Transthoracic Echocardiography for Diagnosing Pulmonary Embolism: A Systematic Review and Meta-Analysis

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Objective: Pulmonary embolism (PE) is a common diagnosis with significant mortality if not appropriately treated. The use of transthoracic echocardiography in patients with PE is common; however, its diagnostic capabilities in this use are unclear. With the increased use of ultrasonography in medical settings, it is important to understand the strengths and limitations of echocardiography for the diagnosis of PE.

Methods: We conducted a systematic review of PubMed, CINAHL, and EMBASE through 2016 for articles assessing the diagnostic accuracy of transthoracic echocardiography for PE. Two authors independently abstracted relevant data from the studies. We assessed quality using the QUADAS-2 tool for diagnostic studies.

Results: Undefined "right heart strain" was the most common sign used, and it had a sensitivity of 53% (95% CI, 45%–61%) and a specificity of 83% (95% CI, 74%–90%). Eleven other distinct signs were identified: ventricle size ratio, abnormal septal motion, tricuspid regurgitation, 60/60 sign, McConnell's sign, right heart thrombus, right ventricle hypokinesis, pulmonary hypertension, right ventricular end-diastolic diameter, tricuspid annular plane systolic excursion, and right ventricular systolic pressure.

Conclusions: Studies show a consistently high specificity and low sensitivity for echocardiography in the diagnosis of PE, making it potentially adequate as a rule-in test at the bedside in critical care settings such as the emergency department and intensive care unit for patients with a suspicion of PE, especially those unable to get other confirmatory studies. Future research may continue to clarify the role of bedside echocardiography in conjunction with other tests and imaging in the overall management of PE. (J Am Soc Echocardiogr 2017;■:■-■.)

Keywords: Ultrasound, Ultrasonography, Pulmonary embolism, Critical care

Venous thromboembolism (VTE), a clinical syndrome involving venous thrombosis followed by distant embolism, is the third most common cause of cardiovascular death and the leading cause of preventable hospital death.[1-3] Estimates of the incidence of pulmonary embolism (PE) and VTE range from 1.05 to 1.48 per 1,000 patient-years.[4-6] Of the nearly 300,000 patients who experience VTE each year, 15%–25% present with sudden death or die within 30 days of diagnosis.[7] Approximately half of all PEs are diagnosed in the emergency setting,[8,9] and prompt diagnosis and treatment have been shown to improve outcomes and survival.[10,11]

Echocardiographic signs of right heart (RH) strain are often used as prognostic markers in patients with acute PE[12-14]; however, the ability of echocardiography to diagnose PE is not well understood. It is suspected to be relatively specific for PE in patients without known chronic cardiorespiratory disease.[13,15] Recent guidelines by the European Society of Cardiology do not recommend echocardiography as part of the diagnostic workup in non-high-risk patients; however, signs of right ventricular (RV) overload in high-risk patients without another leading diagnosis justify emergent treatment if computed tomography (CT) or other confirmatory test is not immediately available.[16]

Most systematic reviews on the diagnosis of PE have not focused on echocardiography. The last systematic review that reported test characteristics on echocardiography for diagnosing PE was done in 2005 and found only two studies on the topic.[15] It is possible that the test characteristics have improved in light of the increased use of ultrasonography in the emergency department (ED) and the improvements in technology in recent years. Therefore, we sought to do a systematic review and meta-analysis to summarize the test characteristics of echocardiography using gold standards of CT and

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Abbreviations

CT = Computed tomography

ED = Emergency department

FOCUS = Focused cardiac ultrasound

HSROC = Hierarchical summary receiver operator curve

LV = Left ventricular, ventricle

MeSH = Medical subject headings

PAH = Pulmonary arterial hypertension

PE = Pulmonary embolism

PRISMA = Preferred Reporting in Systematic Reviews and Meta Analyses

RH = Right heart

RHT = Right heart thrombus

RV = Right ventricular, ventricle

RVEDD = Right ventricular end diastolic diameter

RVSP = Right ventricular systolic pressure

TAPSE = Tricuspid annular plane systolic excursion

TR = Tricuspid regurgitation

V/Q = Ventilation/perfusion

VTE = Venous thromboembolism

surgery in the diagnosis of PE in adult patients presenting to any health care provider with signs or symptoms of PE.

METHODS

Search Techniques

We conducted a thorough and systematic literature search of English language articles published on transthoracic echocardiography used for the diagnosis of PE from January 1, 1980, to the end of year 2014 (exact search dates in Supplemental Appendix 1, available at www.onlinejase.com) using PubMed (National Library of Medicine), CINAHL (EBSCO), and EMBASE (Elsevier). For the searches, we selected medical subject headings (MeSH) and keywords to capture the concepts of ultrasonography, echocardiography, RV, and PE. The search results were combined and exported to EndNote bibliographic management tool, and duplicate results were removed. The search was conducted in compliance with the Preferred Reporting in Systematic Reviews and Meta Analyses (PRISMA) guidelines.[17] We updated the search using the same criteria in November 2016. Complete details of the search strategies including search terms are available (Supplemental Appendix 1, available at www.onlinejase.com).

All titles were independently reviewed for possible inclusion by two trained reviewers (J.D. and L.G.). Prior to beginning the review, both reviewers agreed to err on the side of inclusion. If either reviewer selected a reference, the full text was ordered for further review. Using this strategy, 464 articles were selected for further review. The reference sections of all included articles were checked for additional potentially relevant articles (Figure 1).

Inclusion and Exclusion Criteria

Articles meeting the following criteria were eligible for review: English language, research of any design that reported quantitative data, focus on diagnosis of acute PE using echocardiography, and reporting of data that allowed for calculation of both sensitivity and specificity. Exclusion criteria included articles that were anecdotal or had no data; on >50% pregnant patients; prognostic studies; single case reports or had a sample size less than 10; studies that used healthy controls; or experimental studies using animals, animal tissue, or cadavers.

A priori, we defined the positive reference standard as either CT, pulmonary angiogram, high-probability ventilation/perfusion (V/Q) scan, intermediate-probability V/Q scan with any other confirmatory study (including leg ultrasound for venous thrombosis), surgery, or autopsy. We chose a wide range of gold standard studies to reflect the large amount of diagnostic studies that are used in practice and to ensure we did not bias our sample if different confirmatory tests were used on patients with different pretest probabilities of PE.

Data Collection and Processing

The team developed an abstraction tool designed to confirm final eligibility for full review, assess article characteristics, and extract data relevant to the study question, which was used by two reviewers (J.D. and L.G.) to independently abstract data from the articles. Data included test characteristics, reported results, location of study, gold standard test used, sonographer experience, and other ultrasonography studies done. If data important to the meta-analysis, specifically data related to the sensitivity and specificity, were needed, the corresponding author of the study was asked for the information by a single e-mail. The two abstractors and two senior team members (A.A. and J.M.F.) discussed the two independent abstractions and combined them into a final abstraction. All abstraction disagreements were minor and were quickly resolved via consensus discussion among the four team members.

In order to perform subgroup analyses, articles were categorized into those performed only in the ED, as focused cardiac ultrasound (FOCUS, previously referred to as "point of care"), and performed by a physician (instead of an cardiac sonographer, nurse, or other health care professional). These groups were not mutually exclusive, and studies could be in more than one group. For example, studies performed in ED patients could be comprehensive exams performed by cardiac sonographers or focused exams performed by physicians. Studies that did not report this information specifically were not included in these analyses.

Quality Assessment

Two reviewers (J.D. and L.G.) independently assessed the quality of the articles using the QUADAS-2 tool[18] (University of Bristol, Bristol, UK) modified to conform to this meta-analysis of diagnostic accuracy. The resultant QUADAS-2 tool was used to assess studies for potential risk of bias involving methodology, reporting, and validity. Study heterogeneity was assessed using χ^2 analysis. All disagreements were minor and resolved via consensus of several members of the team (A.A., L.G., J.D., and J.M.F.).

We decided a priori the characteristics of each study that would meet the criteria for low risk of bias in each section of the QUADAS-2 tool. A more detailed description of the QUADAS-2 tool can be found in the Supplemental Appendix 2 (available at www.onlinejase.com).

Statistical Analysis

All statistical analyses were performed using R version 3.1.[19] For interrater reliability, we determined both percent agreement and Cohen's kappa. For the diagnostic accuracy meta-analysis, a hierarchical summary receiver operator curve (HSROC) was constructed that allows both fixed and random effects (for threshold and accuracy). The HSROC models were used to obtain sensitivity, specificity, positive and negative likelihood ratios, and diagnostic odds ratios. HSROC was chosen because it has been shown to be superior to other commonly used methods,[20,21] it takes into account the correlation between sensitivity and 1-specificity and models

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