Original Research

Pulmonary Embolism: CT Signs and Cardiac Biomarkers for Predicting Right Ventricular Dysfunction

Thomas Henzler, MD¹,²*, Susanne Roeger, MD²*, Mathias Meyer, BS¹,², U. Joseph Schoepf, MD⁴, John W. Nance Jr., MD⁴, Dariush Haghi, MD³, Wolfgang E. Kaminski, MD³, Michael Neumaier, MD³, Stefan O. Schoenberg, MD¹, Christian Fink, MD¹

1. Institute of Clinical Radiology and Nuclear Medicine,
2. 1st. Department of Medicine
3. Institute of Clinical Chemistry
   University Medical Center Mannheim, Medical Faculty Mannheim – Heidelberg University, Germany
4. Department of Radiology and Radiological Science,
   Medical University of South Carolina,
   Charleston, South Carolina

*Drs Henzler and Roeger contributed equally to this study

Address for correspondence: Thomas Henzler, MD
Institute of Clinical Radiology and Nuclear Medicine
University Medical Center Mannheim
Medical Faculty Mannheim – Heidelberg University
Theodor-Kutzer-Ufer 1-3
D-68167 Mannheim, Germany
Tel: 0621 383 2067
Fax: 0621 383 3817
E-Mail: thomas.henzler@medma.uni-heidelberg.de
Abstract

To prospectively evaluate the accuracy of quantitative cardiac CT parameters and two cardiac biomarkers (NT-pro-Brain Natriuretic Peptide (NT-pro-BNP); troponin I), alone and in combination, for predicting right ventricular dysfunction (RVD) in patients with acute pulmonary embolism (PE).

557 consecutive patients with suspected PE underwent pulmonary CTA. Patients with PE also underwent echocardiography and NT-pro-BNP/troponin I serum level measurements. 3 different CT measurements were obtained (RV/LVaxial, RV/LV4CH), and RV/LVvolume). CT measurements and NT-pro-BNP/ troponin I serum levels were correlated with RVD at echocardiography.

Patients with RVD (n=77) showed significantly higher RV/LV ratios and NT-pro-BNP/troponin I levels compared to those without RVD (RV/LVaxial 1.68±0.84 vs. 1.00±0.21; RV/LV4ch 1.52±0.45 vs. 1.01±0.21; RV/LVvolume 1.97±0.53 vs. 1.07±0.52; serum NT-pro-BNP 6372±2319 vs. 1032±1559 ng/L; troponin I 0.18±0.41 vs. 0.06±0.18). The area under the curve for the detection of RVD of RV/LVaxial, RV/LV4Ch, RV/LVvolume, NT-pro-BNP and troponin I were 0.84, 0.87, 0.93, 0.83 and 0.70 respectively. The combination of biomarkers and RV/LVvolume increased the AUC to 0.95 (RV/LVvolume with NT-pro-BNP) and 0.93 (RV/LVvolume with troponin I).

RV/LVvolume is the most accurate CT parameter for identifying patients with RVD. A combination of RV/LVvolume with NT-pro-BNP or troponin I measurements improves the diagnostic accuracy of either test alone.
Introduction

Right ventricular dysfunction (RVD) is a predictor of poor outcome in patients with acute pulmonary embolism (PE) [1]. Thus, risk stratification relies on early detection of RVD in order to identify normotensive high-risk patients who might benefit from more aggressive therapies, such as thrombolysis or embolectomy [2, 3].

While echocardiography is considered the reference standard for assessing RVD in patients with acute PE [4-6], a multitude of recent studies have evaluated various morphometric parameters from pulmonary CT angiography (CTA) for predicting adverse outcomes or early death in patients with acute PE [7-13]. One of the most frequently investigated parameters is the ratio of right ventricular (RV) to left ventricular (LV) diameters as measured on transverse CT images or reconstructed four-chamber (4-CH) views [7, 12]. Recent reports suggest that 3D assessment of ventricular volumes is superior to diameter measurements for determining RVD in patients with PE [14-16]. However, studies that specifically compare the accuracy of CT signs for predicting RVD, as assessed by echocardiography, are limited and to date have not included ventricular volume measurements [17, 18].

Beyond imaging signs, cardiac biomarkers such as N-terminal pro-B-type Natriuretic Peptide (NT-pro-BNP) and troponin I have been proposed as predictors of clinical outcome in patients with acute PE [1, 19, 20]. NT-pro-BNP is secreted due to RV shear stress whereas increased levels of cardiac troponin I results from myocardial necrosis after severe RV pressure overload or a long duration of pressure overload that causes RV myocardial necrosis.
The aim of this study therefore was to prospectively evaluate the accuracy of quantitative cardiac CT parameters, obtained from pulmonary CTA, and two cardiac biomarkers (NT-pro-BNP; troponin I), alone and in combination, for predicting RVD on echocardiography in patients with acute PE.
Materials and methods

Study population

Our local ethics committees approved this prospective study, and all patients gave written informed consent. Between August 2008 and June 2009, 575 consecutive patients with suspected PE underwent pulmonary CTA. Of those, 77 (13.4%) had acute PE and were enrolled in the study. These included 42 men and 35 women with a mean age of 63±15.8 years. Medical records of all patients were reviewed for presence of congestive heart failure, cancer, myocardial infarction, chronic kidney disease, pulmonary hypertension, and sepsis at the time point of admission to CT and/or two weeks prior to admission.

Echocardiographic assessment of RVD

Echocardiography data were acquired with Vivid 7 and Vivid 1 (GE Healthcare, Chalfont St Giles, UK) ultrasound scanners. All examinations were performed within 24 hours after the onset of symptoms by two cardiologists (S.R/D.H), who were blinded to NT-pro-BNP serum levels and CT measurements. The echocardiographic protocol included apical two-, three- and four-chamber views, parasternal long- and short-axis views and subcostal views. Digitized echocardiographic data were analyzed by both investigators in a consensus reading using the EchoPAC PC (GE Medical Systems, Milwaukee, Wisconsin) software package. Specifically, the RV was evaluated for the presence or absence of the following signs [4, 21]: RV > 30 mm or RV/LV end-diastolic ratio > 1 from the apical four-chamber view, dyskinesia or hypokinesia of the free right ventricular wall, hypokinesia of the infundibular RV region with normal contraction of the RV apex (McConnell sign), tricuspid annular plane systolic excursion (TAPSE) < 15
mm, RV/atrial gradient > 30 mm Hg. A diagnosis of RV dysfunction was established in the presence of two or more of these criteria [21, 22]. In addition, if bulging of the interventricular septum into the LV was observed, RVD was classified as severe [22, 23]. All other forms of RVD were classified as moderate.

**CT Protocol**

All standard pulmonary CTA examinations were performed on multi detector-row CT (MDCT) systems. 40 patients were examined on a 16 slice MDCT system (Somatom Emotion, Siemens Healthcare, Forchheim, Germany). The remaining 37 patients were examined using 64-slice dual-source CT system (Somatom Definition, Siemens). 100 ml iodinated contrast material (Imeron 400, Bracco Imaging S.p.A., Milan, Italy) was injected in an antecubital vein using a power injector (Stellant D, Medrad, Warrendale, USA) at a rate of 4 ml/s, followed by a 20 ml saline chaser. In all examinations the entire chest was scanned in caudo-cranial direction during an inspiratory breath hold.
**CT Analysis**

All CT studies were analyzed on a multi-modality 3D-enabled workstation (Syngo VE36A, Siemens). CT studies were evaluated by two radiologists (C.F/T.H) in consensus, who were blinded to the echocardiographic and laboratory results.

**RV/LV axial diameter ratio**

The axial section displaying the maximal distance between the ventricular endocardium and the interventricular septum, perpendicular to the long axis of the heart, was identified for both the right and left ventricle. The maximum short axis diameters were measured for the RV and LV and the RV/LV_{axial} ratio was subsequently calculated (Figure 1).

**RV/LV 4-CH view ratio**

4-CH views were reconstructed as previously described [12]. The two levels on the reconstructed 4-CH views that showed the maximal distance between the ventricular endocardium and the interventricular septum for the RV and LV were identified. The RV and LV 4-CH diameters were measured, and from this the RV/LV_{4-CH} ratio was calculated (Figure 1).

**RV/LV volume ratio**

The 3D volumetric analysis of both ventricles was performed by using dedicated volume analysis software (Volume analysis, Syngo VE31A, Siemens). The endocardial contours were semi-automatically segmented from the valvular plane to the apex of both ventricles and the RV/LV_{volume} ratio was subsequently calculated as previously described [15] (Figure 1).

**Laboratory measurements**
NT-pro-BNP and troponin I serum levels were quantified from a venous blood sample, which was drawn within 24 hours after the diagnosis of PE. Plasma NT-pro-BNP concentration was determined using an NT-pro-BNP enzyme immunoassay and a Dimension RxL analyzer (Siemens Healthcare Diagnostics, Eschborn, Germany). The manufacturer’s proposed decision threshold for excluding heart failure in patients without renal insufficiency is 84 ng/L in males and 155 ng/L in females ≤50 years old and 194 ng/L in males and 222 ng/L in females >50 years old.

Troponin I levels were measured with a two-site immunoenzymatic immunoassay (Access AccuTnI, Beckmann Coulter, GmbH - Diagnostic, Krefeld, Germany). Per manufacturer, the cut point level for an upper limit of normal (with an assay coefficient of variation <10%) was 0.06 g/ L.

Statistical analysis

Statistical analysis was performed using JMP 7.0 (SAS Institute, Cary, North Carolina, USA). Continuous variables are expressed as mean ± SD. The Shapiro-Wilk test was applied to determine probability distribution; a two-tailed Student’s t-test was subsequently used to compare groups with normal distribution, while the Mann–Whitney U-test was used if the data were not normally distributed. The $X^2$ test was applied for dichotomous variables. Pearson’s correlation was used to correlate serum levels of NT-pro-BNP with $RV/LV_{axial}$, $RV/LV_{4Ch}$, $RV/LV_{volume}$, and echocardiographic assessment of RVD. To determine the diagnostic accuracy of cardiac biomarkers and CT parameters for RVD, receiver operating characteristic (ROC) plots were analyzed and areas under the curve (AUCs) were calculated. Differences between AUC values were compared using the Hanley and McNeil method. Multivariate analysis was performed with logistic
regression analysis using block entry of the following variables: NT-pro-BNP, troponin I, 
RV/LV\textsubscript{axial}, RV/LV\textsubscript{ach}, and RV/LV\textsubscript{volume}. The results are presented as estimated odds 
ratios (OR) and relative risk with the corresponding 95% confidence intervals. A 2-tailed 
p-value of <0.05 was considered statistically significant.
Results

Among the 77 patients with acute PE, congestive heart failure was present in 13 patients, cancer in 11, myocardial infarction in 8, chronic kidney disease in 4, pulmonary hypertension in 4, and sepsis in 2 patients. Echocardiography showed RVD in 27/77 patients (35%) of whom 15 (56%) were classified as severe and 12 (44%) as moderate.

Overall detection of RVD

Patients with RVD showed significantly higher RV/LV ratios and cardiac biomarker levels compared to those without RVD (RV/LVaxial 1.68 ± 0.84 vs. 1.00 ± 0.21 (p=0.003); RV/LV4ch 1.52 ± 0.45 vs. 1.01 ± 0.21 (p=0.002); RV/LVvolume 1.97 ± 0.53 vs. 1.07 ± 0.52 (p = 0.0001); serum NT-pro-BNP 6372 ± 2319 vs. 1032 ± 1559 ng/L (p=0.002); troponin I 0.179 ± 0.411 vs. 0.061 ± 0.176 g/L (p=0.0375)).

The correlation coefficient of the three different CT parameters with serum NT-pro-BNP was weak for RV/LVaxial with NT-pro-BNP (r= 0.38), moderate for RV/LV4ch with NT-pro-BNP (r= 0.52), and good for RV/LVvolume with NT-pro-BNP (r= 0.68). No correlation was found between the three different CT parameters with troponin I: RV/LVaxial with troponin I (r= 0.10), RV/LV4ch with troponin I (r= 0.12), and RV/LVvolume with troponin I (r= 0.19).

The area under the curve (AUC) of RV/LVaxial, RV/LV4Ch, RV/LVvolume, serum NT-pro-BNP and troponin I for predicting RVD was 0.84, 0.87, 0.93, 0.83 and 0.70 respectively (Figure 2). ROC analysis of CT parameters and cardiac biomarkers revealed the following cut-off values for the prediction of RVD: 1.18 for RV/LVaxial, 1.29 for RV/LV4ch, 1.34 for RV/LVvolume, 1617 ng/L for NT-pro-BNP and 0.07 g/L for troponin I.
Table 1 summarizes the diagnostic characteristics of RV/LV axial, RV/LV 4Ch, RV/LV volume, serum NT-pro-BNP and troponin I using the specified cutoff values.

A combination of NT-pro-BNP and the three different CT parameters increased the AUC for RV/LV axial, RV/LV 4Ch, RV/LV volume to 0.87, 0.90, and 0.95, respectively (all p-values > 0.05). Table 2 summarizes the diagnostic accuracy of RV/LV axial, RV/LV 4Ch, and RV/LV volume in combination with NT-pro-BNP for the detection of RVD. A combination of troponin I and the three different CT parameters increased the AUC of RV/LV axial, RV/LV 4Ch, and RV/LV volume to 0.85, 0.88, and 0.93, respectively (all p-values > 0.05). Table 2 summarizes the diagnostic accuracy of RV/LV axial, RV/LV 4Ch, RV/LV volume in combination with troponin I serum levels for the detection of moderate RVD.

Multiple logistic regression analysis revealed that RV/LV axial (OR 37.5; 95%CI 8 – 190; p=0.0001), RV/LV 4Ch (OR 45.7; 95%CI 10 – 215; p=0.0001), RV/LV volume (OR 67.5; 95%CI 12 – 370; p=0.0001), NT-pro-BNP (OR 12; 95% CI 3.0 – 47.2; p=0.002) and troponin I (OR 5; 95% CI 1.6 – 15.9; p=0.019) were all independent predictors of RVD.

Detection of moderate RVD

ROC analysis of the patient group with moderate RVD revealed the following cut-off values for RV/LV axial, RV/LV 4Ch, RV/LV volume, serum NT-pro-BNP and troponin I for detecting patients with echocardiographically confirmed moderate RVD: 1.23, 1.31, 1.33, 1427 ng/L and 0.09 g/L, respectively. Using those cut-off values the AUCs of RV/LV axial, RV/LV 4Ch, RV/LV volume, serum NT-pro-BNP and troponin I were 0.87, 0.89, 0.90, 0.80 and 0.71, respectively. Table 3 summarizes the diagnostic accuracy of RV/LV axial,
Detection of moderate RVD

A combination of NT-pro-BNP and the three different CT parameters increased the AUC of RV/LV\textsubscript{axial}, RV/LV\textsubscript{4Ch}, and RV/LV\textsubscript{volume} to 0.90, 0.91, and 0.93, respectively (all p-values > 0.05). Table 4 summarizes the diagnostic accuracy of RV/LV\textsubscript{axial}, RV/LV\textsubscript{4Ch}, RV/LV\textsubscript{volume} in combination with NT-pro-BNP serum levels for the detection of moderate RVD. A combination of troponin I and the three different CT parameters increased the AUC of RV/LV\textsubscript{axial}, RV/LV\textsubscript{4Ch}, and RV/LV\textsubscript{volume} to 0.88, 0.90, and 0.91, respectively (all p-values > 0.05). Table 4 summarizes the diagnostic accuracy of RV/LV\textsubscript{axial}, RV/LV\textsubscript{4Ch}, RV/LV\textsubscript{volume} in combination with troponin I serum levels for the detection of moderate RVD.

Detection of severe RVD

ROC analysis of the patient group with severe RVD revealed the following cut-off values for RV/LV\textsubscript{axial}, RV/LV\textsubscript{4Ch}, RV/LV\textsubscript{volume}, serum NT-pro-BNP and troponin for detecting patients with echocardiographically confirmed severe RVD: 1.28, 1.39, 1.72, 1840 ng/L and 0.1 g/L, respectively. Using those cut-off values the AUCs of RV/LV\textsubscript{axial}, RV/LV\textsubscript{4Ch}, RV/LV\textsubscript{volume}, serum NT-pro-BNP and troponin I were 0.80, 0.79, 0.94, 0.93 and 0.73, respectively (Figure. 3). Table 5 summarizes the diagnostic accuracy of RV/LV\textsubscript{axial}, RV/LV\textsubscript{4Ch}, RV/LV\textsubscript{volume}, serum NT-pro-BNP and troponin I for the detection of severe RVD.

A combination of NT-pro-BNP and the three different CT parameters increased the AUC of RV/LV\textsubscript{axial}, RV/LV\textsubscript{4Ch}, and RV/LV\textsubscript{volume} statistically significant to 0.91, 0.93, and 0.98, respectively (all p-values < 0.05). Table 6 summarizes the diagnostic accuracy
of RV/LV$_{axial}$, RV/LV$_{4Ch}$, RV/LV$_{volume}$ in combination with NT-pro-BNP serum levels for the detection of severe RVD. A combination of troponin I and the three different CT parameters increased the AUC of RV/LV$_{axial}$, RV/LV$_{4Ch}$, and RV/LV$_{volume}$ statistically significant to 0.81, 0.80, and 0.94, respectively (all p-values < 0.05). Table 6 summarizes the diagnostic accuracy of RV/LV$_{axial}$, RV/LV$_{4Ch}$, RV/LV$_{volume}$ in combination with troponin I serum levels for the detection of severe RVD.
Discussion

We show that, in a consecutive cohort of unselected patients with acute PE, 3D measurements of ventricular volumes and elevated cardiac biomarker serum levels are superior to uni-dimensional RV/LV diameter ratios for the prediction of RVD. Moreover, we show that a combination of RV/LV volume and cardiac biomarker measurements increased the diagnostic accuracy when compared to either parameter alone.

Echocardiography is considered the reference standard for the assessment of RVD in patients with PE because it can assess RV size and function as well as measure pulmonary artery pressures. Echocardiography can be performed at the bedside and allows for repetitive noninvasive assessment of hemodynamic status and response to treatment. However, accurate echocardiographic imaging of the RV free wall can be technically challenging and at times impossible in a patient with dyspnea, especially in the presence of obesity or chronic lung disease [24]. Second, at many institutions the availability of this test is limited to weekday daytime hours, whereas pulmonary CTA typically has much greater circadian availability, even in small centers [24]. The measurement of serum NT-pro-BNP levels has become routinely available at most clinical laboratories. Accordingly, the combination of cardiac biomarkers and quantitative cardiac CT parameters from pulmonary CTA could be a cost-effective alternative for detecting RVD and for stratifying patient risk in clinical scenarios where echocardiography is not readily available.

An increased RV/LV diameter ratio on pulmonary CTA has been suggested by several studies [7-9, 12, 13, 25] as a surrogate marker for RVD and shown to be a predictor of short-term mortality and adverse clinical events in patients with acute PE.
However, only three studies with a limited number of patients have directly compared CT findings with echocardiography [10, 17, 18]. Lim et al. (18) retrospectively reviewed CT studies of 14 patients with acute, massive PE during a 52-month period, with CT showing a sensitivity of 91.6% and a specificity of 100% for the detection of RVD compared to echocardiography. Likewise, Contractor et al. [17] evaluated 25 patients with PE and showed a sensitivity of 78% and a specificity of 100%. However, those studies limited their evaluation to qualitative parameters (right ventricular dilation or septal bowing) for diagnosing RVD. Quantification of RV/LV ratios, as performed by Mansencal et al [10], may provide a more reproducible parameter for identifying RVD. Their study evaluated 46 consecutive patients with PE who underwent pulmonary CTA and echocardiography. A RV/LV area ratio >1 on CT was shown to provide 88% sensitivity and 88% specificity for diagnosing RVD compared with echocardiography, which is comparable to the performance of RV/LV\textsubscript{volume} found in our present investigation.

In this current investigation, RV/LV\textsubscript{volume} was more accurate than both uni-dimensional RV/LV diameter ratios (RV/LV\textsubscript{axial} and RV/LV\textsubscript{4ch}) for predicting echocardiographically confirmed RVD in patients with acute PE. These findings support those of previous feasibility studies in which RV/LV\textsubscript{volume} was more accurate than RV/LV\textsubscript{axial} and RV/LV\textsubscript{4ch} for differentiating patients with and without central PE [14, 15]. The better correlation of RV/LV\textsubscript{volume} with NT-pro-BNP serum levels compared to RV/LV\textsubscript{axial} and RV/LV\textsubscript{4ch} may be explained by the notion that volumetric analysis of the entire ventricle may better reflect right ventricular overload and thus may be superior for assessing the myocardial strain which causes NT-pro-BNP and troponin I release. Although RV/LV\textsubscript{4ch} and RV/LV\textsubscript{volume} showed higher AUC values than NT-pro-BNP for
the detection of all patients with RVD, NT-pro-BNP showed the highest sensitivity when compared to all CT parameters for detecting those patients with severe RVD. Troponin I showed a lower diagnostic performance when compared to RV/LV\textsubscript{volume} and NT-pro-BNP whereas a combination between RV/LV\textsubscript{volume} and troponin I led to almost similar diagnostic results than a combination of RV/LV\textsubscript{volume} and NT-pro-BNP. Since troponin I is a marker of myocardial cell damage, significant serum elevation might not be found within the first 24 hours after PE in patients with only moderate RVD. However, newer assays for cardiac troponin that have been developed recently are able to detect changes in concentration of the biomarker at or below the 99th percentile for a normal population [26]. Therefore, future studies have to investigate whether new high-sensitivity troponin assays are superior to conventional troponin I for the diagnosis of RVD in patients with PE.

Serum NT-pro-BNP and troponin I levels have been proposed as a non-imaging biomarker for improved risk stratification in patients with acute PE. A recent meta-analysis on the prognostic value of NT–pro-BNP for predicting 30-day adverse events showed an overall sensitivity and specificity of 93% and 58%, respectively. The negative predictive and the positive predictive values were 81% and 63% [1]. These results document the high sensitivity and the favorable negative predictive value of NT–pro-BNP assessment. In another meta-analysis about the prognostic value of troponins in acute PE, Becattini et al. found an unadjusted OR of 5.2 (95% CI 3.3 – 8.4) of elevated cardiac troponin for the prediction of death in patients with PE [27]. Similar values were observed in our study for the prediction of severe RVD (Table 2). Binder et al. [28] also demonstrated that NT-pro-BNP combined with echocardiography may reliably identify
both low-risk and high-risk patients with PE. This data suggests that while cardiac biomarkers do not have high enough specificity as a stand-alone test to identify high-risk patients, it may have value in combination with other diagnostic tests, such as imaging. We therefore evaluated three reported markers of poor prognosis, RVD as seen on pulmonary CTA, serum NT-pro-BNP and troponin I, and compared them with the established first-line risk stratification tool, echocardiography. Vuilleumier et al. [29] evaluated the correlation between NT-pro-BNP and RV/LV_{4ch} and found a correlation of 0.36 between both parameters, which is similar to our uni-dimensional measurement results. However, their study did not evaluate the combination of both parameters and RVD was not confirmed by echocardiography.

There are several limitations to our study, which have to be considered. First, we did not exclude patients with underlying other disease states that may have led to an increase in serum NT-pro-BNP and troponin I levels. Moreover, we based our observations on routine pulmonary CTA techniques rather than ECG-synchronized scan protocols. Non-ECG synchronized CT has some potential limitations for measuring ventricular chamber size, because the images are not acquired during a specific phases of the cardiac cycle. However, it has been previously demonstrated that the use of ECG-synchronized CT protocols is only of limited incremental diagnostic value when compared to routine techniques [30]. More importantly, because of the additional radiation exposure involved with retrospective ECG-gated techniques of the whole chest, this approach is not currently used for routine PE imaging [31], whereas our results obtained in non ECG-gated pulmonary CT angiography studies are directly transferable to clinical practice. However, recently published studies have demonstrated that high
pitch CTPA as well as prospectively ECG-gated CTPA protocols are able to acquire studies with less motion artifacts and an even lower radiation dose when compared to standard non ECG-gated CTPA protocols [32, 33]. Another limitation of our findings that has to be mentioned concerns the broad clinical applicability. Although we observed superiority of RV/LV_{volume} over RV/LV_{ax} and RV/LV_{4ch} for the assessment of RVD, it has to be mentioned that simple diameter measurements are less time consuming when compared to a volumetric analysis that requires dedicated software tools. Thus, it remains unclear whether the technique is suitable for smaller medical centers, which may not have the software or personal recourses.

Lastly, we did not evaluate adverse outcomes of our patients since this study aimed to compare the diagnostic accuracy of cardiac CT parameters and cardiac biomarkers for the detection of RVD with echocardiography as the established imaging modality to assess RVD in patients with acute PE. Future studies should evaluate whether a combination of cardiac CT parameters – in particular RV/LV_{volume} – and cardiac biomarkers allow an improved prediction of adverse outcomes in patients with acute PE compared with echocardiography.

In conclusion, CT-derived RV/LV_{volume} compares favorably with echocardiography for the diagnosis of RVD in patients with acute PE and shows good correlation with cardiac biomarker serum levels. A combination of RV/LV_{volume} and NT-pro-BNP or troponin I has higher diagnostic accuracy than either parameter in isolation. Accordingly, quantitative cardiac CT parameters obtained from pulmonary CTA in combination with cardiac biomarker measurements could be used as an alternative to
echocardiography for the detection of right ventricular dysfunction in patients with acute PE.
References


21. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ. Recommendations for chamber quantification: a report from the American Society of Echocardiography’s Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005; 18: 1440-1463.


Figure legends

**FIGURE 1.** Pulmonary CT angiography study in a 67 year old woman with acute PE. RV/LV assessed on an axial section (A) and on a reconstructed four-chamber view (B). The widest diameter of each ventricle was not necessarily located on the same section. (C) illustrates volumetric analysis of the right ventricle using a threshold-dependent algorithm. The manually segmented contours were automatically propagated to the neighboring sections. Voxels with attenuation in the range of myocardium were automatically excluded from the volume analysis, after the attenuation of the septal myocardium was measured three times for each patient.
FIGURE 2. ROC curves of the three different CT parameters and cardiac biomarkers for predicting right ventricular dysfunction on echocardiography in patients with acute PE.
FIGURE 3. ROC curves of the three different CT parameters and cardiac biomarkers for the prediction of echocardiographically confirmed severe right ventricular dysfunction in patients with acute PE.
<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Area under the curve</th>
<th>Cut off value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV/LV$_{axial}$</td>
<td>82%</td>
<td>83%</td>
<td>68%</td>
<td>92%</td>
<td>0.84</td>
<td>1.18</td>
</tr>
<tr>
<td>RV/LV$_{4ch}$</td>
<td>88%</td>
<td>83%</td>
<td>71%</td>
<td>92%</td>
<td>0.87</td>
<td>1.29</td>
</tr>
<tr>
<td>RV/LV$_{volume}$</td>
<td>88%</td>
<td>85%</td>
<td>82%</td>
<td>95%</td>
<td>0.93</td>
<td>1.34</td>
</tr>
<tr>
<td>NT-pro-BNP (ng/L)</td>
<td>75%</td>
<td>80%</td>
<td>60%</td>
<td>88%</td>
<td>0.83</td>
<td>1617</td>
</tr>
<tr>
<td>Troponin I</td>
<td>67%</td>
<td>72%</td>
<td>56%</td>
<td>80%</td>
<td>0.70</td>
<td>0.07 g/L</td>
</tr>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Positive predictive value</td>
<td>Negative predictive value</td>
<td>Area under the curve</td>
<td>Cut off value</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
<td>-------------</td>
<td>---------------------------</td>
<td>---------------------------</td>
<td>-----------------------</td>
<td>---------------</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;axial&lt;/sub&gt; with NT-pro-BNP</td>
<td>79%</td>
<td>87%</td>
<td>69%</td>
<td>92%</td>
<td>0.87</td>
<td>1.18 + 1617 ng/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;4ch&lt;/sub&gt; with NT-pro-BNP</td>
<td>84%</td>
<td>92%</td>
<td>77%</td>
<td>93%</td>
<td>0.90</td>
<td>1.29 + 1617 ng/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;volume&lt;/sub&gt; with NT-pro-BNP</td>
<td>92%</td>
<td>95%</td>
<td>85%</td>
<td>97%</td>
<td>0.95</td>
<td>1.34 + 1617 ng/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;axial&lt;/sub&gt; with troponin I</td>
<td>85%</td>
<td>78%</td>
<td>67%</td>
<td>91%</td>
<td>0.85</td>
<td>1.18 + 0.07 g/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;4ch&lt;/sub&gt; with troponin I</td>
<td>89%</td>
<td>80%</td>
<td>71%</td>
<td>93%</td>
<td>0.88</td>
<td>1.29 + 0.07 g/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;volume&lt;/sub&gt; with troponin I</td>
<td>93%</td>
<td>90%</td>
<td>84%</td>
<td>96%</td>
<td>0.93</td>
<td>1.34 + 0.07 g/L</td>
</tr>
</tbody>
</table>
Table 3-Diagnostic accuracy of RV/LV\textsubscript{axial}, RV/LV\textsubscript{4Ch}, RV/LV\textsubscript{volume}, and cardiac biomarkers for the detection of moderate right ventricular dysfunction

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Area under the curve</th>
<th>Cut off value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV/LV\textsubscript{axial}</td>
<td>83%</td>
<td>80%</td>
<td>50%</td>
<td>95%</td>
<td>0.87</td>
<td>1.23</td>
</tr>
<tr>
<td>RV/LV\textsubscript{4ch}</td>
<td>83%</td>
<td>88%</td>
<td>63%</td>
<td>96%</td>
<td>0.89</td>
<td>1.31</td>
</tr>
<tr>
<td>RV/LV\textsubscript{volume}</td>
<td>92%</td>
<td>88%</td>
<td>65%</td>
<td>98%</td>
<td>0.90</td>
<td>1.33</td>
</tr>
<tr>
<td>NT-pro-BNP (ng/L)</td>
<td>75%</td>
<td>72%</td>
<td>40%</td>
<td>92%</td>
<td>0.80</td>
<td>1427</td>
</tr>
<tr>
<td>Troponin I (g/L)</td>
<td>66%</td>
<td>70%</td>
<td>33%</td>
<td>90%</td>
<td>0.71</td>
<td>0.09</td>
</tr>
</tbody>
</table>
Table 4: Diagnostic accuracy of RV/LV<sub>axial</sub>; RV/LV<sub>4Ch</sub>; RV/LV<sub>volume</sub> in combination with cardiac biomarkers for the detection of moderate RVD

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Area under the curve</th>
<th>Cut off value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV/LV&lt;sub&gt;axial&lt;/sub&gt; with NT-pro-BNP</td>
<td>92%</td>
<td>90%</td>
<td>70%</td>
<td>98%</td>
<td>0.90</td>
<td>1.23 +1427 ng/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;4ch&lt;/sub&gt; with NT-pro-BNP</td>
<td>92%</td>
<td>92%</td>
<td>74%</td>
<td>98%</td>
<td>0.91</td>
<td>1.31 + 1427 ng/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;volume&lt;/sub&gt; with NT-pro-BNP</td>
<td>100%</td>
<td>94%</td>
<td>82%</td>
<td>95%</td>
<td>0.93</td>
<td>1.33 + 1427 ng/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;axial&lt;/sub&gt; with troponin I</td>
<td>92%</td>
<td>86%</td>
<td>65%</td>
<td>98%</td>
<td>0.88</td>
<td>1.23 + 0.09 g/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;4ch&lt;/sub&gt; with troponin I</td>
<td>83%</td>
<td>94%</td>
<td>77%</td>
<td>96%</td>
<td>0.90</td>
<td>1.31 + 0.09 g/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;volume&lt;/sub&gt; with troponin I</td>
<td>100%</td>
<td>94%</td>
<td>82%</td>
<td>95%</td>
<td>0.93</td>
<td>1.33 + 0.09 g/L</td>
</tr>
</tbody>
</table>
Table 5-Diagnostic accuracy of RV/LV<sub>axial</sub>, RV/LV<sub>4Ch</sub>, RV/LV<sub>volume</sub>, and cardiac biomarkers for the detection of severe right ventricular dysfunction

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Area under the curve</th>
<th>Cut off value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV/LV&lt;sub&gt;axial&lt;/sub&gt;</td>
<td>81%</td>
<td>74%</td>
<td>42%</td>
<td>94%</td>
<td>0.8</td>
<td>1.28</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;4ch&lt;/sub&gt;</td>
<td>73%</td>
<td>90%</td>
<td>73%</td>
<td>93%</td>
<td>0.79</td>
<td>1.39</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;volume&lt;/sub&gt;</td>
<td>90%</td>
<td>91%</td>
<td>75%</td>
<td>98%</td>
<td>0.94</td>
<td>1.72</td>
</tr>
<tr>
<td>NT-pro-BNP (ng/L)</td>
<td>100%</td>
<td>81%</td>
<td>52%</td>
<td>100%</td>
<td>0.93</td>
<td>1840</td>
</tr>
<tr>
<td>Troponin I (g/L)</td>
<td>73%</td>
<td>75%</td>
<td>42%</td>
<td>92%</td>
<td>0.73</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Positive predictive value</td>
<td>Negative predictive value</td>
<td>Area under the curve</td>
<td>Cut off value</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
<td>-------------</td>
<td>----------------------------</td>
<td>---------------------------</td>
<td>-----------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;axial&lt;/sub&gt; with NT-pro-BNP</td>
<td>100%</td>
<td>98%</td>
<td>90%</td>
<td>100%</td>
<td>0.91</td>
<td>1.28 +1840 ng/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;4ch&lt;/sub&gt; with NT-pro-BNP</td>
<td>100%</td>
<td>98%</td>
<td>90%</td>
<td>100%</td>
<td>0.93</td>
<td>1.39 +1840 ng/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;volume&lt;/sub&gt; with NT-pro-BNP</td>
<td>90%</td>
<td>100%</td>
<td>100%</td>
<td>98%</td>
<td>0.98</td>
<td>1.72 +1840 ng/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;axial&lt;/sub&gt; with troponin I</td>
<td>87%</td>
<td>89%</td>
<td>67%</td>
<td>97%</td>
<td>0.81</td>
<td>1.28 + 0.1 g/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;4ch&lt;/sub&gt; with troponin I</td>
<td>87%</td>
<td>87%</td>
<td>65%</td>
<td>97%</td>
<td>0.80</td>
<td>1.39 + 0.1 g/L</td>
</tr>
<tr>
<td>RV/LV&lt;sub&gt;volume&lt;/sub&gt; with troponin I</td>
<td>100%</td>
<td>98%</td>
<td>94%</td>
<td>100%</td>
<td>0.94</td>
<td>1.72 + 0.1 g/L</td>
</tr>
</tbody>
</table>