Long-Term Cardiovascular and Noncardiovascular Mortality of 1023 Patients With Confirmed Acute Pulmonary Embolism

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Background—There are currently no guidelines advising long-term surveillance of patients following an acute pulmonary embolism (PE), because long-term outcome studies are rare. We investigated the long-term cardiovascular and all-cause mortality of a large patient cohort with confirmed PE in relation to baseline cardiovascular disease (CVD).

Methods and Results—Clinical details of all patients presenting with acute PE to a tertiary hospital were retrieved from medical records, and their survival tracked from a statewide death registry. There were 1023 (45% males) patients admitted with confirmed PE from 2000 to 2007. During a mean follow-up of 3.8±2.6 years, 363 patients died (35.5%), of whom only 31 (3.0%) died in-hospital during the index PE admission. The 3-month, 6-month, 1-year, 3-year, and 5-year cumulative mortality rates were 8.3%, 11.1%, 16.3%, 26.7%, and 31.6% respectively. Annual mortality did not improve over the 7-year period. The postdischarge mortality of 8.5%/patient-year was 2.5-fold that of an age- and sex-matched general population, being 12.6-fold in the youngest quintile (<55 years) and 1.9-fold in the oldest quintile (≥85 years). Patients with known CVD at baseline had 2.2-fold greater all-cause mortality than those without CVD, and this effect, although at a lower level of risk, remained significant after multivariate analysis. Of the 332 deaths occurring postdischarge, 40% were attributed to cardiovascular causes.

Conclusions—In a contemporary adult population, PE is associated with a substantially increased long-term mortality, of which nearly half is cardiovascular. Our study highlights the urgent need to develop long-term surveillance strategies in this population. (Circ Cardiovasc Qual Outcomes. 2011;4:00-00.)

Key Words: pulmonary embolism ■ long-term ■ mortality ■ predictors ■ cardiovascular ■ heart disease ■ thrombosis

Venous thromboembolic disease is a worldwide problem, with acute pulmonary embolism (PE) its most severe manifestation.¹ The outcome of patients with acute PE is only partly (and to a small extent) determined by the size and extent of thrombus burden, and much more by the presence and extent of right ventricular dysfunction.² Symptomatic PE can cause death within 1 hour of onset in up to 10% of cases³; it is the third largest cause of cardiovascular death after coronary artery disease and stroke,⁴ occurring in up to 7% to 30% of all autopsy series.¹ Predictors of acute mortality following acute PE include: age >70 years, coexistent malignancy, heart failure, pulmonary disease, systemic hypotension, right ventricular dysfunction, and biomarkers such as cardiac troponins and B-type natriuretic peptide.⁵–⁸

In contrast to the abundant data regarding acute outcome, predictors of long-term mortality remain poorly defined because of the rarity of large cohort studies. The few studies extending beyond 6 months have indicated an increased 1-year mortality rate after PE, which may be as high as 25%.⁹⁻¹¹ Increased long-term risk of recurrent PE, cancer, and cardiovascular events have been reported in patients presenting with acute PE,¹²⁻¹⁴ However, almost all of these studies have excluded patients with baseline cardiovascular disease, or have not reported this and other baseline comorbidities, making risk stratification for long-term outcome in contemporary, more elderly populations difficult. The focus on short-term mortality in PE literature is reflected in current European² and American guidelines¹⁵ such that there are no...
recommendations regarding follow-up beyond 3 months for patients with acute PE.

The primary aim of our study was to investigate the long-term all-cause mortality posthospital admission for an acute PE and to identify its major clinical predictors. The secondary aim was to investigate cause specific mortality and its relationship to baseline comorbidities, including baseline cardiovascular disease.

WHAT IS KNOWN

- There is a substantial increased risk of death in-hospital after acute pulmonary embolism, and current international guidelines all focus on its acute management.
- In contrast, large long-term cohort studies of these patients are rare, and current guidelines fail to provide any guidance for the long-term care of these patients.

WHAT THE STUDY ADDS

- The current article presents long-term outcome results from the largest contemporary cohort of patients with confirmed pulmonary embolism.
- There is substantially increased long-term all-cause mortality in these patients, of which nearly half is attributable to cardiovascular causes. The current study highlights the urgent need to develop long-term surveillance strategies in this population.

Methods

Study Population

Consecutive patients admitted with a principle diagnosis of acute PE between January 2000 and December 2007 were identified retrospectively from a single tertiary institution (Concord Repatriation General Hospital, Sydney, Australia). The medical records of all identified patients were then reviewed for formal confirmation of diagnosis of acute PE. Confirmed PE was defined according to published guidelines,2 and required both documented clinical diagnosis and/or treatment of acute PE by the attending physician and an imaging study consistent with the diagnosis (intermediate-high probability nuclear pulmonary ventilation-perfusion scintigraphy or computed-tomography pulmonary angiogram showing thrombus within pulmonary arterial circulation). For those patients who presented on more than one occasion with acute PE during the study period (recurrent PE), only the initial presentation was included. Those patients who were not residents of the local state (New South Wales) during their PE presentation were excluded from the study to minimize incomplete tracking of long-term outcomes. The study was approved by the institutional Human Research Ethics Committee.

Data Sources

Details of the patients' admission history, including the type of imaging modality used to diagnose the PE (nuclear pulmonary ventilation-perfusion scintigraphy or computed-tomography pulmonary angiogram), whether deep vein thrombosis was documented, the admitting physician's specialty, length of admission, and inhospital outcomes were recorded. Important comorbidities during index PE admission, such as history of cardiovascular disease (including ischemic heart disease, prior coronary artery bypass surgery, heart failure, valvular heart disease, prosthetic heart valves, atrial fibrillation/flutter, peripheral vascular disease, stroke), cardiac risk factors (hypertension, hyperlipidemia, diabetes, current or ex-smoker), types of malignancy, pulmonary disease (asthma and/or emphysema), neurodegenerative disease (dementia and/or Parkinson’s disease), and chronic renal disease coded by diagnosis-related group based on the International Classification of Disease, Tenth Revision (ICD-10), were recorded for each patient. In addition, the overall comorbid status of each patient was assessed and given a Charlson Comorbidity Index score.16

Statistical Analysis

All continuous variables are expressed as mean (standard deviation), unless otherwise stated, and categorical data given in proportions and percentages. Comparison between groups used the unpaired t test for continuous variables and χ² tests or the Fisher exact test for dichotomous variables. Kaplan-Meier survival methods were used to compare unadjusted survival rates. Cox proportional hazards regression analysis was used to assess for univariate predictors of mortality, which included age, sex, recurrent PE, cardiovascular and noncardiovascular comorbidities, and cardiac risk factors. Only univariate variables with P<0.10 were included in the multivariate Cox proportional hazards regression analysis. Analysis was performed using SPSS version 13.0 (SPSS Inc., Chicago, Ill.). A 2-tailed probability value P<0.05 was considered statistically significant.

Results

Between 2000 and 2007, 1112 patients were admitted to our institution with a diagnosis of PE. Of these, 97 patients had 118 readmissions after their index PE presentation, and in these patients, only their index hospitalization was included. Of the 1112 patients, 89 were excluded from further analysis: 77 patients did not fulfill both clinical and imaging criteria for confirmed PE, and 12 were nonlocal state residents. None of the nonlocal state residents died during their hospital admission. The final study cohort of 1023 patients had a mean follow-up of 3.8 (2.6) years, or 3923 patient-years of follow-up. The mean number of patients presenting with confirmed PE was 128 (39) patients per year (range, 80 to 175 patients per year) during the 7-year study period.
Table 1 shows the baseline clinical characteristics of the study cohort. The mean age of the cohort was 68 (16) years with slightly more females than males (55% versus 45%, respectively). The majority of patients were non-Asian. More than a quarter of the patients (27%) were younger than 60 years (online-only Data Supplement Figure 1). When stratified into year of their PE presentation, the mean age of the cohort did not change significantly with each consecutive year of the study. Most patients were admitted under medical subspecialties, the most common being thoracic medicine (51%), followed by cardiology (21%), geriatric medicine (7%), and oncology (6%). Most cases of PE (84%) were identified on nuclear pulmonary ventilation-perfusion scintigraphy, with 88% showing a high-probability scan. In addition, 25% had their pulmonary embolus identified by computed tomography, whereas 10% of patients had both imaging studies performed during their admission. The mean length of admission was 8 (6) days, and this did not change significantly during the study period.

Prior history of cardiovascular disease was recorded in 44% of patients during their index admission, whereas 22% of patients admitted had underlying malignancy. Malignancies were most commonly hematologic (20%), gastrointestinal (15%), breast (15%), lung (13%), urinary tract (8%), and prostate (8%). More than half of the cohort (57%) had at least one recorded cardiac risk factor. The mean Charlson Comorbidity Index score for the cohort was 3.6 (3.2). There were 351 patients who had an index score of 0 at the time of their PE presentation, whereas nearly 60% of patients had a score ≥3, indicating a substantial burden of chronic disease.16

The overall all-cause mortality was 35.5% (363 patients). There were 31 in-hospital deaths. Of the 992 patients surviving to discharge, most (86%) were discharged home, 11% were transferred to other health facilities, and 332 died during follow-up. The 3-month, 6-month, 1-year, 3-year, and 5-year cumulative mortality rates were 8.3%, 11.1%, 16.3%, 26.7%, and 31.6%, respectively, with an overall mortality rate of 9.3% per patient-year. Figure 1 shows the Kaplan-Meier survival curve of the study cohort following discharge from hospital (excluded in-hospital death).

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cumulative mortality of 13.2%. Neither the in-hospital nor the 1-year mortality rates changed significantly during the study period (online-only Data Supplement Figure 2). There was, however, a significant trend toward fewer numbers of patients admitted with confirmed PE with each successive year of the period. Of the patients who survived to hospital discharge (n=992), 95% were discharged on warfarin and 5% on enoxaparin only. There were 27 (2.7%) patients who additionally received aspirin, and only 4 (0.4%) received additional clopidogrel. Only 1 (0.1%) patient received aspirin and clopidogrel in addition to warfarin. The mean international normalized ratio (INR) of the cohort at time of discharge was 2.3 (0.8). Only 70% of the patient population had a therapeutic INR (≥2.0) on discharge (83% had INR ≥1.5).

Table 2 shows the all-cause mortality of the study cohort stratified into age quintiles. For all age groups, more deaths occurred after discharge than during the index hospitalization. The postdischarge mortality rate of the study cohort (8.5% per patient-year) was 2.5-fold that of the general population, adjusted for age and sex (P<0.0001). The oldest quintile (≥83 years) had a mortality of 19.8% per patient-year compared with 1.89% per patient-year in the youngest quintile (<55 years). In comparison, the expected mortality rates for local state residents stratified into the same age quintiles as our study cohort and adjusted for sex were 10.6% in the oldest quintile and 0.15% in the youngest. This represents a relative increase in risk of death of 12.6-fold for our study cohort compared with the general population. For the oldest quintile, the relative risk increase was 1.9-fold.

We compared the characteristics of patients who died in-hospital and postdischarge (the nonsurvivors) to the survivors (online-only Data Supplement Table 1). No significant differences in baseline comorbidities were observed in those patients who died in-hospital following their acute PE admission compared with those who survived to discharge except for underlying malignancy, which was significantly more common in the former group. In comparison, patients who died after discharge were older, had longer admissions during their index acute PE presentation, and had more comorbidities, including history of cardiovascular disease, malignancy, chronic pulmonary disease, neurodegenerative disease, and chronic renal disease, than the survivors during long-term follow-up.

In total, 40% of deaths were attributed to cardiovascular causes, whereas malignancy (25%) and sepsis (20%) were the 2 most common noncardiovascular causes (Table 3). Among the 31 in-hospital deaths, 24 (77.4%) were due directly to the acute PE. Of the 332 deaths that occurred after discharge, 119 (35.8%) were due to a cardiovascular cause. These included 16 (4.8%) recurrent acute PE, 24 (7.2%) strokes (ischemic and hemorrhagic), and 79 (23.8%) cardiac deaths (myocardial infarction [n=31], heart failure [n=27], cardiac arrest [n=3], and cardiac-related cause of death [n=18]). Among the 213 noncardiovascular causes of death, 89 (26.8%) were due to malignancy, 71 (21.4%) were due to sepsis, 8 (2.4%) were undefined, and 45 (13.6%) deaths were due to other causes. There were five patients who had pulmonary hypertension recorded as a contributing comorbidity to their deaths postdischarge (1.5%, 5/332), which were all ascribed to noncardiovascular causes. During their index PE presentation, none of these patients had recorded pulmonary hypertension. One patient had documented systemic lupus erythematosus and another had associated heart failure with preserved systolic function on echocardiogram, both of which could independently contribute to the development of pulmonary hypertension.

Table 4 shows the univariate and multivariate predictors of all-cause mortality postdischarge. Patients with underlying cardiovascular disease at baseline had a 2.2-fold increased risk of death during long-term follow-up compared with those without baseline cardiovascular disease when presenting with...
an acute PE (Figure 2). Other significant univariate predictors of increased mortality included older age, underlying malignancy, pulmonary disease, neurodegenerative disease, and chronic renal disease. Race was not a predictor of long-term survival.

Older age and underlying comorbidities, including cardiovascular disease, malignancy, neurodegenerative disease, and chronic renal disease, were all independent predictors of postdischarge mortality.

We next investigated to what extent baseline comorbidities, particularly cardiovascular disease or malignancy, predicted cause-specific mortality postdischarge for acute PE (online-only Data Supplement Table 2). Of the total 119 cardiovascular deaths that occurred postdischarge, 90 occurred in patients with baseline cardiovascular disease (other than PE), and 29 occurred in patients with no known cardiovascular disease (7 from recurrent PE, 9 from myocardial infarction, 6 from stroke, 3 from heart failure, 3 from cardiac-related causes of death and 1 from cardiac arrest). A history of atrial arrhythmias (atrial fibrillation/flutter) without other known cardiovascular disease was a notable univariate predictor of adverse outcome (online-only Data Supplement Table 1). Of the 50 patients with only a history of atrial fibrillation/flutter as their underlying cardiovascular disease, 22 (44%) died during follow-up, and 12 of these deaths were cardiovascular (four deaths from myocardial infarction, four deaths from heart failure, two deaths from stroke and two from cardiac arrest).

Of a total of 89 deaths attributed to malignancy (online-only Data Supplement Table 2), 70 occurred in patients with documented known malignancy at the time of their index PE presentation (4/70 were due to a new malignancy, whereas 66/70 were due to the underlying malignancy), and 19 occurred in patients without baseline malignancy. Thus, 23 of 89 malignant deaths (26%) during follow-up were due to a new malignancy.

It is important to note that the increased mortality in this population could not be solely assigned to baseline comorbidity. In 351 patients with a Charlson Comorbidity Index score of 0 at baseline (ie, no comorbidities), there were 44 (13%) deaths postdischarge, of which 19 (43%) were cardiovascular (3 due to recurrent PE, 6 to myocardial infarction, 4 to heart failure, 2 to cardiac-related causes, and 4 to stroke) and 4 (9%) were due to malignancy.

**Discussion**

In this large contemporary adult population hospitalized with acute PE, we found substantially increased long-term mortality. Older age and underlying comorbidities, including cardiovascular disease, malignancy, neurodegenerative disease, and chronic renal disease, were all independent predictors of all-cause mortality during long-term follow-up. Approximately 36% of postdischarge mortality was attributed to cardiovascular causes, and only 5% of deaths were due to recurrent PE.

Acute PE is common and life-threatening, with 3- to 6-month mortality varying between 4% and 13% from registry data.6,19 We found a similar short-term mortality in our PE cohort validating the diagnostic entry criteria in our study. Our study also confirms previous findings that patients with PE have a guarded long-term prognosis, and baseline characteristics help predict postdischarge mortality.9,11 Miniati et al20 reported that in patients with PE, there was a progressive decline in survival during a median follow-up of 2.1 years through non-PE–related deaths. Klok et al21 recently reported a 30% all-cause mortality rate after PE after a median follow-up of 3.3 years. Our study supports and substantially

### Table 4. Predictors of All-Cause Mortality Postdischarge After Acute PE

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per 1 year</td>
<td>1.05 (1.04–1.06)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Male</td>
<td>1.13 (0.91–1.40)</td>
<td>0.29</td>
</tr>
<tr>
<td>Recurrent PE</td>
<td>0.72 (0.49–1.06)</td>
<td>0.09</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>2.18 (1.75–2.72)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.01 (0.80–1.28)</td>
<td>0.91</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>0.76 (0.54–1.05)</td>
<td>0.10</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.21 (0.91–1.61)</td>
<td>0.18</td>
</tr>
<tr>
<td>Current smoker</td>
<td>0.57 (0.35–0.91)</td>
<td>0.02</td>
</tr>
<tr>
<td>Malignancy</td>
<td>3.49 (2.79–4.37)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>1.30 (0.98–1.73)</td>
<td>0.07</td>
</tr>
<tr>
<td>Neurodegenerative disease</td>
<td>3.17 (2.31–4.35)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Chronic renal disease</td>
<td>2.19 (1.51–3.18)</td>
<td>&lt;.0001</td>
</tr>
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### Figure 2. Kaplan-Meier survival curve (unadjusted) of patients with versus those without baseline cardiovascular disease postdischarge following acute PE. The broken line represents the survival curve of patients without baseline cardiovascular disease (CVD), whereas the continuous line represents those with baseline CVD, during long-term follow-up. CVD includes history of ischemic heart disease, stroke, heart failure, peripheral vascular disease, valvular heart disease (with or without prosthetic valve), and/or atrial fibrillation/flutter.
extends previous literature in describing the long-term outcome of PE in relation to patient’s age, baseline comorbidities, and cause-specific mortality. We found that although most cardiovascular and malignant deaths occurred in patients with these diseases at baseline, a substantial number of deaths also occurred in those without these baseline comorbidities at the time of their index PE presentation. No difference was seen in long-term outcome between patients of different racial backgrounds, although only a minority of the cohort was of Asian descent. Compared with local age- and sex-matched population data, the greatest increase in the relative risk of death (12.6-fold) was in the youngest quintile (15 to 54 years). Even in patients with no known comorbidities (Charlson score 0), there was 13% mortality, and most of these postdischarge deaths were cardiovascular. Therefore, in those patients with baseline comorbidity, acute PE should serve as a “flag” to intensify the chronic management of these existing comorbidities, and to screen those without baseline cardiovascular disease for unrecognized cardiovascular disease and its risk factors.

The baseline comorbidities identified in our patients are consistent with what would be expected for a contemporary, older cohort with pulmonary embolism. Neurodegenerative diseases such as Parkinson disease and Alzheimer’s disease significantly impair mobility, and the prothrombotic effects of malignancy and renal disease are well known. Not previously reported is the significance of baseline cardiovascular disease, including atrial fibrillation/flutter (online-only Data Supplement Table 1) on long-term survival in patients with PE. Of 435 patients with baseline cardiovascular disease, 150 had a history of atrial fibrillation/flutter. That 22 of the 50 patients with atrial fibrillation/flutter and no other cardiovascular disease died during follow-up (12 deaths being cardiovascular) is of concern. Patients with acute PE and a history of atrial fibrillation/flutter may therefore warrant particularly careful screening for unrecognized structural heart disease following discharge.

Douketis et al22 examined the long-term risk of malignancy in a cohort of patients with a first episode of venous thromboembolism and found an annual risk of malignancy of 1.32 (95% confidence interval, 1.09 to 1.60) per 100 person-years. We found that in our population, 74% of malignant deaths were due to malignancy present at the time of acute PE, and 26% of malignant deaths during follow-up were due to a new malignancy. In our older population, cardiovascular death was at least as common as malignant death during long-term follow-up.

The long-term mortality of patients with PE compares unfavorably with other chronic cardiovascular diseases, most of which, unlike PE, have clear guidelines for long-term follow-up (online-only Data Supplement Table 3). In outpatients with stable coronary artery disease, Jabbour et al31 reported an annual mortality rate of 1.4%. In the Australian ACACIA registry, patients with ST-elevation myocardial infarction had a cumulative 1-year mortality rate of 8%/24 whereas in community-based chronic heart failure patients, Roger et al reported an annual mortality rate approaching 11%.25 By comparison, we found an annual mortality rate of 12.7% (cumulative 1-year mortality rate of 14.5%) in patients with PE who had underlying cardiovascular disease. Hence, the prognosis of patients with PE is clearly worse than many patients with stable or unstable coronary disease, and at best similar to those with stable chronic heart failure. Whereas there are well-developed guidelines for the long-term follow-up of patients with coronary disease and heart failure,26,27 current guidelines do not recommend the long-term follow-up of patients post-PE.3 The current study shows that this is unsupported for any age group, including those in the youngest quintile and those without baseline comorbidities.

Limitations
To the best of our knowledge, this patient group is the single largest contemporary cohort reported to date relating baseline cardiovascular disease to long-term outcome. However, our study does have limitations, including its single-center source of patients and its retrospective design. Because our outcome data were obtained from a statewide death registry, we cannot exclude the possibility that some of the survivors died in other states. However, based on known migration rates, the estimated noncaptured deaths during the study period is expected to be at most 0.6%.18 Moreover, including the patients who died out of state would only further emphasize the high long-term mortality rates in post-PE patients. We used a classification of death recommended by the World Health Organization that is based on death certificate.17 However, without formal autopsy, it is possible that some of the deaths may have been misclassified. Our overall autopsy rate was only 2.8% (10 of 363 deaths). This low rate is consistent with a known general trend toward fewer autopsies being performed in recent decades.28,29 We do not have accurate information on the duration of anticoagulation therapy in these patients. It is reasonable to expect that almost all of our patients would have received therapy according to national and international guidelines and received between 3 to 6 months of anticoagulation for a first (nonrecurrent) PE.30 Because >90% of deaths in our cohort were not attributable to PE recurrence, our overall conclusions regarding all-cause mortality and non-PE-related cause-specific mortality are unlikely to be influenced by the duration of anticoagulation therapy. This conclusion would be consistent with findings of Schulman et al,31 who found that the duration of anticoagulation did not impact long-term outcomes after venous thromboembolism. Other limitations include the lack of systematic venous ultrasonography, which explains the low number of patients with documented deep vein thrombosis and the relatively low use of echocardiography (37% of patients) that precludes assessment of the predictive value on long-term outcome of echocardiographic findings. By performing echocardiograms at baseline and 6 months post-PE, Kline et al32 reported that, although >90% of patients showed resolution of right ventricular dysfunction, one-half of patients had unchanged or increased right ventricular systolic pressure. The long-term consequences of these changes remain to be determined, but they do suggest that the incidence of milder or subclinical pulmonary hypertension in our population may be underestimated.

Conclusions
In summary, we have identified a very poor long-term outcome in a large adult population hospitalized with confirmed acute PE. There is an urgent need for further studies to
assess the feasibility of long-term surveillance for these patients and to develop management strategies, as some cardiovascular deaths may be preventable.

Acknowledgments
We thank Natasha Smith and Dr Chadi Ayoob for assistance with data collection and professor Jenny Peat for assistance with statistical analyses of the study.

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Disclosures
None.

References

Long-Term Cardiovascular and Noncardiovascular Mortality of 1023 Patients With Confirmed Acute Pulmonary Embolism
Austin Chin Chwan Ng, Tommy Chung, Andy Sze Chiang Yong, Helen Siu Ping Wong, Vincent Chow, David Stephen Celermajer and Leonard Kritharides

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SUPPLEMENTAL MATERIAL
## Supplementary Table 1. Comparison between Survivors and Non-survivors Post Acute PE.

<table>
<thead>
<tr>
<th>Variables</th>
<th>In-hospital survival</th>
<th>Post-discharge survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Survivors (N = 992)</td>
<td>Non-survivors (N = 31)</td>
</tr>
<tr>
<td>Mean age (SD), years</td>
<td>68 (16)</td>
<td>74 (11)</td>
</tr>
<tr>
<td>Male, no.(%)</td>
<td>442 (45)</td>
<td>15 (48)</td>
</tr>
<tr>
<td>Asians, no.(%)</td>
<td>50 (5)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Mean length of stay (SD), days</td>
<td>8 (6)</td>
<td>10 (7)</td>
</tr>
<tr>
<td>Cardiovascular disease, no.(%)</td>
<td>435 (44)</td>
<td>46 (52)</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>204 (21)</td>
<td>6 (19)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>126 (13)</td>
<td>7 (23)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>118 (12)</td>
<td>5 (16)</td>
</tr>
<tr>
<td>Stroke</td>
<td>30 (3)</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Atrial fibrillation/flutter</td>
<td>150 (15)</td>
<td>7 (23)</td>
</tr>
<tr>
<td>Cardiac risk factors, no.(%)</td>
<td>566 (57)</td>
<td>15 (48)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>307 (31)</td>
<td>9 (29)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>139 (14)</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>155 (16)</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>173 (17)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>85 (9)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Malignancy, no.(%)</td>
<td>213 (21)</td>
<td>16 (52)</td>
</tr>
<tr>
<td>Chronic pulmonary disease, no.(%)</td>
<td>136 (14)</td>
<td>8 (26)</td>
</tr>
<tr>
<td>Neurodegenerative disease, no.(%)</td>
<td>65 (7)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Chronic renal disease, no.(%)</td>
<td>57 (6)</td>
<td>2 (6)</td>
</tr>
</tbody>
</table>
Online Data Supplementary

**Supplementary Table 2.** Baseline Cardiovascular Disease and Malignancy and Cause of Death Post-discharge for Acute PE.

<table>
<thead>
<tr>
<th>Baseline comorbidities</th>
<th>Cohort</th>
<th>All-cause death</th>
<th>Cardiovascular death</th>
<th>Malignant death</th>
<th>Others (Proportion of death - %)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total no.</td>
<td>Total no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>435</td>
<td>200 (46%)</td>
<td>90/200 (45%)</td>
<td>35/200 (18%)</td>
<td>75/200 (37%)</td>
</tr>
<tr>
<td>No</td>
<td>557</td>
<td>132 (24%)</td>
<td>29/132 (22%)</td>
<td>54/132 (41%)</td>
<td>49/132 (37%)</td>
</tr>
<tr>
<td>Malignancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>213</td>
<td>123 (58%)</td>
<td>22/123 (18%)</td>
<td>70/123 (57%)</td>
<td>31/123 (25%)</td>
</tr>
<tr>
<td>No</td>
<td>779</td>
<td>209 (27%)</td>
<td>97/209 (46%)</td>
<td>19/209 (9%)</td>
<td>93/209 (44%)</td>
</tr>
<tr>
<td>Both cardiovascular and malignancy</td>
<td>86</td>
<td>51 (59%)</td>
<td>15/51 (29%)</td>
<td>21/51 (41%)</td>
<td>15/51 (29%)</td>
</tr>
<tr>
<td>No comorbidities (CCI* score of 0)</td>
<td>351</td>
<td>44 (13%)</td>
<td>19/44 (43%)</td>
<td>4/44 (9%)</td>
<td>21/44 (48%)</td>
</tr>
</tbody>
</table>

* CCI indicates Charlson Comorbidity Index

**References**

Online Data Supplementary

**Supplementary Table 3.** Mortality Outcome between Different Chronic Cardiovascular Diseases

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Mortality Outcome</th>
<th>Recommended Long-term Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatients with stable coronary artery disease(^1)</td>
<td>Annual rate 1.4%</td>
<td>4 – 12 monthly review(^3)</td>
</tr>
<tr>
<td>Patients with ST-elevation myocardial infarction(^3)</td>
<td>1-yr cumulative rate 8.0%</td>
<td></td>
</tr>
<tr>
<td>Chronic heart failure(^4)</td>
<td>Annual rate 10.9%</td>
<td>3 – 6 monthly review(^5)</td>
</tr>
<tr>
<td>Current PE cohort</td>
<td>Annual rate 12.7%</td>
<td>1-yr cumulative rate 14.5%</td>
</tr>
<tr>
<td>Total cohort *</td>
<td>8.5%</td>
<td>13.2%</td>
</tr>
<tr>
<td>With cardiovascular disease</td>
<td></td>
<td>No recommendation(^6)</td>
</tr>
</tbody>
</table>

* All-cause mortality rate (excluded in-hospital deaths).

References

Online Data Supplementary

Supplementary Figure 1. Age Distribution of Cohort Stratified by Sex.

The graph shows the age distribution of the cohort in decades, stratified into males (dark columns) and females (light columns). The numbers above each column indicate the total number of patients in the age group.
Online Data Supplementary

Supplementary Figure 2. Trend of One-year Mortality Rate during the Study Period.

The dark-coloured columns show the 1-year mortality rates of the cohort (excluding in-hospital death) based on year of PE presentation. The light-coloured columns represent the in-hospital mortality rates during the study period. There was no significant difference in the 1-year mortality over the 7-year study period \((P=0.44 \text{ chi-square test; } P=0.10 \text{ for trend})\). The table below the graph shows the total number of patients admitted during each year of the study. In the year 2007, there were 82 patients admitted with confirmed PE. There was a significant trend towards lesser number of patients admitted with confirmed PE with each successive year during the study \((P=0.004 \text{ for linear trend})\).