (*n* = 808)	2019 (*n* = 816)	2020 (*n* = 780)	
Age, years, mean (SD)	70 (15)	68 (16)	69 (17)	68 (17)	69 (16)	69 (16)	71 (16)	70 (16)	70 (16)	69 (16)	68 (17)	0.94
Men, *n* (%)	162 (37.2)	214 (34.6)	268 (35.8)	288 (39.9)	273 (36.5)	277 (38.0)	323 (37.4)	325 (38.3)	321 (39.7)	320 (39.2)	317 (40.6)	0.02
Body mass index on the day of admission, kg/m^2, mean (SD)	23.5 (5.2)	23.0 (4.6)	23.3 (5.1)	23.5 (5.2)	23.6 (5.2)	23.6 (5.3)	23.5 (5.1)	23.7 (5.0)	23.7 (5.2)	24.1 (5.1)	24.1 (5.2)	0.001
Out-of-hospital cardiac arrest, *n* (%)	114 (26.2)	157 (25.4)	206 (27.5)	232 (32.1)	229 (30.6)	255 (35.0)	302 (35.0)	341 (40.2)	271 (33.5)	293 (35.9)	298 (38.2)	<0.001
Intensive care unit admission, *n* (%)	211 (48.5)	309 (50.0)	375 (50.1)	403 (55.8)	382 (51.1)	387 (53.2)	418 (48.4)	404 (47.6)	398 (49.3)	401 (49.1)	385 (49.4)	0.16
High dependency care unit admission, *n* (%)	81 (18.6)	106 (17.2)	138 (18.4)	127 (17.6)	157 (21.0)	149 (20.5)	204 (23.6)	240 (28.3)	207 (25.6)	227 (27.8)	239 (30.6)	<0.001
Procedures on the day of admission, *n* (%)												
Cardiopulmonary resuscitation	178 (40.9)	210 (34.0)	264 (35.2)	274 (38.0)	267 (35.7)	260 (35.7)	310 (35.9)	338 (39.9)	291 (36.0)	284 (34.8)	301 (38.6)	0.76
Extracorporeal membrane oxygenation	48 (11.0)	76 (12.3)	116 (15.5)	126 (17.5)	112 (15.0)	128 (17.6)	132 (15.3)	158 (18.6)	122 (15.1)	142 (17.4)	166 (21.3)	<0.001
Surgical embolectomy	22 (5.1)	40 (6.5)	35 (4.7)	41 (5.7)	41 (5.5)	35 (4.8)	54 (6.3)	49 (5.8)	53 (6.6)	39 (4.8)	43 (5.5)	0.83
Thrombolysis	98 (22.5)	161 (26.1)	190 (25.4)	161 (22.3)	158 (21.1)	141 (19.4)	145 (16.8)	160 (18.9)	121 (15.0)	146 (17.9)	121 (15.5)	<0.001
Inferior vena cava filter	36 (8.3)	66 (10.7)	64 (8.5)	64 (8.9)	75 (10.0)	45 (6.2)	40 (4.6)	24 (2.8)	23 (2.8)	23 (2.8)	19 (2.4)	<0.001
Anticoagulant agents on the day of admission, *n* (%)												
Rivaroxaban	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	6 (0.8)	10 (1.2)	20 (2.4)	29 (3.6)	30 (3.7)	26 (3.3)	<0.001
Apixaban	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (0.7)	14 (1.6)	15 (1.8)	24 (3.0)	37 (4.5)	26 (3.3)	<0.001

Edoxaban	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	9 (1.2)	14 (1.6)	11 (1.3)	17 (2.1)	7 (0.9)	8 (1.0)	<0.001
Warfarin	34 (7.8)	55 (8.9)	55 (7.3)	57 (7.9)	62 (8.3)	23 (3.2)	11 (1.3)	7 (0.8)	8 (1.0)	9 (1.1)	2 (0.3)	<0.001
Heparin	310	436	569	559	539	532	619	616	582	602	579	1.00
	(71.3)	(70.6)	(76.0)	(77.4)	(72.1)	(73.1)	(71.6)	(72.6)	(72.0)	(73.8)	(74.2)	
Outcomes												
In-hospital mortality, *n* (%)	222	306	319	331	345	346	408	397	365	357	341	0.04
	(51.0)	(49.5)	(42.6)	(45.8)	(46.1)	(47.5)	(47.2)	(46.8)	(45.2)	(43.8)	(43.7)	
Length of hospital stay, days, mean (SD)	22.3	22.0	27.2	24.6	22.4	24.2	20.7	21.9	19.9	22.1	20.6	0.052
	(41.0)	(34.5)	(46.2)	(35.5)	(38.5)	(59.9)	(28.2)	(28.6)	(25.6)	(31.5)	(28.7)	
Total hospitalization cost, $\times 10^3$ dollars, mean (SD)	13.3	14.6	16.3	17.4	16.0	16.9	15.1	16.7	15.3	16.6	18.1	0.10
	(14.2)	(18.9)	(19.7)	(21.4)	(21.6)	(22.1)	(18.2)	(21.0)	(18.2)	(20.4)	(22.0)	
Major bleeding in a critical area or organ, *n* (%)	2 (0.5)	2 (0.3)	8 (1.1)	4 (0.6)	6 (0.8)	10 (1.4)	12 (1.4)	9 (1.1)	13 (1.6)	5 (0.6)	8 (1.0)	0.11
Red blood cell transfusions, ml, mean (SD)	672	813	1,325	1061	904	996	840	988	885	825	1,008	0.82
	(1,595)	(2,229)	(17,921)	(2,918)	(2,399)	(2,253)	(2,093)	(2,172)	(2057)	(1,701)	(1,952)	

Each fiscal year started on 01 April and ended on 31 March. SD, standard deviation

Table S4. Patient characteristics and outcomes on an annual basis in non-high-risk pulmonary embolism patients.

	Fiscal year											*P* for trend
	2010 (*n* = 4,146)	2011 (*n* = 6,464)	2012 (*n* = 7,198)	2013 (*n* = 6,923)	2014 (*n* = 8,058)	2015 (*n* = 7,744)	2016 (*n* = 8,389)	2017 (*n* = 7,967)	2018 (*n* = 8,126)	2019 (*n* = 7,798)	2020 (*n* = 8,037)	
Age, years, mean (SD)	68 (16)	68 (16)	68 (16)	68 (16)	68 (16)	69 (16)	69 (16)	69 (16)	69 (16)	69 (16)	70 (16)	0.002
Men, *n* (%)	1,657 (40.0)	2,560 (39.6)	2,913 (40.5)	2,800 (40.4)	3,345 (41.5)	3,182 (41.1)	3,476 (41.4)	3,254 (40.8)	3,448 (42.4)	3,337 (42.8)	3,486 (43.4)	<0.001
Body mass index on the day of admission, kg/m^2, mean (SD)	23.7 (4.4)	23.8 (4.5)	23.7 (4.5)	23.7 (4.5)	23.7 (4.6)	23.7 (4.6)	23.9 (4.6)	23.8 (4.6)	24.0 (4.6)	23.9 (4.6)	24.0 (4.7)	0.01
Intensive care unit admission, *n* (%)	621 (15.0)	897 (13.9)	1,050 (14.6)	1,090 (15.7)	1,104 (13.7)	1,067 (13.8)	945 (11.3)	758 (9.5)	779 (9.6)	697 (8.9)	652 (8.1)	<0.001
High dependency care unit admission, *n* (%)	373 (9.0)	615 (9.5)	808 (11.2)	816 (11.8)	1,148 (14.2)	1,180 (15.2)	1,374 (16.4)	1,427 (17.9)	1,479 (18.2)	1,452 (18.6)	1,431 (17.8)	<0.001
Procedures on the day of admission, *n* (%)												
Thrombolysis	568 (13.7)	826 (12.8)	835 (11.6)	706 (10.2)	747 (9.3)	634 (8.2)	556 (6.6)	456 (5.7)	358 (4.4)	309 (4.0)	271 (3.4)	<0.001
Inferior vena cava filter	638 (15.4)	899 (13.9)	1,008 (14.0)	821 (11.9)	974 (12.1)	798 (10.3)	596 (7.1)	494 (6.2)	387 (4.8)	312 (4.0)	297 (3.7)	<0.001
Anticoagulant agents on the day of admission, *n* (%)												
Rivaroxaban	0 (0.0)	0 (0.0)	4 (0.1)	19 (0.3)	18 (0.2)	282 (3.6)	723 (8.6)	884 (11.1)	1,055 (13.0)	1,110 (14.2)	1,090 (13.6)	<0.001
Apixaban	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	19 (0.2)	112 (1.4)	761 (9.1)	858 (10.8)	1,180 (14.5)	1,366 (17.5)	1,525 (19.0)	<0.001
Edoxaban	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	168 (2.1)	534 (6.9)	543 (6.5)	645 (8.1)	587 (7.2)	520 (6.7)	472 (5.9)	<0.001
Warfarin	1,134	1,713	2,073	1,998	2,003	799	446 (5.3)	294 (3.7)	213 (2.6)	177 (2.3)	166 (2.1)	<0.001

	(27.4)	(26.5)	(28.8)	(28.9)	(24.9)	(10.3)						
Heparin	2,640	4,147	4,802	4,620	5,470	5,047	4,987	4,597	4,461	4,198	4,290	<0.001
	(63.7)	(64.2)	(66.7)	(66.7)	(67.9)	(65.2)	(59.4)	(57.7)	(54.9)	(53.8)	(53.4)	
Outcomes												
In-hospital mortality, *n* (%)	327 (7.9)	512 (7.9)	487 (6.8)	427 (6.2)	533 (6.6)	470 (6.1)	493 (5.9)	456 (5.7)	420 (5.2)	369 (4.7)	434 (5.4)	<0.001
Length of hospital stay, days, mean (SD)	25.7	25.3	25.3	24.6	23.2	22.1	22.4	21.8	20.5	19.6	19.4	<0.001
	(32.1)	(36.9)	(34.5)	(25.8)	(22.6)	(26.9)	(72.3)	(40.9)	(28.4)	(24.3)	(23.6)	
Total hospitalization cost, $\times 10^3$ dollars, mean (SD)	9.5 (8.6)	9.4 (9.1)	9.7 (10.2)	9.6 (10.2)	9.0 (8.6)	8.8 (9.5)	8.5 (12.6)	8.4 (10.0)	8.1 (8.9)	7.8 (8.3)	8.1 (9.0)	<0.001
Major bleeding in a critical area or organ, *n* (%)	5 (0.1)	13 (0.2)	18 (0.3)	13 (0.2)	24 (0.3)	15 (0.2)	18 (0.2)	14 (0.2)	14 (0.2)	9 (0.1)	11 (0.1)	0.11
Red blood cell transfusions, ml, mean (SD)	247	334	516	486	322	409	363	468	500	444	545	0.07
	(767)	(1,090)	(5,433)	(4,169)	(940)	(1,317)	(1,006)	(1,371)	(1,161)	(1,174)	(1,217)	

Each fiscal year started on 01 April and ended on 31 March. SD, standard deviation

Table S5. Patient characteristics and outcomes across the age categories in overall pulmonary embolism patients.

	Age category							*P* for trend
	0–39 (*n* = 4,623)	40–49 (*n* = 7,981)	50–59 (*n* = 9,877)	60–69 (*n* = 17,187)	70–79 (*n* = 24,808)	80–89 (*n* = 20,038)	≥ 90 (*n* = 4,452)	
Men, *n* (%)	2,302 (49.8)	3,609 (45.2)	5,300 (53.7)	8,556 (49.8)	9,815 (39.6)	6,108 (30.5)	856 (19.2)	<0.001
Body mass index on the day of admission, kg/m^2, mean (SD)	25.4 (5.9)	26.1 (5.6)	25.2 (5.0)	23.9 (4.2)	23.5 (4.0)	22.6 (4.0)	21.2 (3.8)	0.004
Out-of-hospital cardiac arrest, *n* (%)	182 (3.9)	348 (4.4)	340 (3.4)	488 (2.8)	656 (2.6)	562 (2.8)	122 (2.7)	<0.001
Intensive care unit admission, *n* (%)	891 (19.3)	1,656 (20.7)	1,722 (17.4)	2,764 (16.1)	3,747 (15.1)	2,589 (12.9)	364 (8.2)	<0.001
High dependency care unit admission, *n* (%)	701 (15.2)	1,210 (15.2)	1,516 (15.3)	2,495 (14.5)	3,871 (15.6)	3,413 (17.0)	772 (17.3)	<0.001
Procedures on the day of admission, *n* (%)								
Cardiopulmonary resuscitation	160 (3.5)	320 (4.0)	356 (3.6)	481 (2.8)	759 (3.1)	730 (3.6)	171 (3.8)	0.69
Extracorporeal membrane oxygenation	142 (3.1)	261 (3.3)	244 (2.5)	262 (1.5)	301 (1.2)	108 (0.5)	8 (0.2)	<0.001
Surgical embolectomy	59 (1.3)	68 (0.9)	78 (0.8)	117 (0.7)	132 (0.5)	45 (0.2)	1 (0.0)	<0.001
Thrombolysis	621 (13.4)	975 (12.2)	1,070 (10.8)	1,717 (10.0)	2,121 (8.5)	1,219 (6.1)	145 (3.3)	<0.001
Inferior vena cava filter	554 (12.0)	852 (10.7)	1,043 (10.6)	1,677 (9.8)	2,079 (8.4)	1,343 (6.7)	155 (3.5)	<0.001
Anticoagulant agents on the day of admission, *n* (%)								
Rivaroxaban	302 (6.5)	578 (7.2)	739 (7.5)	1,151 (6.7)	1,634 (6.6)	810 (4.0)	94 (2.1)	<0.001
Apixaban	254 (5.5)	508 (6.4)	651 (6.6)	1,134 (6.6)	1,915 (7.7)	1,258 (6.3)	223 (5.0)	0.40
Edoxaban	133 (2.9)	278 (3.5)	350 (3.5)	693 (4.0)	936 (3.8)	933 (4.7)	214 (4.8)	<0.001
Warfarin	641 (13.9)	1,145 (14.3)	1,326 (13.4)	2,467 (14.4)	3,193 (12.9)	2,220 (11.1)	347 (7.8)	<0.001
Heparin	3,056 (66.1)	5,394 (67.6)	6,396 (64.8)	11,035 (64.2)	15,226 (61.4)	11,689 (58.3)	2,406 (54.0)	<0.001
Outcomes								
In-hospital mortality, *n* (%)	252 (5.5)	559 (7.0)	716 (7.2)	1,321 (7.7)	2,221 (9.0)	2,622 (13.1)	974 (21.9)	<0.001
Length of hospital stay, days, mean (SD)	21.8 (77.6)	19.3 (30.9)	19.5 (20.6)	21.0 (36.2)	22.6 (36.9)	25.7 (32.3)	25.8 (25.5)	0.02
Total hospitalization cost, ×10^3 dollars, mean (SD)	10.9 (17.4)	9.8 (12.2)	9.5 (11.9)	9.4 (12.0)	9.4 (11.1)	9.2 (9.0)	8.4 (6.7)	0.002
Major bleeding in a critical area or organ, *n* (%)	13 (0.3)	18 (0.2)	23 (0.2)	45 (0.3)	85 (0.3)	43 (0.2)	6 (0.1)	0.67
Red blood cell transfusions, ml, mean (SD)	731 (2,028)	732 (1,669)	710 (3,298)	622 (2,976)	553 (2,614)	426 (6,469)	207 (723)	0.004

SD, standard deviation

Table S6. In-hospital mortality on an annual basis across the age categories in the overall, high-risk, and non-high-risk PE patients.

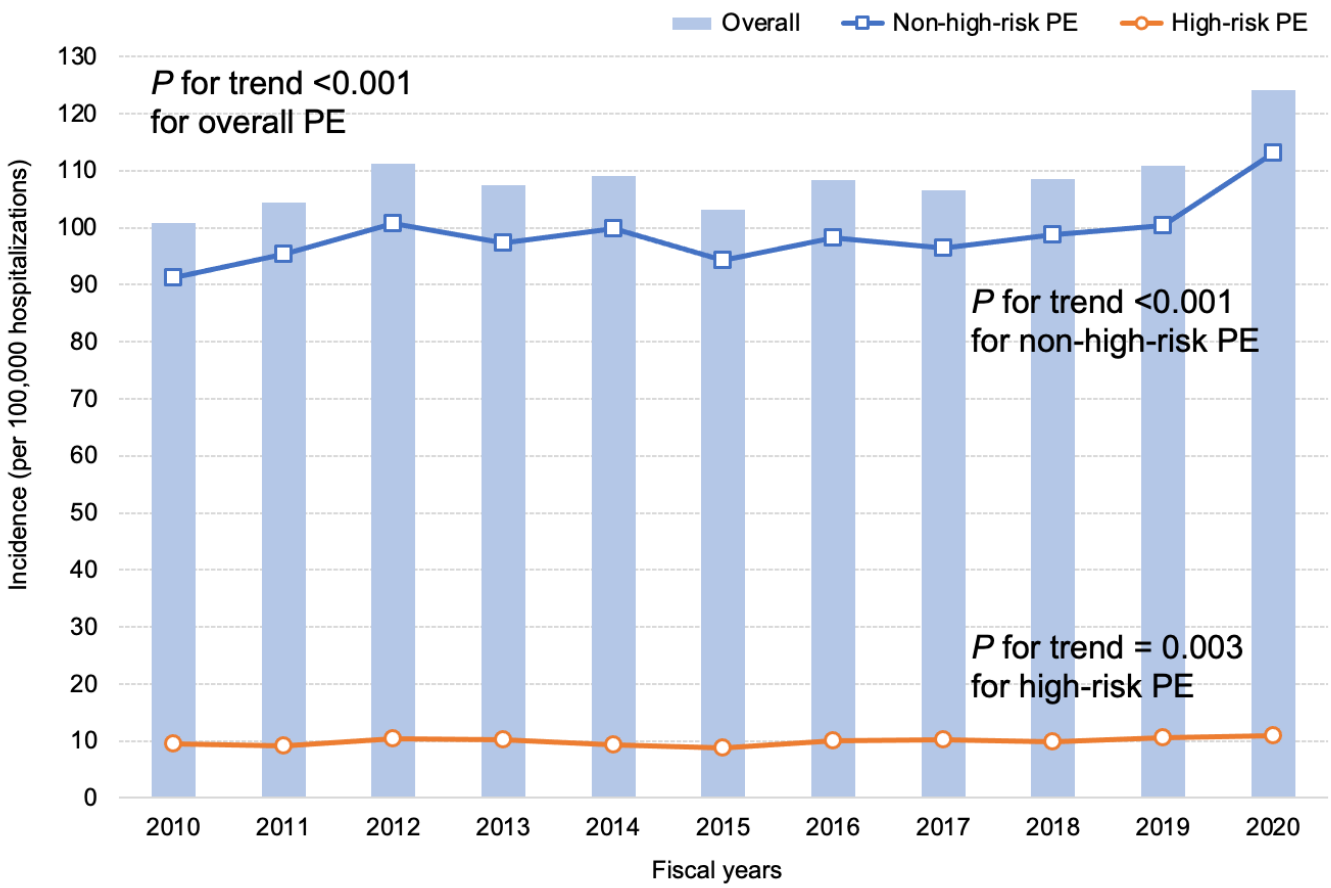
	Fiscal year											*P* for trend
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	
Aged 0-39	(*n* = 248)	(*n* = 394)	(*n* = 483)	(*n* = 443)	(*n* = 476)	(*n* = 416)	(*n* = 441)	(*n* = 433)	(*n* = 438)	(*n* = 423)	(*n* = 428)	
In-hospital mortality, *n* (%)												
Overall PE	14 (5.6)	29 (7.4)	22 (4.6)	25 (5.6)	20 (4.2)	28 (6.7)	23 (5.2)	23 (5.3)	22 (5.0)	20 (4.7)	26 (6.1)	0.64
High-risk PE	7 (36.8)	17 (40.5)	13 (29.5)	13 (32.5)	17 (39.5)	18 (56.3)	13 (36.1)	20 (50.0)	16 (36.4)	14 (35.0)	16 (36.4)	0.76
ECMO	2 (100.0)	6 (54.5)	5 (38.5)	5 (31.3)	8 (53.3)	3 (75.0)	7 (46.7)	12 (63.2)	8 (50.0)	5 (50.0)	12 (57.1)	0.45
Thrombolysis	1 (16.7)	4 (28.6)	3 (15.8)	2 (14.3)	6 (60.0)	2 (50.0)	1 (20.0)	1 (25.0)	2 (28.6)	2 (22.2)	4 (44.4)	0.28
Non-high-risk PE	7 (3.1)	12 (3.4)	9 (2.1)	12 (3.0)	3 (0.7)	10 (2.6)	10 (2.5)	3 (0.8)	6 (1.5)	6 (1.6)	10 (2.6)	0.12
DOAC	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	3 (2.2)	0.048
Thrombolysis	0 (0.0)	2 (2.7)	2 (2.9)	0 (0.0)	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	1 (2.6)	0 (0.0)	1 (4.2)	0.84
Aged 40-49	(*n* = 400)	(*n* = 632)	(*n* = 753)	(*n* = 756)	(*n* = 825)	(*n* = 761)	(*n* = 826)	(*n* = 787)	(*n* = 782)	(*n* = 712)	(*n* = 747)	
In-hospital mortality, *n* (%)												
Overall PE	32 (8.0)	43 (6.8)	52 (6.9)	68 (9.0)	59 (7.2)	61 (8.0)	44 (5.3)	54 (6.9)	53 (6.8)	47 (6.6)	46 (6.2)	0.11
High-risk PE	19 (52.8)	25 (41.0)	28 (37.8)	38 (48.1)	32 (47.1)	43 (51.8)	27 (40.9)	40 (50.6)	36 (48.6)	33 (45.2)	29 (33.3)	0.48
ECMO	3 (60.0)	9 (56.3)	12 (60.0)	18 (60.0)	15 (83.3)	19 (67.9)	16 (59.3)	18 (66.7)	14 (56.0)	16 (59.3)	13 (34.2)	0.04
Thrombolysis	5 (50.0)	6 (33.3)	5 (20.8)	12 (52.2)	3 (20.0)	6 (42.9)	8 (44.4)	6 (37.5)	6 (35.3)	6 (31.6)	6 (28.6)	0.68
Non-high-risk PE	13 (3.6)	18 (3.2)	24 (3.5)	30 (4.4)	27 (3.6)	18 (2.7)	17 (2.2)	14 (2.0)	17 (2.4)	14 (2.2)	17 (2.6)	0.007
DOAC	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.2)	0 (0.0)	0 (0.0)	3 (1.1)	1 (0.4)	5 (1.8)	0.33
Thrombolysis	2 (3.0)	1 (0.9)	0 (0.0)	4 (4.3)	4 (3.8)	1 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.17
Aged 50-59	(*n* = 539)	(*n* = 792)	(*n* = 870)	(*n* = 833)	(*n* = 992)	(*n* = 909)	(*n* = 942)	(*n* = 1,004)	(*n* = 995)	(*n* = 1,007)	(*n* = 994)	
In-hospital mortality, *n* (%)												
Overall PE	44 (8.2)	63 (8.0)	65 (7.5)	56 (6.7)	86 (8.7)	57 (6.3)	68 (7.2)	70 (7.0)	57 (5.7)	76 (7.5)	74 (7.4)	0.26
High-risk PE	19 (38.8)	25 (46.3)	28 (36.8)	33 (39.8)	36 (46.8)	35 (50.7)	39 (44.3)	34 (34.7)	30 (39.0)	48 (43.2)	41 (45.6)	0.79
ECMO	7 (70.0)	9 (75.0)	6 (28.6)	10 (62.5)	10 (47.6)	18 (85.7)	11 (47.8)	12 (32.4)	12 (60.0)	19 (63.3)	18 (54.5)	0.82
Thrombolysis	2 (18.2)	8 (44.4)	4 (28.6)	7 (33.3)	7 (38.9)	9 (45.0)	6 (31.6)	5 (20.8)	5 (23.8)	6 (40.0)	3 (25.0)	0.53

Non-high-risk PE	25 (5.1)	38 (5.1)	37 (4.7)	23 (3.1)	50 (5.5)	22 (2.6)	29 (3.4)	36 (4.0)	27 (2.9)	28 (3.1)	33 (3.7)	0.006
DOAC	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	1 (0.4)	0 (0.0)	7 (2.0)	7 (2.0)	6 (1.7)	0.046
Thrombolysis	3 (3.7)	1 (0.7)	3 (2.7)	1 (1.0)	3 (3.1)	1 (1.4)	2 (2.5)	1 (2.1)	0 (0.0)	1 (2.3)	1 (2.0)	0.79
Aged 60-69	(*n* = 962)	(*n* = 1,458)	(*n* = 1,593)	(*n* = 1,605)	(*n* = 1,692)	(*n* = 1,688)	(*n* = 1,820)	(*n* = 1,639)	(*n* = 1,673)	(*n* = 1,543)	(*n* = 1,514)	
In-hospital mortality, *n* (%)												
Overall PE	99 (10.3)	150 (10.3)	111 (7.0)	137 (8.5)	138 (8.2)	134 (7.9)	129 (7.1)	108 (6.6)	109 (6.5)	102 (6.6)	104 (6.9)	<0.001
High-risk PE	39 (49.4)	54 (46.2)	38 (31.1)	48 (36.9)	53 (42.7)	62 (43.7)	55 (39.3)	53 (39.3)	55 (37.9)	54 (37.8)	45 (37.5)	0.22
ECMO	9 (64.3)	7 (53.8)	10 (50.0)	15 (51.7)	11 (47.8)	16 (59.3)	13 (52.0)	13 (50.0)	12 (50.0)	13 (39.4)	14 (50.0)	0.26
Thrombolysis	12 (48.0)	10 (29.4)	13 (31.0)	6 (26.1)	8 (27.6)	9 (26.5)	9 (32.1)	11 (30.6)	6 (22.2)	7 (23.3)	4 (21.1)	0.09
Non-high-risk PE	60 (6.8)	96 (7.2)	73 (5.0)	89 (6.0)	85 (5.4)	72 (4.7)	74 (4.4)	55 (3.7)	54 (3.5)	48 (3.4)	59 (4.2)	<0.001
DOAC	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)	4 (2.0)	12 (2.7)	9 (1.9)	7 (1.2)	5 (0.8)	9 (1.6)	0.10
Thrombolysis	3 (2.3)	3 (1.7)	1 (0.5)	5 (2.9)	3 (2.1)	1 (0.7)	1 (0.8)	2 (1.9)	1 (1.1)	2 (3.2)	0 (0.0)	0.65
Aged 70-79	(*n* = 1,295)	(*n* = 1,962)	(*n* = 2,217)	(*n* = 2,140)	(*n* = 2,471)	(*n* = 2,315)	(*n* = 2,491)	(*n* = 2,336)	(*n* = 2,551)	(*n* = 2,487)	(*n* = 2,543)	
In-hospital mortality, *n* (%)												
Overall PE	152 (11.7)	209 (10.7)	207 (9.3)	176 (8.2)	239 (9.7)	202 (8.7)	240 (9.6)	202 (8.6)	213 (8.3)	179 (7.2)	202 (7.9)	<0.001
High-risk PE	59 (55.7)	82 (50.0)	76 (38.8)	76 (42.9)	86 (42.2)	68 (38.0)	105 (46.3)	86 (45.3)	93 (43.1)	78 (39.2)	98 (48.0)	0.41
ECMO	8 (66.7)	13 (65.0)	16 (48.5)	16 (64.0)	17 (65.4)	17 (56.7)	21 (65.6)	16 (47.1)	17 (60.7)	15 (51.7)	14 (43.8)	0.15
Thrombolysis	10 (41.7)	16 (39.0)	19 (31.7)	18 (35.3)	12 (26.1)	14 (37.8)	17 (41.5)	14 (37.8)	10 (32.3)	18 (43.9)	8 (24.2)	0.70
Non-high-risk PE	93 (7.8)	127 (7.1)	131 (6.5)	100 (5.1)	153 (6.7)	134 (6.3)	135 (6.0)	116 (5.4)	120 (5.1)	101 (4.4)	104 (4.4)	<0.001
DOAC	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.9)	6 (2.2)	8 (1.4)	14 (2.0)	19 (2.2)	23 (2.5)	17 (1.7)	0.87
Thrombolysis	4 (2.3)	5 (2.4)	3 (1.4)	1 (0.5)	11 (5.3)	1 (0.5)	5 (3.7)	3 (2.7)	1 (1.2)	2 (2.2)	2 (2.4)	0.79
Aged 80-89	(*n* = 957)	(*n* = 1,575)	(*n* = 1,692)	(*n* = 1,573)	(*n* = 1,926)	(*n* = 1,957)	(*n* = 2,218)	(*n* = 2,134)	(*n* = 2,009)	(*n* = 1,948)	(*n* = 2,049)	
In-hospital mortality, *n* (%)												
Overall PE	164 (17.1)	261 (16.6)	267 (15.8)	221 (14.0)	243 (12.6)	235 (12.0)	291 (13.1)	278 (13.0)	221 (11.0)	222 (11.4)	219 (10.7)	<0.001
High-risk PE	65 (52.8)	89 (58.2)	102 (56.4)	104 (57.8)	87 (48.3)	87 (50.3)	141 (56.2)	123 (49.8)	101 (50.0)	97 (49.0)	78 (41.9)	0.002
ECMO	5 (100.0)	3 (75.0)	6 (66.7)	5 (50.0)	6 (66.7)	12 (75.0)	6 (85.7)	9 (60.0)	4 (44.4)	10 (83.3)	4 (33.3)	0.10
Thrombolysis	11 (50.0)	14 (45.2)	14 (46.7)	14 (53.8)	12 (33.3)	12 (48.0)	14 (42.4)	13 (44.8)	6 (35.3)	8 (34.8)	5 (20.8)	0.04

Non-high-risk PE	99 (11.9)	172 (12.1)	165 (10.9)	117 (8.4)	156 (8.9)	148 (8.3)	150 (7.6)	155 (8.2)	120 (6.6)	125 (7.1)	141 (7.6)	<0.001
DOAC	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.4)	4 (2.0)	13 (3.3)	11 (2.1)	13 (2.5)	18 (3.1)	21 (3.3)	0.50
Thrombolysis	5 (7.4)	8 (7.8)	9 (7.3)	3 (3.3)	8 (7.3)	6 (6.2)	4 (3.8)	3 (3.8)	3 (5.2)	0 (0.0)	4 (10.8)	0.20
Aged ≥ 90	(*n* = 180)	(*n* = 269)	(*n* = 339)	(*n* = 295)	(*n* = 424)	(*n* = 426)	(*n* = 515)	(*n* = 482)	(*n* = 486)	(*n* = 494)	(*n* = 542)	
In-hospital mortality, *n* (%)												
Overall PE	44 (24.4)	63 (23.4)	82 (24.2)	75 (25.4)	93 (21.9)	99 (23.2)	106 (20.6)	118 (24.5)	110 (22.6)	80 (16.2)	104 (19.2)	0.003
High-risk PE	14 (60.9)	14 (51.9)	34 (60.7)	19 (57.6)	34 (65.4)	33 (66.0)	28 (50.0)	41 (69.5)	34 (68.0)	33 (63.5)	34 (69.4)	0.15
ECMO	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	2 (66.7)	0 (0.0)	0 (0.0)	1 (100.0)	2 (100.0)	0.55
Thrombolysis	0 (0.0)	3 (60.0)	0 (0.0)	0 (0.0)	2 (50.0)	5 (71.4)	0 (0.0)	1 (16.7)	0 (0.0)	5 (55.6)	2 (66.7)	0.76
Non-high-risk PE	30 (19.1)	49 (20.2)	48 (17.0)	56 (21.4)	59 (15.9)	66 (17.6)	78 (17.0)	77 (18.2)	76 (17.4)	47 (10.6)	70 (14.2)	0.002
DOAC	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	1 (3.6)	4 (6.3)	6 (6.8)	5 (5.5)	6 (5.0)	8 (6.7)	0.89
Thrombolysis	1 (33.3)	1 (20.0)	3 (20.0)	2 (20.0)	0 (0.0)	1 (6.3)	1 (10.0)	1 (12.5)	1 (14.3)	2 (22.2)	0 (0.0)	0.53

Each fiscal year started on 01 April and ended on 31 March. DOAC, direct oral anticoagulant; ECMO, extracorporeal membrane oxygenation; PE, pulmonary embolism

Figure S1. Annual incidence of overall, high-risk and non-high-risk PE.



Each fiscal year started on 01 April and ended on 31 March. PE, pulmonary embolism