Clinical Policy: Critical Issues in the Evaluation and Management of Adult Patients With Suspected Acute Nontraumatic Thoracic Aortic Dissection

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ABSTRACT

This clinical policy from the American College of Emergency Physicians addresses key issues in the evaluation and management of patients with suspected acute nontraumatic thoracic aortic dissection. A writing subcommittee conducted a systematic review of the literature to derive evidence-based recommendations to answer the following clinical questions: (1) In adult patients with suspected acute nontraumatic thoracic

aortic dissection, are there clinical decision rules that identify a group of patients at very low risk for the diagnosis of thoracic aortic dissection? (2) In adult patients with suspected acute nontraumatic thoracic aortic dissection, is a negative serum D-dimer sufficient to identify a group of patients at very low risk for the diagnosis of thoracic aortic dissection? (3) In adult patients with suspected acute nontraumatic thoracic aortic dissection, is the diagnostic accuracy of a computed tomography angiogram at least equivalent to transesophageal echocardiogram or magnetic resonance angiogram to exclude the diagnosis of thoracic aortic dissection? (4) In adult patients with suspected acute nontraumatic thoracic aortic dissection, does an abnormal bedside transthoracic echocardiogram establish the diagnosis of thoracic aortic dissection? (5) In adult patients with acute nontraumatic thoracic aortic dissection, does targeted heart rate and blood pressure lowering reduce morbidity or mortality? Evidence was graded and recommendations were made based on the strength of the available data.

INTRODUCTION

Thoracic aortic dissection is one of the deadliest cardiovascular diseases encountered in the emergency department (ED) setting. Inhospital mortality has been reported to be as high as 27%, even under optimal conditions.[1] Unfortunately, acute aortic dissection is also a difficult disease to diagnose and study because of the very low incidence of cases (3.5/100,000 per year)[2] and varied clinical presentations. The emergency physician must walk a careful line between the significant risks of missing the diagnosis and the considerable clinical and financial burden of overtesting for this rare entity. Compounding the difficulty of decisionmaking, there are no high-quality studies to guide the approach to diagnosis. As a result, the misdiagnosis of aortic dissection is a substantial medicolegal concern.[3]

Aortic dissection is a result of weakness and disruption of the intima (innermost layer of the aortic wall). This may be a result of hemodynamic stressors, connective tissue disorders, or abnormal flow caused by anatomic abnormalities such as a bicuspid aortic valve. The disruption in the intimal layer may result in extension of the dissection, leading to external rupture if the adventitial layers of the aortic wall are weak, obstruction of coronary arteries, or chronic hematomas. Prognosis and management are largely based on the anatomic location of the dissection. The most commonly used classification of the location of the dissection is the Stanford classification, dividing the dissection into type A, which involves the ascending aorta and/or arch, and type B, which involves the descending aorta or arch (distal to the L subclavian artery). The majority of dissections are type A and these are typically associated with higher mortality.* Surgical management has been shown to reduce mortality rates in type A dissections.[4]

*The American Heart Association classifies dissection as: type A, in which all dissections involve the ascending aorta regardless of site of origin. Type B dissections do not involve the ascending aorta and include involvement of the aortic arch, as long as the ascending aorta is not involved.

Clinical presentation differs by type of aortic dissection. The classic presentation has been described as a tearing chest pain that radiates to the back. In the International Registry of Acute Aortic Dissection (IRAD), a prospective registry of aortic dissection started in 1996 and including more than 2,000 patients from at least 26 sites, the most common presenting symptom was abrupt onset of pain that was described as severe and was present in 84% of all patients with dissection. However, pain such as that associated with dissection may also be described in other cardiovascular disease states such as acute coronary syndrome or pulmonary embolus. Back and abdominal pain is more often described in patients with a type B dissection. The location and severity of the dissection may also result in varying presentations, including syncope, hypotension, pulse deficits, and hypoperfusion, resulting in mesenteric and myocardial ischemia.[5] Hypotension is more commonly associated with a type A dissection and is also associated with a high rate of mortality in the acute setting.[6]

With respect to nontraumatic thoracic aortic dissection, the first critical question discusses what evidence there is for the role of clinical decision rules in identifying patients with suspected thoracic aortic dissection. The emergency physician must consider this diagnosis in patients with a variety of chief complaints and then make a clinical decision about which patients with suspected thoracic aortic dissection need further testing versus which patients' symptoms are below the clinician's testing threshold. Most emergency physicians have become accustomed to the use of a risk stratification algorithm for the diagnosis of pulmonary embolism. This incorporates the concept of a "testing threshold," the point of equipoise for risk-benefit of testing, and an acceptable rate of "missed" diagnosis. Risk stratification and the testing threshold for thoracic aortic dissection are not well established. A recent decision analysis proposes a "very low" testing threshold for the point of equipoise of risk-benefit of testing in suspected aortic dissection, 0.6% (1 in 167), which is much lower than the testing threshold that emergency physicians have become accustomed to in the diagnostic evaluation for pulmonary embolism. This threshold has not been incorporated into any prospective evaluations of decision rules or diagnostic algorithms.[7]

Once the decision has been made to pursue the diagnosis of dissection, the clinician must decide which diagnostic testing modalities to use. Strategies have evolved during the last decade as rapid imaging tools have become more readily available. The newest debate is the role of D-dimer in the screening of these patients, reflecting the hope that this could increase the identification of this disease without the overuse of time-consuming and expensive imaging studies. The role of D-dimer is discussed in the second critical question, and the third and fourth questions evaluate the role of computed tomography angiogram (CTA), transesophageal echocardiogram (TEE), transthoracic echocardiogram (TTE), and magnetic resonance angiogram (MRA).

Although initial management of the dissection in the ED is largely based on decreasing hemodynamic stress in patients with elevated blood pressure, the definitive management of the dissection varies according to the location of the dissection. In contrast to the benefit shown for patients with a type A dissection,

there has been no benefit shown from surgical intervention for the majority of patients with type B dissection.[8] The final critical question in this policy assesses the evidence for whether heart rate and blood pressure management impact morbidity and mortality for patients with thoracic aortic dissection.

METHODOLOGY

This clinical policy was created after careful review and critical analysis of the medical literature and was based on a systematic review of the literature. Searches of MEDLINE, MEDLINE InProcess, Cochrane Database of Abstracts of Reviews of Effects, Web of Science's Cited Reference Search, and Scopus were performed. All searches were limited to English-language sources, human studies, adults, and years January 2000 through April 2012; searches were conducted on April 30, 2012, and May 3, 2012. Specific key words/phrases and years used in the searches are identified under each critical question. In addition, relevant articles from the bibliographies of included studies and more recent articles identified by committee members and reviewers were included.

This policy is a product of the American College of Emergency Physicians (ACEP) clinical policy development process, including expert review, and is based on the existing literature; when literature was not available, consensus of emergency physicians was used. Expert review comments were received from emergency physicians, cardiologists, and vascular surgeons, including individual members of the American Heart Association and the Society for Vascular Surgery, and ACEP's Quality and Performance Committee. Comments were received from ACEP members during a 60-day open comment period, with notices of the comment period sent in e-mails, published in *EM Today*, and posted on the ACEP Web site. The responses were used to further refine and enhance this policy; however, the responses do not imply endorsement of this clinical policy. Clinical policies are scheduled for revision every 3 years; however, interim reviews are conducted when technology or the practice environment changes significantly. ACEP was the funding source for this clinical policy.

Assessment of Classes of Evidence

All articles used in the formulation of this clinical policy were graded by at least 2 subcommittee members and assigned a Class of Evidence. In doing so, subcommittee members assigned design classes to each article, with design 1 representing the strongest study design and subsequent design classes (eg, design 2, design 3) representing respectively weaker study designs for therapeutic, diagnostic, or prognostic clinical reports, or meta-analyses (Appendix A). Articles were then graded on dimensions related to the study's methodological features, including but not necessarily limited to randomization processes, blinding, allocation concealment, methods of data collection, outcome measures and their assessment, selection and misclassification biases, sample size, and generalizability. Using predetermined formulas related to the study's design, methodological quality, and applicability to the critical question, articles received a final Class of Evidence grade (ie, Class I, Class II, Class III, or Class X) (Appendix B). Articles identified with fatal flaws or that were not applicable to the critical question received a Class of Evidence grade "X" and were not used in formulating recommendations for this policy. Grading was done with respect to the specific critical questions; thus, the level of evidence for any one study may vary according to the question for which it is being considered. As such, it was possible for a single article to receive different Classes of Evidence as different critical questions were answered from the same study. Question-specific Classes of Evidence grading may be found in the Evidentiary Table (available online at www.annemergmed.com).

Translation of Classes of Evidence to Recommendation Levels

Strength of recommendations regarding each critical question were made by subcommittee members using results from strength of evidence grading, expert opinion, and consensus among subcommittee members according to the following guidelines:

Level A recommendations. Generally accepted principles for patient care that reflect a high degree of clinical certainty (ie, based on evidence from 1 or more Class of Evidence I or multiple Class of Evidence II studies).

Level B recommendations. Recommendations for patient care that may identify a particular strategy or range of strategies that reflect moderate clinical certainty (ie, based on evidence from 1 or more Class of Evidence II studies or strong consensus of Class of Evidence III studies).

Level C recommendations. Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of any adequate published literature, based on expert consensus. In instances where consensus recommendations are made, "consensus" is placed in parentheses at the end of the recommendation.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, and publication bias, among others, might lead to such a downgrading of recommendations.

When possible, clinically oriented statistics (eg, likelihood ratios, number needed to treat) were presented to help the reader better understand how the results may be applied to the individual patient. For a definition of these statistical concepts, see Appendix C.

This policy is not intended to be a complete manual on the evaluation and management of patients with suspected acute nontraumatic thoracic aortic dissection but rather a focused examination of critical issues that have particular relevance to the current practice of emergency medicine.

It is the goal of the Clinical Policies Committee to provide an evidence-based recommendation when the medical literature provides enough quality information to answer a critical question. When the medical literature does not contain adequate empirical data to answer a critical question, the members of the Clinical Policies Committee believe that it is equally important to alert emergency physicians to this fact.

This clinical policy is not intended to represent a legal standard of care for emergency physicians. Recommendations offered in

this policy are not intended to represent the only diagnostic or management options available to the emergency physician. ACEP recognizes the importance of the individual physician's judgment and patient preferences. This guideline defines for the physician those strategies for which medical literature exists to provide support for answers to the critical questions addressed in this policy.

Scope of Application. This guideline is intended for physicians working in EDs.

Inclusion Criteria. This guideline is intended for adult patients aged 18 years and older presenting to the ED with suspected acute nontraumatic thoracic aortic dissection.

Exclusion Criteria. This guideline is not intended to be used for patients with traumatic aortic dissection, for pediatric patients, or for pregnant patients.

For potential benefits and harms of implementing the recommendations, see Appendix D.

CRITICAL QUESTIONS

1. In adult patients with suspected acute nontraumatic thoracic aortic dissection, are there clinical decision rules that identify a group of patients at very low risk for the diagnosis of thoracic aortic dissection?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. In an attempt to identify patients at very low risk for acute nontraumatic thoracic aortic dissection, do not use existing clinical decision rules alone. The decision to pursue further workup for acute nontraumatic aortic dissection should be at the discretion of the treating physician.

Key words/phrases for literature searches: thoracic aortic dissection, dissecting, aneurysm, diagnosis, predictive value of tests, sensitivity and specificity, likelihood functions, dissecting, aneurysm, and variations and combinations of the key words/phrases.

Study Selection: Forty-five articles were identified in the search. Seventeen articles were selected from the search results for further review. One additional article was identified and added at the review stage, with 4 studies included for this critical question recommendation.

The exclusion of the diagnosis of nontraumatic aortic dissection can be challenging for emergency providers. Approximately 8% to 10% of all patients present with chest pain to EDs across the country.[9] The majority of these patients do not have aortic dissections. The development of clinical decision rules to identify a very-low-risk group for whom it may be appropriate to avoid advanced imaging would be extremely useful. Ideally, a combination of historical and physical examination findings, low-risk diagnostic imaging, or laboratory testing would be optimal. However, the prevalence of this disease is so low that challenges exist in the prospective development of decision rules. As a result, only 4 Class III studies were identified that addressed this clinical question.

In a Class III observational study of 250 patients with chest pain, back pain, or both, von Kodolitsch et al[10] attempted to define clinical predictors of acute aortic dissection prior to emergency imaging. A cohort of 250 patients was identified from 41,495 ED patients meeting the inclusion criteria as having suspected thoracic aortic dissection. Of the 250 patients, 128 had a thoracic aortic dissection, which raises the question of selection bias. Analysis of 26 clinical variables identified 3 independent predictors: (1) acute onset of pain and/or tearing/ripping pain; (2) mediastinal widening and/or aortic widening on chest radiograph (portable or posterior to anterior and lateral); and (3) pulse differential (absence of proximal extremity pulse or carotid pulse) and/or blood pressure differentials (difference of >20 mm Hg between arms). In the absence of all 3 predictors, the prevalence of an aortic dissection among the 250 patients with suspected disease was 7% (95% confidence interval [CI] 2.6% to 11.4%). In this cohort, the presence of all 3 clinical predictors had a prevalence of 100% (95% CI 90% to 100%) for the identification of aortic dissection.

In a Class III comprehensive review, Klompas[11] evaluated the clinical history, physical examination, and utility of a chest radiograph in the detection of acute thoracic aortic dissections. Twenty-one studies were included in this evaluation: 16 were retrospective reviews, the study by von Kodolitsch et al[10] discussed above was a large observational study, and all included nonindependently selected patients. Four[10,12-14] of the 21 studies in Klompas[11] were reviewed by the subcommittee. Two[13,14] of those 4 studies and the remaining 17 studies in Klompas[11] did not individually meet inclusion criteria for this clinical policy. Approximately half of the patients in this review received a diagnosis of aortic dissection. As a result of selection bias, this review likely overestimated sensitivity and underestimated specificity of the test. The author noted that most of the studies in his analysis used pulse differentials (loss or diminishment of pulses between carotids or similar extremities). Klompas[11] referenced 1 older study from the 1950s that used blood pressure differentials greater than 20 mm Hg between arms, and referenced the findings from von Kodolitsch et al[10] that blood pressure differentials greater than 20 mm Hg were found to be an independent predictor. However, Singer and Hollander,[15] in a prospective convenience sample to assess the range of normal interarm blood pressure differentials, found that 19% of patients had blood pressure differentials greater than 20 mm Hg. This questions the benefit of routine use of blood pressure differentials in patients with possible nontraumatic aortic dissection. The absence of the sudden onset of pain decreased acute aortic dissection risk (negative likelihood ratio [LR-] 0.3; 95% CI 0.2 to 0.5). A completely normal chest radiograph result (absence of widened mediastinum and absence of abnormal aortic contour) decreased the likelihood of aortic dissection (LR- 0.3; 95% CI 0.2 to 0.4); however, interobserver agreement for the radiograph read was only fair. Other findings in isolation were found to be very low yield for excluding aortic dissection. However, a combination of findings was shown to improve accuracy. Patients without all of the following were unlikely to have aortic dissection (LR- 0.07; 95% CI 0.03 to

0.17): pain (sudden onset, tearing/ripping, or both), blood pressure or pulse differential, and widened mediastinum. Four percent of the patients in this subgroup ultimately received a diagnosis of aortic dissection. The findings have not been validated in a prospective study.

A Class III study by Rogers et al[16] examined patients enrolled in the International Registry of Acute Aortic Dissection (IRAD) from 1996 to 2009. A risk assessment score (aortic dissection detection [ADD] risk score) was developed from a risk assessment tool based on a guideline published by multiple professional societies.[17] The risk score was developed to provide a simple method to screen large numbers of patients. It used high-risk predisposing conditions, pain features, and physical examination findings to group patients into 3 different categories based on a pretest risk. High-risk predisposing conditions were defined as Marfan syndrome, family history of aortic disease, known aortic valve disease, recent aortic manipulation, or known thoracic aneurysm. Three high-risk pain features were defined as chest, back, or abdominal pain described as abrupt in onset, severe, or ripping/tearing. High-risk examination features were defined as pulse deficit, systolic blood pressure differential, focal neurologic deficit with pain, murmur of aortic insufficiency (new or not known to be old) with pain, or hypotension/shock. An ADD risk score was created from 0 to 3 based on the number of categories in which a patient had at least 1 high-risk marker present. This was incorporated into an algorithm that used chest radiograph and ECG with the ADD risk score to help risk-stratify patients. This had not been validated previously and the study retrospectively applied this score to the IRAD database. Of the 2,538 patients with aortic dissection, 108 would have been categorized as low risk (4.3%) with an ADD risk score of 0. In another Class III retrospective validation of the ADD risk score, Nazerian et al[18] described the diagnostic accuracy of the ADD risk score in 1,328 patients, with 291 (22%) having acute aortic dissection. In patients with an ADD score of less than 1, the prevalence of disease was 5% and the LR- was 0.22 (95% CI 0.15 to 0.33). The authors concluded that an ADD score of 0 was insufficient to accurately exclude the diagnosis of aortic dissection.[18]

Future Research - Large prospective studies are needed to better assess historical information, physical examination findings, and diagnostic testing combinations for the diagnosis of acute nontraumatic aortic dissection.

2. In adult patients with suspected acute nontraumatic thoracic aortic dissection, is a negative serum D-dimer sufficient to identify a group of patients at very low risk for the diagnosis of thoracic aortic dissection?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. In adult patients with suspected nontraumatic thoracic aortic dissection, do not rely on D-dimer alone to exclude the diagnosis of aortic dissection.

Key words/phrases for literature searches: thoracic aortic dissection, dissecting, aneurysm, D-dimer, diagnosis, predictive value of tests, sensitivity and specificity, likelihood functions, and variations and combinations of the key words/phrases.

Study Selection: Eighty-two articles were identified in the search. Twenty-four articles were selected from the search results for further review. One additional article was identified and added at the review stage, with 11 studies included for this critical question recommendation.

Traditionally, the diagnosis of acute nontraumatic thoracic aortic dissection has been based on diagnostic imaging. The use of a laboratory test to exclude the diagnosis of acute thoracic aortic dissection, similar to the use of D-dimer for ruling out acute pulmonary embolism, is appealing and could potentially save time and money.

Eleven Class III studies, including 2 meta-analyses, have evaluated the performance of D-dimer in diagnosing acute thoracic aortic dissection.[19-29] These studies suffer from selection bias and vary widely in the assays used to measure D-dimer. Even though the cutoff value for a positive test result, as well as the type of assays used to measure D-dimer values, varied in the studies reviewed, D-dimer was highly sensitive for diagnosing acute thoracic aortic dissection, with sensitivities ranging from 91% to 100%. However, given the low quality of these Class III studies, strong recommendations about the routine use of D-dimer testing alone cannot be made. One Class III article evaluated the diagnostic accuracy of a negative D-dimer test result in conjunction with a risk-stratification score of 0.[29] In those patients, none had an aortic dissection. In nonhigh-risk patients, the LR- was 0.04 (95% CI 0.01 to 0.15).[29] This approach, however, needs prospective validation because of methodologic limitations of this study.

The following conditions, however, may result in a low or false-negative D-dimer value in patients with proven thoracic aortic dissection: chronicity, time from symptom onset, presence of thrombosis or intramural hematoma, short length of dissection, and young age of patient. Eggebrecht et al[20] found a significant negative correlation between the absolute D-dimer values and time from onset of symptoms. D-dimer levels were higher in patients with acute versus chronic thoracic aortic dissections.[20] Eggebrecht et al[20] also noted that D-dimer levels were higher in patients with thoracic aortic dissection who died early, underwent emergency endovascular or surgical procedure, or had complications. Thrombosed false lumens or intramural hematomas may affect D-dimer levels. In multiple studies, D-dimer levels were lower in patients with thoracic aortic dissection and a thrombosed false lumen than in patients without a thrombosed false lumen.[22,25,28] Hazui et al,[23] in a 2006 study, found that patients with thoracic aortic dissection who were younger or had short dissection lengths and thrombosed false lumens without ulcerlike projections may have false-negative D-dimer results. Ohlmann et al[25] identified 1 of 94 patients with a false-negative D-dimer test with a localized intramural hematoma without an intimal flap.

If a patient has a positive D-dimer result, the diagnosis of thoracic aortic dissection cannot be made definitively without

imaging. D-dimer elevations are not specific for thoracic aortic dissection. Elevated D-dimer measurements can be found in patients presenting to the ED with many conditions, including but not limited to acute thoracic aortic dissection, pulmonary embolism, acute myocardial infarction, and inflammatory conditions. Based on the clinical presentation, a positive D-dimer result may prompt the physician to order an imaging study to further investigate the diagnosis. Sakamoto et al[30] reported a sensitivity of diagnosing acute thoracic aortic dissection of 68.4%. According to Sakamoto et al,[30] D-dimer levels were higher in patients with acute thoracic aortic dissection and pulmonary embolism compared with levels in patients with acute myocardial infarction. D-dimer was not able to reliably differentiate an acute thoracic aortic dissection from a pulmonary embolism with D-dimer values of 32.9 μg/mL (SD 66.7 μg/mL) for acute thoracic dissection and 28.5 μg/mL (SD 23.6 μg/mL) for pulmonary embolism. Because D-dimer is nonspecific, routinely obtaining this test in a large population of patients with symptoms suspicious for aortic dissection can result in harm, most notably, exposure to radiation and cost associated with advanced imaging.

Future Research

A prospective study evaluating D-dimer levels on undifferentiated ED patients who present with signs and symptoms concerning for thoracic aortic dissection is warranted. Studies clarifying the best way to integrate D-dimer testing into clinical algorithms that include risk stratification are needed.

3. In adult patients with suspected acute nontraumatic thoracic aortic dissection, is the diagnostic accuracy of CTA at least equivalent to TEE or MRA to exclude the diagnosis of thoracic aortic dissection?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. In adult patients with suspected nontraumatic thoracic aortic dissection, emergency physicians may use CTA to exclude thoracic aortic dissection because it has accuracy similar to that of TEE and MRA.

Level C recommendations. None specified.

Key words/phrases for literature searches: thoracic aortic dissection, dissecting, aneurysm, x-ray computed tomography, CT angiogram, spiral computed tomography, gadolinium diagnostic use, magnetic resonance imaging, MRI, MRA, MR imaging, MR angiogram, transesophageal echocardiography, diagnosis, predictive value of tests, sensitivity and specificity, likelihood functions, and variations and combinations of the key words/phrases.

Study Selection: Sixty-nine articles were identified in the search. Fifteen articles were selected from the search results for further review, with 6 studies included for this critical question recommendation.

Because CTA has become the preferred diagnostic test among emergency physicians suspecting aortic dissection in the ED, this critical question focuses on whether CTA (compared with TEE or MRA) can accurately exclude the diagnosis of aortic dissection. The literature review focused on the diagnostic accuracy for aortic dissection and did not address details such as gating, phase, and timing. A Class I meta-analysis by Shiga et al[31] addressed this critical question related to TEE and MRA. It identified 3 prospective studies evaluating helical computed tomography (CT), with a total of 114 aortic dissections among 193 patients.[32-34] The reference standard for diagnosis of thoracic aortic dissection was surgery, autopsy, or another confirmatory imaging study. Although the quality of the 3 studies[32-34] varied (Grades I, II, and III), the results were consistent and the meta-analysis resulted in a sensitivity of 100% (95% CI 96% to 100%) and specificity of 98% (95% CI 87% to 99%). In comparison, TEE had a sensitivity of 98% (95% CI 95% to 99%) and specificity of 95% (95% CI 92% to 97%); magnetic resonance imaging (MRI) had a sensitivity of 98% (95% CI 95% to 99%) and specificity of 98% (95% CI 95% to 100%).

A Class II large retrospective study (N=373) evaluating patients for suspicion of aortic dissections in the emergency setting found a high level of accuracy of multidetector CTA to detect an aortic disorder, with sensitivity of 99% (95% CI 91% to 100%) and specificity of 100% (95% CI 99% to 100%).[35] The reference standard for confirmation was surgical/pathologic diagnoses, clinical follow-up findings, or subsequent imaging. This study also demonstrated an additional benefit of CT over TEE: the ability to detect alternative findings that were identified in 13% of the cases without aortic disorders.

In a Class III study from the IRAD, sensitivities for TEE, CT, and MRI were found to be 88% (95% CI 82% to 92%), 93% (95% CI 90% to 95%), and 100% (95% CI 70% to 100%), respectively.[36] It is difficult to generalize these particular findings without a clear understanding of the spectrum of cases enrolled. The study population was a convenience sample of patients with a known diagnosis of aortic dissection. Unlike the other studies reviewed, there was no criterion standard used for the diagnosis of aortic dissection.

Future Research

Future research should attempt to clarify the risk of harm from ionizing radiation and intravenous contrast administration associated with CTA. The study of ECG-gated versus nongated CT imaging to reduce motion artifact and improve image quality should also be evaluated.

4. In adult patients with suspected acute nontraumatic thoracic aortic dissection, does an abnormal bedside TTE establish the diagnosis of thoracic aortic dissection?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. In adult patients with suspected nontraumatic thoracic aortic dissection, do not rely on an abnormal bedside TTE result to definitively establish the diagnosis of thoracic aortic dissection.

Level C recommendations. In adult patients with suspected nontraumatic thoracic aortic dissection, immediate

surgical consultation or transfer to a higher level of care should be considered if a TTE is suggestive of aortic dissection. (Consensus recommendation)

Key words/phrases for literature searches: aortic dissection, aortic aneurysm, thoracic, aneurysm, dissecting, transthoracic, echocardiography, bedside or point-of-care, diagnosis, predictive value of tests, sensitivity and specificity, likelihood functions, and variations and combinations of the key words/phrases.

Study Selection: Fifty-one articles were identified in the search. Thirty-six articles were selected from the search results for further review, with 6 studies included for this critical question recommendation.

The diagnosis of thoracic aortic dissection is time sensitive and is frequently complicated by hemodynamic instability, limiting the ability to send the patient for tests such as CT or MRI. TTE is an attractive diagnostic modality for thoracic aortic dissection, because it can be conducted at the bedside for an unstable patient. Additionally, as the number of emergency physicians trained to perform TTE increases, this diagnostic modality is immediately available in an increasing number of EDs. However, there are few high-quality studies addressing this important diagnostic question in ED populations. All studies suffered from some degree of spectrum bias[37] because they enrolled a population with a higher prevalence of thoracic aortic dissection (19% to 93%) than that typically reported in ED patients being evaluated for thoracic aortic dissection. Additionally, many studies of TTE included TTEs that were performed after a diagnosis of thoracic aortic dissection was already established, likely inflating the sensitivity. All included studies, except for 2, are older than 20 years, limiting the generalizability to current ultrasound technology that has since improved. Despite these limitations, a number of studies provide useful data about the diagnostic characteristics of bedside TTE for thoracic aortic dissection. None of the studies evaluated emergency physician–performed TTE; rather they evaluated TTE performed by echo technicians or cardiologists.

In a Class II study, Evangelista et al[38] evaluated TTE in 143 consecutive patients, of whom 8 had immediate indications for surgery due to hemodynamic instability and TTE findings consistent with thoracic aortic dissection, 7 had inadequate echocardiography windows, and 128 had adequate echocardiography windows. Prevalence of thoracic aortic dissection was 60% among the entire enrolled population. Diagnostic test characteristics were sensitivity 74% (95% CI 65% to 84%) and specificity 74% (95% CI 62% to 85%).

In 5 Class III studies with varying prevalence of disease, TTE was reported to have sensitivity ranging from 59% to 80% and specificity 0% to 100%.[39-43]

Future Research

Future research should address the diagnostic characteristics of bedside TTE by emergency physicians in ED patients with acute presentations concerning for thoracic aortic dissection. To be most useful, such a study should prospectively evaluate unstable patients with a high suspicion of having thoracic aortic dissection. Research also needs to be conducted to determine optimal methods for teaching emergency physicians how to perform a TTE to maximize diagnostic accuracy.

5. In adult patients with acute nontraumatic thoracic aortic dissection, does targeted heart rate and blood pressure lowering reduce morbidity or mortality?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. In adult patients with acute nontraumatic thoracic aortic dissection, decrease blood pressure and pulse if elevated. However, there are no specific targets that have demonstrated a reduction in morbidity and mortality.

Key words/phrases for literature searches: aortic dissection, aortic aneurysm, thoracic, dissecting aneurysm, heart rate, pulse rate, blood pressure, intensive medical management, antihypertensive agents, diagnosis, sensitivity and specificity, likelihood functions, methods and results, and variations and combinations of the key words/phrases.

Study Selection: Fifty-five articles were identified in the search. Thirty-seven articles were selected from the search results for further review, with 1 study included for this critical question recommendation.

The leading cause of death in patients with an aortic dissection is not the initial intimal tear, but progressive dissection that results in rupture.[44] Progression of dissection has been attributed to the pulsatile nature of blood flow.[45] Wheat et al[44] described that the pulsatile flow is a result of 2 key forces that may be targeted. The first is the kinetic energy of the blood flow that can be reduced if the velocity of the blood flow is reduced, and the second is the pressure differentials throughout the aorta.[44] Basic science studies largely conducted in animals and modeling aortic dissection provide the body of evidence that shear force and the pulsatile nature of blood flow are directly associated with progression of aortic dissection.[45-48] Medications that reduce heart rate and blood pressure have been recommended in the acute treatment of aortic dissection based on the principles described by Wheat et al.[44] In their study from 1968, Wheat and Palmer[49] suggested lowering the systolic blood pressure to 100 mm Hg to 120 mm Hg. They inferred that the optimal blood pressure is the lowest one that maintains mentation and urine output. Major specialty consensus guidelines currently present therapeutic targets of a heart rate of 60 beats/min and a systolic blood pressure less than 120 mm Hg[17,50]; however, there is limited data to support specific blood pressure and heart rate targets in the acute setting. The majority of studies on hemodynamic control describe the success of therapeutic protocols that include various blood pressure and heart rates.[51-54] In a Class III study by Kodama et al,[55] 171 patients with a thoracic aortic dissection were followed for 27 months with 32 meeting the target heart rate control of less than 60 beats/min. Heart rate was measured at 6 AM, noon, and 6 PM every day during the acute treatment with β-blockers. The target heart rate was defined as an average of heart rate 3, 5, and 7 days after onset of treatment. In patients with tight blood pressure control, the rate of

adverse events was lower in those who also met the heart rate target (odds ratio 0.25; 95% CI 0.08 to 0.77). Maintaining a systolic blood pressure greater than 140 mm Hg has not been independently associated with an increase in aortic size in a multivariate analysis.[56] In addition, there are no prospective human studies that demonstrate preferential treatment order of lowering heart rate before the blood pressure when selecting the initiating pharmacologic agent.

Future Research

Research needs to be conducted to define ideal hemodynamic targets and agents in patients with an acute thoracic aortic dissection.

Relevant industry relationships: There were no relevant industry relationships disclosed by the subcommittee members.

Relevant industry relationships are those relationships with companies associated with products or services that significantly impact the specific aspect of disease addressed in the critical question.

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Appendix A. Literature classification schema.*

Design/Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized, controlled trial or meta-analysis of randomized trials	Prospective cohort using a criterion standard or meta-analysis of prospective studies	Population prospective cohort or meta-analysis of prospective studies
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)

*Some designs (eg, surveys) will not fit this schema and should be assessed individually.
†Objective is to measure therapeutic efficacy comparing interventions.
‡Objective is to determine the sensitivity and specificity of diagnostic tests.
§Objective is to predict outcome, including mortality and morbidity.

Appendix B. Approach to downgrading strength of evidence.

	Design/Class		
Downgrading	**1**	**2**	**3**
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

Appendix C. Likelihood ratios and number needed to treat.*

LR (+)	LR (−)	
1.0	1.0	Does not change pretest probability
1-5	0.5-1	Minimally changes pretest probability
10	0.1	May be diagnostic if the result is concordant with pretest probability
20	0.05	Usually diagnostic
100	0.01	Almost always diagnostic even in the setting of low or high pretest probability

LR, likelihood ratio.
*Number needed to treat (NNT): number of patients who need to be treated to achieve 1 additional good outcome; NNT=1/absolute risk reductionx100, where absolute risk reduction is the risk difference between 2 event rates (ie, experimental and control groups).

Appendix D. Potential benefits and harms of implementing the recommendations.

1. In adult patients with suspected acute nontraumatic thoracic aortic dissection, are there clinical decision rules that identify a group of patients at very low risk for the diagnosis of thoracic aortic dissection?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. In an attempt to identify patients at very low risk for acute nontraumatic thoracic aortic dissection, do not use existing clinical decision rules alone. The decision to pursue further workup for acute nontraumatic aortic dissection should be at the discretion of the treating physician.

Potential Benefit of Implementing the Recommendations: Clinicians recognize the limitations of using clinical decision rules alone to risk stratify patients with suspected acute nontraumatic thoracic aortic dissection.

Potential Harm of Implementing the Recommendations: Harm of implementation of this recommendation is unknown at this time.

2. In adult patients with suspected acute nontraumatic thoracic aortic dissection, is a negative serum D-dimer sufficient to identify a group of patients at very low risk for the diagnosis of thoracic aortic dissection?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. In adult patients with suspected nontraumatic thoracic aortic dissection, do not rely on D-dimer alone to exclude the diagnosis of aortic dissection.

Potential Benefit of Implementing the Recommendations: In ED patients with suspected acute nontraumatic thoracic aortic dissection, the recommendations can help clinicians recognize the limitations of a negative D-dimer result in the setting of suspicion for disease.

Potential Harm of Implementing the Recommendations: The use of D-dimer may lead to unnecessary advanced imaging and exposure to radiation.

3. In adult patients with suspected acute nontraumatic thoracic aortic dissection, is the diagnostic accuracy of CTA at least equivalent to TEE or MRA to exclude the diagnosis of thoracic aortic dissection?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. In adult patients with suspected nontraumatic thoracic aortic dissection, emergency physicians may use CTA to exclude thoracic aortic dissection because it has accuracy similar to that of TEE and MRA.

Level C recommendations. None specified.

Potential Benefit of Implementing the Recommendations: Potential benefits of CT angiogram include ready availability, rapid diagnosis of nontraumatic aortic dissection, and potential identification of alternative disorders.

Potential Harm of Implementing the Recommendations: Potential harms of CT angiogram include adverse events due to risks of intravenous contrast administration such as anaphylaxis, contrast-induced nephropathy, local contrast extravasation, and radiation exposure.

4. In adult patients with suspected acute nontraumatic thoracic aortic dissection, does an abnormal bedside TTE establish the diagnosis of thoracic aortic dissection?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. In adult patients with suspected nontraumatic thoracic aortic dissection, do not rely on an abnormal bedside TTE result to definitively establish the diagnosis of thoracic aortic dissection.

Level C recommendations. In adults patients with suspected nontraumatic thoracic aortic dissection, immediate surgical consultation or transfer to a higher level of care should be considered if a TTE is suggestive of aortic dissection. (Consensus recommendation)

Potential Benefit of Implementing the Recommendations: In adult patients with suspected acute nontraumatic thoracic aortic dissection, implementing the recommendation will avoid patients being directed to inappropriate intervention on the basis of a false-positive echocardiography result.

Potential Harm of Implementing the Recommendations: Lack of reliance on bedside TTE results to establish the diagnosis may result in delay of diagnosis and additional testing.

5. In adult patients with acute nontraumatic thoracic aortic dissection, does targeted heart rate and blood pressure lowering reduce morbidity or mortality?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. In adult patients with acute nontraumatic thoracic aortic dissection, decrease blood pressure and pulse if elevated. However, there are no specific targets that have demonstrated a reduction in morbidity and mortality.

Potential Benefit of Implementing the Recommendations: Deceasing heart rate and blood pressure may reduce the risk of further dissection and improve outcomes.

Potential Harm of Implementing the Recommendations: Reducing blood pressure and heart rate aggressively in select patients may result in adverse events, such as in patients with severe aortic insufficiency or pericardial tamponade.

Evidentiary Table.

Study and Year Published	Class of Evidence	Setting and Study Design	Methods and Outcome Measures	Results	Limitations and Comments
von Kodolitsch et al[10] (2000)	III	Observational study	41,495 patients evaluated with chest pain, back pain, or both; 38,819 excluded cases with evidence of alternative diagnosis (eg, acute coronary syndrome); 2 emergency physicians agreed on exclusion of 2,426 for low clinical concerns for thoracic aortic dissection and shared clinical suspicion for thoracic aortic dissection in N=250 patients; diagnostic imaging studies plus findings at surgery or autopsy established final diagnosis; 128 patients had thoracic aortic dissection, 122 did not; 26 clinical variables were evaluated; stepwise logistic regression model	3 independent clinical variables permitted identification of thoracic aortic dissection and risk stratification; probability of thoracic aortic dissection was low (7%) in absence of 3 variables (aortic pain with acute onset of pain and/or tearing/ripping pain; mediastinal widening and/or aortic widening on chest radiograph [portable or PA and lateral]; and pulse differentials [absence of proximal extremity pulse or carotid pulse] and/or blood pressure differentials [difference of >20 mm Hg between arms])	Selection bias
Klompas[11] (2002)	III	Meta-analysis and comprehensive review	Structured literature search; original studies describing clinical findings with 18 or more consecutive patients with confirmed thoracic aortic dissection; Outcome: review accuracy of clinical history, physical examination, and chest radiograph in thoracic aortic dissection diagnosis	N=1,848 cases from 21 studies; patients with 0 of 3 triad ("aortic pain" of sudden onset tearing/ripping pain or both; blood pressure or pulse differential; and widened mediastinum) were unlikely to have thoracic aortic dissection; LR- 0.07 (95% CI 0.03 to 0.17)	Roughly half of the patients in this review were diagnosed with thoracic aortic dissection; inclusion or selection bias; study may overestimate sensitivity and underestimate specificity; only 1 reviewer; not blinded; only 4 studies had controls; physical and history examination still cannot exclude diagnosis (4% still had thoracic aortic dissection even if 0 of 3 triad); LR- extends to 0.17

Evidentiary Table (continued).

Study and Year Published	Class of Evidence	Setting and Study Design	Methods and Outcome Measures	Results	Limitations and Comments
Rogers et al[16] (2011)	III	Prospective multinational study from 24 centers; 2,538 patients with thoracic aortic dissection	Assessment of patients enrolled in IRAD database 1996-2009; diagnosis based on diagnostic imaging studies, surgery, or autopsy; 290 variables recorded; evaluated sensitivity of thoracic aortic dissection guideline diagnostic algorithm published in Hiratzaka et al[17]; ADD risk score (0 to 3) calculated based on number of risk categories (high-risk predisposing conditions, pain features, examination features); low-risk ADD score: 0	ADD score 0: 108 patients (4.3%) were identified as low risk; of the 108 low-risk patients with thoracic aortic dissection 72 had chest radiographs; 35 of 72 (48.6%) chest radiographs showed wide mediastinum	ADD score may not work as well in general or undifferentiated populations because patients in database were likely typical thoracic aortic dissection cases; study design may lead to overtesting; patients were misidentified
Nazerian et al[18] (2014)	III	Retrospective study at 2 cardiovascular centers	Included patients with suspected aortic dissection enrolled prospectively in a registry prior to diagnosis of dissection; ADD risk scores were calculated; diagnosis was based on a 2-physician review of imaging, autopsy, or surgical reports	ADD score 0: 439 patients (33.1%) were identified as low risk; of the low-risk patients 26 (2%) were diagnosed with acute aortic dissection; LR- was 0.22 (95% CI 0.15 to 0.22)	Selection bias is likely because all patients were referred to the registry by the treating physician based on suspicion

Evidentiary Table (continued).

Study and Year Published	Class of Evidence	Setting and Study Design	Methods and Outcome Measures	Results	Limitations and Comments
Akutsu et al[19] (2005)	III	Academic critical care unit; prospective cohort	Patients with suspected acute aortic dissection, sudden-onset chest or back pain with nonischemic ECG had a bedside D-dimer and CT scan and were compared with a reference group; 78 patients, 30 with acute aortic dissection	D-dimer >0.5 µg/mL; sensitivity 100%; specificity 54%; PPV 58%; NPV 100%; LR+: 2.17; LR-: 0; median D-dimer values (µg/mL): without acute aortic dissection: 0.42; with acute aortic dissection: 1.80	Rapid bedside assay Roche cardiac D-dimer; exact D-dimer levels not assessed in 9 patients (12%) secondary to levels being too high or too low to detect with the bedside assay
Eggebrecht et al[20] (2004)	III	Netherlands study; unclear setting; prospective cohort	Analyzed blood from patients with chest pain presenting within 48 h of symptom onset and compared with asymptomatic patients with previously diagnosed chronic, stable aortic dissection; diagnosis of aortic dissection confirmed by 2 imaging modalities; 96 patients, 16 with acute aortic dissection	D-dimer highly elevated in pulmonary embolism and aortic dissection; D-dimer cutoff value of 626 µg/L; sensitivity 100%; specificity 73%; LR+: 3.7; LR-: 0; D-dimer cutoff value of 500 µg/L; sensitivity 100%; specificity 67%; LR+: 3.0 LR-: 0	Dade Behring D-dimer latex-enhanced turbidimetric test; only patients with aortic dissection in whom a clear timeline for onset of symptoms that could be delineated were included

Evidentiary Table (continued).

Study and Year Published	Class of Evidence	Setting and Study Design	Methods and Outcome Measures	Results	Limitations and Comments
Ersel et al[21] (2010)	III	Turkish retrospective chart review of ED patients; tertiary care setting	Patients with chest pain who received D-dimers in the ED and acute aortic dissection confirmed with CT showing intimal flap; 99 patients, 30 with acute aortic dissection	D-dimer ≥0.246 μg/mL; sensitivity 96.6%; specificity 52.2%; NPV 97.3%; PPV 46.8%; LR+: 2.02; LR-: 0.06	Dade Behring immunoturbidimetric assay; 1 patient with negative D-dimer result had an aortic dissection but it was "chronic aortic dissection" (presented nearly 2 wk after onset of symptoms); 8 patients with chronic aortic dissection were categorized into the nonaortic dissection group for statistical calculations
Hazui et al[22] (2005)	III	Japanese retrospective, case control study	Analyzed blood from patients with aortic dissection and myocardial infarction who presented within 4 h of symptom onset; aortic dissection confirmed by CT; 78 patients, 29 with acute aortic dissection	D-dimer ≥0.8 μg/mL; sensitivity 93.1%; 2 patients with D-dimer <0.8 g/mL had an acute aortic dissection with a thrombosed false lumen	Roche latex agglutination; patients with an aortic dissection and thrombosed false lumen exhibit significantly lower D-dimer levels

Evidentiary Table (continued).

Study and Year Published	Class of Evidence	Setting and Study Design	Methods and Outcome Measures	Results	Limitations and Comments
Hazui et al[23] (2006)	III	Japanese retrospective chart review	Patients with CT-confirmed acute aortic dissection had blood for D-dimer testing drawn in the ED; 113 patients with acute aortic dissection (29 previously reported by Hazui et al, 2005[22])	D-dimer cutoff value of 0.4 μg/mL; sensitivity 91.35%; 9 (8%) patients with acute aortic dissection had negative D-dimer result	Roche latex agglutination; first report to demonstrate a limitation concerning sensitivity of D-dimer
Marill[24] (2008)	III	Meta-analysis	Literature review of patients with confirmed aortic dissection and D-dimer; 349 patients, 327 with acute aortic dissection	349 pooled patients; D-dimer >0.5 μg/mL; sensitivity 94%; specificity 40% to 100%	Test type varied; 11 studies reviewed
Ohlmann et al[25] (2006)	III	French study; single center; retrospective case control study	94 acute aortic dissection (<15 days) and 94 control patients with suspected dissection but later ruled out who had D-dimer testing; aortic dissection confirmed by imaging or autopsy; 188 patients, 94 with aortic dissection	D-dimer >400 ng/mL; sensitivity 99%; specificity 34%; LR+: 1.5; LR-: 0.3; 93 of 94 patients with aortic dissection had a positive D-dimer result	Sta-Liatest D-DI immunoturbidimetric assay (Diagnostica Stago); 1 normal D-dimer result had localized intramural hematoma without intimal flap; D-dimer level significantly lower in patients with intramural hematoma vs patients with patent false lumen
Shimony et al[26] (2011)	III	Meta-analysis	7 studies; 298 patients with acute (within 2 wk) aortic dissection	D-dimer threshold of 500 ng/mL; sensitivity 97% (95% CI 0.94% to 0.99%); specificity 56% (95% CI 0.51% to 0.60%); NPV: .96 (95% CI 0.93 to 0.98); PPV: .60 (95% CI 0.55 to 0.66); LR-: 0.06 (95% CI 0.03 to 0.12); LR+: 2.43 (95% CI 1.89 to 3.12)	Assays varied

Evidentiary Table (continued).

Study and Year Published	Class of Evidence	Setting and Study Design	Methods and Outcome Measures	Results	Limitations and Comments
Sodeck et al[27] (2007)	III	Austrian study; single site; tertiary care; prospective cohort	D-dimer ordered immediately after diagnosis of ascending aortic dissection established; 65 patients	D-dimer >0.1 μg/mL; sensitivity 100%; D-dimer >0.5 μg/mL; sensitivity 98%; D-dimer >0.9 μg/mL; sensitivity 86%; NPV ranged from 92% to 100%	STA latex agglutination (Roche)
Suzuki et al[28] (2009)	III	Multicenter; prospective cohort	220 patients; 87 with acute aortic dissection; 133 control	D-dimer cutoff value of 500 ng/mL; sensitivity 96.6% (95% CI 90.3% to 99.3%); specificity 46.6% (95% CI 37.9% to 55.5%); LR+: 1.8; LR-: 0.07; PPV 37.6; NPV 97.6	Triage D-dimer; predictive values based on prevalence of disease estimated at 25%; slight trend for false lumen patency to be associated with higher D-dimer level but it was not statistically significant
Nazerian et al[29] (2014)	III	Retrospective study at 2 cardiovascular centers	Included patients with suspected aortic dissection enrolled prospectively in a registry prior to diagnosis of dissection; D-dimer was obtained at physician discretion; latex agglutination test was performed with a threshold of 500 ng/mL; ADD was retrospectively applied; diagnosis was based on a 2-physician review of imaging, autopsy, or surgical reports	Risk score and D-dimer were obtained for 1,035 patients; the ADD was 0 in 322 patients and 1.8% had an aortic dissection; the D-dimer LR- was 0 in these patients; in the overall patient population of 1,035 the D-dimer LR- was 0.05 (95% CI 0.02 to 0.13)	Selection bias is likely because all patients were referred to the registry by the treating physician based on suspicion; not all patients with a suspected aortic dissection had a D-dimer obtained

Evidentiary Table (continued).

Study and Year Published	Class of Evidence	Setting and Study Design	Methods and Outcome Measures	Results	Limitations and Comments
Shiga et al[31] (2006)	I	Systematic review and meta-analysis of diagnostic accuracy of TEE, CT, and MRI	Selected studies: prospective, at least 1 imaging technique was used, reported absolute numbers of true-positive, false-negative, true-negative, and false-positive results, reference standard for diagnosing thoracic aortic dissection was clearly indicated	16 studies including 1,139 patients met inclusion criteria; TEE (10 studies): sensitivity 98% (95% CI 95% to 99%), specificity 95% (95% CI 92% to 97%); LR+: 14.1; LR-: 0.4; helical CT (3 studies): sensitivity 100% (95% CI 96% to 100%), specificity 98% (95% CI 87% to 99%); LR+: 13.9; LR-:0.02; MRI (7 studies): sensitivity 98% (95% CI 95% to 99%), specificity 98% (95% CI 95% to 100%); LR+: 25.3; LR-: 0.05	Only 3 helical CT studies included with a total of 117 patients with aortic dissection (18 of whom had subacute or chronic aortic dissections); the sensitivity is likely overly optimistic given the high percentage of patients with the disease in this population cohort

Evidentiary Table (continued).

Study and Year Published	Class of Evidence	Setting and Study Design	Methods and Outcome Measures	Results	Limitations and Comments
Sommer et al[32] (1996)	II	German academic medical center; prospective cohort	Symptomatic patients clinically suspected to have aortic dissection who were able to have TEE followed by spiral CT and MRI within 48 h; outcome: aortic dissection diagnosis on autopsy, intraoperative exploration, angiography, or follow-up	N=49; sensitivity 100% (95% CI 89% to 100%) for all 3 study modalities; CT specificity 100% (95% CI 79% to 100%); TEE specificity 94% (95% CI 70% to 100%) MRI specificity 94% (95% CI 70% to 100%)	10 of 49 enrolled patients had previous repair of Stanford type A dissection; only 1 interpreter for each imaging modality but the interpreter was blinded and followed strict diagnostic criteria
Yoshida et al[33] (2003)	I	Japanese academic medical center; prospective cohort	Patients receiving emergency helical CT for suspected aortic dissection or intramural hematoma; outcome: aortic dissection confirmed with surgery	N=121 (58 aortic dissection diagnoses and 1 refused surgery); sensitivity 100%; specificity 100%; LR+: undefined; LR-: 0.12 (95% CI 0.02 to 0.78)	Two interpreters of CT imaging before surgery were aware of clinical history but blinded to other imaging
Zeman et al[34] (1995)	III	Academic medical center; prospective study	Patients with chest pain or abnormal chest radiograph referred for helical CT; outcome: aortic dissection based on surgery, angiography, or clinical outcome	N=23 with 7 true positives, 15 true negatives, and 1 false positive; sensitivity 93.8%; specificity 100%	Very small sample (7 aortic dissections)
Hayter et al[35] (2006)	II	Urban academic medical center; retrospective cohort	Patients undergoing multidetector CTA for suspicion of aortic dissection in emergency setting; electronic chart review; outcome: diagnosis of aortic disorder	N=373; sensitivity 99% (67/68), 95% CI 91% to 100%; specificity100% (304/304), 95% CI 99% to 100%; PPV 100% (67/67); NPV 99.7% (304/305); LR+: undefined; LR-: 0.01 (95% CI 0 to 0.10); accuracy 99.5% (371/373)	CT depicted alternative findings accounting for acute presentation in 12.9% (48) of the negative cases; test characteristics are for diagnosis of aortic disorders (not aortic dissection specifically)

Evidentiary Table (continued).

Study and Year Published	Class of Evidence	Setting and Study Design	Methods and Outcome Measures	Results	Limitations and Comments
Moore et al[36] (2002)	III	IRAD; retrospective cohort	Physicians completed form developed by IRAD investigators for all acute aortic dissections (onset within 14 days)	N=628 registry patients; TEE: sensitivity 88% (170/193) CT: sensitivity 93% (353/379) MRI: sensitivity 100% (9/9) aortography: sensitivity 87% (21/24)	Does not report consecutive sample; therefore, likely a convenience sample; no single criterion standard used for aortic dissection diagnosis
Evangelista et al[38] (2010)	II	Academic hospital in Spain; specific clinical environment unclear; prospective cohort study	Conventional and contrast-enhanced TTE and TEE were performed in 143 consecutive patients with clinically suspected acute aortic dissection; aortic dissection was diagnosed by the presence of 2 vascular lumina separated by an intimal flap; results were validated independently against criterion standard of intraoperative findings in 45 patients and CT information in 90; outcome measures: diagnostic characteristics of TTE and TEE	143 consecutive patients enrolled; 8 excluded due to type A dissections with hemodynamic shock in which surgical treatment was indicated directly after conventional or contrast-enhanced TTE; 7 excluded because of poor windows; 128 enrolled in study; results for 143 with TTE done and criterion standard test: prevalence 60% (95% CI 52% to 68%), sensitivity 74% (95% CI 65% to 84%), specificity 74% (95% CI 62% to 85%), LR+: 2.8 (95% CI 1.8 to 4.4), LR-: 0.35 (95% CI 0.23 to 0.51)	Enrolled consecutive patients with suspicion of acute aortic dissection from the ED; the prevalence of 60% is higher than typically tested for thoracic aortic dissection in the ED; the published data excluded 15 patients: 8 with positive TTE and 7 with poor windows; test characteristics were calculated based on complete data obtained by e-mail from author

Evidentiary Table (continued).

Study and Year Published	Class of Evidence	Setting and Study Design	Methods and Outcome Measures	Results	Limitations and Comments
Khandheria et al[39] (1989)	III	Urban, single-center, academic hospital; retrospective cohort	Retrospective review of TTE among patients with a diagnosis of thoracic aortic dissection; TTE definition of thoracic aortic dissection was not explicit; criterion standard was operative or autopsy diagnosis; outcome measures: diagnostic characteristics of TTE	67 patients: 31 type I, 21 type II, 10 type III, 5 false positive; prevalence 93% (95% CI 86% to 99%), sensitivity 79% (95% CI 70% to 90%), specificity 0% (95% CI 0% to 52%), LR+: 0.8 (95% CI 0.7 to 0.9), LR-: undefined	Retrospective review of 'cases' of thoracic aortic dissection; did not include: patients with suspicion of thoracic aortic dissection on whom TTE was performed and who did not have criterion diagnosis of thoracic aortic dissection, or patients with inadequate studies; this falsely elevates sensitivity
Kodolitsch et al[40] (1999)	III	Urban, academic hospital in Germany; specific clinical environment unclear; retrospective cohort	Retrospective review of TTE compared with a variable criterion standard or surgical results, angiography, or autopsy; TTE definition of thoracic aortic dissection required evidence of 2 vascular lumina separated by a flap; further classified as definite with presence of at least 1 other sign (demonstration of an entry-site, flow phenomena, or thrombus formation in the false lumen, mediastinal hematoma, side-branch occlusion, aortic valve incompetence, pericardial effusion, or aortic dilatation); outcome measures: diagnostic characteristics of TTE	Enrolled 168 patients over 10 y with clinical suspicion of aortic dissection; diagnostic characteristics of TTE calculated based on the 86 patients who had TTE and criterion; prevalence 45% (95% CI 35% to 56%), sensitivity 67% (95% CI 52% to 81%), specificity 70% (95% CI 57% to 83%), LR+: 2.2 (95% CI 1.4 to 3.7), LR–: 0.47 (95% CI 0.29 to 0.77)	Population of 168 patients over 10 y with clinical suspicion of aortic dissection is not consistent with ED practice in United States, because a larger number of patients are evaluated for thoracic aortic dissection; a variable criterion standard was used: surgical results, angiography, or autopsy

Evidentiary Table (continued).

Study and Year Published	Class of Evidence	Setting and Study Design	Methods and Outcome Measures	Results	Limitations and Comments
Nienaber et al[41] (1993)	III	2 urban, academic hospitals in Germany; prospective cohort	Included adults referred to hospitals with suspected thoracic aortic dissection; TTE, TEE, CT, and MRI were the diagnostic tests under study; angiography, surgical and postmortem evaluations were the criterion standard; each modality had clear definitions for thoracic aortic dissection; TTE criteria were presence of 2 vascular lumens separated by an intimal flap; imaging readers were blinded to other results and came to consensus on image interpretations; results: diagnostic characteristics of TTE, TEE, CT, and MRI	All 110 patients with suspected thoracic aortic dissection underwent TTE during 5 y; prevalence 56% (95% CI 47% to 66%), sensitivity 59% (95% CI 47% to 72%), specificity 83% (95% CI 73% to 94%), LR+: 3.5 (95% CI 1.8 to 7.0), LR–: 0.48 (95% CI 0.35 to 0.67)	A variable criterion standard was used; authors report diagnostic characteristics for type A and B thoracic aortic dissection separately (and acute and subacute); for this clinical policy one 2x2 table was rebuilt for all types of thoracic aortic dissection, which produces slightly different results from what is published in the article; the results published in the article were reported here
Roudaut et al[42] (1988)	III	Urban, academic hospitals in France; prospective cohort	Over 6 y, 673 patients underwent TTE and had a criterion standard test; TTE standards for diagnosing TTE were defined: aortic dilatation, intimal flap; criterion standard: CT, angiography, surgery, or autopsy; outcomes: diagnostic characteristics of TTE	673 patients with a clinical suspicion of aortic dissection, over a 6-y period; prevalence 19% (95% CI 16% to 22%), sensitivity 67% (95% CI 59% to 75%), specificity 100% (95% CI 99% to 100%), LR+: undefined, LR–: 0.33 (95% CI 0.26 to 0.42)	Use of angiography, 1 criterion standard, changed during study from first test to follow-up test in some patients; specificity of 100% does not fit in the range of other studies and suggests that the TTE was not interpreted in isolation or blindly because there were no false positives; dropout: echocardiogram was technically difficult and of poor quality in 13 cases of aortic dissection (10%)

Evidentiary Table (continued).

Study and Year Published	Class of Evidence	Setting and Study Design	Methods and Outcome Measures	Results	Limitations and Comments
Victor et al[43] (1981)	III	Urban, single-center, academic hospital; prospective cohort	Included patients referred for TTE because of a clinical suspicion of aortic dissection; diagnostic accuracy of TTE, using presence of an intimal flap as diagnostic definition; criterion standard: angiography or pathology	42 patients; prevalence 36% (95% CI 21% to 50%); sensitivity 80% (95% CI 60% to 100%); specificity 96% (95% CI 89% to 100%); LR+: 21.6 (95% CI 3.1 to 150); LR-: 0.21 95% CI (0.08 to 0.57)	
Kodama et al[55] (2008)	III	Single center, prospective study of type B acute aortic dissection	Heart rate was measured at 6 AM, noon, and 6 PM every day; all patients received β-blockers unless contraindicated; tight heart rate control defined as average heart rate at 3, 5, and 7 days after onset and had heart rate <60 beats/min; aortic events: composite ischemia, rupture, expansion, recurrent dissection during study period	171 patients followed a median of 27 mo with 32 meeting definition of tight heart rate control; total adverse events: tight heart rate 4 (12.5%), control 50 (36%) OR 0.25, 95% CI 0.08 to 0.77, *P*<.01	Excluded subjects who did not meet systolic blood pressure (<120 mm Hg) within 3 days; outpatient management not adjusted for (84% confirmed compliance); heart rate control averaged over 3 days

ADD, aortic dissection detection; *CI*, confidence interval; *CT*, computed tomography; *CTA*, computed tomography angiogram; *ECG*, electrocardiogram; *ED*, emergency department; *h*, hour; *IRAD*, International Registry of Acute Aortic Dissection; *LR*, likelihood ratio; *min*, minute; *mm Hg*, millimeters of mercury; *mo*, month; *MRI*, magnetic resonance imaging; *NPV*, negative predictive value; *OR*, odds ratio; *PA*, posterior to anterior; *PPV*, positive predictive value; *TEE*, transesophageal echocardiogram; *TTE*, transthoracic echocardiogram; *wk*, week; *y*, year.