



Predictors for congestive heart failure hospitalization or death following acute pulmonary embolism: A population-linkage study



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ABSTRACT

Background: Congestive heart failure (CHF) is a risk factor for pulmonary embolism (PE). PE is also an independent predictor of death or re-hospitalization among CHF patients. We assessed the incidence of CHF admission following acute PE using population-linkage analysis.

Methods: Patients were identified from a comprehensive single-center PE database and CHF admissions or death after their PE were tracked from the statewide Admitted Patient Data Collection and Death registries respectively. Patients were divided into two groups: Group-1 were patients without a history of CHF and left ventricular ejection fraction (LVEF) $\geq 50\%$; Group-2 were patients with a history of CHF and/or LVEF $< 50\%$. Cox regression was used to identify independent predictors for post-PE CHF admission or death.

Results: The study cohort comprised 515 patients (Group-1: $n = 338$ [65.6%]; Group-2: $n = 177$ [34.4%]). The incidence of first CHF hospitalization after discharge for acute PE over a mean (\pm SD) follow-up period of 4.7 ± 3.7 years for the total cohort was 71 (13.8%), with the rate significantly higher in Group-2 than Group-1 (Group-2: [$n = 58$] 9.11 per-100-patient-years vs Group-1: [$n = 13$] 0.73 per-100-patient-years). Independent predictors for CHF admission or death after acute PE were older age, male gender, history of CHF or malignancy, low day-1 serum hemoglobin, on diuretics during index PE admission, LVEF $< 50\%$, and elevated right ventricular-atrial pressure gradient on echocardiography.

Conclusion: We report a high incidence of CHF requiring hospital admission after acute PE. Surveillance for new-onset heart failure and close monitoring for heart failure decompensation following acute PE particularly in at-risk groups may be warranted.

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1. Introduction

Pulmonary embolism (PE) is the most severe manifestation of venous thromboembolism (VTE) [1] and has a close bidirectional relationship with congestive heart failure (CHF). Previous studies have demonstrated that CHF is a risk factor for the development of PE [2,3], and the risk of PE among patients with CHF increases as left ventricular systolic function declines [3]. CHF is an independent predictor of mortality in patients presenting with acute PE [4,5]. Conversely, PE is also an independent predictor of death or re-hospitalization among heart failure patients [6]. Although a prior study reported that patients diagnosed with a first unprovoked PE were at higher risk of developing

subsequent arterial cardiovascular events than patients with a provoked PE or the control population without PE, the cardiovascular events did not include heart failure [7]. To date, no study has adequately defined the incidence or the predictors for CHF hospitalization during long-term follow-up after acute PE.

In this study, we report on the incidence of hospitalization for CHF during long-term follow-up of patients with acute PE using population-linkage analysis. We further identify independent predictors for CHF hospitalization or death in these patients according to prior history of CHF and left ventricular systolic function at baseline.

2. Methods

2.1. Study population

Outcomes of patients admitted to our institution (Concord Hospital, University of Sydney, Australia) with confirmed PE have been reported previously [8,9]. For the purpose of this study, patients with confirmed acute PE between 1 January 2001 and 31 December 2012 were identified from our PE database. Confirmed PE was defined as per published guidelines, requiring both a documented clinical diagnosis and/or treatment of acute PE,

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together with a consistent imaging study (intermediate-high probability nuclear pulmonary ventilation-perfusion scintigraphy or computed-tomography pulmonary angiogram showing thrombus within pulmonary arterial circulation) [10].

The Concord Hospital PE database is maintained by the Cardiology Department, and contains details of patients' admission history, including their presenting symptoms, heart rate, blood pressure, oxyhemoglobin saturation, admission medications, blood test results, transthoracic echocardiogram results (if performed during admission) and in-hospital outcomes.

2.2. Inclusion and exclusion criteria

For patients that presented with recurrent PE during the study period, only the index PE admission was included in this study. Furthermore, only patients with transthoracic echocardiogram (TTE) were included. This is to identify patients with asymptomatic left ventricular dysfunction despite no prior history of congestive heart failure admission. Patients who were non-residents of the local state (New South Wales [NSW]) were excluded from the study to minimize incomplete tracking of outcomes.

To determine predictors for CHF admission or death post-acute PE, we pre-specified the following variables for consideration – age, gender, cardiovascular and noncardiovascular comorbidities, hemodynamic and blood profiles on admission and admission medications. Clinical transthoracic echocardiogram assessments including left ventricular ejection fraction (LVEF), right ventricular (RV) size, right ventricular – right atrial (RV-RA) pressure gradient, and major valvular disease of moderate to severe degree were extracted from finalized report and stratified in a standardized fashion. For patients without reported RV-RA pressure gradient (usually due to insufficient tricuspid regurgitation), the median value for the whole cohort was imputed. Comorbidities were coded based on the International Classification of Diseases 10th revision (ICD-10). Each patient also had their simplified Pulmonary Embolism Severity Index (sPESI) score calculated from the extracted data [11]. The sPESI score was calculated by assigning a point to the following: age > 80 years, heart rate \geq 110 beats/min, systolic blood pressure < 100 mmHg, oxyhemoglobin saturation < 90%, history of malignancy, and history of cardiopulmonary disease. For the purpose of this study, CHF is defined as patients with ICD-10 code I50.

The study cohort was divided into two groups: Group-1 consisted of patients without a history of CHF and LVEF reported as \geq 50% during index PE admission; Group-2 consisted of patients with a history of CHF prior to or during their acute PE presentation and/or LVEF <50% on transthoracic echocardiogram performed during the index PE admission.

2.3. Study outcomes

The Centre for Health Record Linkage (CHeReL) was established in July 2000 and holds one of the largest data linkage systems in Australia, containing high-quality linked health data of all people in the state of New South Wales. The mortality and morbidity outcomes of our PE cohort were tracked from the statewide death registry and the Admission Patient Data Collection registry respectively. Both are part of CHeReL-derived Master Linkage Key databases. A censored date (study end date) of 31 December 2013 was predetermined to allow a minimum follow-up of 1 year for each patient. For the purpose of this study, the primary outcome of interest is re-hospitalization with a primary diagnosis of CHF (ICD-10 code I50). In order to factor in the competing risk of death, we used a composite end-point of death or first CHF re-hospitalization after acute PE. Patients who died or had an admission episode for CHF after their index acute PE were identified and the admission date recorded.

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. For the Concord Hospital PE cohort, approval was granted by Concord Hospital Ethics Committee, reference number: CH62/6/2008–009. For the population-linkage analysis, approval was granted by the NSW Population and Health Services Research Ethics Committee, reference number: 2013/09/479. All patients' data were de-identified and analyzed anonymously.

2.4. Statistical analysis

All continuous variables were expressed as either mean \pm standard deviation or median (interquartile range) based on Shapiro-Wilk test of normality, with categorical variables expressed as frequencies and percentages. Comparisons between two groups were performed using independent-samples *t*-test or Mann-Whitney *U* test for continuous variables, and Pearson's chi square test for dichotomous variables. Unadjusted survival to first CHF admission or death was performed using Kaplan-Meier method and comparison between groups performed using logrank test. Cox proportional hazard regression method was used to determine predictors for first CHF admission or death after PE based on pooled total study cohort. Only univariables with $p < 0.05$ were included in the multivariable Cox regression analysis, except for age and gender which were included irrespectively of their *p* value into the model, to identify independent predictors for first CHF admission or death after acute PE. To avoid significant co-linearity, only univariable predictors with a correlation coefficient ≤ 0.7 were chosen for the multivariable modelling. Separate univariable and multivariable analyses based on above criteria were performed for patients without baseline CHF and those with baseline CHF. All analyses were performed using SPSS v24.0 (IBM, USA). A 2-tailed probability value <0.05 was considered statistically significant.

3. Results

The study cohort comprised 515 patients who were admitted with confirmed acute PE and had inpatient echocardiograms. Of the 515 patients, 338 (65.6%) (Group-1) had LVEF \geq 50% and no history of CHF (Supplementary Fig. 1). There was a total of 177 (34.4%) patients in Group-2, consisting of 59 patients with a history of CHF and LVEF \geq 50% at index PE admission, another 48 patients with a history of CHF and LVEF <50%, and 70 patients without a history of CHF but LVEF was <50% (asymptomatic LV dysfunction) at index PE admission.

3.1. Baseline characteristics across groups

The baseline characteristics of the study groups are shown in Table 1. The median age for the overall cohort ($n = 515$) was 72.5 (60.7–80.6)

Table 1
Baseline characteristics during index PE admission.

Parameters	No CHF, LVEF \geq 50%	CHF or LVEF < 50%	<i>p</i> value
	Group-1 (N = 338)	Group-2 (N = 177)	
Age, years	69.7 (56.9–79.0)	76.5 (68.6–83.8)	<0.001
Males	133 (39.3)	100 (56.5)	<0.001
Documented deep vein thrombosis	91 (26.9)	33 (18.6)	0.04
Length of stay, days	7 (5–10)	9 (7–13)	<0.001
Initial symptoms			
Syncope	36 (10.7)	10 (5.6)	0.10
Chest pain	210 (62.1)	76 (42.9)	<0.001
Dyspnea	239 (70.7)	129 (72.9)	0.08
Admission hemodynamics			
Heart rate, beats/min	87.0 (75.0–100.0)	91.0 (75.0–106.5)	0.10
Systolic blood pressure, mmHg	140 (122.3–159.0)	139 (120.0–159.5)	0.68
Oxyhemoglobin saturation, %	96.0 (94.0–98.0)	96 (93–98)	0.06
Simplified PESI score	1 (0–1)	1 (1–2)	<0.001
Imaging modality			
Ventilation-perfusion scintigraphy	226 (66.9)	144 (81.4)	<0.001
CT pulmonary angiography	150 (44.4)	54 (30.5)	0.002
Both modalities used	37 (10.9)	21 (11.9)	0.77
Cardiac comorbidities			
Cardiovascular disease ^a	102 (30.2)	147 (83.1)	<0.001
Ischemic heart disease	40 (11.8)	66 (37.3)	<0.001
Prior CABG or PCI	10 (3.0)	24 (13.6)	<0.001
Stroke	5 (1.5)	8 (4.5)	0.07
Heart failure	0 (0)	107 (60.5)	<0.001
Valvular heart disease	7 (2.1)	9 (5.1)	0.11
Peripheral vascular disease	27 (8.0)	30 (16.9)	0.003
Prosthetic heart valve	0 (0)	3 (1.7)	0.04
Atrial fibrillation/flutter	45 (13.3)	51 (28.8)	<0.001
Cardiac risk factors	168 (49.7)	112 (63.3)	0.004
Hypertension	82 (24.3)	65 (36.7)	0.004
Hyperlipidemia	36 (10.7)	28 (15.8)	0.09
Diabetes	42 (12.4)	47 (26.6)	<0.001
Current smoker	29 (8.6)	8 (4.5)	0.11
Non-cardiac comorbidities			
Malignancy	51 (15.1)	31 (17.5)	0.53
Chronic pulmonary disease	36 (10.7)	15 (8.5)	0.54
Dementia	8 (2.4)	9 (5.1)	0.12
Chronic renal disease	15 (4.4)	24 (13.6)	<0.001

Continuous variables are expressed as medians with interquartile range in brackets; all others represent numbers of patients with values in brackets representing percentages. CABG, coronary artery bypass grafting; CHF, congestive heart failure; CT, computed-tomography; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; PE, pulmonary embolism; simplified PESI, simplified pulmonary embolism severity index incorporates age, history of malignancy, heart failure/chronic lung disease, heart rate \geq 110 beats/min, systolic blood pressure < 100 mmHg and oxyhemoglobin saturation < 90%.

^a Cardiovascular disease includes ischemic heart disease, prior CABG or PCI, stroke, heart failure, valvular heart disease, peripheral vascular disease, prosthetic heart valve or atrial fibrillation/flutter.

years, with patients in Group-2 significantly older than patients in Group-1 (median age: 76.5 vs 69.7 respectively, $p < 0.001$). Group-2 had proportionally more males (56.5% vs 39.3%, $p < 0.001$), whilst Group-1 patients were more likely to present with chest pain (62.1% vs 42.9%, $p < 0.001$) and have documented deep vein thrombosis (26.9% vs 18.6%, $p = 0.04$) at index PE admission. A greater proportion of patients in Group-2 had cardiac risk factors, baseline cardiovascular disease and chronic renal disease compared to patients in Group-1.

Table 2 compares the baseline blood profiles, medications and echocardiographic parameters of study groups on admission. Group-1 patients had significantly higher median estimated glomerular filtration rate, while significantly greater proportion of patients in Group-2 were taking aspirin, angiotensin-converting-enzyme inhibitors, diuretics, statin and beta-blocker than Group-1 patients on admission.

3.2. Echocardiographic parameters

All Group-1 patients had LVEF $\geq 50\%$, whilst 118 (66.7%) patients in Group-2 had LVEF $< 50\%$ at index PE admission (Table 2). There were more patients in Group-2 with RV dilatation (37.3% vs 34.0%, $p = 0.03$). There were also more patients in Group-2 with moderate to severe valvular pathologies including aortic stenosis (4.5% vs 0.6%, $p = 0.004$), mitral regurgitation (17.5% vs 2.1%, $p < 0.001$) and tricuspid regurgitation (27.1% vs 7.4%, $p < 0.001$) than in Group-1.

3.3. Incidence of admission for CHF after acute PE episode

The mean follow-up time for the total cohort to either death, first CHF admission or last censored date, 31 December 2013, is $4.7 \pm$

Table 2
Blood, medications and echocardiographic parameters during index PE admission.

Parameters	No CHF, LVEF $\geq 50\%$	CHF or LVEF $< 50\%$	p value
	Group-1 (N = 338)	Group-2 (N = 177)	
Blood profile on admission			
Day-1 sodium, mmol/L	139 (137–141)	139 (137–141)	0.73
Day-1 hemoglobin, g/L	133 (121–144)	131 (113–142)	0.10
Day-1 eGFR, ml/min/1.73m ²	79 (60–95)	64 (45–81)	<0.001
Admission medications			
Aspirin	78 (23.1)	59 (33.3)	0.004
Clopidogrel	18 (5.3)	11 (6.2)	0.55
Thrombolysis	3 (0.9)	2 (1.1)	0.67
Warfarin	18 (5.3)	14 (7.9)	0.18
Enoxaparin	14 (4.1)	3 (1.7)	0.20
DOAC	0	0	
ACE-inhibitor	54 (16.0)	45 (25.4)	0.004
Angiotensin receptor blocker	64 (18.9)	39 (22.0)	0.24
Diuretics ^a	62 (18.3)	64 (36.2)	<0.001
Statin	84 (24.9)	59 (33.3)	0.01
Beta-blockers	55 (16.3)	52 (29.4)	<0.001
Echocardiographic parameters			
LVEF $< 50\%$	0 (0)	118 (66.7)	<0.001
Right ventricular dilatation	115 (34.0)	66 (37.3)	0.03
RV-RA pressure gradient, mmHg	32 (26–44)	36 (30–45)	0.003
Valvular lesions (moderate-severe)			
Aortic stenosis	2 (0.6)	8 (4.5)	0.004
Aortic regurgitation	1 (0.3)	4 (2.3)	0.05
Mitral stenosis	1 (0.3)	0 (0)	1.00
Mitral regurgitation	7 (2.1)	31 (17.5)	<0.001
Tricuspid regurgitation	25 (7.4)	48 (27.1)	<0.001

Continuous variables are expressed as medians with interquartile range in brackets; all others represent numbers of patients with values in brackets representing percentages. ACE, angiotensin-converting-enzyme; CHF, congestive heart failure; eGFR = $186 \times ([\text{SCr}/88.4]^{-1.154}) \times (\text{age})^{-0.203} \times (0.742 \text{ if female})$, where eGFR = estimated glomerular filtration rate (ml/min/1.73m²), SCr = serum creatinine concentration ($\mu\text{mol/L}$), and age is expressed in years; DOAC, direct-acting oral anticoagulant including dabigatran, rivaroxaban, and apixaban; INR, international normalized ratio; LVEF, left ventricular ejection fraction; RV, right ventricular; RV-RA, right ventricular to right atrial.

^a Include both thiazide and loop diuretics.

3.7 years. During this period, there were a total of 110 CHF admissions or deaths in Group-1, while Group-2 had 132 CHF admissions or deaths. The incidence of subsequent admission for CHF post-acute PE was significantly higher in Group-2 than in Group-1 (Group-2: 58 [32.8%] patients, 9.11 per 100-patient-years vs Group-1: 13 [3.85%] patients, 0.73 per 100-patient-years). Fig. 1 shows the Kaplan-Meier curves for first CHF hospitalization or death after index PE admission: Group-2 patients had a significantly higher rate of admission for CHF or death after an acute PE episode compared to Group-1 patients ($p < 0.001$).

3.4. Predictors for CHF admission or death following acute PE

The independent predictors for first CHF admission or death after acute PE based on pooled analysis of the whole study cohort were age (adjusted hazard ratio [aHR] 1.04, 95% confidence interval [CI] 1.02–1.06), male gender (aHR 1.38, 95% CI 1.01–1.89), history of congestive heart failure (aHR 1.57, 95% CI 1.12–2.20) or malignancy (aHR 2.75, 95% CI 1.94–3.91), day-1 serum hemoglobin (aHR 0.99, 95% CI 0.98–0.99), on diuretics at index PE admission (aHR 1.70, 95% CI 1.21–2.37), LVEF $< 50\%$ (aHR 1.63, 95% CI 1.16–2.29), and RV-RA pressure gradient (aHR 1.02, 95% CI 1.01–1.04) on transthoracic echocardiogram during index PE admission (all $p < 0.05$) (Table 3; Supplementary Table S1 for univariable analysis).

For Group-1 (patients without history of CHF and LVEF $\geq 50\%$), the independent predictors for first CHF (new-onset) admission or death were age (aHR 1.07, 95% CI 1.04–1.09), history of atrial fibrillation / flutter (aHR 1.74, 95% CI 1.10–2.98), malignancy (aHR 2.38, 95% CI 1.42–4.00), chronic pulmonary disease (aHR 2.17, 95% CI 1.26–3.74), and day-1 hemoglobin (aHR 0.98, 95% CI 0.97–0.99) (all $p < 0.05$) (Supplementary Table S2 for univariable analysis; Supplementary Table S3 for multivariable analysis). For Group-2 (patients with a history of CHF or LVEF $< 50\%$ during index PE admission), history of stroke (aHR 2.66, 95% CI 1.15–6.15), malignancy (aHR 2.16, 95% CI 1.29–3.60), on diuretics during index PE admission (aHR 2.96, 95% CI 1.94–4.52), and RV-

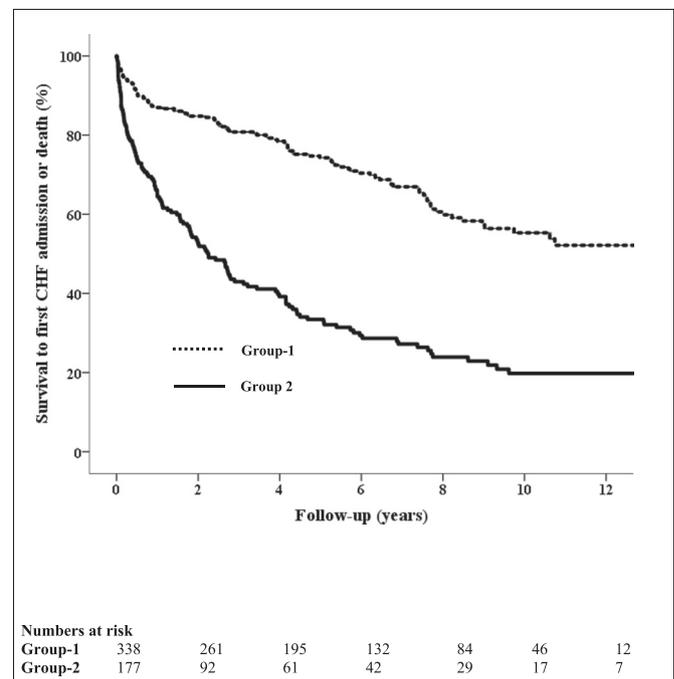


Fig. 1. Kaplan-Meier survival curves for first CHF hospitalization or death after index PE admission. The dotted line represents the survival curve of the cohort without baseline CHF and LVEF $\geq 50\%$ during index PE admission (Group-1), while the un-dotted line represents the survival curve of the cohort with baseline history of CHF and/or LVEF $< 50\%$ during index PE admission (Group-2). The survival curves differed significantly (logrank $p < 0.001$). CHF, congestive heart failure; LVEF, left ventricular ejection fraction; PE, pulmonary embolism.

Table 3

Independent predictors for first CHF hospitalization or death after acute PE (Pooled analysis).

Multivariable analyses ^a	Adjusted hazard ratio	95% CI	p value
Age at episode, per 1-year	1.04	1.02–1.06	<0.001
Males	1.38	1.01–1.89	0.04
Congestive heart failure	1.57	1.12–2.20	0.009
Malignancy	2.75	1.94–3.91	<0.001
Day-1 hemoglobin, per 1 g/L	0.99	0.98–0.99	<0.001
On diuretics at admission ^b	1.70	1.21–2.37	0.002
LVEF <50%	1.63	1.16–2.29	0.005
RV-RA pressure gradient, per 1 mmHg	1.02	1.01–1.04	0.001

CI, confidence interval; CHF, congestive heart failure; LVEF, left ventricular ejection fraction; PE, pulmonary embolism; RV-RA, right ventricular to right atrial.

^a Multivariable Cox proportional hazards regression method was used to identify independent predictors for first CHF hospitalization or death after acute PE for the whole study cohort. Only univariables with $p < 0.05$ (except for age and gender which were included irrespectively) were included in the multivariable analysis (see Supplementary material online Table S1 for univariable analysis). Only independent predictors with $p < 0.05$ are presented in the Table.

^b Include both thiazide and loop diuretics.

RA pressure gradient (aHR 1.04, 95% CI 1.02–1.06) (all $p < 0.05$) were independent predictors for subsequent CHF admission or death after acute PE.

3.5. Subgroup analyses

We performed two additional exploratory analyses: 1) determine if there was difference over time in outcomes within Group-1 and Group-2; and 2) within Group-2, was there a difference in outcomes between those with a prior history of clinical heart failure (107/177 patients, 60.5%) and those with asymptomatic LV dysfunction (70/177 patients, 39.5%). Firstly, patients from earlier years (2001–2006) had similar survival outcomes to first CHF admission or death compared to those from later years (2007–2012) within each group (Group-1: logrank $p = 0.29$; Group 2: logrank $p = 0.06$). Secondly, within Group-2 patients, those with a prior history of clinical heart failure had a significantly higher risk for CHF admission or death compared to those with asymptomatic LV dysfunction ($p = 0.02$) (Supplementary Fig. 2).

4. Discussion

In the present study, we report a high incidence of subsequent hospitalization for CHF after acute PE, the risk of which can be further stratified by simple clinical, biochemical and echocardiographic criteria. Acute admission with PE can therefore be considered an opportunity for screening and preventing subsequent CHF hospitalization.

To the best of our knowledge, our study is the first to carefully discern the prevalence and incidence of CHF in acute PE, and to identify its predictors. Klok et al. showed that prior arterial cardiovascular events in patients presenting with acute PE predicted their recurrence [7], however heart failure was not reported. At the time of acute PE admission, we identify that 34% had a history of prior or intercurrent CHF. In one of our previous studies, Hee et al. demonstrated that patients with underlying cardiovascular disease, who presented with an acute PE, had a 2.3 fold increased risk of death during follow-up compared to those without [12]. However, there was no data on the re-hospitalization rates and etiology of these patients. In our current study, patients with a history of CHF and/or LVEF <50% had approximately 12.4 times the risk of developing subsequent CHF than patients without these characteristics following an acute PE event. Furthermore, our study showed that the readmission rates continues to climb in the long-term.

The present study confirmed the importance of traditional risk factors for CHF in the prediction of subsequent CHF hospitalization. Age was found to be an independent predictor for CHF hospitalization

after acute PE in Group-1 patients, consistent with other studies showing that the incidence, prevalence and mortality of CHF increases with advancing age [13–15]. Interestingly, chronic pulmonary disease was found to be an independent predictor of CHF after acute PE in Group-1 patients. This may be attributable to low-grade systemic inflammation in patients with chronic obstructive pulmonary disease (COPD) [16] as the incidence of heart failure was higher among Framingham subjects with elevated C-reactive protein (CRP) and cytokine levels, independent of established cardiac risk factors [17]. There may also be a contribution from the high incidence of left ventricular function in moderate to severe COPD patients [16]. An acute PE event will not only likely worsen pre-existing LV dysfunction via hypoxia and hemodynamic stress, but also has the potential to contribute to new RV dysfunction, leading to an overall significant reduction in cardiac output and increasing the likelihood of CHF presentation [18].

We hypothesize several mechanisms to explain the occurrence of CHF after acute PE. PE-induced pulmonary vasoconstriction and anatomical obstruction increase pulmonary vascular resistance, resulting in RV dilatation [10,18]. Subsequent RV failure due to pressure overload is associated with worse outcomes in acute PE and is the main cause of death in these patients in the acute setting [10,19,20]. The prolongation of RV contraction time into early diastole, coupled with increased right ventricular end-diastolic pressure, leads to leftward bowing of the interventricular septum. As a result, LV filling is impeded in early diastole, potentially contributing to further reduction in cardiac output with clinical manifestation of systemic hypotension and hemodynamic instability. It is also likely that the imbalance between oxygen supply and demand can result in damage to cardiomyocytes and further reduce contractile forces [10]. Systemic inflammation in patients with comorbidities such as malignancy, chronic heart failure and ischemic heart disease may also be implicated in the pathogenesis of CHF by promoting myocardial dysfunction and inducing pathological consequences in other organs and tissues [21]. In patients with ischemic heart disease, endothelial dysfunction and increased vascular oxidative stress have also been shown to predict the risk of cardiovascular events [22]. Although anemia is associated with high-output CHF due to increased metabolic demand [23], we recently reported that red blood cell transfusion in patients hospitalized with acute PE is rare and appears to be associated with increased risk of short and long-term mortality [24].

4.1. Study strengths

Strengths of this study include a well-characterized cohort of patients with confirmed PE, linkage to a state-wide hospital admission data registry enabling adequate capture of all CHF hospitalization, availability of a control group without baseline CHF, a significant follow-up period with a minimum follow-up time of at least 1 year for all patients and identification of important predictors for subsequent CHF admission or death in patients with acute PE. In addition, the study analysis is stratified into patients with either normal or impaired left ventricular systolic function based on echocardiographic assessment at the time of index PE admission.

4.2. Study limitations

Our study has several limitations. As a single-center study with a retrospective design, selection bias is unavoidable. We also did not conduct a cause-specific mortality analysis. Given that CHF is a clinical diagnosis with potential overlap of symptoms with other diseases, our results could have underestimated the number of patients with CHF. We minimized this limitation by only including patients who had an echocardiogram during their index PE admission. As the CHeReL registry does not contain echocardiogram data, we were unable to compare the echocardiographic parameters of patients obtained during their index PE admission with those obtained during subsequent CHF admissions. It is also not possible to distinguish whether the readmissions for CHF

were for right heart failure, left heart failure or biventricular failure. However, it has already been established that acute PE can lead to RV failure due to pressure overload, as well as LV failure due to underfilling, hypoxia and hemodynamic stress [10,18]. Hence, the main purpose of the study was to determine CHF hospitalization as reported. Although it is well established that a number of biomarkers such as natriuretic peptides, high-sensitive troponin, procalcitonin and others are associated with heart failure [25], these biomarkers were not available in this study.

5. Conclusion

We report a high prevalence of CHF in patients admitted with acute PE, and a high incidence for subsequent CHF hospitalization with or without baseline CHF after acute PE. The results of our study highlight the need for closer surveillance measures for new-onset CHF in the PE cohort. Patients with asymptomatic left ventricular dysfunction will also need to be closely monitored to reduce their risk of developing overt heart failure. Furthermore, there is a need to establish prospective registries to collect accurate outcome data so that strategies to reduce mortality and prevent the development of new-onset heart failure after PE can be developed.

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Conflict of interest

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