Multimodality Assessment of Right Ventricular Strain in Patients With Acute Pulmonary Embolism

Brett J. Carroll, MD[a,b,*], Benedikt H. Heidinger, MD[c], Dominique C. Dabreo, MD[c], Jason D. Matos, MD[a,b], Donya Mohebali, MD[a,b], Stephanie A. Feldman, MD[a], Ian McCormick, MD[a,b], Diana Litmanovich, MD[c], and Warren J. Manning, MD[a,b,c]

Optimal risk stratification is essential in managing patients with an acute pulmonary embolism (PE). There are limited data evaluating the potential additive value of various methods of evaluation of right ventricular (RV) strain in PE. We retrospectively evaluated RV strain by computed tomography (CT), transthoracic echocardiography (TTE), electrocardiography (ECG), and troponin levels in consecutive hospitalized patients with acute PE (May 2007 to December 2014). Four-hundred and seventy-seven patients met inclusion criteria. RV strain on ECG (odds ratio [OR] 1.9, confidence interval [CI] 1.1 to 3.3; p = 0.03), CT (OR 2.7, CI 1.5 to 4.8, p <0.001), TTE (OR 2.8, CI 1.5 to 5.4, p <0.001), or a positive troponin (OR 2.7, CI 2.0 to 6.9, p <0.001) were associated with adverse events. In patients with ECG, CT, and TTE data, increased risk was only elevated with RV strain on all 3 parameters (OR 4.6, CI 1.8 to 11.3, p <0.001). In all patients with troponin measurements, risk was only elevated with RV strain on all 3 parameters plus a positive troponin (OR 8.8, CI 2.8 to 28.1, p <0.001) and was similar in intermediate-risk PE (OR 11.1, CI 1.2 to 103.8, p = 0.04). In conclusion, in patients with an acute PE and evaluation of RV strain by ECG, CT, and TTE, risk of adverse events is only elevated when RV strain is present on all 3 modalities. Troponin further aids in discriminating high-risk patients. Multimodality assessment of RV strain is identified as a superior approach to risk assessment. **(Am J Cardiol 2018;122:175–181)**

Pulmonary embolism (PE) is one of the leading causes of cardiovascular death with an increasing incidence.[1–3] There is a subset of high-risk patients that may benefit from advanced therapy to decrease the risk of hemodynamic decompensation or death.[4–6] Advanced therapies portend significant morbidity, particularly bleeding.[2,7,8] Thus, risk stratification is essential in patients with PE to limit the exposure of these treatments to those most likely to benefit. Previous analyses of electrocardiography (ECG),[9] computed tomography (CT),[10] and transthoracic echocardiography (TTE)[11] have shown that evidence of right ventricular (RV) strain in each modality are individually associated with adverse outcomes in acute PE; however, the positive predictive value of such a finding is low.[4] The measurement of troponin in addition to imaging evaluation of RV strain is recommended in guidelines to further differentiate high-risk patients.[4] Although previous studies have evaluated various combinations of RV strain parameters in the same cohort,[12–18] there are no studies evaluating ECG, CT, and TTE findings, along with troponin levels, in the same patient cohort. We therefore sought to determine the potential additive value of multiple parameters of RV strain and to evaluate the association of each individual parameter with adverse events in acute PE.

Methods

We retrospectively identified all consecutively hospitalized patients between May 1, 2007 and December 31, 2014 with an International Classification of Diseases code for PE, diagnosed with acute PE by CT, and had a TTE performed 24 hours before or 48 hours after the diagnostic CT scan. If available, ECGs from the same time period were also reviewed. Patient demographics, clinical characteristics, and patient outcomes were extracted from the patient's electronic medical record. PE severity was defined as (1) high risk if there was demonstration of hypotension (systolic blood pressure <90 mm Hg for >15 minutes), cardiac arrest, and respiratory failure necessitating mechanical ventilation, or vasopressors were instituted; (2) intermediate risk if the previously mentioned criteria were absent but evidence of RV strain was present on CT or TTE; and (3) low risk if none of the previously mentioned characteristics were present. Adverse events included 30-day mortality related to PE, advanced therapy (e.g., systemic fibrinolysis, catheter-directed therapy, or pulmonary embolectomy), or need for vasopressors.[19] Mortality was considered related to PE if classified as death secondary or possibly secondary to PE by 2 or more of the 3 physicians who independently adjudicated each case.

Assessment of RV strain on ECG, CT, and TTE was performed by 3 physicians (JDM, DCD, and BJC, respectively) who were blinded to the clinical outcomes and to the analysis of the other modalities. ECG evidence of RV strain was defined as (1) an S wave in lead I, a Q wave in lead III,

[a]Beth Israel Deaconess Medical Center, Department of Medicine, Boston, Massachusetts; [b]Beth Israel Deaconess Medical Center, Cardiovascular Division, Boston, Massachusetts; and [c]Beth Israel Deaconess Medical Center, Radiology and Harvard Medical School, Boston, Massachusetts. Manuscript received December 20, 2017; revised manuscript received and accepted March 1, 2018.

See page 180 for disclosure information.

*Corresponding author: Tel: (617) 632-7493; fax: (617) 632-7620.
E-mail address: Bcarrol2@bidmc.harvard.edu (B.J. Carroll).

0002-9149/
https://doi.org/10.1016/j.amjcard.2018.03.013

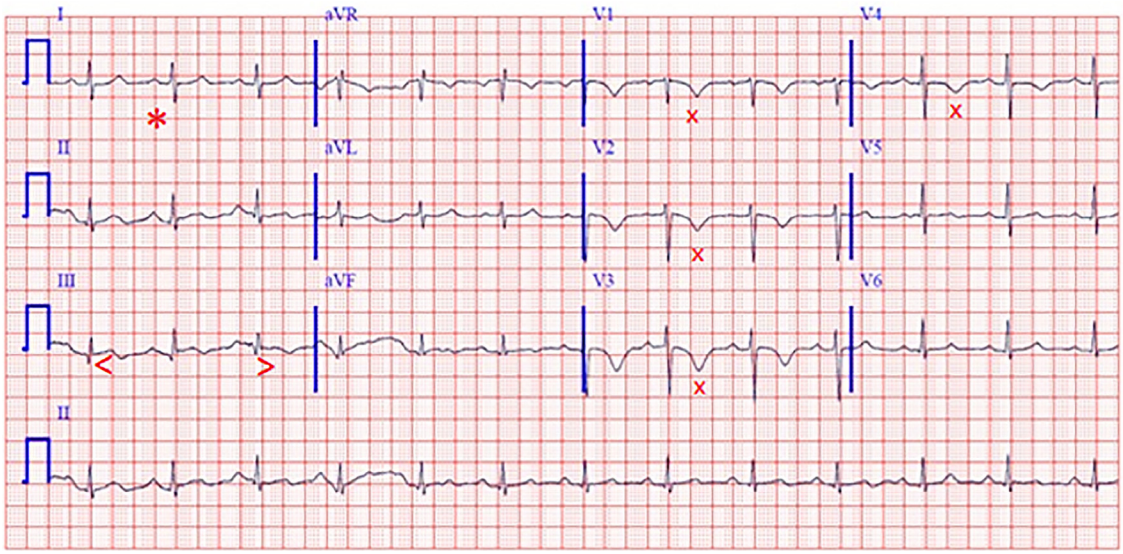

Figure 1. Electrocardiographic evidence of RV strain. Electrocardiogram with S wave in I (*), Q wave in III (<), T wave in III (>), and precordial T wave inversions (x).

and a T-wave inversion in lead III; (2) right bundle branch block (RBBB); (3) T-wave inversions in the early precordial leads (if present in leads V_1 to V_2, V_1 to V_3, or V_1 to V_4) (Figure 1).[9,19,20]

Contrast-enhanced CT scans were performed with 64-detector MDCT scanners (VCT or HD 750, General Electric Medical Systems, Milwaukee, Wisconsin), a 64-detector row unit (Discovery CT750 with Gemstone Spectral Imaging, General Electric Medical Systems), or Toshiba 64-row MDCT scanners (Toshiba America Medical Systems, Tustin, CA). Images were acquired after the administration of 70–100 ml of iodinated contrast media timed for optimal opacification of the pulmonary arteries and reconstructed at a thickness of 0.5 to 2.4 mm. One fellowship-trained cardiothoracic radiologist assessed the transverse CT images for RV strain by measuring the maximum distance from the interventricular septum to the endocardial border, perpendicular to the long axis of the respective ventricle. The RV/left ventricular (LV) diameter ratio was then calculated, with an abnormal ratio defined by current literature: (1) ≥0.9 and (2) ≥1.0 (Figure 2).[21]

TTEs were performed with an echocardiograph (Vivid q, Vivid 7, or Vivid 9, General Electric Medical Systems). Each TTE was over-read by an American Board of Echocardiography Special Competency in Adult Echocardiography–certified attending blinded to the other imaging modalities and to outcomes. The RV/LV ratio was calculated by measurement of the basal RV end-diastolic dimension on the apical 4-chamber view[22] and the basal LV end-diastolic dimension on the parasternal long-axis view (Figure 3). Again, the RV/LV ratio was considered to be abnormal by using the thresholds (1) ≥0.9 and (2) ≥1.0.[23] Tricuspid annular plane systolic excursion (TAPSE) was assessed in the M-mode presentation by placing the cursor at the level of the lateral aspect of the tricuspid annulus and measuring the maximum displacement with systole. A TAPSE of <16 mm was considered abnormal (Figure 3).[11,22] Visual assessment of RV free wall systolic function was categorized as normal or mild, moderate, or severe hypokinesia.[24] The presence and severity of RV hypokinesia were evaluated qualitatively, as was the presence of McConnell's sign.[25] Troponin T was considered positive if peak value was >0.10 ng/ml. The study was approved by our institutional review board, which waived informed consent.

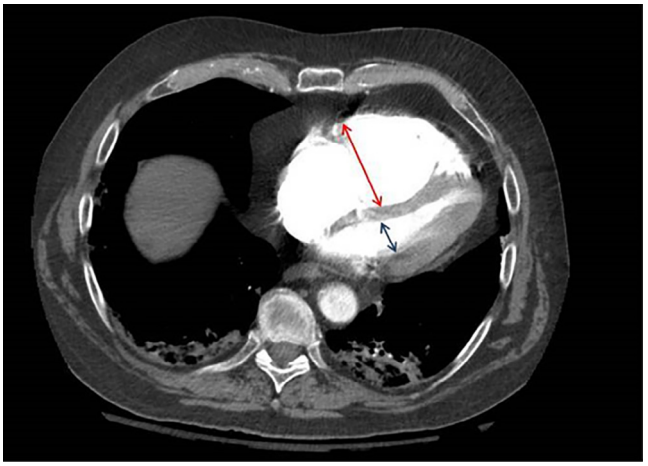

Figure 2. Increased RV-to-LV diameter ratio. CT measurement of RV diameter (red)-to-LV diameter (blue) ratio on transverse CT image of 2.3. (Color version available online.)

All analyses were performed with STATA (v14.2, StataCorp LP, College Station, Texas). Continuous variables are expressed as mean ± SD or as median (interquartile range) as appropriate. Categorical variables are expressed as number (percentage). Association of RV strain and troponin with adverse events was performed by calculating the odds ratio (OR) and testing for statistical significance using logistic regression analyses. A 2-sided p value of <0.05 was used to indicate statistical significance.

Results

Between May 2007 and December 2014, 2,168 hospitalized patients had an International Classification of Diseases

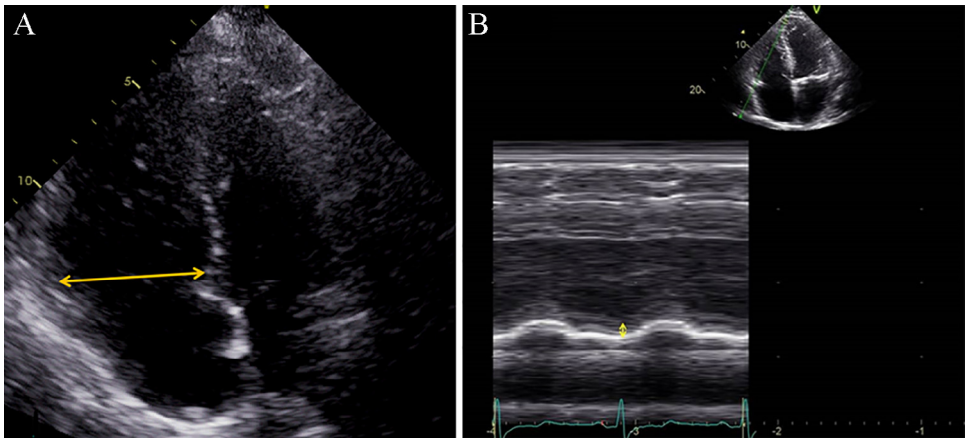

Figure 3. RV strain on TTE. (A) Transthoracic echocardiographic measurement of basal RV diameter at end diastole in the apical 4-chamber view. (B) Transthoracic echocardiographic measurement of the TAPSE.

Table 1
Patient demographics and clinical characteristics

Variable	(N = 477)
Age (years)	63.0 ± 16.2
Male	226 (47%)
Smoker	
Current	49 (11%)
Former	170 (37%)
Never	243 (53%)
Hypertension	291 (61%)
Hyperlipidemia	181 (38%)
Diabetes mellitus	83 (17%)
Coronary artery disease	62 (13%)
Atrial fibrillation	44 (9%)
Prior stroke	16 (3%)
Congestive heart failure	34 (7%)
Chronic obstructive pulmonary disease	37 (8%)
Chronic kidney disease	22 (5%)
Prior pulmonary embolism	37 (8%)
Prior deep vein thrombosis	42 (9%)
Active malignancy	163 (34%)
Surgery within 90 days	81 (17%)
Hospitalization within 90 days	129 (27%)
Medications prior to pulmonary embolism	
Anti-platelet	152 (32%)
Anticoagulation	44 (9%)

code diagnosis for PE, of which 477 (63.0 ± 16.2 years, 47% male) had an acute PE, CT images available for review, and a TTE within the designated time frame (Table 1). The mean time intervals between CT diagnosis of PE and performance of the ECG and TTE are summarized in Table 2. Sixty-one patients (13%) had 1 or more adverse events (Table 2). Mortality attributable to a PE was low in those with low-risk PE (1 of 59, 2%) and intermediate-risk PE (7 of 372, 2%) but was elevated in those with high-risk PE (11 of 46, 24%).

A total of 415 patients (87%) had an ECG available for review in the designated time frame. The presence of S1Q3T3 was the only ECG marker associated with adverse events (OR 2.5, confidence interval [CI] 1.3 to 4.7, p = 0.004) (Table 3). However, when the 3 ECG parameters were analyzed as a

Table 2
Timing of testing and pulmonary embolism characteristics and outcomes

Variable	(N = 477*)
Computed tomography to echocardiography timing (hours)	
Mean	16.3 ± 14.9
-24 to <0	68 (14%)
0 to ≤24	289 (61%)
>24 to 48	120 (25%)
Computed tomography to electrocardiography timing (hours) (N = 415)	
Mean	-1.1 ± 8.2
-24 to <0	294 (71%)
0 to ≤24	117 (28%)
>24 to 48	4 (1%)
Most proximal clot location on computed tomography	
Central (saddle or main pulmonary artery)	166 (35%)
Lobar	115 (24%)
Segmental	141 (27%)
Subsegmental	54 (11%)
Right Atrial/Right Ventricular Thrombus	4 (1%)
Concomitant deep vein thrombosis	184 (40%)
Pulmonary embolism clinical severity	
Low	59 (12%)
Intermediate	372 (78%)
High	46 (10%)
Elevated troponin† (N = 367)	76 (21%)
Anticoagulation	457 (96%)
Inferior vena cava filter	80 (17%)
Intubated	47 (10%)
Adverse events	
Vasopressor support	32 (7%)
Systemic thrombolysis	22 (5%)
Catheter-directed thrombolysis	3 (1%)
Catheter-directed thrombectomy	3 (1%)
Surgical embolectomy	1 (0.2%)
Overall 30-day mortality	41 (9%)
Pulmonary embolism-related mortality	19 (4%)
Advanced therapy, vasopressor support, and/or pulmonary embolism-related mortality	61 (13%)

Values are mean ± SD or n (%).
* N = 477 unless otherwise specified.
† Troponin T > 0.10 ng/ml.

Table 3
Electrocardiographic, computed tomographic, and echocardiographic parameters of right ventricular strain and adverse outcomes

Parameter	N	Present	Present + Adverse Event	OR (CI)	p-value
Electrocardiogram					
S1Q3T3	415	72 (17%)	18	2.5 (1.3–4.7)	0.004
Precordial T wave inversions	415	120 (29%)	21	1.4 (0.8–2.7)	0.18
Right bundle branch block	415	35 (8%)	5	1.0 (0.4–2.8)	0.96
Any positive electrocardiographic parameter	415	166 (40%)	31	1.9 (1.1–3.3)	0.03
Computed Tomogram					
Right ventricular-left ventricular ratio ≥ 0.9	473	326 (69%)	48	1.9 (1.0–3.8)	0.05
Right ventricular-left ventricular ratio ≥ 1.0	473	244 (52%)	43	2.7 (1.5–4.8)	<0.001
Echocardiogram					
Right ventricular-left ventricular ratio ≥ 0.9	431	246 (57%)	35	1.5 (0.8–2.8)	0.162
Right ventricular-left ventricular ratio ≥ 1.0	431	187 (43%)	32	2.2 (1.2–3.9)	0.009
Tricuspid annular plane systolic excursion < 16 mm	429	115 (27%)	28	4.1 (2.2–7.4)	<0.001
At least mild right ventricular hypokinesis	455	186 (41%)	42	4.9 (2.6–9.2)	<0.001
At least moderate right ventricular hypokinesis	455	94 (21%)	29	5.3 (3.0–9.5)	<0.001
McConnell's sign	450	63 (14%)	17	3.4 (1.8–6.5)	<0.001
Tricuspid annular plane systolic excursion < 16 mm and/or RV/LV ratio ≥ 1.0	427	236 (55%)	40	2.8 (1.5–5.4)	0.002
Elevated Troponin*	367	76 (21%)	24	3.7 (2.0–6.9)	<0.001

Values as n (%).
* Considered elevated if >0.10 ng/ml.

group, any ECG evidence of RV strain was associated with adverse events (OR 1.9, CI 1.1 to 3.3, p = 0.03). The presence of sinus tachycardia was not significantly associated with adverse events (OR 1.5, CI 0.89 to 2.6, p = 0.12). Neither ST elevation in aVR (3 patients, OR 3.1, CI 0.3 to 34.9, p = 0.38) nor ST elevation in V_1 (5 patients, OR 1.5, CI 0.2 to 14.1, p = 0.70) were associated with adverse events. On CT, an RV/LV diameter ratio was measured in 473 patients (99%) (Table 3). The OR of an adverse event was 1.9 for an RV/LV diameter ratio ≥0.9 (CI 1.0 to 3.8, p = 0.05) and 2.7 for an RV/LV diameter ratio ≥1.0 (CI 1.5 to 4.8, p = 0.001).

On TTE, an RV/LV diameter ratio could be measured in 431 patients (90%). Image quality was not sufficient in the remainder. The OR was only significant when utilizing the ≥1.0 threshold (2.2, CI 1.2 to 3.9, p = 0.009). The remainder of TTE parameters were also individually associated with adverse events (Table 3). More severe abnormal values of each parameter had similar associations with adverse events (TAPSE <12 mm: OR 3.2, CI 1.5 to 7.1, p = 0.004; RV/LV diameter ratio ≥1.5: OR 3.0, CI 1.6 to 5.5, p = < 0.001; severe RV hypokinesia: OR 3.3, 1.2 to 8.8, p = 0.02). When including all parameters of RV strain assessed on TTE to a multivariable logistic regression model, only a depressed TAPSE was associated with adverse events (OR 2.7, CI 1.2 to 5.7, p = 0.01).

In the 368 patients who had RV strain assessment by all 3 modalities (ECG, CT, TTE), 50 (13.6%) experienced an adverse event. Increased risk was only seen in those patients who had evidence of RV strain on all three modalities (OR 4.6, CI 1.8 to 11.3, p <0.001) (Tables 4 and 5). In the 295 patients with an intermediate-risk PE, there was a trend toward the association of RV strain present on all three modalities and adverse events (OR 3.6, CI 0.9 to 21.3, p = 0.06) (Table 5).

Troponin was measured in a subset of patients (367; 77%) and was elevated in 76 patients (21%). An elevated troponin was associated with an increased risk of adverse events (OR 3.7, CI 2.0 to 6.9, p <0.001). Of those patients with a troponin and the 3 modes of RV assessment evaluated, the odds of an adverse event was only elevated in those with positive RV strain on all three modalities and a positive troponin (OR 8.8, CI 2.8 to 28.1, p <0.001) (Table 6). This was also true of the subset of patients presenting with an intermediate-risk PE (OR 11.1, CI 1.2 to 103.8, p = 0.04) (Table 6).

Table 4
Risk of adverse event based on combination of evidence of right ventricular strain

Parameter*	Number† (N = 368)	Positive + Adverse Event (%) (N = 50)	OR (CI)	p-value
-ECG/-TTE/-CT	87	7 (14%)	Reference	
+ECG/-TTE/-CT	26	0 (0%)	NA‡	NA
-ECG/ + TTE/-CT	43	5 (10%)	1.5 (0.5–5.0)	0.51
-ECG/-TTE/ + CT	36	4 (8%)	1.4 (0.4–5.2)	0.59
+ECG/ + TTE/-CT	22	2 (4%)	1.1 (0.2–5.9)	0.87
+ECG/-TTE/ + CT	17	2 (4%)	1.5 (0.3–8.1)	0.62
-ECG/ + TTE/ + CT	53	6 (12%)	1.5 (0.5–4.6)	0.64
+ECG/ + TTE/ + CT	84	24 (48%)	4.6 (1.8–11.3)	<0.001

* + Electrocardiogram = any of the three ECG signs of right ventricular strain; +Echocardiogram = tricuspid annular systolic plane excursion <16 mm and/or right ventricular-to-left ventricular ratio ≥1.0; +Computed tomogram = right ventricular-to-left ventricular ratio ≥1.0.
CT = computed tomogram; ECG = electrocardiogram; TTE = transthoracic echocardiogram.
† Only patients with values available for all parameters above were included in the analysis.
‡ OR could not be calculated as no adverse events occurred.

Discussion

In this retrospective study of nearly 500 consecutive patients presenting with an acute PE, we identify the presence of RV strain on all three (ECG, CT, TTE) noninvasive methods

Table 5
(a)Additive value of positive right ventricular strain. (b)Additive value of positive right ventricular strain in intermediate-risk pulmonary embolism

a

Number of Modalities Positive*	Number† (N = 368)	Positive + Adverse Event (%) (N = 50)	OR (CI)	p-value
0	87	7 (14%)	Reference	
1	105	9 (18%)	1.1 (0.5–3.8)	0.90
2	92	10 (22%)	1.4 (0.5–3.8)	0.64
3	84	24 (48%)	4.6 (1.8–11.3)	<0.001

b

Number of Modalities Positive*	Number† (N = 295)	Positive + Adverse Event (%) (N = 28)	OR (CI)	p-value
0	51	2 (7%)	Reference	
1	89	7 (25%)	2.1 (0.4–10.5)	0.37
2	90	9 (32%)	2.7 (0.6–13.1)	0.21
3	65	10 (36%)	3.6 (0.93–21.3)	0.06

* + ECG = any of the three signs of right ventricular strain; +TTE = tricuspid annular systolic plane excursion <16 mm and/or right ventricular-to-left ventricular ratio ≥1.0; +CT = right ventricular-to-left ventricular ratio ≥1.0.

† Only patients with values available for all parameters above were included in the analysis.

Table 6
(a)Troponin plus right ventricular strain (b) Troponin plus right ventricular strain in intermediate-risk pulmonary embolism

a

Number of Modalities Positive for Right Ventricular Strain	Number* (N = 293)	Positive + Adverse Event (%) (N = 47)	OR (CI)	p-value
0 (-) troponin	52	5 (11%)	Reference	
0 (+) troponin	10	1 (2%)	1.0 (0.1–10.0))	0.97
1 (-) troponin	73	6 (13%)	0.8 (0.2–2.9)	0.79
1 (+) troponin	11	2 (4%)	2.1 (0.3–12.5)	0.42
2 (-) troponin	57	6 (13%)	1.1 (0.3–3.9)	0.86
2 (+) troponin	14	4 (9%)	3.8 (0.9–16.5)	0.08
3 (-) troponin	45	8 (17%)	2.0 (0.6–6.7)	0.25
3 (+) troponin	31	15 (32%)	8.8 (2.8–28.1)	<0.001

b

Number of Modalities Positive for Right Ventricular Strain	Number* (N = 240)	Positive + Adverse Event (%) (N = 27)	OR (CI)	p-value
0 (-) troponin	32	1 (4%)	Reference	
0 (+) troponin	9	1 (4%)	3.9 (0.2–68.9)	0.36
1 (-) troponin	61	4 (15%)	2.2 (0.2–20.3)	0.50
1 (+) troponin	10	2 (7%)	7.7 (0.6–96.7	0.11
2 (-) troponin	57	6 (22%)	3.6 (0.4–31.7)	0.24
2 (+) troponin	13	3 (11%)	9.3 (0.9–99.8)	0.07
3 (-) troponin	39	5 (19%)	4.6 (0.5–41.2)	0.18
3 (+) troponin	19	5 (19%)	11.1 (1.2–103.8)	0.04

* Only patients with values available for electrocardiogram, tricuspid annular plane systolic excursion, right ventricular-to-left ventricular diameter ratio on echocardiography and computed tomography, along with troponin value were included in the analysis.

as the best marker for an elevated risk of an adverse outcome. The addition of troponin to the assessment of RV strain further risk-stratified PE patients, including those presenting with an intermediate-risk PE.

Previous literature suggests there is a correlation between ECG and TTE or CT evidence of RV strain,[15,26,27] and that CT and TTE similarly predict adverse outcomes.[14] There is minimal evidence regarding the potential additive value of ECG, CT, and TTE. Dudzinski et al reviewed 104 patients with both a CT and a TTE performed and found higher rates of clinical deterioration in patients with RV strain on both compared with either method alone.[16] Our data support this smaller series.

In an attempt to improve risk stratification, there have been analyses showing the utility of an elevated troponin to predict adverse events,[28] as was also seen in our study. Elevated troponin, in addition to imaging evidence of RV strain, has been shown to further delineate risk[13] and has been incorporated into the guidelines for risk stratification.[4] Kukla et al demonstrated a trend toward an association between PE mortality and patients with TTE evidence of RV strain, an elevated troponin, and ischemic ECG changes.[18]

There are no previous studies describing the risk of adverse events with RV strain in ECG, CT, and TTE, along with troponin in the same patient cohort. We demonstrate that in patients with all 3 methods performed, risk was only elevated in patients with RV strain present in all 3 methods. Patients with RV strain on all 3 methods represent a higher risk group as these patients may have more significant RV dysfunction, thus displaying strain regardless of method. Another potential explanation of this finding is that these patients have RV strain over a greater period of time as, expectedly, most patients had an ECG before CT, whereas a TTE was often performed after PE diagnosis.

Our subanalysis of patients with intermediate-risk PE also found a trend toward increased risk only when RV strain was present in all 3 methods. This analysis was limited by a lower event rate compared with the cohort as a whole. However, when including troponin, only those patients with a positive troponin and RV strain present in all 3 methods had an elevated risk of adverse events in both the total cohort of patients presenting with PE and in the subgroup with an intermediate-risk PE.

The selection of appropriate patients in whom to pursue therapy beyond anticoagulation in the setting of acute PE remains a difficult clinical decision given the significant risks that these treatments possess, particularly in those that initially present with hemodynamic stability.[7,8] The guidelines offer some assistance in these challenging decisions but also note the limitations of any one factor in determining which patients may benefit from such treatment.[4,29] In addition to clinical assessment, our findings suggest the incorporation of multiple modes of evaluation of RV strain along with troponin is preferred to utilizing 1 or 2 of these methods in isolation and may improve risk stratification and aid in the complex decision making required for patients with acute PE.

Although large and consecutive, our study is retrospective. Thus, analyses were limited to data available in the medical record, and not all patients had an available ECG, troponin, or adequate CT and TTE images. CT examinations were acquired on different CT scanners; however, similar widely accepted clinical protocols were applied. The timing

of the ECG and TTE relative to CT varied among patients, but the distribution is representative of real-world acquisition of these studies. Selection bias of particular patients with acute PE is likely present in our cohort, as it represented only a subset of patients hospitalized with PE. Very low-risk patients may have been less likely to have a TTE performed, and very high-risk patients (e.g., patients in active cardiac arrest) may not have survived long enough for a TTE to be acquired. Although clinical patient features and vital signs are important in the assessment of patients with PE, we did not have sufficiently accurate data available to incorporate clinical risk scores or vital signs outside of the differentiation of high-risk, intermediate-risk, and low-risk clinical severity.

In patients with acute PE, the presence of RV strain on ECG, CT, and TTE identifies a patient cohort with increased risk of an adverse event than if present on only 1 or 2 of the methods. The addition of troponin further aids in discriminating high-risk patients in the presence of RV strain, including in the subset of patients with intermediate-risk PE.

Disclosures

All authors have no conflicts of interests to disclose.

1. Huang W, Goldberg RJ, Anderson FA, Kiefe CI, Spencer FA. Secular trends in occurrence of acute venous thromboembolism: the Worcester VTE study (1985–2009). *Am J Med* 2014;127:829–839.
2. Cohen AT, Agnelli G, Anderson FA, Arcelus JI, Bergqvist D, Brecht JG, Greer IA, Heit JA, Hutchinson JL, Kakkar AK, Mottier D, Oger E, Samama M-M, Spannagl M. Venous thromboembolism in Europe. The number of VTE events and associated morbidity and mortality. *Thromb Haemost* 2007;98:756–764.
3. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Das SR, de Ferranti S, Despres JP, Fullerton HJ, Howard VJ, Huffman MD, Isasi CR, Jimenez MC, Judd SE, Kissela BM, Lichtman JH, Lisabeth LD, Liu S, Mackey RH, Magid DJ, McGuire DK, Mohler ER 3rd, Moy CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichol G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Rosamond W, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Woo D, Yeh RW, Turner MB. Heart disease and stroke statistics-2016 update: a report from the American Heart Association. *Circulation* 2016;133:e38–e360.
4. Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galie N, Gibbs JS, Huisman MV, Humbert M, Kucher N, Lang I, Lankeit M, Lekakis J, Maack C, Mayer E, Meneveau N, Perrier A, Pruszczyk P, Rasmussen LH, Schindler TH, Svitil P, Vonk Noordegraaf A, Zamorano JL, Zompatori M. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J* 2014;35:3033–3069.
5. Chatterjee S, Chakraborty A, Weinberg I, Kadakia M, Wilensky RL, Sardar P, Kumbhani DJ, Mukherjee D, Jaff MR, Giri J. Thrombolysis for pulmonary embolism and risk of all-cause mortality, major bleeding, and intracranial hemorrhage: a meta-analysis. *JAMA* 2014;311:2414–2421.
6. Meyer G, Vicaut E, Danays T, Agnelli G, Becattini C, Beyer-Westendorf J, Bluhmki E, Bouvaist H, Brenner B, Couturaud F, Dellas C, Empen K, Franca A, Galie N, Geibel A, Goldhaber SZ, Jimenez D, Kozak M, Kupatt C, Kucher N, Lang IM, Lankeit M, Meneveau N, Pacouret G, Palazzini M, Petris A, Pruszczyk P, Rugolotto M, Salvi A, Schellong S, Sebbane M, Sobkowicz B, Stefanovic BS, Thiele H, Torbicki A, Verschuren F, Konstantinides SV, PEITHO Investigators. Fibrinolysis for patients with intermediate-risk pulmonary embolism. *N Engl J Med* 2014;370:1402–1411.
7. Piazza G, Hohlfelder B, Jaff MR, Ouriel K, Engelhardt TC, Sterling KM, Jones NJ, Gurley JC, Bhatheja R, Kennedy RJ, Goswami N, Natarajan K, Rundback J, Sadiq IR, Liu SK, Bhalla N, Raja ML, Weinstock BS, Cynamon J, Elmasri FF, Garcia MJ, Kumar M, Ayerdi J, Soukas P, Kuo W, Liu PY, Goldhaber SZ. A prospective, single-arm, multicenter trial of ultrasound-facilitated, catheter-directed, low-dose fibrinolysis for acute massive and submassive pulmonary embolism: the SEATTLE II study. *JACC Cardiovasc Interv* 2015;8:1382–1392.
8. Fiumara K, Kucher N, Fanikos J, Goldhaber SZ. Predictors of major hemorrhage following fibrinolysis for acute pulmonary embolism. *Am J Cardiol* 2006;97:127–129.
9. Shopp JD, Stewart LK, Emmett TW, Kline JA. Findings from 12-lead electrocardiography that predict circulatory shock from pulmonary embolism: systematic review and meta-analysis. *Acad Emerg Med* 2015;22:1127–1137.
10. Schoepf UJ, Kucher N, Kipfmueller F, Quiroz R, Costello P, Goldhaber SZ. Right ventricular enlargement on chest computed tomography: a predictor of early death in acute pulmonary embolism. *Circulation* 2004;110:3276–3280.
11. Pruszczyk P, Goliszek S, Lichodziejewska B, Kostrubiec M, Ciurzynski M, Kurnicka K, Dzikowska-Diduch O, Palczewski P, Wyzgal A. Prognostic value of echocardiography in normotensive patients with acute pulmonary embolism. *JACC Cardiovasc Imaging* 2014;7:553–560.
12. Stein PD, Matta F, Sabra MJ, Treadaway B, Vijapura C, Warren R, Joshi P, Sadiq M, Kofoed JT, Hughes P, Chabala SD, Keyes DC, Kakish E, Hughes MJ. Relation of electrocardiographic changes in pulmonary embolism to right ventricular enlargement. *Am J Cardiol* 2013;112:1958–1961.
13. Stein PD, Matta F, Janjua M, Yaekoub AY, Jaweesh F, Alrifai A. Outcome in stable patients with acute pulmonary embolism who had right ventricular enlargement and/or elevated levels of troponin I. *Am J Cardiol* 2010;106:558–563.
14. George E, Kumamaru K, Ghosh N, Quesada C, Wake N, Bedayat A, Dunne R, Saboo S, Khandelwal A, Hunsaker A, Rybicki F, Gerhard-Herman M. Computed tomography and echocardiography in patients with acute pulmonary embolism: Part 2. *J Thorac Imaging* 2014;29:7–12.
15. Hariharan P, Dudzinski DM, Okechukwu I, Takayesu JK, Chang Y, Kabrhel C. Association between electrocardiographic findings, right heart strain, and short-term adverse clinical events in patients with acute pulmonary embolism. *Clin Cardiol* 2015;38:236–242.
16. Dudzinski DM, Hariharan P, Parry BA, Chang Y, Kabrhel C. Assessment of right ventricular strain by computed tomography versus echocardiography in acute pulmonary embolism. *Acad Emerg Med* 2017;24:337–343.
17. Kucher N, Walpoth N, Wustmann K, Noveanu M, Gertsch M. Qr in v1 – an ECG sign associated with right ventricular strain and adverse clinical outcome in pulmonary embolism. *Eur Heart J* 2003;24:1113–1119.
18. Kukla P, McIntyre WF, Fijorek K, Krupa E, Mirek-Bryniarska E, Jastrzebski M, Bryniarski KL, Zajchowski W, Bryniarski L, Baranchuk A. Use of ischemic ECG patterns for risk stratification in intermediate-risk patients with acute PE. *Am J Emerg Med* 2014;32:1248–1252.
19. Daniel KR, Courtney DM, Kline JA. Assessment of cardiac stress from massive pulmonary embolism with 12-lead ECG. *Chest* 2001;120:474–481.
20. Kukla P, McIntyre WF, Fijorek K, Mirek-Bryniarska E, Bryniarski L, Krupa E, Jastrzebski M, Bryniarski KL, Zhong-qun Z, Baranchuk A. Electrocardiographic abnormalities in patients with acute pulmonary embolism complicated by cardiogenic shock. *Am J Emerg Med* 2014;32:507–510.
21. Trujillo-Santos J, den Exter PL, Gomez V, Del Castillo H, Moreno C, Van der Hulle T, Husiman MV, Monreal M, Yusen RD, Jimenez D. Computed tomography-assessed right ventricular dysfunction and risk stratification of patients with acute non-massive pulmonary embolism: systematic review and meta-analysis. *J Thromb Haemost* 2013;11:1823–1832.
22. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, Solomon SD, Louie EK, Schiller NB. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr* 2010;23:685–713.
23. Khemasuwan D, Yingchoncharoen T, Tunsupon P, Kusunose K, Moghekar A, Klein A, Tonelli AR. Right ventricular echocardiographic parameters are associated with mortality after acute pulmonary embolism. *J Am Soc Echocardiogr* 2015;28:355–362.
24. Kucher N, Rossi E, De Rosa M, Goldhaber SZ. Prognostic role of echocardiography among patients with acute pulmonary embolism and

a systolic arterial pressure of 90 mm Hg or higher. *Arch Intern Med* 2005;165:1777–1781.
25. McConnell MV, Solomon SD, Rayan ME, Come PC, Goldhaber SZ, Lee RT. Regional right ventricular dysfunction detected by echocardiography in acute pulmonary embolism. *Am J Cardiol* 1996;78:469–473.
26. Keller K, Beule J, Balzer JO, Dippold W. Right bundle branch block and SIQIII-type patterns for risk stratification in acute pulmonary embolism. *J Electrocardiol* 2016;49:512–518.
27. Punukollu G, Gowda RM, Vasavada BC, Khan IA. Role of electrocardiography in identifying right ventricular dysfunction in acute pulmonary embolism. *Am J Cardiol* 2005;96:450–452.
28. Becattini C, Vedovati MC, Agnelli G. Prognostic value of troponins in acute pulmonary embolism: a meta-analysis. *Circulation* 2007;116:427–433.
29. Kearon C, Akl EA, Ornelas J, Blaivas A, Jimenez D, Bounameaux H, Huisman M, King CS, Morris TA, Sood N, Stevens SM, Vintch JR, Wells P, Woller SC, Moores L. Antithrombotic therapy for VTE disease: chest guideline and expert panel report. *Chest* 2016;149:315–352.