Increased Sensitivity of Focused Cardiac Ultrasound for Pulmonary Embolism in Emergency Department Patients With Abnormal Vital Signs

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ABSTRACT

Background: Focused cardiac ultrasound (FOCUS) is insensitive for pulmonary embolism (PE). Theoretically, when a clot is large enough to cause vital sign abnormalities, it is more likely to show signs of right ventricular dysfunction on FOCUS, although this has not been well quantified. A rapid bedside test that could quickly and reliably exclude PE in patients with abnormal vital signs could be of high utility in emergency department (ED) patients. We hypothesized that in patients with tachycardia or hypotension, the sensitivity of FOCUS for PE would increase substantially.

Methods: We performed a prospective observational multicenter cohort study involving a convenience sample of patients from six urban academic EDs. Patients suspected to have PE with tachycardia (heart rate [HR] ≥ 100 beats/min) or hypotension (systolic blood pressure [sBP] < 90 mm Hg) underwent FOCUS before computed tomography angiography (CTA). FOCUS included assessment for right ventricular dilation, McConnell's sign, septal flattening, tricuspid regurgitation, and tricuspid annular plane systolic excursion. If any of these were abnormal, FOCUS was considered positive, while if all were normal, FOCUS was considered negative. We a priori planned a subgroup analysis of all patients with a HR ≥ 110 beats/min (regardless of their sBP). We then determined the diagnostic test characteristics of FOCUS for PE in the entire patient population and in the predefined subgroup, based on CTA as the criterion standard. Inter-rater reliability of FOCUS was determined by blinded review of images by an emergency physician with fellowship training in ultrasound.

Results: A total of 143 subjects were assessed for enrollment and 136 were enrolled; four were excluded because they were non–English-speaking and three because of inability to obtain any FOCUS windows. The mean (±SD) age of enrolled subjects was 56 (±7) years, mean (±SD) HR was 114 (±12) beats/min, and 37 (27.2%) subjects were diagnosed with PE on CTA. In all subjects, FOCUS was 92% (95% confidence interval [CI] = 78% to 98%) sensitive and 64% specific (95% CI = 53% to 73%) for PE. In the subgroup of 98 subjects with a HR ≥ 110 beats/min, FOCUS was 100% sensitive (95% CI = 88% to 100%) and 63% specific (95% CI = 51% to 74%) for PE. There was substantial interobserver agreement for FOCUS (κ = 1.0, 95% CI = 0.31 to 1.0).

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Conclusions: A negative FOCUS examination may significantly lower the likelihood of the diagnosis of PE in most patients who are suspected of PE and have abnormal vital signs. This was especially true in those patients with a HR ≥ 110 beats/min. Our results suggest that FOCUS can be an important tool in the initial evaluation of ED patients with suspected PE and abnormal vital signs.

The evaluation of a patient with chest pain or dyspnea in the emergency department (ED) often prompts the emergency physician (EP) to consider the diagnosis of pulmonary embolism (PE). A rapid bedside test that could quickly and reliably exclude PE in patients with tachycardia or hypotension could be of high utility in the management of these ED patients. Focused cardiac ultrasound (FOCUS) can be used to assess for signs of right ventricular dysfunction (RVD) due to PE. The routine application of FOCUS in all patients suspected of PE is not recommended as FOCUS is relatively insensitive for PE. A recent systematic review and meta-analysis concluded that the overall sensitivity of FOCUS for PE is 53% (95% confidence interval [CI] = 45% to 61%).[1] However, ED patients with tachycardia who have a PE are more likely to show signs of RVD on FOCUS.[2] RVD occurs in between 30% and 70% of patients with PE, and the absence of RVD in patients with hemodynamic compromise makes PE an unlikely etiology.[2,3] EP-performed FOCUS has been shown to be effective in detecting findings of RVD.[2,4–8] Typical findings of RVD on FOCUS include right ventricular dilation, the presence of McConnell's sign, septal flattening, and tricuspid regurgitation (with regurgitant jet velocity on continuous-wave Doppler > 2.6 m/sec).[9]

Recent literature has demonstrated that a less commonly utilized measure of RVD known as tricuspid annular plane systolic excursion (TAPSE) is more sensitive for the diagnosis of PE than other signs, is relatively easy to perform, and may be more reproducible as an objective measurement.[2] TAPSE assesses for RVD by using M-mode to measure the dynamic movement of the tricuspid valve annulus over the course of a contraction (Figure 1).[10] Any value over 1.7 cm is typically considered normal, while any value below 1.7 cm is considered indicative of RVD.[2] TAPSE correlates well with other modalities that measure RVD[11–18] and has been shown to have high degrees of inter-rater reliability among cardiologists and EPs with experience in FOCUS.[2,19]

Our group recently described the diagnostic utility of TAPSE for PE by EPs.[2] With a testing threshold of 2.0 cm (compared to the 1.7 cm threshold most commonly found in the literature), TAPSE was 72% (95% CI = 38% to 74%) sensitive for PE. However, we conducted a post hoc subgroup analysis of 17 patients that presented to the ED with tachycardia (heart rate [HR] ≥ 100 beats/min) and/or hypotension (systolic blood pressure [sBP] < 90 mm Hg) and found that FOCUS was 100% (95% CI = 80% to 100%) sensitive for PE and the sensitivity of TAPSE for PE was 94% (95% CI = 71% to 99%) in this group. If FOCUS is shown to be sensitive in this population, it may allow for the exclusion of PE in patients who are too unstable to leave the ED for definitive imaging, who are in a resource-limited practice environment without access to computed tomography angiography (CTA), or who have a contraindication to CTA such as contrast allergy or acute kidney injury.

The objectives of the current study were to determine the diagnostic test characteristics of FOCUS and its components for PE in patients with tachycardia and/or hypotension. We hypothesized that in patients with a HR ≥ 100 beats/min or sBP < 90 mm Hg, the sensitivity of FOCUS would be over 90%. Additionally, we planned a subgroup analysis of patients with a HR ≥ 110 beats/min a priori and hypothesized

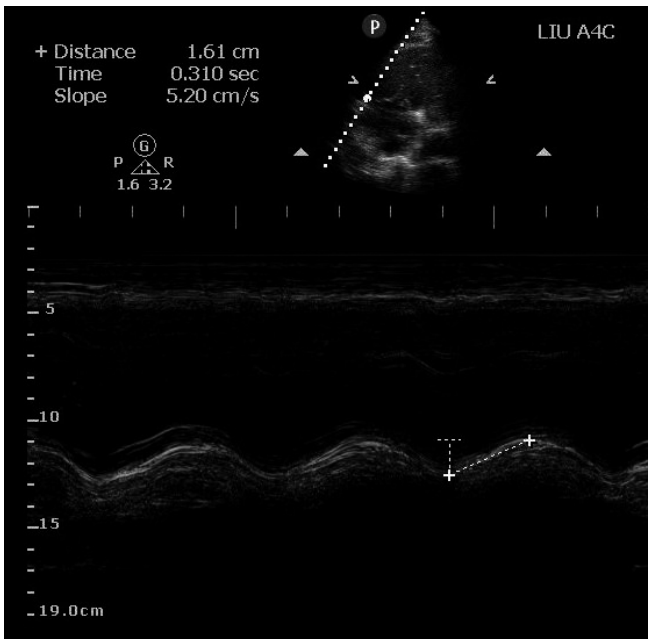

Figure 1. Measuring TAPSE. TAPSE is measured in the apical four-chamber view with the M-mode cursor placed over the lateral tricuspid valve annulus. This creates a wave form, which can then be measured from trough to peak. TAPSE = tricuspid annular plane systolic excursion.

that the sensitivity of FOCUS would be over 95% in this subgroup.

METHODS

Study Design

We performed a prospective observational multicenter cohort study involving a convenience sample of ED patients undergoing evaluation for suspected PE with CTA who underwent FOCUS. Enrollment took place from April 2016 to November 2018. This study was approved by the institutional review board (IRB) and conducted in accordance with the STARD guidelines for reporting diagnostic accuracy studies.[20]

Study Setting and Population

Subjects were recruited from six urban academic medical centers with annual ED visits ranging from 60,000 to 120,000 annually. Subjects were enrolled when an EP or study investigator trained in obtaining FOCUS was available. Subjects were eligible for enrollment if they were adults (18 years of age or older) with tachycardia and/or hypotension undergoing CTA for evaluation of possible PE in the ED. Investigators initially identified potential subjects by scanning the ED track board for patients undergoing CTA with abnormal vital signs to evaluate for PE. Investigators then confirmed the abnormal vital signs immediately prior to the FOCUS examination at the bedside. If a subject was enrolled due to hypotension alone, investigators measured their blood pressure twice and the subject was only enrolled if both measurements were believed to be reliable and were below 90 mm Hg. Prisoners, wards of the state, non–English-speaking patients, and those where investigators could not obtain any echocardiographic data due to technical challenges were excluded.

Study Protocol

Study personnel included seven ultrasound fellowship–trained attending EPs, three emergency medicine resident physicians, and three medical students. Subjects were primarily enrolled when study personnel were working clinically in the ED. At the primary study site, three medical students who were trained in the acquisition of FOCUS worked on a part-time basis in the ED to enroll subjects by screening the ED track board for patients who were undergoing CTA for suspected PE. When a potential subject was identified, subjects were then assessed for enrollment eligibility, and if deemed eligible, written consent was obtained. Vital signs were assessed by the investigator at the time of the FOCUS examination. Three patients were unable to provide consent at the time of enrollment due to the severity of their illness and provided consent later in their hospital stay, as permitted by the IRB.

All personnel received standardized training that consisted of a brief video and a 1-hour didactic meeting to ensure that standardized images were being obtained. Two of the resident physicians underwent an additional didactic session conducted by an ultrasound fellowship–trained EP. Residents later performed supervised practice examinations until the ultrasound fellowship–trained EP was satisfied that they could reliably perform all the components of FOCUS prior to enrolling patients in the study. These residents were PGY-3 in emergency medicine and had prior ultrasound experience consistent with their level of residency training. The third resident, the primary author, already had significant experience in FOCUS (including TAPSE) and did not undergo additional training for study purposes.[2] The three medical students underwent a 1-hour didactic and 1-hour hands-on training session by the primary author. Medical students were in their third year of medical school and did not have significant experience in bedside ultrasound prior to becoming involved in this study. Each student then completed 20 FOCUS examinations with feedback under the supervision of the primary author prior to enrolling patients in the study.

Investigators performed and interpreted FOCUS at the bedside during the subject's ED stay, if possible, prior to the patient undergoing CTA. If performed after CTA, echocardiographers were blinded to CTA results. Investigators conducted the FOCUS examination using four echocardiographic windows: the parasternal long, parasternal short, apical four chamber, and subxiphoid. Components of FOCUS included the measurement of TAPSE and evaluation for other measures of RVD, defined as right ventricular enlargement (visual appearance of the right ventricle being equal to or greater in size than the left ventricle), septal flattening (flattening of the interventricular septum typically seen on parasternal short axis, sometimes referred to as the "D-sign"), tricuspid regurgitation, and McConnell's sign (hypokinesis of the right ventricle with apical sparing). While some degree of tricuspid regurgitation can be normal (if measured on continuous wave Doppler at less than 2.6 cm/sec), for the purposes of this study and to simplify FOCUS acquisition for novice users, any presence of tricuspid

regurgitation viewed on color doppler was considered abnormal. The normal testing threshold for TAPSE when used for the prognosis of disease was 1.7 cm.[2] This study defined an abnormal TAPSE as <2.0 cm because prior research by the primary author that employed receiver operating characteristic curve analysis demonstrated that a higher testing threshold of 2.0 cm provided increased sensitivity for PE, while maintaining moderate specificity.[2] TAPSE was obtained in the apical four-chamber view by placing the M-mode cursor along the lateral tricuspid valve annulus and measuring the change in height of the resultant tracing from trough to peak (Figure 1).[10]

If any of the components of FOCUS were abnormal, then the FOCUS examination was considered positive, while if all components of FOCUS were normal, the FOCUS examination was considered negative. The criterion standard for diagnosing PE was the presence of a filling defect on CTA consistent with PE as reported by radiology. Radiologists were not aware of FOCUS results at any time. All patients who were enrolled underwent CTA in the ED.

Inter-rater reliability of right ventricular enlargement, septal flattening, tricuspid regurgitation, and McConnell's sign were determined by blinded review of images by the site principal investigator in 104 of 136 patients. If there was a disagreement between raters, the interpretation initially made at the bedside was used for statistical analysis to maintain study generalizability. Inter-rater reliability of TAPSE could not be conducted in this manner because TAPSE must be measured at the bedside. In a subset of eight patients, two investigators performed FOCUS on the same patient to determine inter-rater reliability of the entire FOCUS examination and TAPSE. They were blinded to each other's results. These patients were selected based on convenience; if two study investigators were present at the time of enrollment, then each performed FOCUS. Selection was not related to image quality, the clinical condition of the patient, or any other criteria.

Measures

The primary outcome measure was the sensitivity of FOCUS for PE in both predescribed patient populations: 1) those with a HR $\geq$ 100 beats/min or sBP < 90 mm Hg (n = 136) and 2) those with a HR $\geq$ 110 beats/min (n = 98). Secondary outcomes include the specificity and likelihood ratios of FOCUS for PE in each population. Additional secondary outcome measures include the diagnostic test characteristics for PE of the individual component parts of FOCUS.

Data Analysis

All data analyses were performed using Stata 15.1 (StataCorp) by a statistician with a doctorate in statistics and significant work experience. Patient and demographic characteristics were tabulated for patients with and without PE. p-values were calculated using Student's t-tests for continuous variables and chi-square tests for categorical variables. For inter-rater agreement, Fleiss kappa values were calculated for two raters (first operator and second operator), using the Stata "kap" package. Kappa values were interpreted based on recommendations by Landis and Koch.[21] Diagnostic test characteristics of TAPSE and other measures of right heart strain were calculated using the Stata "diagt" package, both for all patients and for a subset of patients with a HR $\geq$ 110 beats/min. To determine sample size, we chose to conduct a power calculation to minimize the 95% CI for the sensitivity of FOCUS in the diagnosis of PE. For the width of the 95% CI to be 20% or less, the authors calculated that it would require 120 subjects, assuming a FOCUS sensitivity greater than 90%.

Some patients had missing data from the FOCUS examination. In some instances, this was because the data were not recorded, while in others, this was because investigators were unable to obtain the required echocardiographic windows. Patients with incompletely documented or recorded FOCUS examinations were still included in the data analysis for the diagnostic test characteristics of the entire FOCUS examination, as the FOCUS examination could still be tabulated as positive or negative based on incomplete data. For example, a patient may have had data recorded for right ventricular enlargement, TAPSE, septal flattening, and McConnell's sign, but nothing recorded for tricuspid regurgitation. In this example, it would still be possible to determine if the patient had a positive or negative FOCUS examination; however, presence or absence of tricuspid regurgitation would not contribute to that categorization, nor would this patient's data have been used to determine the individual diagnostic test characteristics for tricuspid regurgitation.

RESULTS

There were 143 patients that underwent CTA during the study period. Four were not eligible for enrollment

because they did not speak English, while three were excluded because personnel were unable to obtain any FOCUS windows (none of these subjects were diagnosed with a PE on CTA). There were 136 patients enrolled during the study period (Figure 2) and 37 (27.2%) were diagnosed as having a PE (Table 1). Of the 37 patients diagnosed with PE, six (16.2%) were in patients whose sBP was below 90 mm Hg, 28 (75.6%) were in normotensive patients who had evidence of RVD on FOCUS, and three (8.1%) were in normotensive patients without evidence of RVD on FOCUS. Patients diagnosed with a PE were more likely to be admitted to the hospital and had higher rates of admission to the step-down or intensive care unit (Table 1). Data depicting patient enrollment by site and sonographer level of training may be found in the Data Supplement S1 (available as supporting information in the online version of this paper, which is available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13774/full).

In patients with a HR ≥ 100 beats/min or a sBP < 90 mm Hg (n = 136), the sensitivity of FOCUS for PE was 92% (95% CI = 78% to 98%; Table 2). The most sensitive component of FOCUS for PE was TAPSE with a testing threshold of 2.0 cm, which was 88% sensitive (95% CI = 72% to 97%). The sensitivity of TAPSE when using the traditional testing threshold of 1.7 cm was 67% (95% CI = 48% to 82%). The sensitivity for other components of the FOCUS examination ranged from 35% to 51% (Table 2). FOCUS had an overall specificity of 64% (95% CI = 53% to 73%). The most specific component of FOCUS was McConnell's sign with 99% (95% CI = 94% to 100%) specificity. The specificity of other components of FOCUS ranged from 64% to 93% (Table 2).

In the subgroup of patients with a HR ≥ 110 (n = 98), the sensitivity of FOCUS for PE was 100% (95% CI = 88% to 100%; Table 3). The most sensitive component of FOCUS was TAPSE when using a testing threshold of 2.0 cm, which was 93% (95% CI = 75% to 99%) sensitive for PE. The sensitivity of TAPSE with the traditional threshold of 1.7 cm was 77% (95% CI = 56% to 91%).The sensitivity for other components of the FOCUS examination ranged from 36% to 57% (Table 3). FOCUS was 63% (95% CI = 51% to 74%) specific for PE in this subgroup. The most specific component of FOCUS was McConnell's sign with 100% (95% CI = 95% to 100%) specificity. The specificity of other components of FOCUS ranged from 63% to 93% (Table 3).

Inter-rater reliability for whether the FOCUS examination was found to be positive or negative by two separate sonographers was substantial with a kappa statistic of 1.0 (95% CI = 0.31 to 1.0). Inter-rater reliability of the components of the FOCUS examination was moderate to high with kappa statistics measuring as 0.61 (95% CI = 0.31 to 1.0) for TAPSE, 0.88 (95% CI = 0.69 to 1.0) for septal flattening, 0.89 (95% CI = 0.7 to 1.0) for right ventricular enlargement, 0.89 (95% CI = 0.7 to 1.0) for McConnell's sign, and 0.81 (95% CI = 0.64 to 1.0) for tricuspid regurgitation. Nine patients had missing data for

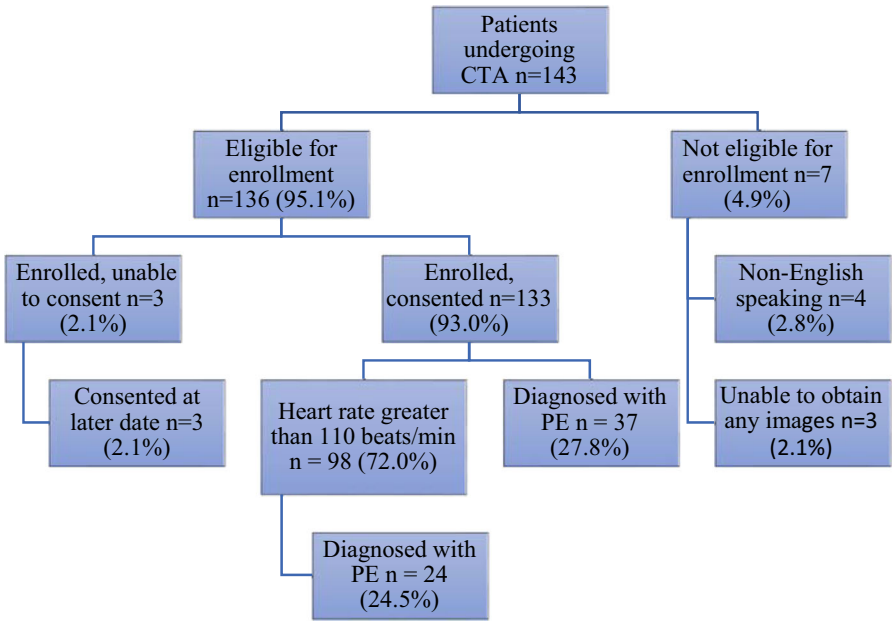

Figure 2. Patient enrollment flow diagram. CTA = Computed tomographic angiogram; PE = pulmonary embolism.

Table 1
Demographic and Clinical Characteristics of Enrolled Subjects by Disease Status

	All Subjects (N = 136)	PE Positive (n = 37)	PE Negative (n = 99)	p-value
Age (years), mean ± SD (range)	56 ± 17 (19–89)	58 ± 16 (24–85)	56 ± 17 (19–89)	0.56
Female	80 (59)	23 (62)	57 (58.0)	0.63
Comorbid conditions				
Congestive heart failure	11 (8.1)	1 (2.7)	10 (10.1)	0.16
COPD	25 (18.4)	6 (16.2)	19 (19.2)	0.69
Asthma	12 (8.8)	1 (2.7)	11 (11.1)	0.12
Pulmonary hypertension	3 (2.2)	0 (0.0)	3 (3.0)	0.28
PE risk factors				
Prior PE or DVT	31 (22.8)	11 (29.7)	20 (20.2)	0.24
Cancer within past 6 months	54 (39.7)	15 (40.5)	39 (39.4)	0.93
Clinical signs or symptoms of DVT	21 (15.4)	14 (37.8)	7 (7.1)	< 0.001
Disposition				
Discharged	17 (13)	0 (0)	17 (18.0)	0.01
Admit to floor	80 (63)	16 (48)	64 (69.0)	0.02
Admit to SDU/ICU	29 (23)	17 (52)	12 (12.0)	<0.01
LOS (days)	7.1 (±6.1)	6.0 (±3.4)	7.5 (±6.8)	0.58
ICU/SDU LOS (days)	2.6 (±1.9)	2.1 (±2.1)	3.1 (±1.7)	0.32
Vital signs				
HR (beats/min)	114.3 (±12.5)	116.2 (±13.2)	113.6 (±12.2)	0.47
sBP (mm Hg)	120.3 (±23.7)	117.9 (±27.7)	121.2 (±22.1)	0.65

Data are reported as n (%) or mean (±SD) unless otherwise reported.
COPD = chronic obstructive pulmonary disease; DVT = deep venous thrombosis; HR = heart rate; ICU = Intensive care unit; LOS = length of stay; PE = pulmonary embolism; SDU = step-down unit.

Table 2
Diagnostic Test Characteristics of FOCUS and Its Components for PE in Subjects With a HR ≥ 100 beats/min and/or sBP < 90 mm Hg (n = 136)

	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
FOCUS	92 (78–98)	64 (53–73)	2.5 (1.9–3.3)	0.13 (0.04–0.38)
TAPSE threshold (cm)				
2.0	88 (72–97)	73 (63–82)	3.3 (2.3–4.7)	0.17 (0.07–0.42)
1.7	66 (48–82)	85 (76–91)	4.5 (2.6–7.6)	0.39 (0.24–0.64)
RVE	51 (34–68)	86 (77–92)	3.6 (2.0–6.3)	0.57 (0.40–0.80)
Septal flattening*	43 (27–61)	93 (86–97)	5.9 (2.7–13.2)	0.61 (0.46–0.82)
TR	50 (26–74)	75 (62–86)	2.0 (1.1–3.8)	0.67 (0.41–1.08)
McConnell's sign†	35 (20–53)	99 (94–100)	33.7 (4.6–249)	0.66 (0.52–0.83)

FOCUS = focused cardiac ultrasound; HR = heart rate; PE = pulmonary embolism; RVE = right ventricular enlargement (appearance of right ventricle as being equal to or larger than the left ventricle); TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation (any regurgitant jet visualized on color Doppler).
*Abnormal flattening of the interventricular septum during systole.
†Visualization of hypokinesis of the right ventricle with apical sparing.

TAPSE, two for right ventricular enlargement, two for septal flattening, two for McConnell's sign, and 60 for tricuspid regurgitation.

DISCUSSION

Our results confirm that FOCUS is highly sensitive for PE in patient populations with abnormal vital signs who are suspected of having PE, especially in those with a HR ≥ 110 beats/min. A rapid bedside test that could reliably exclude or significantly lower the likelihood of PE at the time the history and physical examination is performed in ED patients with abnormal vital signs could be of significant utility. While CTA is the criterion standard for the diagnosis of PE in the ED, there are a variety of common

Table 3
Diagnostic Test Characteristics of FOCUS and Its Components for PE in Subjects With a HR ≥ 110

	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
FOCUS	100 (88–100)	63 (51–74)	2.7 (2.0–3.7)	Undefined
TAPSE threshold (cm)				
2.0	93 (75–99)	73 (60–83)	3.4 (2.3–5.1)	0.11 (0.03–0.40)
1.7	77 (56–91)	88 (78–95)	6.4 (3.2–12.6)	0.26 (0.13–0.53)
RVE	57 (37–76)	84 (73–92)	3.6 (1.9–6.7)	0.51 (0.32–0.79)
Septal flattening*	47 (28–66)	93 (84–98)	6.3 (2.5–16.0)	0.58 (0.41–0.82)
TR	47 (21–73)	75 (59–87)	1.9 (0.9–4.0)	0.71 (0.43–0.89)
McConnell's sign†	36 (19–56)	100 (95–100)	Undefined	0.64 (0.49–0.85)

FOCUS = focused cardiac ultrasound; HR = heart rate; PE = pulmonary embolism; RVE = right ventricular enlargement (appearance of right ventricle as being equal to or larger than the left ventricle); TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation (any regurgitant jet visualized on color Doppler).
*Abnormal flattening of the interventricular septum during systole.
†Visualization of hypokinesis of the right ventricle with apical sparing.

clinical situations that may limit its accessibility, including the evaluation of patients with acute kidney injury, those with a contrast allergy, patients who are too obese to fit in a CT scanner, patients who are too hemodynamically unstable to leave the ED, and those who live in a resource-limited setting where CTA may not be available (e.g., global or rural health facilities).

Our results suggest that CTA may not provide additional diagnostic information regarding PE in patients with abnormal vital signs and a normal FOCUS examination, although given the width of the reported 95% CIs (Tables 3and 4), further study in a larger cohort of patients is required before this can be said with certainty. In this scenario, a clinician may choose to further resuscitate a patient before attempting a potentially hazardous trip to radiology to obtain a CTA. Additionally, in patients with abnormal vital signs where confirmatory imaging is delayed due to a contrast allergy or acute kidney injury, an abnormal FOCUS examination may help the EP in their decision to begin anticoagulation earlier on a potentially unstable patient, since the early initiation of anticoagulation is associated with reduced mortality in patients with PE.[22]

There have been many studies in the literature that delineate the diagnostic test characteristics of the more typical components of the FOCUS examination for PE,[4,23,24] although many of these have not included TAPSE.[2] Our prior work demonstrated the high reliability of EP measured TAPSE in patients with suspected or confirmed PE and suggested a higher testing threshold (2.0 cm vs. 1.7 cm) to increase the examinations sensitivity.[2] Consistent with our prior results, this study demonstrated that TAPSE is the most sensitive measure of PE when compared to other components of the FOCUS exam (Tables 2 and 3). Additionally, using a higher testing threshold yielded increased sensitivity for PE, although the difference was not statistically significant (Tables 2 and 3). While TAPSE is the most sensitive measure of the FOCUS examination, it is important to retain the other components of the FOCUS examination when assessing a patient with abnormal vitals for PE. Four of 37 patients diagnosed with PE in this study had a TAPSE greater than 2.0 cm (normal) but demonstrated other signs of PE on the FOCUS examination.

Of 37 patients diagnosed with PE in this study, three had false-negative FOCUS examinations without any signs of RVD. In all three of these patients, investigators were unable to perform a complete FOCUS examination due to difficult cardiac windows. One patient did not have a TAPSE calculated while in the other two patients, investigators were unable to assess for tricuspid regurgitation. Additionally, these patients had a high pretest probability of PE (all three were being treated for cancer and had a prior history of PE). Furthermore, these patients were younger (aged 28, 46, and 62 years) and in good cardiovascular health, which makes it less likely that their heart would manifest signs of RVD on FOCUS. For these reasons, we caution the use of FOCUS to exclude PE in patients with an incomplete FOCUS examination, younger patients, those with a high pretest probability of PE, or those with a HR < 110 beats/min.

While FOCUS demonstrates high sensitivity for PE in this patient population, it is not surprising that the specificity of FOCUS for PE is only moderate (63%). This is in part explained by the fact that only one

component of the FOCUS examination had to be abnormal for the examination to be deemed positive for PE, which maximizes the examination's sensitivity at the expense of its specificity. Additionally, higher false-positive rates were noted in patients with heart failure or obstructive lung disease (e.g., chronic obstructive pulmonary disease, asthma), likely due to underlying mild right heart failure secondary to these disease processes. However, conditions that lead to chronic right heart strain will lead to global thickening of the RV which may help determine if the noted RVD is acute or chronic.[25]

While the overall specificity of FOCUS is moderate, our results demonstrate that certain components of FOCUS have a very high specificity for PE. McConnell's sign was 99% specific for PE and septal flattening was 93% specific for PE (Tables 2 and 3). When present, especially in the absence of a prior history of pulmonary hypertension, McConnell's sign, and septal flattening suggest an extremely high likelihood that the patient has a PE. Patients with these findings may merit empiric anticoagulation or thrombolysis if the EP is unable to obtain a CTA within a reasonable period of time.

LIMITATIONS

This study was limited by derivation of subjects from a convenience sample of patients, which may introduce selection bias. Additionally, the observational nature of the study introduces potential for bias. In two subjects, investigators were unintentionally unblinded to results and had a high suspicion that the subjects had been diagnosed with PE, due to the fact that the they were receiving a heparin infusion during the FOCUS examination (however, independent blinded review of these particular subjects agreed with the initial FOCUS results).

Some patients had missing data concerning various components of the FOCUS examination (e.g., missing tricuspid regurgitation data). Because the FOCUS examination only required one abnormal component to be categorized as a positive examination, the missing data may have contributed to a reported sensitivity that is lower than the actual sensitivity and a reported specificity that is higher than the actual specificity of the FOCUS examination.

Investigators chose to power the study so the width of the 95% CI for the sensitivity of the FOCUS examination was no greater than 20%. Investigators felt that a 20% width would most appropriately balance the need for diagnostic data and the team's ability to meet the required enrollment numbers given limited resources.

Investigators had significant experience in bedside echocardiography and received dedicated training in measuring TAPSE, which limits the generalizability of these results to EP populations with more variable ultrasound experience. However, three medical students with limited experience in bedside echocardiography were able to learn the technique, suggesting that EPs with less experience in bedside ultrasound could also acquire the necessary skill set. Prior work by this author has demonstrated high rates of interobserver reliability between medical students who were taught the FOCUS examination and EPs with significant experience in bedside echocardiography.[2]

CONCLUSIONS

Focused cardiac ultrasound performed by emergency physicians with advanced training in emergency ultrasound may significantly lower the likelihood of the diagnosis of pulmonary embolism in most patients who are suspected of pulmonary embolism and have abnormal vital signs. This was especially true in those patients with a heart rate > 110 beats/min. Further study in a larger cohort of patients (which would yield narrower 95% confidence intervals) is required before focused cardiac ultrasound can be used to reliably exclude pulmonary embolism in this patient population. Our results suggest that focused cardiac ultrasound can be an important tool in the initial evaluation of ED patients with suspected pulmonary embolism and abnormal vital signs.

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Supporting Information

The following supporting information is available in the online version of this paper available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13774/full

Data Supplement S1. Patient enrollment by site and level of experience.