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CT Signs of Right Ventricular Dysfunction

Prognostic Role in Acute Pulmonary Embolism

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OBJECTIVES The purpose of this study was to compare the prognostic role of various computed tomography (CT) signs of right ventricular (RV) dysfunction, including 3-dimensional ventricular volume measurements, to predict adverse outcomes in patients with acute pulmonary embolism (PE).

BACKGROUND Three-dimensional ventricular volume measurements based on chest CT have become feasible for routine clinical application; however, their prognostic role in patients with acute PE has not been assessed.

METHODS We evaluated 260 patients with acute PE for the following CT signs of RV dysfunction obtained on routine chest CT: abnormal position of the interventricular septum, inferior vena cava contrast reflux, right ventricle diameter (RVD) to left ventricle diameter (LVD) ratio on axial sections and 4-chamber (4-CH) views, and 3-dimensional right ventricle volume (RVV) to left ventricle volume (LVV) ratio. Comorbidities and fatal and nonfatal adverse outcomes according to the MAPPET-3 (Management Strategies and Prognosis in Pulmonary Embolism Trial-3) criteria within 30 days were recorded.

RESULTS Fifty-seven patients (21.9%) had adverse outcomes, including 20 patients (7.7%) who died within 30 days. An RVD_{axial}/LVD_{axial} ratio >1.0 was not predictive for adverse outcomes. On multivariate analysis (adjusting for comorbidities), abnormal position of the interventricular septum (hazard ratio [HR]: 2.07; $p = 0.007$), inferior vena cava contrast reflux (HR: 2.57; $p = 0.001$), $RVD_{4\text{-CH}}/LVD_{4\text{-CH}}$ ratio >1.0 (HR: 2.51; $p = 0.009$), and RVV/LVV ratio >1.2 (HR: 4.04; $p < 0.001$) were predictive of adverse outcomes, whereas $RVD_{4\text{-CH}}/LVD_{4\text{-CH}}$ ratio >1.0 (HR: 3.68; $p = 0.039$) and RVV/LVV ratio >1.2 (HR: 6.49; $p = 0.005$) were predictive of 30-day death.

CONCLUSIONS Three-dimensional ventricular volume measurement on chest CT is a predictor of early death in patients with acute PE, independent of clinical risk factors and comorbidities. Abnormal position of the interventricular septum, inferior vena cava contrast reflux, and $RVD_{4\text{-CH}}/LVD_{4\text{-CH}}$ ratio are predictive of adverse outcomes, whereas RVD_{axial}/LVD_{axial} ratio >1.0 is not. (J Am Coll Cardiol Img 2011;4:841–9) © 2011 by the American College of Cardiology Foundation

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Right ventricular (RV) failure is the most common cause of early death among patients with acute pulmonary embolism (PE) (1–5). While bedside echocardiography remains the first-line test for diagnosing RV dysfunction (3,5–7), chest computed tomography (CT) has become the preferred imaging modality for PE diagnosis in stable patients, because it is accurate and available 24 h daily at most institutions (8,9). Several studies have evaluated chest CT signs for determining the severity of RV dysfunction and for predicting patient outcome (10–31), including flattening or displacement of the interventricular septum toward the left ventricle, reflux of contrast material into the inferior vena cava (IVC), and measurements of RV diameter (RVD) divided by left ventricular diameters (LVD) on transverse chest CT sections or reconstructed 4-chamber (4-CH) views.

ABBREVIATIONS AND ACRONYMS

AUC = area under the curve

CI = confidence interval

CT = computed tomography

ECG = electrocardiogram

4-CH = four-chamber

IVC = inferior vena cava

LV = left ventricle

LVD = left ventricular diameter

LVV = left ventricular volume

PE = pulmonary embolism

RV = right ventricle

RVD = right ventricular diameter

RVV = right ventricular volume

However, because the ventricles have a complex 3-dimensional (3D) shape, 3D assessment of right ventricular volume (RVV) and left ventricular volume (LVV) may be more useful as a surrogate marker for RV dysfunction in patients with acute PE. Image post-processing methods enabling 3D volumetry of the ventricles have recently become available. A previous study (15) demonstrated that ventricular volume measurements at electrocardiogram (ECG)-gated chest CT were more sensitive for identifying patients with possible RV dysfunction than diameter measurements on non–ECG-gated chest CT. However, routine ECG-gating of chest CT studies for diagnosing PE is not currently recommended because of the additional radiation exposure involved with ECG-gated techniques (8,9) and because of the only limited incremental diagnostic improvement over routine non–ECG-gated chest CT (23).

Accordingly, the purpose of this current investigation was to compare, in patients with acute PE, the prognostic value for adverse outcomes and 30-day mortality of 3D volumetric ventricular analysis based on routine, non–ECG-gated chest CT with all other described chest CT signs of RV dysfunction.

METHODS

Patient population. From April 2007 through August 2009 we performed 1,606 contrast-enhanced chest CT studies for suspected PE, and 302 of these studies were interpreted as positive for new onset, acute PE. Of these, a total of 260 patients were included in the present analysis after 36 patients were excluded because of incomplete follow-up during the study period. Six patients were excluded because of insufficient contrast enhancement of the ventricular chambers for reliable delineation of the endocardial borders.

In all, 173 patients (66.5%) were inpatients already hospitalized at the time of acute PE diagnosis. Primary reasons for hospitalization and complications other than acute PE during the hospital stay included major surgery in 93 patients, trauma in 32, pneumonia in 29, stroke in 14, sepsis in 11, major hemorrhage in 9, myocardial infarction in 2, and multisystem organ failure in 1 patient.

For indicating imaging work-up of suspected PE, our institution generally follows the recommendations as outlined by the Christopher Study Investigators (32) and by Piazza et al. (33). All patients included in this study were hemodynamically stable and had undergone a clinical assessment of the probability of PE, using the original Wells scoring system (34). Our study population included 172 patients (66.2%) with a Wells score >4 and 88 patients (33.8%) with abnormal D-dimer test.

Adverse clinical outcomes. Adverse clinical outcomes were defined as death within 30 days or escalation of therapy, according to the MAPPET-3 (Management Strategies and Prognosis in Pulmonary Embolism Trial-3) study criteria (4), including cardiopulmonary resuscitation, endotracheal intubation, vasopressors for systemic hypotension, thrombolysis, or surgical embolectomy. Demographic information (age and sex) and medical history (history of cancer, coronary artery disease, congestive heart failure, diabetes mellitus, chronic lung disease, and renal insufficiency) were recorded on the basis of patients' medical records.

Chest CT procedures. All patients had undergone non–ECG-gated chest CT on a 64-slice multidetector-row CT system (Somatom Sensation 64, Siemens, Forchheim, Germany). Image acquisition parameters consisted of 0.6 mm collimation, 120 kV, 160 mAseff, pitch of 1.2, and a reconstructed section thickness of 1 mm. Contrast medium enhancement was achieved with 100 ml of a nonionic iodinated contrast medium (Ultravist 370, Bayer-Schering, Wayne, New Jersey) injected at 4 ml/s using a power injector (Stellant D, Medrad, Indianola, Pennsylvania). Automated bolus triggering was used with a region of interest in the main pulmonary artery and a threshold of 100 Hounsfield units for initiating data acquisition.

Chest CT interpretation. In case of multiple CT examinations for serial follow-up, we included only the first CT study performed at the time of the initial presentation. In a pilot investigation (21), chest CT studies of 50 consecutive patients had been independently reviewed by 2 experienced observers (D.K.K., C.T.) for analysis of interobserver variability. The remaining 210 patients were evaluated by 1 of the observers (D.K.K.). Observers were blinded to the patients' clinical characteristics. All CT studies were reviewed and analyzed on a clinical workstation (MultiModality Workplace, Siemens).

SEPTAL BOWING. Deviation of the interventricular septum was evaluated as follows: normal (convex toward the RV), flattened, and septal bowing (convex toward the left ventricle) (25). Flattened septum (Fig. 1A) and septal bowing (Fig. 2A) were considered abnormal positions of the septum indicating RV strain.

IVC REFLUX. The severity of reflux of contrast medium into the IVC or hepatic veins was graded according to a previously published scale (12): 1 = no reflux; 2 = trace of reflux into IVC only; 3 = reflux into IVC but not hepatic veins; 4 = reflux into IVC and proximal hepatic veins; 5 = reflux into IVC and hepatic veins down to the mid-portion of the liver; 6 = reflux into IVC with opacification of distal hepatic veins (Fig. 1B). The degree of reflux was grouped into nonsubstantial (grades 1 to 3) and substantial (grades 4 to 6).

RVD/LVD RATIO. The 2 axial sections that showed the maximal distance between the ventricular endocardium and the interventricular septum, perpendicular to the long axis of the heart, for the RV and LV, respectively, were identified. RVD_{axial} and LVD_{axial} were subsequently measured, and the RVD_{axial}/LVD_{axial} ratio was calculated (Figs. 1 and 2). Next, 4-CH views were reconstructed on the workstation using our previously described approach (21,26), and $RVD_{4\text{-}CH}/LVD_{4\text{-}CH}$ ratios were calculated.

RVV/LVV RATIO. The 3D volumetric analysis of both ventricles was performed by using the volume analysis application of the workstation (Volume Analysis, Siemens). The endocardial contours were semiautomatically segmented from the valvular

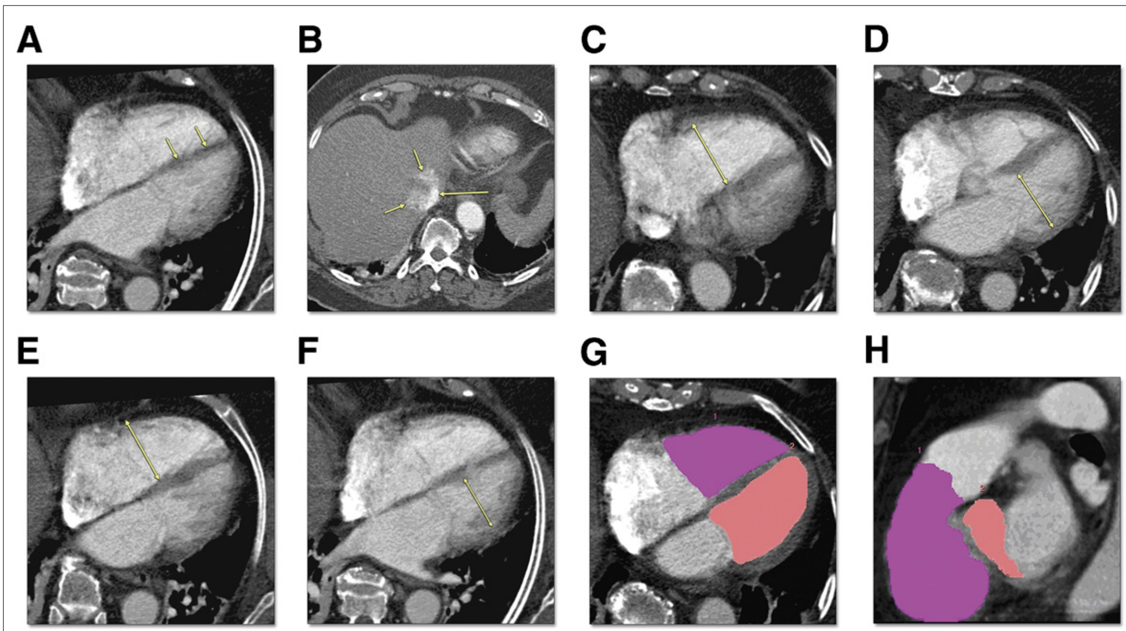

Figure 1. Computed Tomography Signs of RV Dysfunction in a 77-Year-Old Woman

(A) In a 77-year-old woman with acute pulmonary embolism, a 4-chamber (4-CH) view reconstruction of a chest computed tomography scan shows septal flattening **(arrows)**. **(B)** There is also grade 4 reflux of contrast medium into the inferior vena cava **(long arrow)** and proximal hepatic veins **(short arrows)**. Measurements of **(C)** maximal right ventricular diameter (RVD) and **(D)** left ventricular diameter (LVD) on axial sections show RVD axial/LVD axial ratio of 0.98. Measurements of **(E)** maximal RVD and **(F)** LVD on 4-CH views show $RVD_{4\text{-}CH}/LVD_{4\text{-}CH}$ ratio of 1.12. Semiautomated right ventricle volumetry (RVV) **(purple)** and left ventricle volumetry (LVV) **(orange)** displayed **(G)** on axial section and **(H)** on sagittal reformation shows RVV/LVV ratio of 1.62. The patient required mechanical ventilation on the first day of her hospital stay and died on day 28.

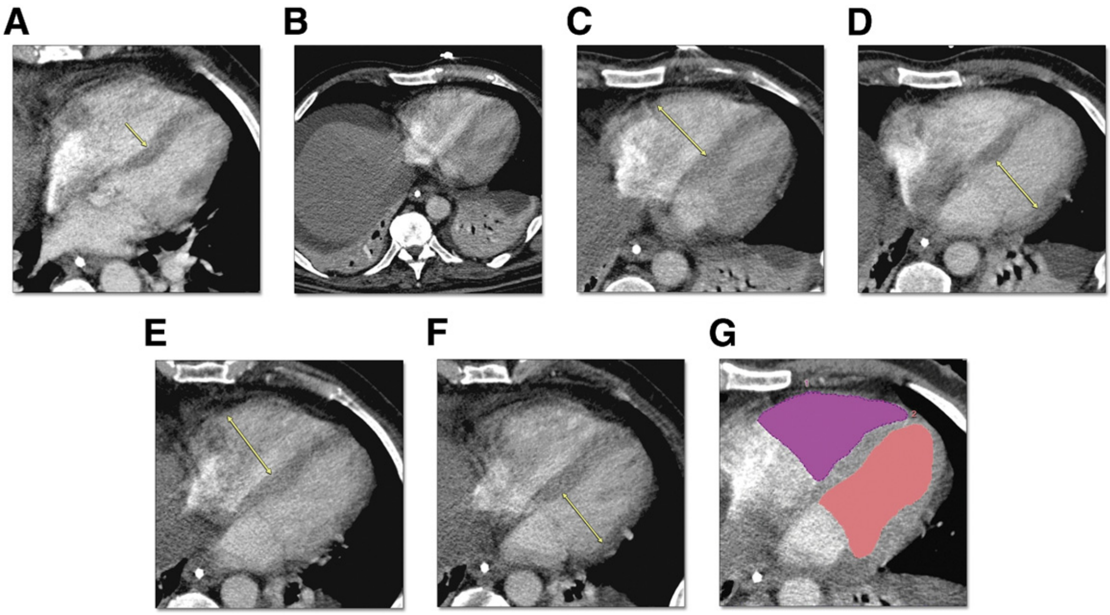

Figure 2. Computed Tomography Signs of RV Dysfunction in a 69-Year-Old Man

(A) In a 69-year-old man with acute pulmonary embolism, a 4-chamber (4-CH) view reconstruction of a chest computed tomography scan shows septal bowing **(arrows)**, convex toward the left ventricle. **(B)** There is no contrast reflux into the inferior vena cava. Measurements of **(C)** maximal right ventricular diameter (RVD) and **(D)** left ventricular diameter (LVD) on axial sections show RVD_{axial}/LVD_{axial} ratio of 0.97. Measurements of maximal **(E)** RVD and **(F)** LVD on 4-CH views show $RVD_{4\text{-}CH}/LVD_{4\text{-}CH}$ ratio of 1.4. Semiautomated right ventricle volumetry (RVV) **(purple)** and left ventricle volumetry (LVV) **(orange)** displayed **(G)** on transverse section and **(H)** on coronal reformation show an RVV/LVV ratio of 1.54. The patient died on hospital day 4.

plane down to the apex of both ventricles. That involved manually outlining the endocardial contours on the transverse sections comprising the minimal and maximal expanse of the ventricle, which were then automatically propagated to the neighboring sections. The RVV/LVV ratio was subsequently calculated (Figs. 1 and 2). The time needed to perform the volumetric measurements ranged between 3.7 min and 10.9 min (21).

Statistical analysis. We used MedCalc (version 10.4.8, MedCalc Software, Mariakerke, Belgium) for all statistical analyses. We used the chi-square test or Fisher exact test for comparisons of categorical variables and the Mann-Whitney test for comparisons in the distributions of continuous variables. Using receiver-operator characteristic curves (in accordance with the methods of DeLong et al. [35]), the area under the curve (AUC) of RVD_{axial}/LVD_{axial}, $RVD_{4\text{-}CH}/LVD_{4\text{-}CH}$, and RVV/LVV for predicting adverse events and 30-day death were compared, and optimal cutoff values, weighted for higher sensitivity, for the above ratios were assigned, similar to previous investigations (26,28); these cutoffs were used for subsequent analyses. The Cox proportional hazard model was used to calculate the hazard ratio of clinical variables and CT measurements for predicting adverse outcomes. Multivariate analysis was then performed to identify predictors of adverse outcomes, using the proportional hazards model with calculation of 95% confidence intervals (CIs). Each CT sign was evaluated in a separate model accounting for clinical characteristics and comorbidities that were significant ($p < 0.05$) predictors of adverse outcomes and 30-day death.

RESULTS

Clinical characteristics of study population. The mean age of the patient population was 55 ± 18 years, and there were 139 (53.5%) men. In all patients, the initial clinical diagnosis of PE was confirmed by the presence of at least 1 filling defect in the pulmonary artery tree (8,9). One hundred forty-five patients (71.4%) had relevant comorbidities, including cancer in 59, coronary artery disease in 35, congestive heart failure in 13, diabetes mellitus in 40, chronic interstitial lung disease in 26, and renal insufficiency in 36. There were no statistical differences between the demographics or CT findings of the 36 excluded patients and final study population ($p > 0.05$ for all measures).

Fifty-seven patients (21.9%) had adverse clinical outcomes, including 20 (7.7%) who died within 30 days. Of the 37 (14.2%) surviving patients with adverse outcomes, 35 required endotracheal intubations, 15 were treated with vasopressors, 11 received thrombolysis, 7 required cardiopulmonary resuscitation, and 4 underwent surgical embolectomy. Adverse outcomes occurred in the range from 1 day to 30 days (mean 10.4 ± 9.6 days) from the time of diagnosis. Patients with adverse outcomes were older and more commonly had diabetes mellitus, renal insufficiency, and sepsis (Table 1), whereas cancer, diabetes mellitus, renal insufficiency, and sepsis were more common among patients who died within 30 days (Table 2); these parameters were subsequently included in the relevant multivariate analyses.

Interobserver reproducibility. The pilot investigation (21) in 50 patients had shown fair interobserver reproducibility for describing the position of the ventricular septum ($k = 0.32$), with moderate reproducibility ($k = 0.44$) for differentiating normal versus abnormal (i.e., flattening or bowing) position. There was good agreement ($k = 0.68$) for classifying the degree of contrast medium reflux into the IVC and hepatic veins as nonsubstantial versus substantial. Correlation coefficients for measurements of RVD_{axial}/LVD_{axial} ratio, $RVD_{4\text{-}CH}/LVD_{4\text{-}CH}$ ratio, and RVV/LVV ratio measurements between the 2 observers were 0.88, 0.85, and 0.93 respectively ($p < 0.001$ for all correlations).

Prognostic value of CT signs. There were no differences in the AUC of RVD_{axial}/LVD_{axial}, $RVD_{4\text{-}CH}/LVD_{4\text{-}CH}$, and RVV/LVV with AUCs of 0.658 (95% CI: 0.597 to 0.715), 0.659 (95% CI: 0.598 to 0.717), and 0.677 (95% CI: 0.617 to 0.734), respectively, for predicting adverse events ($p = 0.565$ to 0.940); and AUCs of 0.698 (95% CI: 0.638 to 0.753), 0.694 (95% CI: 0.634 to 0.750), and 0.664 (95% CI: 0.603 to 0.721), respectively, for predicting 30-day death ($p = 0.603$ to 0.937). Receiver-operator characteristic analysis identified RVD_{axial}/LVD_{axial} >1.0, $RVD_{4\text{-}CH}/LVD_{4\text{-}CH}$ >1.0, and RVV/LVV >1.2 as optimal cutoffs with high sensitivity (>70%) for predicting 30-day death; these values were used for subsequent analyses. Table 3 illustrates the prevalence of the measured CT signs in patients with and without adverse events and 30-day death. The sensitivities and specificities of CT signs for predicting adverse outcomes and 30-day death are presented in Table 4.

Table 1. Clinical Characteristics and Comorbidities in Patients With and Without Adverse Outcomes

	Adverse Outcome (n = 57)	No Adverse Outcome (n = 203)	p Value
Age, yrs, mean ± SD	59 ± 16	54 ± 18	0.021*
Men	34 (59.6%)	105 (51.7%)	0.298
Within 30 days before PE diagnosis			
Major surgery	19 (33.3%)	74 (36.5%)	0.755
Pneumonia	10 (17.5%)	19 (9.4%)	0.096
Sepsis	8 (14.0%)	3 (1.5%)	<0.001*
Trauma	9 (15.8%)	23 (11.3%)	0.366
Stroke	4 (7.0%)	10 (4.9%)	0.515
Major hemorrhage	2 (3.5%)	7 (3.4%)	1.000
Myocardial infarction	1 (1.8%)	1 (0.5%)	0.391
Multisystem organ failure	1 (1.8%)	0 (0.0%)	0.219
Comorbidities			
Cancer	15 (26.3%)	44 (21.7%)	0.477
Coronary artery disease	9 (15.8%)	26 (12.8%)	0.519
Congestive heart failure	4 (7.0%)	9 (4.4%)	0.490
Diabetes mellitus	14 (24.6%)	26 (12.8%)	0.038*
Chronic lung disease	5 (8.8%)	21 (10.3%)	1.000
Renal insufficiency	20 (35.1%)	16 (7.9%)	<0.001*

*Statistically significant p value.
PE = pulmonary embolism.

Table 2. Clinical Characteristics and Comorbidities of Patients Who Died Versus Patients Who Survived

	Death (n = 20)	Survival (n = 240)	p Value
Age, yrs, mean ± SD	61 ± 15	54 ± 17	0.064
Men	15 (75.0%)	124 (51.7%)	0.061
Within 30 days before PE diagnosis			
Major surgery	6 (30.0%)	87 (36.3%)	0.636
Pneumonia	4 (20.0%)	25 (10.4%)	0.255
Sepsis	5 (25.0%)	6 (2.5%)	<0.001*
Trauma	1 (5.0%)	31 (12.9%)	0.484
Stroke	0 (0.0%)	14 (5.8%)	0.610
Major hemorrhage	1 (5.0%)	8 (3.3%)	0.519
Myocardial infarction	1 (5.0%)	1 (0.4%)	0.148
Multisystem organ failure	1 (5.0%)	0 (0.0%)	0.077
Comorbidities			
Cancer	9 (45.0%)	50 (20.8%)	0.023*
Coronary artery disease	4 (20.0%)	31 (12.9%)	0.324
Congestive heart failure	3 (15.0%)	10 (4.2%)	0.068
Diabetes mellitus	7 (35.0%)	33 (13.8%)	0.020*
Chronic lung disease	3 (15.0%)	23 (9.6%)	0.433
Renal insufficiency	12 (60.0%)	24 (10.0%)	<0.001*

*Statistically significant p value.
PE = pulmonary embolism.

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Table 3. Computed Tomography Signs of Right Ventricular Dysfunction for Predicting Adverse Outcomes and 30-Day Death

	Adverse Outcomes (n = 57)	No Adverse Outcomes (n = 203)	
CT Sign of RV Dysfunction	Death (n = 20)	Survival (n = 240)	p Value
Abnormal position of septum	29 (50.9%)	62 (30.5%)	0.014*
	9 (45.0%)	82 (34.2%)	0.338
IVC contrast reflux	22 (38.6%)	29 (14.3%)	<0.001*
	5 (25.0%)	46 (19.2%)	0.558
$RVD_{axial}/LVD_{axial} > 1.0$	36 (63.2%)	112 (55.2%)	0.355
	15 (75.0%)	133 (55.4%)	0.104
$RVD_{4\text{-}CH}/LVD_{4\text{-}CH} > 1.0$	45 (78.9%)	117 (57.6%)	0.006*
	17 (85.0%)	145 (60.4%)	0.031*
RVV/LVV >1.2	45 (78.9%)	104 (51.2%)	<0.001*
	17 (85.0%)	132 (55.0%)	0.009*

Values are n (%).
CT = computed tomography; 4-CH = 4-channel; IVC = inferior vena cava; LVD = left ventricular diameter; LVV = left ventricular volume; RV = right ventricular; RVD = right ventricular diameter; RVV = right ventricular volume.

Multivariate analysis demonstrated that $RVD_{axial}/LVD_{axial} > 1.0$ was not independently predictive of adverse outcomes or 30-day death. Abnormal position of the interventricular septum, substantial IVC contrast reflux, $RVD_{4\text{-}CH}/LVD_{4\text{-}CH} > 1.0$, and RVV/LVV >1.2 were independent predictors of adverse events, while $RVD_{4\text{-}CH}/LVD_{4\text{-}CH} > 1.0$ and RVV/LVV were predictive of 30-day death, with hazard ratios of 3.68 (95% CI: 1.08 to 12.60; p = 0.039) and 6.49 (95% CI: 1.77 to 23.84; p = 0.005), respectively (Table 5). Among 149 patients with RVV/LVV ratio >1.2, 45 had adverse events within 30 days (representing a positive predictive value of 30.2%), and 17 died (positive predictive value of 11.4%). Among 111 patients with RVV/LVV ≤1.2, 99 experienced no adverse events (negative predictive value 89.2%) and 108 survived (negative predictive value 97.3%).

Table 4. Sensitivity and Specificity Values of CT Signs for Predicting Adverse Outcome and 30-Day Death

CT Sign of RV Dysfunction	Sensitivity	Specificity
Abnormal position of septum		
For predicting adverse outcomes	50.9% (29/57)	69.5% (141/203)
For predicting 30-day death	45% (9/20)	65.8% (158/240)
IVC contrast reflux		
For predicting adverse outcomes	38.6% (22/57)	85.7% (174/203)
For predicting 30-day death	25.0% (5/20)	80.8% (194/240)
$RVD_{axial}/LVD_{axial} > 1.0$		
For predicting adverse outcomes	63.2% (36/57)	44.8% (91/203)
For predicting 30-day death	75% (15/20)	44.6% (107/240)
$RVD_{4\text{-}CH}/LVD_{4\text{-}CH} > 1.0$		
For predicting adverse outcomes	78.9% (45/57)	42.4% (86/203)
For predicting 30-day death	85.0% (17/20)	39.6% (95/240)
RVV/LVV >1.2		
For predicting adverse outcomes	78.9% (45/57)	48.8% (99/203)
For predicting 30-day death	85.0% (17/20)	45.0% (108/240)

Values are % (n/N).
Abbreviations as in Table 3.

DISCUSSION

We show that 3D measurement of ventricular volumes is superior to other chest CT signs of RV dysfunction for predicting adverse outcomes and 30-day death in patients with acute PE. In our cohort, among 149 patients with RVV/LVV ratio >1.2, 45 (30.2%) had adverse events within 30 days, and the risk of death within 30 days increased approximately 6-fold. Conversely, in the absence of an RVV/LVV ratio >1.2, most patients (97.3%) survived. The routine availability of contemporary advanced image post-processing workstations, which automatically propagate the segmentation of cardiac chambers, has greatly facilitated the performance of 3D ventricular volume measurement. Performing 3D volumetric ventricular measurements can be accomplished on most current image post-processing platforms. This evaluation method may more appropriately account for the complex shape of the cardiac ventricles than a single image or plane.

In our cohort, the mortality rate was 7.7% within 30 days, and thus was very similar to the mortality rates in other studies (3,5,36,37). The proportion of patients who had nonfatal in-hospital adverse events or required escalation of therapy was similar to that in the MAPPET-3 study (4). The patients enrolled in our study suffered from a variety of severe diseases and may therefore have died of other reasons than PE. However, although, overall, most deaths in PE patients occur because of pre-existing underlying disease (37), the main cause of early death, namely, within 30 days as in our study, is acute RV failure (1,3).

The interventricular septum, which normally bows toward the RV, may shift toward the LV related to increased right-side heart pressure with severe pulmonary arterial obstruction (16). Several studies reported that ventricular septal bowing indicated severe PE (13,25) as manifested by RV dysfunction (14,20,22) and predicted short-term death (10). Conversely, Araoz et al. (11), Van der Meer et al. (31), Ghaye et al. (17), and Aviram et al. (12) did not find this sign to be predictive of death from acute PE. These latter findings correspond to our current results, where abnormal position of the interventricular septum was overall predictive of adverse events but not of 30-day death.

Reflux of contrast medium into the IVC is an indirect sign of increased RV pressure and can be seen in various underlying conditions (21). While substantial IVC reflux was predictive of adverse outcomes in our study, it failed to identify patients at risk of early death. Increased RVD/LVD ratio on chest CT has been proposed as a sign of RV dysfunction. However, multiple quantitative methods and cutoff points have been described to assess dilatation of the complex-shaped RV in patients with acute PE. Araoz et al. (10) and Contractor et al. (14) measured both ventricles at the level of the atrioventricular valves, whereas van der Meer et al. (31) used maximum minor axis measurements. Contractor et al. (14) and Lim et al. (22) found a RVD_{axial}/LVD_{axial} ratio of >1 as measured on transverse sections indicative of severe PE, while others proposed a threshold of >1.5 (13,27). Several studies report that an increased RVD_{axial}/LVD_{axial} ratio on transverse chest CT sections indicates RV dysfunction (14,20,22) and predicts short-term death (10), although others found this sign not to be associated with increased mortality in stable patients without shock (29).

Although a recent report (30) described no statistically significant difference between measurements of RV enlargement on axial and 4-CH views, Dogan et al. (15) reported significant differences for $RVD_{4\text{-}CH}/LVD_{4\text{-}CH}$ ratios between patients with and without PE but not for RVD_{axial}/LVD_{axial} ratios on transverse sections. These findings correspond to our own prior investigations (26,28), where we found that the proportion of patients with increased RVD_{axial}/LVD_{axial} ratios on transverse sections was similar for patients with and without adverse events. However, ventricular measurements on 4-CH views were superior, with an AUC of 0.753 of $RVD_{4\text{-}CH}/LVD_{4\text{-}CH}$ >0.9 versus an AUC of 0.667 of RVD_{axial}/LVD_{axial} >0.9, for predicting adverse outcomes. In our current investigation, although RVD_{axial}/LVD_{axial} >1.0 was more common in patients who died within 30 days, this parameter was neither predictive of adverse outcomes overall nor of early death. Compared with our previous studies (26,28), receiver-operator characteristic analysis in our current investigation revealed a slightly higher $RVD_{4\text{-}CH}/LVD_{4\text{-}CH}$ ratio cutoff (1.0 vs. 0.9), which, however, is identical to the RVD/LVD cutoff of 1.0 used in the MAPPET-2 trial (3) and the PIOPED (Prospective Investigation of Pulmonary Embolism Diagnosis) II study (38).

Table 5. Multivariate Analysis of CT Signs for Predicting Adverse Outcomes and 30-Day Death

		Multivariate Analysis		
CT Sign of RV Dysfunction	n	HR	95% CI	p Value
Abnormal position of septum				
For predicting adverse outcomes	29	2.0726	1.2216–3.5164	0.007*
For predicting 30-day death	9	2.3919	0.9349–6.1192	0.070
IVC contrast reflux				
For predicting adverse outcomes	22	2.5718	1.4688–4.5032	0.001*
For predicting 30-day death	5	1.8337	0.6361–5.2864	0.264
RVD_{axial}/LVD_{axial} >1.0				
For predicting adverse outcomes	36	1.4158	0.7948–2.5221	0.240
For predicting 30-day death	15	2.0848	0.7325–5.9339	0.171
$RVD_{4\text{-}CH}/LVD_{4\text{-}CH}$ >1.0				
For predicting adverse outcomes	45	2.5084	1.2622–4.9850	0.009*
For predicting 30-day death	17	3.6839	1.0771–12.5994	0.039*
RVV/LVV >1.2				
For predicting adverse outcomes	45	4.0379	1.9970–8.1646	<0.001*
For predicting 30-day death	17	6.4919	1.7678–23.8402	0.005*

Age, diabetes mellitus, renal insufficiency, and sepsis were statistically significant ($p < 0.05$) predictors of adverse events and subsequently included in the relevant multivariate analysis. Cancer, diabetes mellitus, renal insufficiency, and sepsis were statistically significant ($p < 0.05$) predictors of 30-day death and included in the relevant multivariate analysis. *Statistically significant p value.
CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 3.

Study limitations. The most important limitation of our study is its retrospective nature. Also, we did not include patients without PE as a control group to determine whether these findings are unique to PE positive patients. However, our current investigation is 1 of the largest analyses to date evaluating the prognostic value of chest CT signs of RV dysfunction in patients with acute PE. It is the only study systematically comparing all signs that have been described for this purpose, including the rather recent method of 3D ventricular volumetry. Our study would have been strengthened by correlation with echocardiography findings; unfortunately, only a small percentage of our patients (100 of 260, 38.5%) had echocardiography findings available. Considering that prior studies have established a good correlation between echocardiography and CT findings (18,20,22,24,26), we chose not to formally analyze this small subset of our patients.

Another potential limitation of our present study is that chest CT image acquisition was not ECG gated. Non–ECG-gated CT is inevitably inaccurate for measuring ventricular chamber size, because the images are acquired in different phases of the cardiac cycle. However, the use of ECG-gated CT protocols over routine chest CT has been shown to result in only limited incremental diagnostic improvements (23). More im-

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portantly, because of the additional radiation exposure involved with ECG-gated techniques, this approach is not currently used for routine PE imaging (8), whereas our results obtained in non–ECG-gated chest CT studies are directly transferable to clinical practice. Finally, the clinical applicability of our results is limited by interobserver variability and 3D workstation requirements; however, we believe continuing evolution and implementation of CT technology should mitigate this limitation in the future.

CONCLUSIONS

In conclusion, we show that abnormal position of the interventricular septum, IVC contrast reflux, and $RVD_{4\text{-CH}}/LVD_{4\text{-CH}}$ ratio are predictive of adverse outcomes. However, 3D measurement of ventricular volumes is superior to all other chest CT signs of RV dysfunction for predicting adverse outcomes and 30-day death in patients with acute PE. Future studies are needed to investigate the benefit of cardiac volumetric measurements for prospectively guiding patient management in comparison to and in combination with other risk assessment tools, such as echocardiography or cardiac biomarkers (39–43).

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