Right Ventricular Enlargement on Chest Computed Tomography
A Predictor of Early Death in Acute Pulmonary Embolism

U. Joseph Schoepf, MD*; Nils Kucher, MD*; Florian Kipfmueller, BS; Rene Quiroz, MD, MPH; Philip Costello, MD; Samuel Z. Goldhaber, MD

Background—In patients with acute pulmonary embolism (PE), rapid and accurate risk assessment is paramount in selecting the appropriate treatment strategy. Right ventricular (RV) enlargement on chest CT has previously been shown to correlate with an unstable hospital course, but its role as a predictor of death is unknown.

Methods and Results—We evaluated 431 consecutive patients (mean age, 59±16 years; 55% women) with acute PE confirmed by multidetector-row chest CT. With the use of multiplanar reformats of axial CT data, CT 4-chamber (4-CH) views were reconstructed and right and left ventricular dimensions (RVD, LVD) were measured. RV enlargement, defined as RVD/LVD >0.9, was present in 276 (64.0%; 95% CI, 59.5% to 68.6%) patients. Thirty-day mortality rate was 15.6% (95% CI, 11.3% to 19.9%) in patients with and 7.7% (95% CI, 3.5% to 12.0%) without RV enlargement (log rank, P=0.018). The hazard ratio of RVD/LVD >0.9 for predicting 30-day death was 3.36 (95% CI, 1.13 to 9.97; P=0.029). On multivariable analysis, RV enlargement predicted 30-day death (hazard ratio, 5.17; 95% CI, 1.63 to 16.35; P=0.005) after adjusting for pneumonia (hazard ratio, 2.95; 95% CI, 1.19 to 3.83; P=0.002), cancer (hazard ratio, 2.13; 95% CI, 1.19 to 3.83; P=0.011), chronic lung disease (hazard ratio, 2.00; 95% CI, 1.04 to 3.86; P=0.039), and age (hazard ratio, 1.03; 95% CI, 1.01 to 1.05; P=0.005).

Conclusions—In patients with acute PE, RV enlargement on reconstructed CT 4-CH view helps predict early death. (Circulation. 2004;110:3276-3280.)

Key Words: tomography • prognosis • mortality • embolism

A cute pulmonary embolism (PE) spans a wide spectrum of prognoses, with an overall 30-day mortality rate that exceeds 10%.

Although most late deaths are due to underlying disease, such as cancer, chronic lung disease, or congestive heart failure, the main cause of death within 30 days is right ventricular (RV) failure. Rapid risk stratification is paramount for identifying high-risk patients and helps select the appropriate treatment strategy. Thrombolysis, catheter intervention, or surgical embolectomy as adjuncts to anticoagulation may rapidly reverse RV failure and reduce the risk of recurrence and death. According to the European Task Force Guidelines on PE, reperfusion therapy is indicated in patients with cardiogenic shock and may be considered in selected patients with preserved systemic pressure and RV dysfunction.

Echocardiography has emerged as an important risk stratification tool because RV dysfunction is a powerful and independent predictor of death. However, echocardiography has limited availability at many institutions, and occasionally, the RV may be difficult to image with the transthoracic approach.

Contrast-enhanced chest CT is increasingly used as the first-line PE imaging test and is available 24 hours daily at most institutions. With newer-generation scanners, standardized cardiac views are easily obtained in almost all patients who undergo contrast-enhanced chest CT. In acute PE, RV enlargement on the reconstructed CT 4-chamber (4-CH) view correlates with RV dysfunction on the echocardiogram, but its role as a predictor of death is unknown. We investigated the prognostic role of RV enlargement on the 2-dimensional reconstructed CT 4-CH view for predicting early death in a large consecutive cohort of patients with acute PE.

Methods

Study Sample
We retrospectively identified 454 consecutive patients hospitalized at Brigham and Women’s Hospital from May 2001 through July
2003 with acute PE confirmed by multidetector-row chest CT. After excluding 23 (5.1%) patients, 431 (94.9%) were eligible for the present study. Twelve patients were excluded because of incomplete imaging of the heart, 9 because of insufficient contrast enhancement of ventricular chambers for reliably delineating the endocardial borders, and 2 had a univentricular heart. The Human Research Committee at Brigham and Women’s Hospital approved the study.

Clinical End Points
Thirty-day death was defined as the primary end point. We also used the composite end point of 30-day death and in-hospital complications, including cardiopulmonary resuscitation, mechanical ventilation, vasopressors for systemic arterial hypotension, thrombolysis, catheter intervention, or surgical embolectomy.

Multidetector-Row Chest CT
Diagnosis
Standard contrast-enhanced PE protocols16 were performed using 4-slice (SOMATOM VolumeZoom, Siemens Medical Solutions) or 16-slice (SOMATOM Sensation16) multidetector-row CT scanners with acquisition of 1.25-mm or 1-mm sections of the entire chest, respectively. The diagnosis of PE was confirmed in the presence of at least one filling defect in the pulmonary artery tree, including the subsegmental level.20 All CT studies were available in standard Digital Imaging and Communications in Medicine (DICOM) format and were analyzed off-line with the use of a stand-alone image processing workstation (Leonardo, Siemens).

Cardiac Measurements
The Leonardo workstation allows 2-D reconstruction of standardized cardiac views, with direct measurement of ventricular dimensions. We developed and validated the methodology of obtaining ventricular measurements from reconstructed 4-CH views by using 2-D multiplanar reformats of the original axial CT data.19 The 4-CH view was obtained by (1) cranio-caudal rotation of the viewport in the coronal CT view and (2) tilting the viewport in the axial CT view until both ventricles were fully depicted. In the reconstructed 4-CH view, RV<sub>0</sub> and LV<sub>0</sub> were then measured by identifying the maximal distance between the ventricular endocardium and the interventricular septum, perpendicular to the long axis of the heart (Figure 1). Measurements were performed by two observers who were blinded to clinical characteristics and outcome data. RV enlargement was defined as RV<sub>0</sub>/LV<sub>0</sub> >0.9 because this cutoff was found most useful for identifying patients at risk for in-hospital complications.19

Statistical Analysis
Before outcome data and CT measurements were obtained, we calculated a power of 81.3% (2-sided type 1 error, 5%) to reject the null hypothesis that the presence of RV enlargement on chest CT will not predict the primary end point in the available sample of 431 patients, using the following assumptions: presence of RV enlargement on chest CT in 70% of the sample, based on the proportion of patients with RV enlargement in our validation study,19 and a 30-day mortality rate of 11% in patients with and 5% without RV enlargement, based on observed mortality rates in patients with and without RV dysfunction from the International Cooperative Pulmonary Embolism Registry.1

We used Wilcoxon rank sum tests for comparisons in the distributions of continuous variables between patients who died or survived within 30 days after PE diagnosis and chi<sup>2</sup> tests or Fisher’s exact test for comparisons of categorical variables. We used receiver operating characteristic analyses to determine the high-sensitivity RV<sub>0</sub>/LV<sub>0</sub> cutoff value for predicting the primary and composite end points. The Kaplan-Meier estimator and log-rank test were used to estimate the cumulative probability of the primary and composite end points in patients with and without RV enlargement. The Cox proportional hazard model was used to calculate the hazard ratio of clinical variables and CT measurements for predicting the primary and composite end points. Multivariable analysis was then performed to identify predictors of 30-day death, using the proportional hazards model with calculation of 95% confidence intervals. We included the following individually significant (<i>P</i> < 0.05) predictors of 30-day death in the multivariable analysis: pneumonia, cancer, chronic lung disease, and age. Because 30-day end point data were complete in the study patients, none of the patients were censored.

Results
Mean age was 59±16 years, and there were 239 (55.4%) women. Overall, 55 (13%) patients died within 30 days,
Cancer was present in 53.8%, coronary artery disease in 12.8%, chronic lung disease in 11.1%, and pneumonia in 9.0%. Compared with surviving patients, those who died within 30 days were older and more often had cancer, pneumonia, or chronic lung disease (Table 1).

Among the 55 patients who died within 30 days, 20% were treated with vasopressors for systemic arterial hypotension, 18% required mechanical ventilation, and 5.5% received thrombolysis. Of 376 surviving patients, 6.6% received thrombolysis, 4.3% vasopressors for systemic arterial hypotension, 3.7% required mechanical ventilation, 2.1% underwent surgical embolectomy, 0.8% catheter interventions, and 0.5% cardiopulmonary resuscitation. Compared with surviving patients, vasopressors (P = 0.001) and mechanical ventilation (P = 0.001) were used more often in patients who died within 30 days. There was no difference in the need for cardiopulmonary resuscitation (P = 1.0), thrombolysis (P = 1.0), catheter intervention (P = 1.0), or surgical embolectomy (P = 0.61) between patients who survived and patients who died, respectively.

The RV/LVp value of 0.9 for RV enlargement was identified as the high-sensitivity cutoff for predicting both the primary and composite end points.

RV enlargement was present in 276 (64.0%; 95% CI, 59.5% to 68.6%) patients. Thirty-day mortality rate was 15.6% (95% CI, 11.3% to 19.9%) in patients with and 7.7% (95% CI, 3.5% to 12.0%) without RV enlargement. The cumulative mortality rate through day 30 was higher in patients with than without RV enlargement (log rank, P = 0.018) (Figure 2A). Median RV/LVp was 1.01 (range, 0.69 to 2.55) in patients who died and 0.95 (range, 0.62 to 1.97) in patients who survived 30 days (P = 0.03). Among patients who died, 43 (78.2%) had RV enlargement. Among the surviving patients, 233 (62.0%) had RV enlargement. The hazard ratio of RV/LVp > 0.9 for predicting 30-day death was 3.36 (95% CI, 1.13 to 9.97; P = 0.029). The prognostic information of RV/LVp > 0.9 on reconstructed CT 4-CH view for identifying patients at risk of death within 30 days (adjusted hazard ratio, 5.17; 95% CI, 1.63 to 16.35; P = 0.005) persisted after adjusting for pneumonia, cancer, chronic lung disease, and age (Table 2).

Overall, 106 (24.6%; 95% CI, 20.5% to 28.7%) patients had the composite end point. Peripheral artery disease (5.7% versus 1.5%; P = 0.03), pneumonia (15.1% versus 7.1%; P = 0.02), and chronic lung disease (17.9% versus 8.9%; P = 0.02) were more common in patients with than in patients without the composite end point, respectively. The composite end point occurred in 30.1% (95% CI, 24.6% to 35.5%) of patients with and 14.8% (95% CI, 9.2% to 20.5%) of patients without RV enlargement. The cumulative probability of the composite end point was higher in patients with than in

### Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Dead at 30 d (n=55)</th>
<th>Alive at 30 d (n=376)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean±SD</td>
<td>65±13</td>
<td>58±16</td>
<td>0.002</td>
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<tr>
<td>Men</td>
<td>27 (49.1)</td>
<td>165 (43.9)</td>
<td>0.47</td>
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<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Cancer</td>
<td>39 (70.9)</td>
<td>193 (51.3)</td>
<td>0.009</td>
</tr>
<tr>
<td>Hypertension</td>
<td>22 (40.0)</td>
<td>120 (31.9)</td>
<td>0.28</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>6 (10.9)</td>
<td>49 (13.0)</td>
<td>0.83</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>8 (14.6)</td>
<td>41 (10.9)</td>
<td>0.49</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>12 (21.8)</td>
<td>36 (9.6)</td>
<td>0.011</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>4 (7.3)</td>
<td>21 (5.6)</td>
<td>0.54</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>3 (5.5)</td>
<td>8 (2.1)</td>
<td>0.15</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>2 (3.6)</td>
<td>14 (3.7)</td>
<td>1.0</td>
</tr>
<tr>
<td>Dialysis</td>
<td>1 (1.8)</td>
<td>5 (1.3)</td>
<td>0.56</td>
</tr>
</tbody>
</table>

Within 30 d before PE diagnosis

<table>
<thead>
<tr>
<th>Event</th>
<th>Dead (n=3)</th>
<th>Alive (n=17)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major surgery</td>
<td>10 (18.2)</td>
<td>111 (29.5)</td>
<td>0.11</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>11 (20.0)</td>
<td>28 (7.5)</td>
<td>0.009</td>
</tr>
<tr>
<td>Sepsis</td>
<td>4 (7.3)</td>
<td>18 (4.8)</td>
<td>0.51</td>
</tr>
<tr>
<td>Trauma</td>
<td>2 (3.6)</td>
<td>17 (4.5)</td>
<td>1.0</td>
</tr>
<tr>
<td>Stroke/transient ischemic attack</td>
<td>3 (5.5)</td>
<td>9 (2.4)</td>
<td>0.19</td>
</tr>
<tr>
<td>Major hemorrhage</td>
<td>5 (9.1)</td>
<td>9 (2.4)</td>
<td>0.013</td>
</tr>
<tr>
<td>ST-elevation myocardial infarction</td>
<td>0 (0.0)</td>
<td>3 (0.8)</td>
<td>1.0</td>
</tr>
<tr>
<td>Non-ST-elevation myocardial infarction</td>
<td>0 (0.0)</td>
<td>3 (0.8)</td>
<td>1.0</td>
</tr>
<tr>
<td>Multisystem organ failure</td>
<td>1 (1.8)</td>
<td>0 (0.0)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Data are given as numbers with proportions in parentheses.
TABLE 2. Multivariable Analysis for Predicting 30-Day Death

<table>
<thead>
<tr>
<th>n*</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV/LV_D &gt;0.9</td>
<td>43</td>
<td>5.17</td>
<td>1.63–16.35</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>11</td>
<td>2.95</td>
<td>1.19–3.83</td>
</tr>
<tr>
<td>Cancer</td>
<td>39</td>
<td>2.13</td>
<td>1.19–3.83</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>12</td>
<td>2.00</td>
<td>1.04–3.86</td>
</tr>
<tr>
<td>Age, y</td>
<td>100</td>
<td>1.03</td>
<td>1.01–1.05</td>
</tr>
</tbody>
</table>

*No. of deaths at 30 days. Overall, 55 patients died during 30 days.

patients without RV enlargement (log rank, P<0.001) (Figure 2B). Median RV/LV_D was 1.02 (range, 0.68 to 2.55) in patients with and 0.94 (range, 0.62 to 1.97) in patients without the composite end point (P<0.001). Among patients with the composite end point, 83 (78.3%) had RV enlargement. Among the patients without the composite end point, 193 (59.4%) had RV enlargement. The hazard ratio of RV/LV_D >0.9 for predicting the composite end point was 2.20 (95% CI, 1.39 to 3.50; P=0.001). The prognostic information of RV/LV_D >0.9 on reconstructed CT 4-CH view for identifying patients at risk of having the composite end point (adjusted hazard ratio, 2.38; 95% CI, 1.49 to 3.79; P<0.001) persisted after adjusting for peripheral artery disease, pneumonia, and chronic lung disease (Table 3).

Sensitivity and specificity (95% CI) of RV enlargement on chest CT for predicting death within 30 days were 78.2% (65.6% to 87.0%) and 38.0% (33.3% to 43.0%), respectively. Negative and positive predictive values of RV enlargement on chest CT for death within 30 days were 92.3% (87.0% to 95.5%) and 15.6% (11.8% to 20.3%), respectively.

Discussion

We found that the presence of RV enlargement on the initial chest CT scan helps predict 30-day death. In our cohort, among those with RV enlargement on the CT 4-CH view, 1 of 4 had major complications within 30 days, and the risk of death within 30 days increased approximately 5-fold. Conversely, in the absence of RV enlargement on CT 4-CH view, most patients (92.3%) survived. RV/LV_D >0.9 also identified patients at risk for the composite end point of death and in-hospital complications, including cardiopulmonary resuscitation, mechanical ventilation, vasopressors, thrombolysis, catheter intervention, and surgical embolectomy. Thirty-day mortality in the present study (12.8%) was similar to the mortality rate observed in the International Cooperative Pulmonary Embolism Registry, suggesting that our single-institution study sample was typical. In our study and in the largest randomized, controlled thrombolysis trial of 256 PE patients, the proportion of patients who had in-hospital complications or escalation of therapy was also similar (24.6% versus 18.4%, respectively).

Reconstructed 4-CH views from routine chest CT provide a static image, obtained without ECG gating. Although endocardial borders are easily identified on reconstructed CT 4-CH view, both overestimation and underestimation of the CT-derived RV/LV_D ratio may occur. Nevertheless, in our previous feasibility study, RV enlargement on CT correlated with RV dysfunction on the echocardiogram, with greater accuracy of measurements from reconstructed 4-CH than from axial views. End-diastolic ventricular dimensions may be obtained if ECG gating is used for chest CT acquisition; however, because of an increase in radiation exposure, use of this technology is not recommended for routine chest CT PE protocols.

In conclusion, RV enlargement on chest CT predicts early death in patients with acute PE. Reconstruction of 4-CH views is performed easily with basic software tools that are available on most contemporary CT scanner platforms. Evaluation of RV enlargement on reconstructed 4-CH views in patients with a positive CT PE protocol is a promising risk stratification tool. The indication for reperfusion therapy in patients with acute PE should not be based on cardiac CT measurements alone, because the positive predictive value of these measurements for early death was relatively low. Prospective PE management studies are needed to investigate whether cardiac measurements on reconstructed CT 4-CH views should guide treatment decisions in combination with other risk assessment tools, such as echocardiography or cardiac biomarkers.

References


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