Impact of reperfusion therapies on clot resolution and long-term outcomes in patients with pulmonary embolism

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ABSTRACT

Objective: Major progress in reperfusion strategies has substantially improved the short-term outcomes of patients with pulmonary embolism (PE), however, up to 50% of patients report persistent dyspnea after acute PE.

Methods: A retrospective study of the PE response team registry and included patients with repeat imaging at 3 to 12 months. The primary outcome was to determine the incidence of residual pulmonary vascular obstruction following acute PE. Secondary outcomes included the development of PE recurrence, right ventricular (RV) dysfunction, chronic thromboembolic pulmonary hypertension, readmission, and mortality at 12 months.

Results: A total of 382 patients were included, and 107 patients received reperfusion therapies followed by anticoagulation. Patients who received reperfusion therapies including systemic thrombolysis, catheter-directed thrombolysis, and mechanical thrombectomy presented with a higher vascular obstructive index (47% vs 28%; $P < .001$) and signs of right heart strain on echocardiogram (81% vs 43%; $P < .001$) at the time of diagnosis. A higher absolute reduction in vascular obstructive index (45% vs 26%; 95% confidence interval, 14.0-25.6; $P < .001$), greater improvement in RV function (82% vs 65%; $P = .021$), and lower 12-month mortality rate (2% vs 7%; $P = .038$) and readmission rate (33% vs 46%; $P = .031$) were observed in the reperfusion group. No statistically significant differences were found between groups in the development of chronic thromboembolic pulmonary hypertension (8% vs 5%; $P = .488$) and PE recurrence (8% vs 6%; $P = .646$).

Conclusions: We observed a favorable survival and greater improvement in clot resolution and RV function in patients treated with reperfusion therapies. (J Vasc Surg Venous Lymphat Disord 2024;12:101823.)

Keywords: Chronic thromboembolic pulmonary hypertension; Dyspnea; Pulmonary embolism; Pulmonary vascular obstruction; RV dysfunction; Venous thromboembolism

Acute pulmonary embolism (PE) remains a leading cause of morbidity and mortality, with around 100,000 deaths annually in the United States.[1] Although major advances in PE management, including diagnostic and therapeutic strategies, have substantially improved the short-term outcomes of PE,[2] few studies have assessed its long-term effects.[3-5] Even with adequate anticoagulation, more than one-half of the patients have persistent dyspnea and functional limitations following acute PE, with proposed attributable causes ranging from clinical post-PE syndrome to persistent pulmonary vascular abnormalities.[6-8] Residual pulmonary vascular obstruction (RPVO) is a frequent sequela following acute PE that has been associated with serious clinical impacts. Although these chronic or slowly resolving thrombi may be asymptomatic, the persistent obstruction of the pulmonary vascular bed could lead to elevation of pulmonary resistance and ultimately right ventricular (RV) dysfunction. The rarest and most severe long-term outcome is the development of chronic thromboembolic pulmonary hypertension (CTEPH).[9] In addition, several studies found that RPVO is an independent predictor of recurrent venous thromboembolism (VTE).[10,11]

Reperfusion therapies have been shown to improve short-term outcomes by rapidly and effectively reversing the hemodynamic burden that PE imposes on the pulmonary circulation and the right heart.[12] Theoretically, the rapid and effective clot resolution exerted by reperfusion therapies could possibly minimize the development

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of long-term consequences of PE, including RV dysfunction and CTEPH. However, whether and to what extent reperfusion therapies could prevent the development of long-term sequelae has not been clearly delineated, either due to limited data or variable parameters used as outcome measures.[3,5] The purpose of the present study is to investigate the role of reperfusion therapies in the reduction of RPVO and its impact on late outcomes.

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective cohort study
- **Key Findings:** In this cohort study of 382 patients who underwent evaluation by the pulmonary embolism response team up to 1 year, we observed a greater extent of clot resolution and improvement in right ventricular function in patients treated with reperfusion therapies compared with anticoagulation alone. A survival benefit at 1-year follow-up was also observed in the reperfusion group.
- **Take Home Message:** The findings suggest the possibility of expanding reperfusion therapies beyond current recommendations. Future randomized control trials are needed to confirm our findings.

METHODS

Study population. We conducted a retrospective review of all hospitalized patients between January 2017 and June 2021 at our institution who underwent evaluation by the pulmonary embolism response team (PERT). The PERT consists of members from interventional cardiology and radiology, pulmonary/critical care, clinical pharmacy, and cardiac surgery. Activation of the PERT occurs either through an on-call phone number or via a single contact to the hospital's transfer center if request arises from an outside hospital. Upon initial activation, a virtual multidisciplinary meeting or conference call among all PERT members is held. Treatment decisions are made through shared decision-making among the PERT members. Finally, the consensus plan is presented to the referring clinician. Patients were included if meeting the following criteria: (1) diagnosis of acute PE confirmed by computed tomography pulmonary angiography (CTPA) or lung perfusion/ventilation (V/Q) scan; (2) completed treatment of therapeutic anticoagulation for at least 3 months; and (3) underwent repeat imaging from 3 to 12 months follow-up after an index PE due to persistent dyspnea. Patients were excluded on account of the following: (1) diagnosis of PE not confirmed by CTPA or V/Q scan; (2) did not receive treatment either due to contraindications to anticoagulation, limited life expectancy or hospice care; (3) unavailability of follow-up; (4) PE-related or non-related in-hospital death; (5) death during follow-up without imaging; and (6) duplicated cases. This study was approved by the Institutional Review Board of our institution (Protocol #26021), and informed consent was waived due to the retrospective nature of the study.

Outcome measures. Demographics, comorbid conditions, and risk factors for VTE were collected and summarized. The main outcome was to determine and compare the incidence of RPVO in patients who received reperfusion therapies plus anticoagulation to those who received anticoagulation alone in 3 to 12 months following acute PE. RPVO was assessed using CTPA or lung V/Q scan, or both if available, and was defined by the presence of persistent filling defects noted on CTPA or residual perfusion defects on V/Q scan. Clot burden was quantified and calculated by using the Qanadli score system.[13] In brief, the arterial tree of each lung was regarded as having 10 segmental arteries (three to the upper lobes, two to the middle lobe/lingula, and five to the lower lobes). The presence of embolus in a segmental artery was scored 1 point, and the embolus at the most proximal arterial level was scored according to the number of segmental arteries arising distally. Each score was assigned to a weighing factor from a scale of 0 to 2 (0 = no defect; 1 = partial occlusion; 2 = complete occlusion). The maximal CT obstructive score is 40, and the vascular obstructive index (VOI) was calculated using the formula: $\Sigma\ (n \times d)/40 \times 100$, where n is the value of proximal thrombus in the pulmonary arterial tree equal to the number of segmental branches arising distally, and d is the degree of obstruction.[13]

The secondary outcomes were to determine the late sequelae of PE in patients who received reperfusion therapies, which included PE recurrence, RV dysfunction, CTEPH, readmission, and mortality at 12 months. PE recurrence was defined by the presence of a new thrombus in a different segmental area than that of the initial PE or a new perfusion defect on the V/Q scan. An echocardiographic assessment of RV function was performed by board-certified cardiologists at the time of PE diagnosis and between 3 and 12 months to determine changes in RV function, which was classified as follows: (1) persistent RV dysfunction; (2) new RV dysfunction; and (3) improvement of RV function. CTEPH was defined by the following two criteria: (1) the presence of pulmonary hypertension (mean pulmonary arterial pressure >20 mmHg) with a pulmonary capillary wedge pressure <15 mmHg confirmed via right heart catheterization; and (2) the presence of thromboembolic occlusion of the pulmonary vasculature, either by V/Q lung scan or CTPA.

Statistical analysis. All continuous variables were tested for normality and presented as mean with a

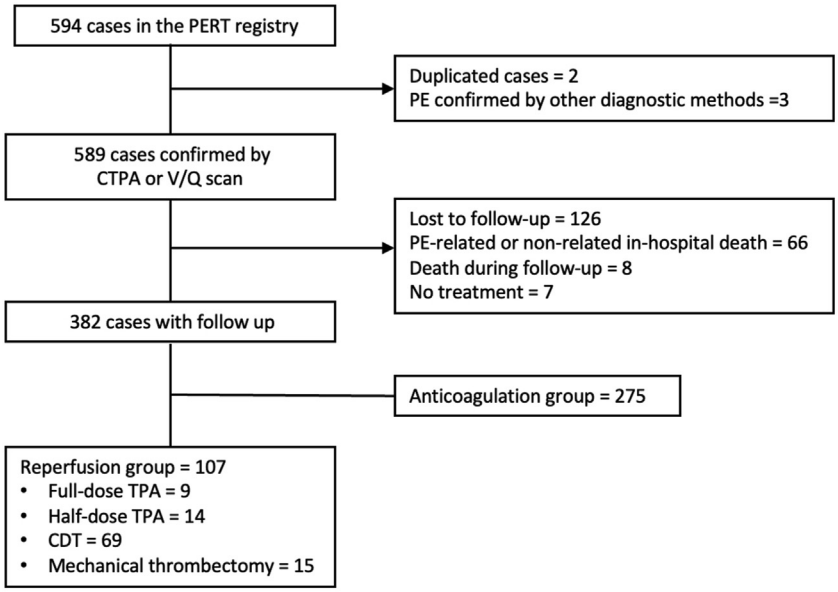

Fig 1. Patient selection flow diagram. *CDT*, Catheter-directed thrombolysis; *CTPA*, computed tomography pulmonary angiography; *PE*, pulmonary embolism; *PERT*, pulmonary embolism response team; *TPA*, tissue-type plasminogen activator; *V/Q*, perfusion/ventilation.

standard deviation, or median with interquartile range if the distribution were skewed. Categorical variables were presented as absolute numbers (percentage). Comparison between the anticoagulation and the reperfusion group was performed using the Student *t*-test or Mann-Whitney *U* test for continuous variables, or the Fischer exact or χ^2 test for categorical variables, as appropriate. Survival distributions at 12 months were estimated by the Kaplan-Meier method and compared using the log-rank test. The software SPSS Statistics for Mac, version 29.0 (IBM Corp) was used for statistical analysis. *P*-values of $< .05$ (two-sided) were considered statistically significant.

RESULTS

Study population and patient characteristics. Of 594 cases between January 2017 and June 2021 identified in the PERT registry, 212 cases were excluded due to the following reasons: duplicated cases (n = 2), diagnosis of PE not confirmed by CTPA or V/Q scan (n = 3), unavailability of repeat imaging (n = 126), PE-related or non-related in-hospital death (n = 62), death during follow-up without repeat imaging (n = 9), and contraindications to anticoagulation, limited life expectancy, or hospice care (n = 10). Fig 1 demonstrates patient selection. A total of 382 patients were included, and the severity of PE was as follows: 106 cases (28%) of low-risk PE, 122 cases (32%) of intermediate-low risk, 132 cases (34%) of intermediate-high risk, and 22 cases (6%) of high-risk PE. The diagnosis of PE was confirmed by CTPA in 97% of patients, whereas 3% of patients were diagnosed by V/Q scan. A total of 107 patients (28%) received reperfusion therapies, which included full-dose thrombolysis (alteplase, 100 mg; n = 9; 8%), half-dose thrombolysis (alteplase, 50 mg; n = 14; 13%), catheter-directed thrombolysis (n = 69; 65%), and mechanical thrombectomy (n = 15; 14%). All patients who received reperfusion therapies had intermediate-risk and high-risk PE.

Baseline patient characteristics of the study cohort are reported in Table I. Among intermediate-risk and high-risk PE group, patients who received reperfusion therapies had a significantly lower prevalence of cardiac diseases (23% vs 50%; $P < .001$), chronic obstructive pulmonary disease (7% vs 16%; $P = .020$), and malignancy (11% vs 24%; $P < .010$). In addition, higher rates of concurrent deep vein thrombosis (69% vs 45%; $P < .001$) and signs of RV strains on CTPA (85% vs 49%; $P < .001$) and echocardiogram (81% vs 56%; $P < .001$) were observed in the reperfusion group.

Assessment of pulmonary vascular obstruction. The mean follow-up time of imaging was 6 months (standard deviation, 3.5 months). RPVO was observed in 21% of patients (n = 23) treated with reperfusion therapies, compared with 9% of patients (n = 25) treated with anticoagulation alone (21% vs 9%; $P = .001$). A higher mean VOI (47% vs 28%; 95% confidence interval [CI], 13.8-24.7; $P < .001$) was observed in patients treated with reperfusion therapies, compared with anticoagulation alone. The VOI was reduced from 47% to 0.5% (a decrease of 99%) in the reperfusion group, and from 28% to 1.5% (a decrease of 95%) in the anticoagulation group. Thus, a significantly greater absolute reduction in VOI (45% vs 26%, 95% CI, 14.0-25.6; $P < .001$) was observed in

Table I. Baseline patient characteristics

	Cohort			Intermediate and high-risk PE		
	AC (n = 275)	Reperfusion (n = 107)	*P* value	AC (n = 169)	Reperfusion (n = 107)	*P* value
Gender (female)	119 (43)	44 (41)	.703	90 (53)	44 (41)	.360
Age, years	57±17.1	56±15.5	.773	60±16.6	56±15.5	.151
Race			.223			.445
Black	140 (51)	58 (54)		93 (55)	58 (54)	
White	50 (18)	25 (23)		30 (18)	25 (23)	
Other	84 (31)	24 (23)		46 (27)	24 (23)	
BMI, kg/m^2	32±9.2	36±8.9	<.001	32±9.0	36±8.9	<.001
Comorbidities						
Cardiac diseases	112 (41)	25 (23)	.005	84 (50)	25 (23)	<.001
COPD/asthma	43 (16)	7 (7)	.018	27 (16)	7 (7)	.020
CKD	26 (9)	9 (8)	.751	21 (12)	9 (8)	.296
ESRD on hemodialysis	5 (2)	0 (0)	.160	4 (2)	0 (0)	.109
Diabetes mellitus	71 (26)	21 (20)	.204	45 (27)	21 (20)	.184
Hypothyroidism	14 (5)	11 (10)	.066	9 (5)	11 (10)	.122
Malignancy	54 (20)	12 (11)	.118	40 (24)	12 (11)	.010
Recent surgery	37 (13)	12 (11)	.557	25 (15)	12 (11)	.395
sPESI score >1	175/236 (74)	93 (87)	.096	149 (88)	93 (87)	.520
Elevated BNP	99/253 (39)	74/101 (73)	<.001	77/161 (48)	74/101 (73)	<.001
Elevated troponin	77 (28)	78 (73)	<.001	62 (37)	78 (73)	<.001
PE severity			<.001			<.001
Low risk	106 (39)	0		0	0	
Intermediate low risk	110 (40)	12 (11)		111 (66)	12 (11)	
Intermediate high risk	53 (19)	79 (74)		52 (31)	79 (74)	
High risk	6 (2)	16 (15)		6 (3)	16 (15)	
RV strain on CT	99/267 (37)	86/104 (82)	<.001	81/167 (49)	86/104 (82)	<.001
RV dysfunction on ECHO	114/265 (43)	85/105 (81)	<.001	93/165 (56)	85/105 (81)	<.001
Presence of DVT	102/252 (40)	71/103 (69)	<.001	70/155 (45)	71/103 (69)	<.001

AC, Anticoagulation; *BMI*, body mass index; *BNP*, B-type natriuretic peptide; *CKD*, chronic kidney disease; *COPD*, chronic obstructive pulmonary disease; *CT*, computed tomography; *DVT*, deep vein thrombosis; *ECHO*, echocardiogram; *ESRD*, end-stage renal disease; *LV*, left ventricular; *PA*, pulmonary artery; *PE*, pulmonary embolism; *RV*, right ventricular; *sPESI*, simplified pulmonary embolism severity index.
Data are presented as number (%) or mean ± standard deviation.

the reperfusion group. Supplementary Table I (online only) summarizes differences in changes of VOI between the anticoagulation and reperfusion groups. Fig 2 demonstrates VOI at the time of diagnosis and follow-up.

Long-term outcomes following acute pulmonary embolism. Table II summarizes all outcome measures at the 12-month follow-up. Of 199 patients who had echocardiographic signs of RV dysfunction at the time of diagnosis, 145 patients (73%) had repeat echocardiography at follow-up (Supplementary Fig, online only). Improvement in RV function was more frequently seen in patients treated with reperfusion therapies (82% vs 65%; $P = .021$). There was no statistical difference in the development of new RV dysfunction (21% vs 18%; $P = .749$) compared with patients treated with anticoagulation alone. No statistically significant differences were found between groups in the development of CTEPH (8% vs 5%; $P = .488$) and PE recurrence (8% vs 6%; $P = .646$).

Readmissions and mortality at 12 months. Patients treated with reperfusion therapies had a lower readmission rate of 33% within a 12-month follow-up period (33% vs 46%; $P = .031$). The in-hospital mortality within the cohort was 14%. For patients who survived acute PE, a higher mortality rate at 12 months was observed in patients who received anticoagulation alone (7% vs 2%; $P = .038$), with the causes of death being cancer (n = 11), respiratory failure (n = 3), COVID (n = 2), septic shock (n = 2), stroke (n = 2), and unknown causes (n = 3). There were no statistically significant differences in in-hospital death (16% vs 13%; $P = .291$) and overall mortality (23% vs 19%; $P = .786$). Fig 3 demonstrates the cumulative risk of death at 12 months.

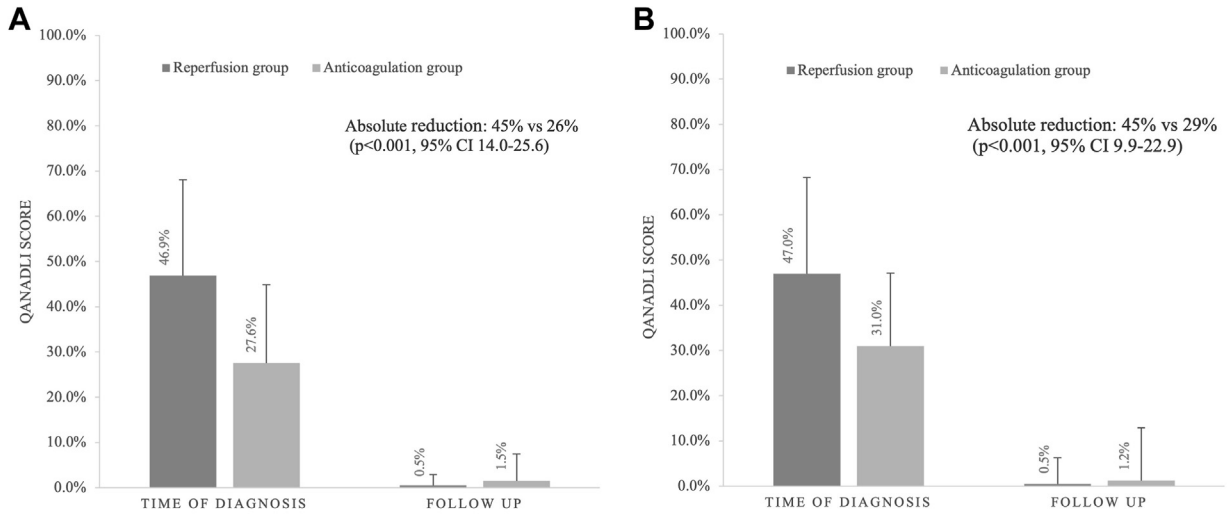

Fig 2. Changes in vascular obstructive index at the time of pulmonary embolism (PE) diagnosis and at follow-up. Changes in pulmonary vascular obstructive index (VOI) between reperfusion group and anticoagulation group in: whole patient cohort **(A)** and patients with intermediate-risk and high-risk PE **(B)**. *CI*, Confidence interval.

Patients with intermediate- and high-risk pulmonary embolism. A stratified analysis of patients with intermediate- and high-risk PE revealed similar findings, notably higher mean VOI at diagnosis (47% vs 31%; 95% CI, 9.8-22.1; $P < .001$), greater absolute reduction in VOI (45 vs 29%; 95% CI, 9.9-22.9; $P < .001$), improvement in RV function (82% vs 66%; $P = .043$), decreased mortality in patients who survived acute PE (2% vs 8%; $P = .024$), and readmission rate (33% vs 47%; $P = .043$) in the reperfusion group (Supplementary Table II, online only).

Table II. Outcome measures at 12-month follow-up

	Cohort			Intermediate and high-risk PE		
	AC (n = 275)	Reperfusion (n = 107)	*P* value	AC (n = 169)	Reperfusion (n = 107)	*P* value
VOI at PE diagnosis	28%	47%	< .001	31%	47%	< .001
RPVO	25 (9)	23 (21)	.001	14 (8)	23 (22)	< .001
Changes in RV function			.021			.043
Persistent RV dysfunction	28/79 (35)	12/66 (18)		21/62 (34)	12/66 (18)	
Improvement in RV function	51/79 (65)	54/66 (82)		41/62 (66)	54/66 (82)	
New RV dysfunction	13/73 (18)	3/14 (21)	.749	6/35 (17)	3/14 (21)	.726
PE recurrence	17 (6)	8 (8)	.646	11 (7)	8 (8)	.757
CTEPH	13 (5)	9 (8)	.488	11 (7)	9 (8)	.721
Readmissions	127 (46)	35 (33)	.031	80 (47)	35 (33)	.043
PE-related	34 (12)	13 (12)		23 (14)	13 (12)	
PE non-related	93 (34)	22 (21)		57 (34)	22 (21)	
In-hospital mortality	41/325 (13)	21/128 (16)	.291	30/208 (14)	21/128 (16)	.623
Mortality (discharge to 1 year)	21/284 (7)	2/107 (2)	.038	15/178 (8)	2/107 (2)	.024
Cancer	11/21 (52)	0		9/15 (60)	0	
Respiratory failure	2/21 (10)	1/2 (50)		1/15 (7)	1/2 (50)	
COVID	2/21 (10)	0		0	0	
Septic shock	1/21 (4)	1/2 (50)		1/15 (7)	1/2 (50)	
Stroke	2/21 (10)	0		2/15 (13)	0	
Unknown	3/21 (14)	0		2/15 (13)	0	
Total mortality	62/325 (19)	23/128 (23)	.786	45/208 (22)	23/128 (18)	.417

AC, Anticoagulation; *CTEPH*, chronic thromboembolic pulmonary hypertension; *PE*, pulmonary embolism; *RPVO*, residual pulmonary vascular obstruction; *RV*, right ventricular; *VOI*, vascular obstructive index.
Data are presented as number/total (%).

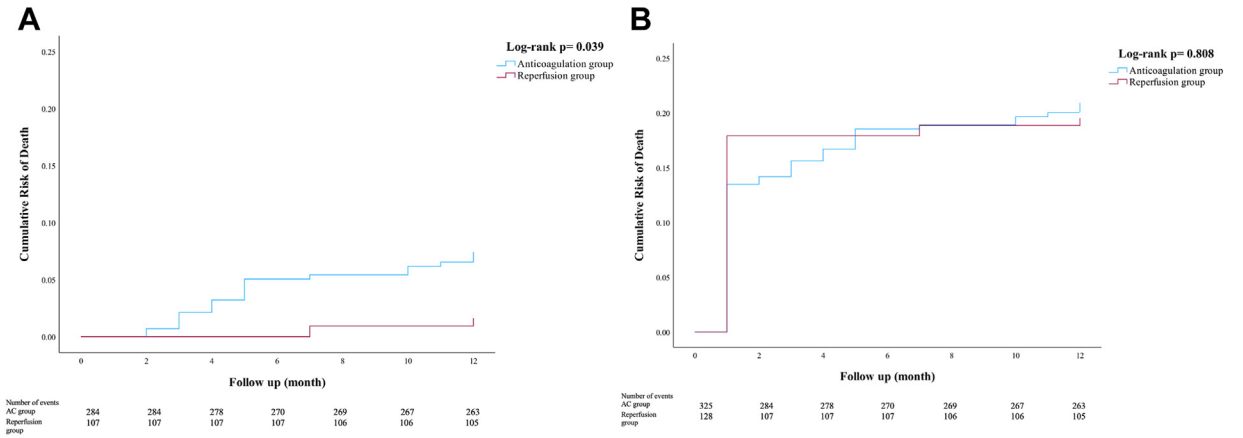

Fig 3. Cumulative risk of death at 12-month: patients who survived pulmonary embolism (PE) hospitalization **(A)**; total mortality including in-hospital death **(B)**. *AC*, Anticoagulation.

DISCUSSION

In this study, RPVO was observed in 21% of patients with acute PE treated with reperfusion therapies up to 1-year follow-up. Patients treated with reperfusion therapies had a higher clot burden as evidenced by a higher VOI and more frequent concomitant deep vein thrombosis at time of diagnosis. Reperfusion therapies resulted in a greater clot reduction, improved RV function, lower readmission rate, and lower 12-month mortality rate in patients who survived acute PE. There was no statistically significant difference in the development of late outcomes, including PE recurrence and CTEPH.

The incidence of RPVO following an index PE is in keeping with previously reported rates ranging from 19% to 51.8%.[10,11,14] There is a paucity of data regarding the long-term effects of reperfusion therapies on PE, and the few studies that investigated its impact came to different conclusions. Two small, prospective randomized trials reported that thrombolysis, compared with anticoagulation, might improve functional capacity and the persistence of pulmonary hypertension at long-term follow-up.[15,16] A retrospective multicenter cohort study by Semaan et al found a survival benefit in patients treated with catheter-directed thrombolysis over anticoagulation without any significant procedure-related complications.[17] On the contrary, Konstantinides et al reported that thrombolysis did not appear to reduce long-term mortality rates, residual dyspnea, or RV dysfunction.[5] Nevertheless, data regarding clot burden and the extent of clot resolution exerted by reperfusion therapies were not available in existing studies, which could have underestimated the long-term benefits of reperfusion therapies.

In this study, it is unsurprising that a higher proportion of patients treated with reperfusion therapies had RPVO on follow-up imaging, as these patients had a higher clot burden at the time of diagnosis and were more likely to present with signs of right heart strain. In fact, our data suggest that, despite the presence of RVPO, reperfusion therapies resulted in a greater extent of clot reduction and a lower VOI at follow-up. In addition, these patients had a significantly greater improvement in RV function compared with anticoagulation alone. These findings highlight the benefits of rapid clot resolution achieved by reperfusion therapies and their potential role in the prevention of long-term sequelae following PE that could contribute to chronic dyspnea.

Our findings may have important implications for daily clinical practice and future clinical research studies. First, current guidelines recommend reservation of reperfusion therapies only to patients with high-risk PE or intermediate-high-risk PE with imminent signs of hemodynamic decompensation, given the concerns of a higher risk of bleeding.[18,19] This study provides insights into the potential long-term benefits of reperfusion therapies, suggesting the feasibility of expanding the role of reperfusion therapies in patients with high clot burden and low bleeding risk. Early involvement of multidisciplinary PERTs can facilitate the careful selection of patients who may be candidates for reperfusion therapies.

Second, the optimal duration of anticoagulation treatment after PE remains controversial. Patients with associated risk factors for VTE recurrence, including unprovoked PE, cancer, or high clot burden at the time of diagnosis often receive prolonged or indefinite anticoagulation.[20,21] The result from our study that reperfusion therapies lead to a greater extent of clot resolution suggests the possibility of shortening the duration of anticoagulation treatment in those treated with reperfusion therapies, provided that serial imaging to observe clot resolution is available and shows the absence of persistent prothrombotic risk factors. Dedicated PE care follow-up allows timely identification of patients who are at risk of developing late outcomes of PE such as CTEPH.

In accordance with existing literature, we did not observe a reduction in the development of CTEPH.[5] A

potential explanation is that CTEPH remains rare, and the sample size may be too small to determine the impact of reperfusion therapies on CTEPH. The pathophysiology of CTEPH remains unknown; further studies are needed to investigate the potential role of reperfusion therapies in the prevention of maladaptive cardiopulmonary remodeling and to elucidate the underlying mechanism that leads to CTEPH.

Study limitations. There are several limitations to our study. First, we did not include parameters that represent exercise tolerances and functional capacity. Thus, a correlation between the radiographic findings of RPVO with the severity of symptoms or the degree of functional impairment could not be delineated. Second, patients with incomplete follow-up were excluded from the study, which might have led to selection bias. Third, patients who had severe symptoms were most likely to seek medical attention, and thus the prevalence of RV dysfunction, PE recurrence, and CTEPH could have been overestimated. Finally, the mean follow-up time is relatively short compared with other existing studies. Other limitations included the retrospective, single-center nature of the data, which may be prone to selection bias.

CONCLUSIONS

In this study, we observed a greater extent of clot resolution and improvement in RV function in patients treated with reperfusion therapies compared with anticoagulation alone. A survival benefit at 1-year follow-up was also observed in the reperfusion group. These findings raise the possibility of expanding the application of reperfusion therapies beyond current recommendations. However, further evidence from future randomized control trials is essential to validate this hypothesis.

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AUTHOR CONTRIBUTIONS

Conception and design: KL, RB, VL, SL, JP, PR
Analysis and interpretation: KL, PR
Data collection: KL
Writing the article: KL, PR
Critical revision of the article: KL, RB, VL, SL, JP, PR
Final approval of the article: KL, RB, VL, SL, JP, PR
Statistical analysis: KL
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Overall responsibility: KL

DISCLOSURES

None.

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Supplementary Table I (online only). Changes in vascular obstructive index (*VOI*) at time of diagnosis and at follow-up

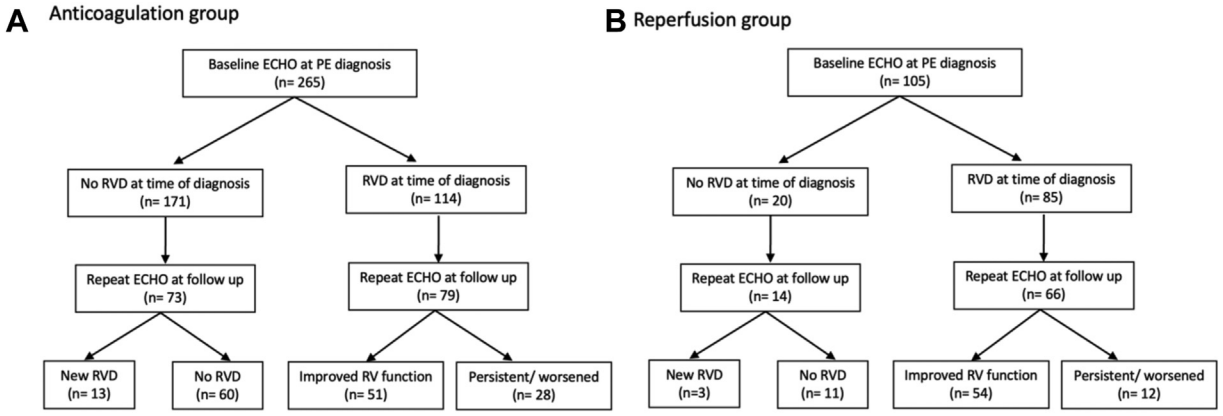
	AC group (n = 275)	Reperfusion group (n = 107)	*P* value	95% CI
VOI at time of diagnosis	27.6 (17.3)	46.9 (21.2)	<.001	13.8-24.7
VOI at follow up	1.5 (5.9)	0.5 (2.4)	.197	13.5-25.0
Absolute reduction in VOI	25.6 (17.6)	45.4 (21.7)	<.001	14.0-25.6
Clot resolution			.001	
Complete resolution	270 (91)	84 (79)		
RPVO	25 (9)	23 (21)		

AC, Anticoagulation; *CI*, confidence level; *RPVO*, residual pulmonary vascular obstruction.
Data are presented as number (%) or mean (standard deviation).

Supplementary Table II (online only). Changes in percentage of pulmonary vascular obstruction at time of diagnosis and at follow up in patients with intermediate-risk and high-risk pulmonary embolism (PE)

	AC group (n = 169)	Reperfusion group (n = 107)	*P* value	95% CI
VOI at time of diagnosis	31 (17.6)	47 (21.2)	<.001	9.8-22.1
VOI at follow-up	1.2 (5.6)	0.5 (2.4)	.316	-2.2-0.7
Absolute reduction in VOI	29 (18.1)	45 (21.7)	<.001	9.9-22.9
Clot resolution			<.001	
Complete resolution	155 (92)	83 (78)		
RPVO	14 (8)	24 (22)		

AC, Anticoagulation; *CI*, confidence level; *RPVO*, residual pulmonary vascular obstruction; *VOI*, vascular obstructive index.
Data are presented as number (%) or mean (standard deviation).



ECHO= echocardiography; RVD= right ventricular dysfunction.

Supplementary Fig (online only). Flow diagram of evaluation of right ventricular (*RV*) function. *ECHO*, Echocardiography; *PE*, pulmonary embolism; *RVD*, right ventricular dysfunction.