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RESEARCH ARTICLE

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Right heart thrombus in acute pulmonary embolism: A single center experience in China

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Abstract

Right heart thrombus (RHT) is a rare but life-threatening condition in acute pulmonary embolism (APE) without clear management guidelines. This study aimed to address the clinical characteristics and outcomes of RHT-APE in Chinese patients. In this study, 17 RHT-APE and 329 non-RHT-APE patients, who were diagnosed between September 2015 and August 2019, were retrospectively recruited with the median follow-up was 360 days. The overall prevalence of RHT was 4.91% in APE. Its prevalence increased along the increase of APE risk stratifications. Comparisons showed that with higher proportion of male gender and younger age, RHT-APE patients also had worse hemodynamic instability and heart function, and higher risk stratification levels than non-RHT-APE patients. After adjusting by age and gender, multivariate logistic regression analysis found high/intermediate-high risk stratification, decreased right ventricular (RV) motion, NT-proBNP >600 pg/mL, and RV dysfunction were risk factors for RHT. Kaplan−Meier analysis showed non-RHT had better prognosis than RHT patients (30-day survival: log-rank: $p < 0.001$; 90-day survival: log-rank: $p = 0.002$). The multivariate logistic regression analysis showed RHT was an independent risk factor for 30-day mortality in APE. The subgroup analysis showed RHT would result in worse outcomes in patients who already had higher APE early mortality risk. RHT would increase the risk of 30- and 90-day mortality in APE. More attention should be paid to young male APE patients with decreased RV motion, NT-proBNP >600 pg/mL, RV dysfunction, or high level of risk stratification, to exclude the coexistence of RHT.

KEYWORDS
acute pulmonary embolism, prevalence, prognosis, right heart thrombus

Wen Li and Zhi-Ying Liu contributed equally to this work as first authors.

INTRODUCTION

Right heart thrombus (RHT) is a rare but potentially life-threatening emergency condition in acute pulmonary embolism (APE) patients. Several studies had reported the prevalence and prognostic significance of RHT. The reported prevalence of RHT in APE varied from 2.6% to 17.6%.[1–7] The majority of these studies showed RHT might increase the mortality risk of APE, especially the short-term death.[2,6,8,9]

The 2019 European Society of Cardiology (ESC) APE Guidelines updated the classification of pulmonary embolism severity and provided the precise definition of hemodynamic instability. In addition, the pulmonary embolism severity index (PESI) was recommended as one of indicators for early mortality risk and the adverse effect of right ventricular (RV) dysfunction was also emphasized.[10] Novel oral anticoagulants (NOACs) were recommended as the first choice for APE anticoagulant therapy.[10] However, cohort studies of RHT-APE were very limited in recent 5 years. Furthermore, published studies had not updated the APE risk assessment according to the 2019 ESC APE Guidelines or reported the use of NOACs in RHT-APE patients.

Though RHT-APE is a rare but severe condition, studies about RHT in China were very limited and there is an urgent need to address the clinical characteristics and outcomes of RHT-APE in Chinese patients. Therefore, we conducted this ambispective cohort study in line with the 2019 ESC classification of pulmonary embolism severity. Based on the experience of a tertiary cardiovascular disease specialized hospital, we focused on RHT-APE, the most uncommon and cryptic type of APE, to study its prevalence, clinical features, and possible risk factors. We also analyzed the 30- and 90-day mortalities to emphasize the adverse prognostic effect of RHT on APE patients. In the end, the treatment experience of RHT-APE was summarized in our center.

METHODS

Study design

This is a single-center, observational, ambispective cohort study. ICD codes including APE and RHT were used for search. Patients with confirmed diagnosis of APE and RHT in our emergency department between January 2003 and August 2019 were included. Since a non-RHT-APE cohort, who were diagnosed between September 2015 and August 2019, were also studied in our emergency department. RHT-APE patients, who were diagnosed during the same period, were selected to compare with non-RHT-APE patients (Supporting Information: Figure 1). Additionally, a 1:4 matched analysis was performed between RHT-APE and non-RHT-APE patients on the basis of gender, age, and BMI. All APE patients received transthoracic echocardiography (TTE) examination within 24 h since they arrived at emergency department to establish the diagnosis of RHT. Baseline demographics, vital signs, comorbidities, risk factors, laboratory results, and TTE indices were collected (details in Supporting Information Materials). The therapeutic strategies for APE, including anticoagulation, thrombolysis + anticoagulation, surgical embolectomy or none, were collected according to the original medical records. This study complied with the Declaration of Helsinki and was approved by the Institutional Review Board of Fuwai Hospital (Ethical approval number: Fuwai 2012-401).

Study outcomes and follow-up

Each patient was followed by outpatient or in hospital examinations in our hospital. Patients who had no follow-up records in hospital would be interviewed by telephone. Data about the survival status, bleeding complications, recurrence of PE, and the usage of anticoagulation therapy were collected. All-cause mortality was designed as the primary end-point.

Statistics analysis

Continuous data were expressed as mean ± standard deviation or quartile (Q1, Q3). Categorical data were expressed as frequency with percentage (%). Differences between two groups were analyzed using two-tailed unpaired Student's *t*-test for normally distributed continuous variables. Mann–Whitney *U* tests were used for non-normally distributed continuous variables. χ^2 or Fisher's exact tests were used for categorical variables. The univariate logistic regression analysis was used to evaluate the potential demographic and clinical risk factors for RHT in APE cohort. Variables with a univariable level of significance of <0.05 were included in a backward, stepwise multivariate logistic regression model with three parameters at one time. The univariable logistic regression analysis was also used to evaluate the risk factors of 30- and 90-day mortality in APE cohort. Multivariable models were fit to investigate the effects of clinical features with RHT on APE survival status.

Kaplan–Meier analyses were performed for the cumulative occurrence of endpoints. Between-group comparisons were made using the log-rank test. A value of $p < 0.05$ was considered to indicate statistical significance. Statistical analyses were performed using SPSS 22.0 (SPSS, Inc.).

RESULTS

The description of baseline clinical characteristics in 32 RHT-APE patients who were diagnosed between 2003 and 2019 (Table 1)

A total of 32 RHT-APE patients, with mean age of 49.94 ± 18.62 years old, were found in our emergency department between Jan 2003 and August 2019. Twenty-two of 32 (68.75%) patients were male. Fifty percent of patients distributed in high/intermediate-high risk stratification. 37.50% of patients had decreased RV motion, 37.50% of patients had estimated SPAP >50 mmHg, and 71.88% of patients had RV dysfunction. The most frequent onset symptoms were dyspnea (96.88%). For treatment choices, the majority (78.13%) of patients received anticoagulation, 6.25% of patients received thrombolysis, and 15.62% of patients received surgical embolectomy.

Comparisons of baseline clinical characteristics and outcomes between RHT-APE and non-RHT-APE patients (Table 2)

A total of 346 APE patients with or without RHT were diagnosed between September 2015 and August 2019. The prevalence of RHT in APE patients was 4.91% (17/346). The prevalence of RHT in high-risk, intermediate-risk, and low risk APE patients were 11.11% (1/9), 6.03% (14/232), and 1.90% (2/105), respectively. Comparisons between RHT ($n = 17$) and non-RHT ($n = 329$) showed RHT patients had higher percentage of male gender (64.71% vs. 38.60%, $p = 0.032$) and younger age (51.63 ± 17.57 vs. 66.48 ± 12.96 years old, $p = 0.003$). Higher proportion of RHT patients were in high/intermediate-high risk group (52.94% vs. 22.80%, $p = 0.008$). RHT patients also had lower SBP (118.88 ± 22.23 vs. 133.02 ± 24.21 mmHg, $p = 0.019$), higher shock index (0.80 ± 0.34 vs. 0.67 ± 0.23, $p = 0.027$), higher percentage with NT-proBNP >600 pg/mL (82.35% vs. 50.15%, $p = 0.016$), and higher level of gamma-GT

TABLE 1 The description of clinical characteristics in RHT-APE patients who were diagnosed between 2003 and 2019.

RHT-APE	
Patient number	32
Gender, male (%)	22 (68.75%)
Age (years)	49.94 ± 18.62
BMI (kg/m)^2	24.88 ± 3.55
SBP (mmHg)	117.94 ± 18.26
HR (bpm)	90.50 ± 21.25
Shock index	0.80 ± 0.28
SaO_2 (%)	94.65 ± 4.06
sPESI score, 0	14 (43.75%)
≥1	18 (57.25%)
Risk stratifications	
High risk	1 (3.12%)
Intermediate-high/intermediate-low risk	15/12 (46.88%/37.50%)
Low risk	4 (12.50%)
Onset symptoms	
Dyspnea	31 (96.88%)
Chest pain	7 (21.88%)
Palpitation	15 (46.88%)
Syncope	7 (21.88%)
Comorbidities and risk factors	
Chronic heart failure	14 (43.75%)
Immobilization >3 days	7 (21.88%)
Chronic lung disease	3 (9.38%)
Surgical history within 1 month	6 (18.75%)
Deep venous thrombosis	19 (59.38%)
Laboratory tests	
NT-proBNP >600 pg/mL	19 (59.38%)
TnI >0.02 ng/mL	7 (21.88%)
HGB (g/L)	140.10 ± 15.91
PLT (10^9/L)	206.10 ± 102.61
ALB (U/L)	37.35 ± 4.50
ALP (U/L)	96.43 ± 43.76
TB (umol/L)	22.20 ± 16.27
DB (umol/L)	7.21 ± 7.40
LDH (U/L)	303.38 ± 152.78
UA (umol/L)	437.29 ± 190.89
D-Dimer (ug/mL)	5.58 ± 5.41

(Continues)

TABLE 1 (Continued)

RHT-APE	
Cr (umol/L)	101.20 ± 54.90
eGFR (mL/min)	82.50 ± 39.95
Transthoracic echocardiographic indices	
RV diameters (mm)	27.83 ± 5.06
LV diameters (mm)	46.69 ± 11.14
LVEF (%)	53.29 ± 14.99
Decreased RV motion	12 (37.50%)
Estimated SPAP (mmHg)	51.68 ± 21.56
Estimated SPAP >50 mmHg	12 (37.50%)
RV dysfunction	23 (71.88%)
Pericardial effusion	7 (21.90%)
Therapeutic strategies	
Thrombolysis + anticoagulation	2 (6.25%)
Surgical embolectomy	5 (15.62%)
Anticoagulation	25 (78.13%)
IVC filter	2 (6.25%)
None	0 (0%)

Abbreviations: ALB, albumin; ALP, alkaline phosphatase; BMI, body mass index; Cr, creatinine; DB, direct bilirubin; EF, ejection fraction; eGFR, estimated glomerular filtration rate; HGB, hemoglobin; HR, heart rate; IVC, inferior vena cava; LDH, lactate dehydrogenase; LV, left ventricle; PLT, platelets; RHT-APE, right heart thrombus-acute pulmonary embolism; RV, right ventricle; SBP, systolic blood pressure; SPAP, systolic pulmonary arterial hypertension; sPESI, simplified pulmonary embolism severity index; TB, total bilirubin; TnI, troponin I; UA, uric acid.

(89.47 ± 53.55 vs. 53.27 ± 64.45 U/L, $p = 0.024$). TTE showed RHT patients had higher percentage with decreased RV motion (47.06% vs. 19.76%, $p = 0.013$) and RV dysfunction (64.71% vs. 30.40%, $p = 0.003$).

Treatment strategies between RHT and non-RHT patients showed significant difference ($p = 0.037$). Though the majority of both groups received anticoagulation therapy (82.36% vs. 88.15%), more RHT patients received heparin or low molecular weight heparin for the initial anticoagulant therapy ($p = 0.001$). In addition, the proportion of patients who received NOACs for the initial anticoagulant therapy was higher in non-RHT than RHT patients (95.53% vs. 66.67%, $p = 0.033$). The medium follow-up periods for RHT and non-RHT patients were 608 and 353 days, respectively ($p = 0.127$). During the follow-up period, two RHT patients and nine non-RHT patients had all-cause mortality ($p = 0.119$).

Comparisons of baseline clinical characteristics and outcomes between RHT-APE and matched non-RHT-APE patients (Supporting Information: Table 2)

A 1:4 matched analysis was performed between RHT ($n = 17$) and non-RHT ($n = 68$) patients on the basis of gender, age, and BMI. All these patients were selected from the same APE cohort (diagnosed between September 2015 and August 2019). Comparisons showed higher proportion of RHT patients were in high/intermediate-high risk group (52.94% vs. 26.47%, $p = 0.036$). Besides, RHT patients also had higher levels of gamma-GT (89.47 ± 53.27 vs. 54.91 ± 37.49, $p = 0.003$) and NT-proBNP (2427.50 vs. 1140.00 pg/mL, $p = 0.022$).

Univariate and multivariate logistic regression analysis for RHT risk factors in APE

Supporting Information: Table 3 listed risk factors for RHT in APE. After adjusting by gender and age, high/intermediate-high risk, decreased RV motion, RV dysfunction, and NT-proBN >600 pg/mL could still be risk factors for RHT in APE (Table 3).

Comparisons between RHT and non-RHT patients in high or intermediate risk stratification (Supporting Information: Table 4)

All intermediate- or high-risk APE with ($n = 15$) or without ($n = 226$) RHT patients were selected from the APE cohort diagnosed between October 2015 and August 2019. Comparisons showed RHT patients had younger age (54.98 ± 15.50 vs. 67.14 ± 13.44, $p = 0.001$), higher levels of NT-proBNP (2578 vs. 1582 pg/mL, $p = 0.042$), and higher proportion of RV dysfunction (73.33% vs. 43.81%, $p = 0.026$).

Kaplan–Meier analysis for the 30- and 90-day survival differences between RHT and non-RHT patients

Kaplan–Meier analysis were performed for the APE cohort (diagnosed between September 2015 and August 2019). In the RHT group ($n = 17$), the median follow-up time was 608 days (Q1–Q3: 213–1103 days). During this period, two patients (11.76%) deceased and one patient

TABLE 2 Comparisons of clinical characteristics and follow-up results between APE with and without RHT patients who were diagnosed between September 2015 and August 2019.

	APE	RHT	Non-RHT	*p*
Patient number	346	17	329	N/A
Gender, male (%)	138 (39.88%)	11 (64.71%)	127 (38.60%)	0.032*
Age (years)	65.78 ± 13.62	51.63 ± 17.57	66.48 ± 12.96	0.003*
BMI (kg/m^2	25.63 ± 3.80	26.27 ± 2.64	25.60 ± 3.86	0.494
SBP (mmHg)	132.42 ± 24.26	118.88 ± 22.23	133.02 ± 24.21	0.019*
SBP <100 mmHg	29 (8.38%)	3 (17.65%)	26 (7.90%)	0.157
HR (bpm)	86.34 ± 20.89	90.71 ± 23.89	86.16 ± 20.79	0.384
HR >110 bpm	48 (13.87%)	5 (29.41%)	43 (13.07%)	0.070
SaO_2 (%)	93.47 ± 4.37	93.88 ± 4.78	93.45 ± 4.36	0.701
sPESI score, 0	164 (47.70%)	7 (41.18%)	157 (47.72%)	0.598
≥1	182 (52.60%)	10 (58.82%)	172 (52.28%)	
Severity and risk stratifications				
High risk	9 (2.60%)	1 (5.88%)	8 (2.43%)	0.066
Intermediate-high/intermediate-low risk	232 (67.05%)	14 (82.36%)	218 (66.26%)	
Low risk	105 (30.35%)	2 (11.76%)	103 (31.31%)	
Severity and risk stratifications				
High/intermediate risk	241 (69.65%)	15 (88.24%)	226 (68.69%)	0.087
Low risk	105 (30.35%)	2 (11.76%)	103 (31.31%)	
Severity and risk stratifications				
High/intermediate-high risk	84 (24.28%)	9 (52.94%)	75 (22.80%)	0.008*
Intermediate-low/low risk	262 (75.72%)	8 (47.06%)	254 (77.20%)	
Comorbidities and risk factors				
Atrial fibrillation	49 (14.16%)	3 (17.65%)	46 (13.98%)	0.719
Coronary atherosclerotic heart disease	91 (26.30%)	3 (17.65%)	88 (26.75%)	0.575
Myocardial infarction	28 (8.09%)	3 (17.65%)	25 (7.60%)	0.150
Chronic heart failure	66 (19.08%)	6 (35.29%)	60 (18.24%)	0.107
Hypertension	182 (52.60%)	6 (35.29%)	176 (53.50%)	0.143
Immobilization	65 (18.79%)	5 (29.41%)	60 (18.24%)	0.334
Infection	65 (18.79%)	5 (29.41%)	60 (18.24%)	0.334
Peripheral arterial disease	35 (10.12%)	4 (23.53%)	31 (9.42%)	0.080
Diabetes mellitus	53 (15.32%)	0 (0%)	53 (16.11%)	0.086
Smoking	49 (14.16%)	5 (29.41%)	44 (13.37%)	0.076
Stroke	65 (18.79%)	3 (17.65%)	62 (18.84%)	0.600
Autoimmune disease	11 (3.18%)	1 (5.88%)	10 (3.04%)	0.430
Chronic lung disease	19 (5.49%)	0 (0%)	19 (5.78%)	0.612
Deep venous thrombosis	193 (55.78%)	11 (64.71%)	182 (55.32%)	0.496
Laboratory tests				
NT-proBNP (Q1–Q3) (pg/mL)	810.00 (123.40–2459.00)	2427.50 (621.05–12,207.30)	698.20 (115.40–2404.40)	0.004*

(Continues)

TABLE 2 (Continued)

	APE	RHT	Non-RHT	*p*
NT-proBNP >600 pg/mL	179 (51.73%)	14 (82.35%)	165 (50.15%)	0.016*
TnI >0.02 ng/mL	95 (27.46%)	5 (29.41%)	90 (27.36%)	0.787
HGB (g/L)	134.68 ± 20.42	141.65 ± 13.87	134.32 ± 20.65	0.149
PLT (10^9/L)	222.99 ± 82.43	229.59 ± 118.04	222.65 ± 80.38	0.814
TB (umol/L)	17.14 ± 12.89	20.52 ± 13.30	16.97 ± 12.86	0.269
DB (umol/L)	4.90 ± 5.66	8.43 ± 8.03	4.72 ± 5.46	0.077
LDH (U/L)	262.87 ± 313.66	316.24 ± 155.36	260.09 ± 319.65	0.473
GGT (U/L)	55.27 ± 64.36	89.47 ± 53.55	53.27 ± 64.45	0.024*
LDL-C (mmol/L)	2.60 ± 0.84	2.51 ± 1.05	2.60 ± 0.83	0.662
D-Dimer (ug/mL)	5.71 ± 6.80	7.12 ± 6.81	5.64 ± 6.80	0.381
Cr (umol/L)	84.34 ± 29.00	111.86 ± 68.54	82.91 ± 24.77	0.102
eGFR (mL/min)	78.36 ± 25.83	79.93 ± 40.34	78.27 ± 24.90	0.873
CCr (mL/min)	75.06 ± 31.09	89.87 ± 57.31	74.25 ± 28.95	0.296
Transthoracic echocardiographic indices				
RV diameters (mm)	25.05 ± 6.24	26.88 ± 5.33	24.94 ± 6.28	0.215
LV diameters (mm)	46.14 ± 8.13	48.00 ± 12.58	46.04 ± 7.85	0.534
Decreased RV motion	73 (21.10%)	8 (47.06%)	65 (19.76%)	0.013*
Estimated SPAP (mmHg)	59.16 ± 19.11	59.08 ± 15.35	59.17 ± 19.42	0.986
Estimated SPAP >50 mmHg	105 (30.35%)	7 (41.18%)	98 (29.79%)	0.319
RV dysfunction	111 (32.08%)	11 (64.71%)	100 (30.40%)	0.003*
Pericardial effusion	25 (7.23%)	2 (11.76%)	23 (6.99%)	0.353
Treatment				
Treatment for APE				
None	18 (5.20%)	0 (0%)	18 (5.47%)	0.037*
Thrombolysis + anticoagulation	23 (6.65%)	2 (11.76%)	21 (6.38%)	
Surgical embolectomy	1 (0.29%)	1 (5.88%)	0 (0%)	
Anticoagulation	304 (87.86%)	14 (82.36%)	290 (88.15%)	
Initial anticoagulant therapy				
Heparin	6 (1.97%)	2 (14.28%)	4 (1.38%)	0.001*
LMWH	46 (15.14%)	6 (42.86%)	40 (13.79%)	
Oral anticoagulants	252 (82.89%)	6 (42.86%)	246 (84.83%)	
Warfarin	13 (5.16%)	2 (33.33%)	11 (4.47%)	0.033*
NOACs	239 (94.84)	4 (66.67%)	235 (95.53%)	
Other treatment				
IVC filter	25 (7.20%)	1 (5.90%)	24 (7.30%)	0.648
Antiplatelet therapy	54 (15.50%)	1 (5.90%)	52 (16.00%)	0.487
Vasoactive agents	38 (10.90%)	3 (17.60%)	35 (10.60%)	0.415
PAH targeted drugs	10 (2.90%)	1 (5.90%)	9 (2.70%)	0.400

TABLE 2 (Continued)

	APE	RHT	Non-RHT	*p*
Follow-up				
Follow-up period (Q1−Q3) (days)	360.00 (114.00−664.00)	608.00 (213.00−1103.00)	353.00 (112.50−650.75)	0.127
All-caused death	11 (3.18%)	2 (11.76%)	9 (2.74%)	0.119

Abbreviations: APE, acute pulmonary embolism; CCr, creatinine clearance rate; GGT, gamma-glutamyl transpeptidase; LDL-C, low-density lipoprotein cholesterol; LMWH, low molecular weight heparin; NOAC, novel oral anticoagulants; RHT, right heart thrombus; RV, right ventricular; sPESI, simplified pulmonary embolism severity index.

*$p < 0.05$.

TABLE 3 Multivariable logistic regression analysis for RHT risk factors in APE patients.

	OR	95% CI	*p*
Male	0.465	0.158−1.366	0.164
Age	1.058	1.025−1.092	<0.001*
High/intermediate-high risk	3.522	1.254−9.894	0.017*
	OR	95% CI	*p*
Male	0.443	0.151−1.304	0.139
Age	1.054	1.022−1.088	0.001*
Decreased RV motion	2.982	1.050−8.469	0.040*
	OR	95% CI	*p*
Male	0.479	0.161−1.428	0.186
Age	1.056	1.024−1.090	0.001*
NT-proBNP >600 pg/mL	4.227	1.153−15.495	0.030*
	OR	95% CI	*p*
Male	0.444	0.151−1.304	0.140
Age	1.054	1.022−1.087	0.001*
RV dysfunction	3.517	1.215−10.183	0.020*

Abbreviations: APE, acute pulmonary embolism; RHT, right heart thrombus; RV, right ventricular.

*$p < 0.05$.

(5.88%) lost to follow-up. For the non-RHT group ($n = 329$), the median follow-up time was 353 days (Q1−Q3: 112.5−650.75 days). During this period, nine patients (2.74%) deceased and 44 patients (13.37%) lost to follow-up. The Kaplan−Meier analysis for the over-all survival between two groups showed no statistically significant difference (log rank: $p = 0.234$, Figure 1a). However, when it comes to the 30- and 90-day survival, non-RHT patients had better prognosis compared to RHT patients (30-day survival: log-rank: $p < 0.001$, Figure 1b; 90-day survival: log-rank: $p = 0.002$, Figure 1c).

Subgroup analysis showed RHT patients still had higher 30- and 90-day mortality than matched non-RHT patients (Figure 2). For APE patients who were in intermediate/high-risk stratification or intermediate-high/high-risk stratification, RHT also had worse 30- and 90-day survival than non-RHT patients (Supporting Information: Figures 2 and 3).

Univariate and multivariate logistic regression analysis for 30- and 90-day mortality risk factors in APE patients

Supporting Information: Table 5 showed the risk factors for the 30- and 90-day mortality in APE patients. After adjusting by simplified pulmonary embolism severity index (sPESI) score[10] or APE risk stratifications, the multivariate logistic regression analysis found RHT were an independent risk factor for 30-day mortality in APE patients (Table 4).

DISCUSSION

RHT is a rare form in the clinical spectrum of APE but would lead to a life-threatening condition. Clinical data about RHT were very limited across the world. By far, the present study was the largest RHT-APE cohort ever reported in China. In this study, the prevalence of RHT was 4.91% in APE and RHT were found to increase the risk of 30- and 90-day mortality. Additionally, young age, male gender, decreased RV motion, NT-proBNP >600 pg/mL, RV dysfunction, and high level of risk stratification were found to be risk factors of RHT.

The exact prevalence of RHT in APE patients is uncertain and it varied from 2.6% to 17.6%[1–7] (Supporting Information: Table 1). The quite variable prevalence of RHT could be attributed to two main reasons: the severity of study population and the application of early TTE screening.[2] In this study, the prevalence of RHT was 4.91% in APE, which was in line with previous registries.[2,4] Besides, RHT's prevalence was also found to vary in different APE risk groups and to increase along the increase of APE risk levels, just as Casazza et al.

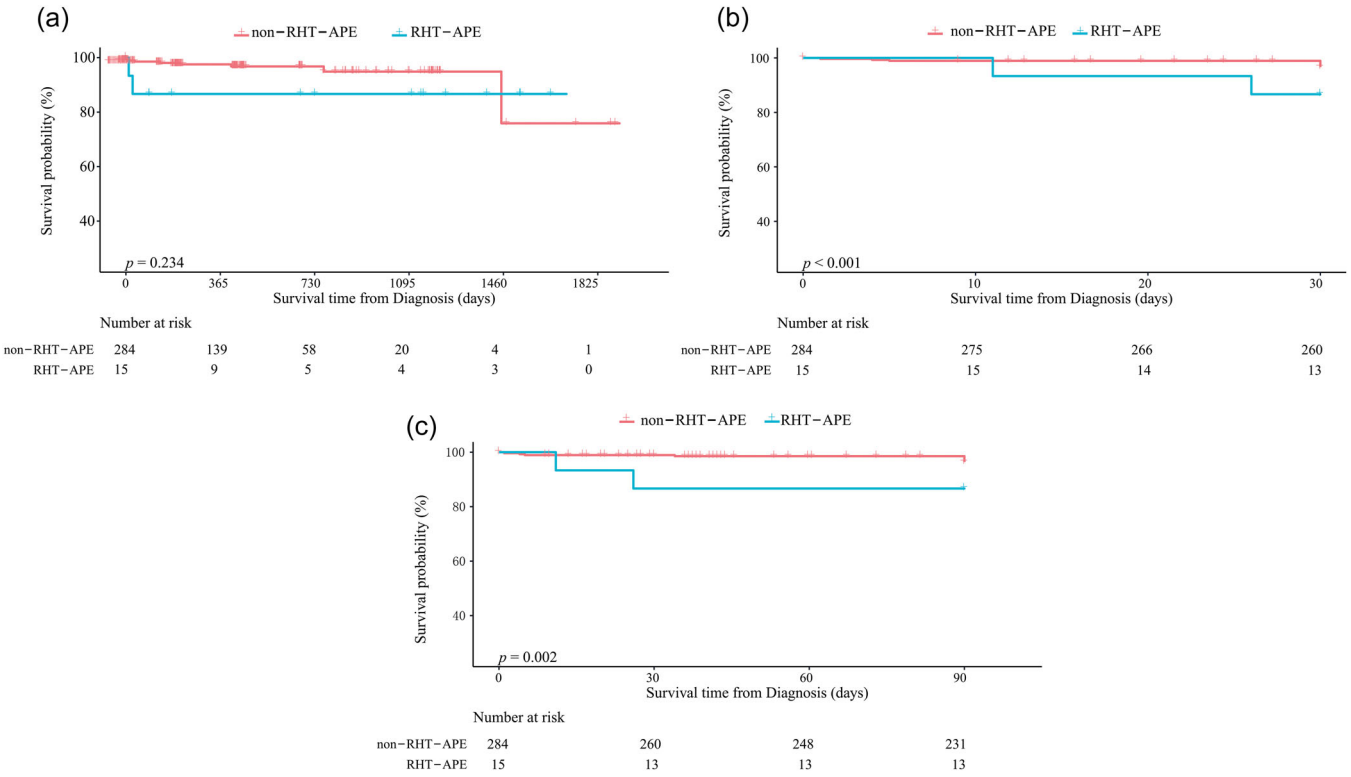

FIGURE 1 Kaplan–Meier analysis for the survival differences between RHT and non-RHT patients. RHT, right heart thrombus.

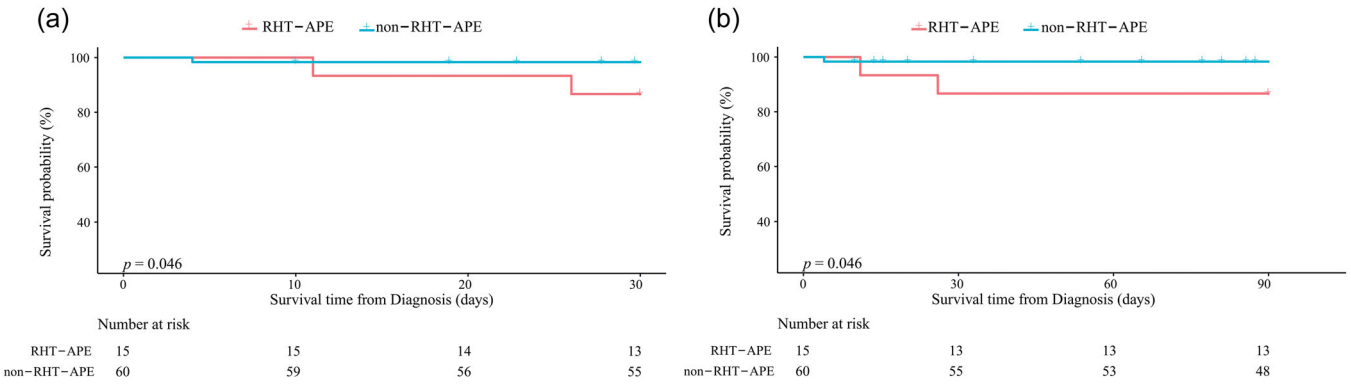

FIGURE 2 Kaplan–Meier analysis for the survival differences between RHT and matched non-RHT patients. RHT, right heart thrombus.

reported.[2] Since the presence of RHT would exacerbate the hemodynamical instability of APE, the source of APE cohort might influence the prevalence of RHT. In this study, the prevalence of RHT in high-risk, intermediate-risk, and low-risk APE patients were 11.11%, 6.03%, and 1.90% respectively, which had the similar trend with the study of Casazza et al. (16%, 3.8%, and 0.3%).[2] However, in our study, the prevalence of RHT in high-risk group was a little lower and in intermediate-risk group was a little higher than the study of Casazza et al.[2] Possible reasons may come down to the tertiary-referral system in China, 23.9% of APE patients in this study had received basic treatment in lower-level medical institutions before attending our emergency department. The prehospital treatment might degrade the risk levels of some severe RHT-APE cases. Besides, some severe RHT-APE cases with unstable condition might have deceased in lower-level medical institutions and could not be included in this study, which leading to a referral bias and was an inevitable limitation of a single center study.

According to a previous meta-analysis, most RHT were diagnosed in patients who were suspected of PE,

TABLE 4 Multivariable logistic regression analysis for 30- and 90-day mortality risk factors in APE patients diagnosed between September 2015 and August 2019.

	OR	95% CI	*p*
30-day mortality			
sPESI score	4.478	1.850−10.840	0.001*
RHT	10.786	1.049−110.893	0.045*
30-day mortality			
Risk stratification	7.494	1.786−31.439	0.006*
RHT	7.575	1.018−56.377	0.048*
90-day mortality			
sPESI score	3.649	1.716−7.761	0.001*
RHT	7.533	0.908−62.482	0.061
90-day mortality			
Risk stratification	4.812	1.493−15.511	0.009*
RHT	5.584	0.862−36.154	0.071

Abbreviations: APE, acute pulmonary embolism; RHT, right heart thrombus; sPESI, simplified pulmonary embolism severity index.
*$p < 0.05$.

and only a few were accidently found during TTE examination for other reasons.[11] The TTE is a reliable method to detect RHT with a sensitivity of 50%−60%.[11] In addition, TTE is widely available, radiation-free, noninvasive, no need for anesthesia, and can be performed at the bedside in critical care settings.[12] However, the diverse timing of receiving TTE examination in different studies would also influence the detection of RHT. In this study, all APE patients received an early bedside TTE within 24 h after they arrived at emergency department. Besides, RV dysfunction and decreased RV motion measured by TTE were found to be risk factors for RHT in APE patients. Furthermore, Bikdeli et al. reported that right atrial enlargement, right ventricular hypokinesis, and RHT measured by TTE were associated with increased odds for PE related mortality.[13] Therefore, an early TTE (better within 24−48 h) is essential for all APE patients to prompt a timely diagnosis and therapeutic decision of RHT, especially in hemodynamically unstable or severely dyspneic patients.[2]

The risk factors for RHT also varied in different studies. Previous studies reported that RHT-APE patients had lower SBP,[4,6] higher APE risk stratification,[6] higher proportion of RV hypokinesis,[4–6,14] and higher BNP levels,[6] which were in consistence with our study. Besides, the present study also reported that RHT patients had younger age,[6] higher proportion of male gender,[15] and higher levels of creatinine,[6] which were also in line with others' studies. However, previous studies reported RHT-APE patients had more risk factors for venous thromboembolism, including prolonged immobilization,[6,15] cancer,[6] and cerebrovascular disorder.[15] In addition, the comorbid chronic heart disease[6,15] or congestive heart failure[4] were also reported to be RHT risk factors. However, these associations between venous thromboembolism risk factors or comorbid chronic heart disease and RHT were not observed in this study. Since our center is a special hospital of cardiovascular diseases, patients with prolonged immobilization, known cancer, or cerebrovascular disorder might be preferred to transfer to other general hospitals. In addition, in the setting of emergency department, a screening for unknown malignance (details in Supporting Information Materials) is unpractical especially in hemodynamically unstable APE patients. Therefore, the data about malignance is not included in this study. In addition, the proportion of RHT patients who had chronic heart failure in this study was almost doubled the proportion of non-RHT (35.29% vs. 18.24%), but the difference didn't reach a statistically significant level. However, in this study, high levels of DB and GGT were reported to be risk factors of RHT, which have not been reported before. The high levels of these two biomarkers might be related with the progressive right heart failure caused by RHT (Supporting Information: Table 6), which should be paid more attention.

The overall mortality of RHT-APE patients, reported by three pooled analyses, were 19%,[16] 20.4%,[17] and 21.3%[11] respectively. The high rate of mortality in RHT-APE patients were reported to depend on the hemodynamic status[11] and the lack of clear management guidelines.[17] However, in the present study, the overall mortality of RHT-APE was only 11.76%, which was quite lower than previous pooled analyses. One nonnegligible reason for the difference of mortality rate is the study period during which patients were recruited. In this study, patients were diagnosed between 2015 and 2019. On the contrary, the three pooled analyses had a very large study-time span, ranging from 10 years to at least 60 years. As the awareness and management strategies of RHT-APE were quite discriminatory at different era, RHT-APE patients who were diagnosed in the past would inevitably have higher mortality than recent diagnosed patients.[16]

Consist with previous studies,[4,6,8,9] this study also found RHT-APE patients had both worse 30- and 90-day survival compared with non-RHT-APE. In addition, after adjusting by sPESI or risk stratification, RHT was an independent predictor for the 30-day mortality. However, the long-term mortality seemed to have no significant difference between two groups. In this study, we for the

first time reported the differences of clinical characteristics and outcomes between RHT and non-RHT patients who were in higher risk stratifications. RHT were found to lead to worse outcomes even in APE patients who already had higher early mortality risk. The hemodynamic instability and worse RV function caused by the coexistence of RHT might be the main reasons for the worse short-term prognosis.

Treatment options for RHT-APE patients include anticoagulation, thrombolysis, surgical embolectomy, and percutaneous thrombectomy. However, the optimal management of RHT-APE remains controversial. Treatment strategies of RHT were made mainly depending on patient clinical conditions, experience of medical institutions, and patient preference. The meta-analysis of Ibrahim et al. reported that thrombolytic therapy and surgical thrombectomy were associated with increased odds of survival.[17] A retrospective pooled analysis showed compared with systemic anticoagulation, systemic thrombolysis might bring favorable odds of survival.[16] The pooled analysis of Burgos et al. reported that anticoagulation alone was not sufficient and would result in increased mortality.[11] In this study, the majority of APE patients received anticoagulation, which was recommended as the corner stone of APE therapy.[10] Further comparisons showed higher percentage of RHT patients received thrombolysis or surgical embolectomy than non-RTH patients. Since this study was not a randomized controlled trial (RCT), we could not draw a conclusion about which treatment was the most effective. In addition, the number of RHT patients who had all-cause death was limited and we could not further analyze the management differences between RHT patients who had different outcomes. Besides, the experience of percutaneous thrombectomy in our center was limited and no RHT-APE patient, diagnosed between 2015 and 2019, received percutaneous thrombectomy. Large RCTs about the management strategies of RHT-APE are still in urgent need.

This study has several limitations. First, our center is a special hospital of cardiovascular diseases, therefore the source of study patients might have selection bias. Second, as RHT-APE is a very rare form of APE, the patient number of this study was relatively limited. Third, as an ambispective observational study, the data might lack some clinical details which might confound study results. Fourth, we could not conclude the effectiveness of each treatment option for RHT-APE patients.

CONCLUSION

RHT would increase the risk of 30- and 90-day mortality in APE. More attention should be paid to young male APE patients, who had decreased RV motion, NT-proBNP >600 pg/mL, RV dysfunction, and high level of risk stratification, to exclude the coexistence of RHT.

AUTHOR CONTRIBUTIONS

Wen Li and Zhi-Ying Liu: Conceptualization; formal analysis; investigation; writing of the original draft; and funding acquisition. **Xiao-Xi Chen, Yu-Ling Qian, and Rui-Lin Quan**: Validation; investigation; resources; and data curation. **Chang-Ming Xiong**: Methodology; investigation; resources; writing, review, and editing; and project administration. **Qing Gu and Jian-Guo He**: Conceptualization; methodology; writing, review, and editing; supervision; project administration; and funding acquisition.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

ETHICS STATEMENT

This study was approved by the Institutional Review Board of Fuwai Hospital (Ethical approval number: Fuwai 2012-401).

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SUPPORTING INFORMATION

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

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