Poor Positive Predictive Value of McConnell's Sign on Transthoracic Echocardiography for the Diagnosis of Acute Pulmonary Embolism

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Abstract

Background: Acute pulmonary embolism (PE) is a life-threatening condition. Making a definitive diagnosis with radiologic studies may delay therapy or be unsafe for the patient. Echocardiography is readily available and can suggest PE by demonstrating right ventricular (RV) dysfunction. McConnell's sign on echocardiogram (ECHO-CG) (RV dysfunction with characteristic sparing of the apex) has been reported to have high sensitivity and specificity for the diagnosis of acute PE. It is hypothesized that McConnell's sign on ECHO-CG in patients hospitalized with suspected acute PE would have a high positive predictive value (PPV). **Methods:** Data, from 2005 to 2010, were retrospectively collected on all patients with an ECHO-CG interpreted as revealing McConnell's sign, who had undergone another diagnostic study (computed tomography pulmonary angiography, ventilation-perfusion scan, upper or lower extremity Doppler ultrasound, or autopsy) for venous thromboembolic disease (VTE). The PPV on transthoracic ECHO-CG was calculated for the diagnostic accuracy of McConnell's sign in all patients. To minimize the potential for ECHO-CG reader bias of patients already confirmed to have had a PE by another modality, the PPV was then recalculated only on the patients in whom the ECHO-GM was the first diagnostic study. **Results:** Seventy-three patients had findings of McConnell's sign on ECHO-CG. The PPV of McConnell's sign on ECHO-CG was 57% (CI, 45%–67%). Of the 37 patients who underwent an ECHO-CG in the first study for suspected acute PE, 15 patients had VTE confirmed; the PPV in this subset was only 40% (CI, 24%–56%). There were 20 patient deaths overall; of these, only 9 of the patients were confirmed to have VTE. **Conclusion:** We concluded that the presence of McConnell's sign has a relatively poor PPV for the diagnosis of acute PE and should not be used in isolation when making a diagnosis of PE in patients.

Keywords: pulmonary embolism; venous thromboembolism; right ventricle; embolism; echocardiography; predictive value of tests

Introduction

An acute pulmonary embolism (PE) can be catastrophic, resulting in patient mortality within minutes to hours. Prompt diagnosis and intervention can be lifesaving, though the risk of death may persist for 24 to 72 hours.[1] Establishing a diagnosis of acute PE in a critically ill, hemodynamically unstable patient is frequently complicated by the inability to transport the patient to obtain a confirmatory radiologic study, such as computed tomography pulmonary angiography (CTA) or ventilation-perfusion scanning. If accurate, echocardiography would provide a useful adjunct in the diagnosis of PE. Right ventricular (RV) dysfunction with a characteristic sparing of the apex has been proposed to be diagnostic for PE. This finding, described by the eponym "McConnell's

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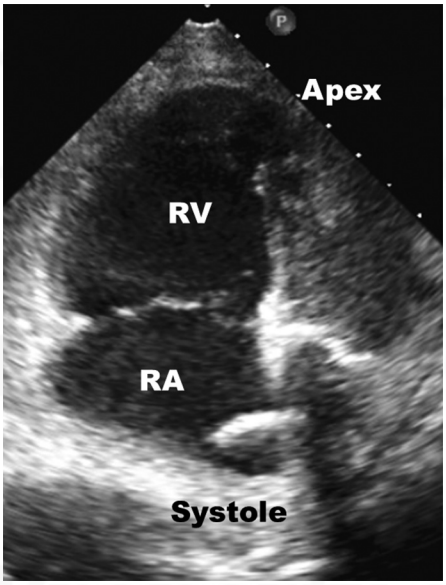
Figure 1. Echocargiographic still of McConnell's sign: RV akinesis with sparing of the apex.



Abbreviations: RA, right atrium; RV, right ventricle.

sign," has been increasingly used in both hemodynamically stable and unstable patients (Figure 1). Furthermore, a recent high quality review on the subject incorporated the finding of RV dysfunction on echocardiogram (ECHO-CG) in the critically ill, hemodynamically unstable patient as a means to confirm the diagnosis of acute PE without any referenced literature supporting this approach.[2]

Several studies have addressed the utility of echocardiography in the diagnosis of acute PE.[3-5] Current literature suggests that intensivists can attain competence in basic critical care echocardiography with a 12-hour structured curriculum,[6] however, only 30% to 50% of patients with acute PE have abnormal ECHO-CGs.[7-9] In rare cases, emboli in transit are demonstrated, thereby establishing the diagnosis. McConnell et al first described akinesis of the mid-RV free wall with preserved wall motion of the RV apex (Figure 2) to have a 77% sensitivity, 94% specificity, positive predictive value (PPV) of 71%, and a negative predictive value of 96% for the presence of PE in patients, based upon a retrospective review of patients already known to have an acute PE.[3] From a prognostic standpoint, there are ample data suggesting the findings of RV dysfunction or "strain" to be associated with worse outcomes.[10,11] Despite these data, it is not clear how specific RV dysfunction, and McConnell's sign in particular, is in making a prospective patient diagnosis of acute PE. In one example, our institution has administered thrombolytic therapy to a hemodynamically unstable patient based on high pre-test probability, and the presence of McConnell's sign on ECHO-CG, even in the face of a negative CTA.[12,13] Our study goal was to determine the PPV of McConnell's sign for diagnosing patients with acute PE at a single institution.

Methods

Patients

This was a retrospective study performed at a single tertiary care center. The inpatient echocardiography reporting database at Thomas Jefferson University Hospital was queried using the key words *McConnell's sign*, *Mc*, *McConnell*, *acute RV strain*, *emboli*, or *clot*. Patients were excluded if they had not undergone another study for determining VTE. Other studies included acute PE on multidetector contrast CTA, ventilation perfusion scan (high or intermediate probability confirming PE), venous Doppler ultrasound, or autopsy. The study protocol was reviewed and approved by the university's institutional review board (IRB Control number 09D.71). All ECHO-CGs were performed by echocardiography technicians and interpreted by American Board of Internal Medicine Cardiovascular Disease-certified and National Board of Echocardiography-certified cardiologists.

Data for each patient were abstracted from the hospital's electronic medical record database. All data entries were independently verified by 2 of the authors. The data collected included: (1) age, sex, admission date, and diagnosis; (2) date and time of diagnostic test for acute PE; (3) results of each study; (4) major clinical endpoint of death; (5) whether VTE was confirmed; (6) administration of thrombolytics or inferior vena cava filter placement; and (7) timing and administration of anticoagulation therapy. Time of each study was defined as the time obtained, not the time that the study was read or reviewed by caregivers.

Statistical Analysis

Data were summarized using percentages, medians, means and ranges. The PPV of McConnell's sign for diagnosing acute PE and the associated 95% confidence interval were calculated for the whole sample and for the subset of patients undergoing ECHO-CG as the first study.

Table 1. PPV of McConnell's Sign

VTE diagnosed, n/N	PPV, % (CI, %)
41/73	57 (45–67)
15/37[a]	40 (24–56)

[a]Of the 73 Patients, 37 had an ECHO-CG as the first assessment modality in suspected VTE and were thus free from possible bias introduced by results of other studies. Of the 37 patients, only 15 were confirmed to have VTE.
Abbreviations: ECHO-CG, echocardiogram; PE, pulmonary embolism; PPV, positive predictive value; VTE, venous thromboembolism.

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Table 2. Baseline Characteristics of the Study Sample

Sex, n (%)	Women 48 (65) Men 25 (35)
Mean age	62 years (range 21–91)
Mean time from hospital admission to first study for suspected PE	8 days (median 2 days)

Abbreviation: PE, pulmonary embolism.

Results

The database of ECHO-CGs contained 35 000 inpatient studies between April 2005 and July 2010. Most (73%) of the studies included in this paper were from 2009/2010. Seventy-three patients had an ECHO-CG report of McConnell's sign along with another study performed for evaluation of VTE (Figure 2). Table 1 depicts the PPV of an ECHO-CG in the detection of acute PE for the entire cohort and for the subset that had an ECHO-CG as the first modality of diagnosis. In the subset, the PPV was only 40%. Table 2 displays the baseline characteristics of the cohort. Table 3 depicts the timing and frequency of the study performed to evaluate patients for acute PE. An ECHO-CG was the first study performed in 37 (51%) patients and was the most frequently used first and second modality. Venous Doppler ultrasound studies were the most frequent third study performed (33/48). Anticoagulation was initiated in 50 of 73 patients (68.4%). Of those patients who did not receive anticoagulation, 3 patients received an inferior vena cava filter and 1 patient received thrombolysis with recombinant tissue plasminogen activator (r-tPA). Of all the patients, a total of 5 received an inferior vena cava filter and 4 were administered thrombolytic therapy with r-tPA. Table 4 illustrates the timing of initiation of anticoagulation in relation to the timing of the studies performed. Anticoagulation was empiric in approximately one-third of the patients, followed by an abnormal ECHO-CG in another third, and was based on other diagnostic studies in the remaining third. There were 20 total deaths among the study patients and 9 of 20 were confirmed to have VTE.

Table 3. Timing and Frequency of Diagnostic Study Performed to Evaluate for Acute PE

Study	Timing of study	n	N	%N
ECHO-CG	First	37	73	51
	Second	28	71	40
	Third	8	48	17
CTA	First	25	73	34
	Second	13	71	18
	Third	2	48	8
Ventilation perfusion scan	First	5	73	7
	Second	10	71	14
	Third	4	48	8
Extremity venous Doppler	First	6	73	8
	Second	20	71	28
	Third	33	48	69

Abbreviations: CTA, computed tomogram pulmonary angiogram; ECHO-CG, echocardiogram; PE, pulmonary embolism.

Discussion

Our retrospective study demonstrates that the finding of McConnell's sign has a poor PPV of only 57% for establishing the diagnosis of acute PE. Eliminating potential ECHO-CG reporting bias by looking only at patients in whom the ECHO-CG was the first assessment used, prior to any other imaging modality, McConnell's sign had an even lower PPV of 40%. The American College of Cardiology/American Heart Association guidelines for the clinical application of ECHO-CG state that pulmonary emboli and suspected clots in the right atrium or ventricle or main pulmonary artery branches are class I indications for performing an ECHO-CG in a patient.[14] In line with our findings, more recent guidelines on the appropriate use of echocardiography recommend against the use of echocardiography to establish the diagnosis of PE in suspected patients.[15]

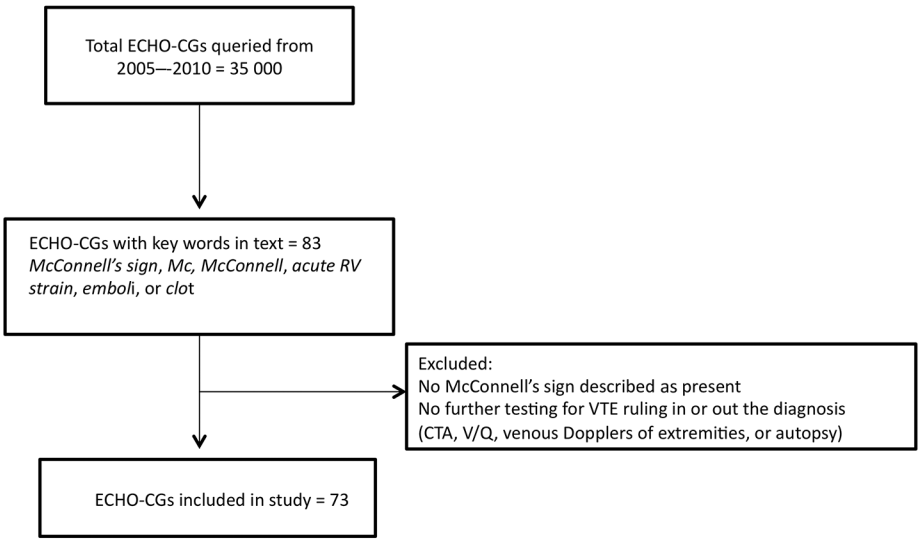
On the other hand, echocardiography appears to have a role in assessing prognosis in acute PE and is, in fact, recommended to assist in guiding further aggressive therapy, be it thrombectomy or thrombolytics.[15] The original study describing McConnell's sign reported a PPV of 71%. Like our review, that study was retrospective in nature. Notably only 13 of the 85 patients in the validation cohort had a diagnosis of acute PE.[3] The other diagnoses included cardiomyopathy (n = 30), chronic pulmonary hypertension (n = 11), valvular heart disease (n = 9), and congenital heart disease (n = 7),

Table 4. Initiation of Anticoagulation With Respect to Study Performed for Suspected VTE

Initiation of anticoagulation	n (%)	Patients with confirmed VTE, n (%)
Empiric (Before any study for VTE)	17 (34)	11 (65)
After ECHO-CG performed raised possibility of VTE	15 (30)	8 (53)
After other studies[a] performed raised possibility of VTE	18 (36)	17 (94)

[a]Other studies include computed tomography pulmonary angiogram, ventilation perfusion scan, upper and lower extremity venous Doppler ultrasound.
Abbreviations: ECHO-CG, echocardiogram; VTE, venous thromboembolism

Figure 2. Flow chart depicting inclusion of patients for the study.



among others. In contrast, 41 of 73 patients had confirmed VTE in our study.

In a retrospective study by Casazza et al,[5] McConnell's sign was detected in 70% of patients with PE and in 67% of patients with RV infarction, thus making it unreliable in distinguishing between the 2 conditions. They reported sensitivity, specificity, PPV, and negative predictive value of McConnell's sign in the diagnosis of acute PE to be 70%, 33%, 67%, and 36%, respectively. Studies have looked at other echocardiography parameters of RV dysfunction in acute PE. Lopez-Candales et al[16] compared regional RV global and RV apical mechanics with longitudinal vector imaging between patients with chronic pulmonary hypertension and acute PE. They reported no significant difference in regional RV wall deformation in the 2 groups of patients. The authors postulated that McConnell's sign with preserved RV apical contractility was a visual illusion created by tethering of the RV apex to a hypercontractile left ventricle in the presence of a dilated hypocontractile RV. A prospective study of 110 patients referred for suspected PE compared ECHO-CG diagnosis of acute PE to the gold standard, pulmonary angiography. Using 2 of 3 echocardiographic criteria (RV end-diastolic diameter $>$ 27 mm without hypertrophy, tricuspid regurgitant velocity $>$ 2.7 m.sec, and/or RV hypokinesis), the study reported a sensitivity of 56% and specificity of 90% in the diagnosis of acute PE.[9] Thus 50% of patients confirmed to have acute PE by angiography were missed by ECHO-CG. The pattern of RV outflow ejection can be useful in the diagnosis of acute PE in the right setting. A short acceleration time followed by a mid-systolic deceleration can indicate an outflow obstruction caused by a PE. The "60/60" sign is defined as an acceleration time $\leq$ 60 milliseconds in the presence of a tricuspid regurgitation pressure gradient of $<$ 60 mm Hg. The sensitivity, specificity, PPV, and negative predictive value of the 60/60 sign in the diagnosis of acute PE was reported to be 25%, 94%, 90%, and 38% respectively.[17]

Our study population was at increased risk of VTE by virtue of being hospitalized with presumably high clinical suspicion. Despite this, the PPV of McConnell's sign was poor. These results differ from the original paper by McConnell et al but reflect more recent literature, as well as current guidelines.[14,15] Thus, our study revealing the poor PPV of McConnell's sign supports the limited utility of the sign in the diagnosis of acute PE and should not be relied on.

We recognize that our study has several limitations. We performed a single institution study with a relatively small number of patients. The retrospective design limited data collection, and clinical probability was not quantified but rather assumed to be high. Our review does not apply solely to hemodynamically unstable, critically ill patients, where the PPV of McConnell's sign is unknown and could possibly be higher. We did not include patients with a McConnell's sign unless another study had been performed in evaluating the patient for VTE, potentially excluding patients with McConnell's sign that were possibly too sick or died before any other studies could be performed, and in whom no autopsy was done. Though, all of the board-certified echocardiographers are familiar with the term "McConnell's sign," it may not have always been used in reports describ-

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ing RV dysfunction with apical sparing, potentially excluding some patients from the study. Furthermore, ECHO-CGs may have been technically limited and inter-observer variation was not accounted for in the identification of McConnell's sign. In addition, 49% of patients had an ECHO-CG after undergoing some other completed evaluation (CTA, ventilation perfusion scans, or venous Doppler ultrasound studies), of which the results may have biased the interpretation of the ECHO-CG. In fact, the PPV of McConnell's sign in diagnosing acute PE in the subset of patients who had an ECHO-CG first was even lower (40% vs 57%). Also of note, we did not aim to determine what the alternative diagnosis was in the study patients with McConnell's sign who did not have PE, and had a negative second confirmatory imaging study.

Despite the unproven role of echocardiography in helping to diagnose acute PE in patients, its role in clarifying the prognosis of patients with documented acute PE and in guiding thrombolytic therapy or surgical decisions (thrombectomy/embolectomy) has been reasonably well established. An obstruction of 30% of pulmonary vasculature in patients with no underlying cardiopulmonary disease results in RV dysfunction.[18] The presence of RV dysfunction is linked to increased mortality in patients with acute PE.[8] An analysis of 7 studies addressing this question concluded that there was at least a 2-fold increase in mortality in patients with acute PE in the presence of RV dysfunction (4%–18% absolute increase).[19]

Conclusion

Due to poor PPV, McConnell's sign should not be relied on in making a diagnosis of acute PE, nor should it solely be used to direct the use of potentially hazardous thrombolytic therapy in hemodynamically stable or unstable patients in the absence of some other diagnostic test for acute PE. Further prospectively designed studies are needed to address the potential utility of echocardiography in the diagnosis of acute PE.

Conflict of Interest Statement

Urvashi Vaid, MD, MS; Esme Singer, MD; Gregary D. Marhefka, MD; Walter K. Kraft, MD; and Michael Baram, MD, FCCM, declare no conflicts of interest.

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