Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

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Circulation 2011;123;2213-2218; originally published online May 9, 2011;
DOI: 10.1161/CIRCULATIONAHA.110.988568
Circulation is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0009-7322. Online ISSN: 1524-4539

Sensitivity of the Aortic Dissection Detection Risk Score, a Novel Guideline-Based Tool for Identification of Acute Aortic Dissection at Initial Presentation

Results From the International Registry of Acute Aortic Dissection

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Background—In 2010, the American Heart Association and American College of Cardiology released guidelines for the diagnosis and management of patients with thoracic aortic disease, which identified high-risk clinical features to assist in the early detection of acute aortic dissection. The sensitivity of these risk markers has not been validated.

Methods and Results—We examined patients enrolled in the International Registry of Acute Aortic Dissection from 1996 to 2009. The number of patients with confirmed acute aortic dissection who presented with 1 or more of 12 proposed clinical risk markers was determined. An aortic dissection detection (ADD) risk score of 0 to 3 was calculated on the basis of the number of risk categories (high-risk predisposing conditions, high-risk pain features, high-risk examination features) in which patients met criteria. The ADD risk score was tested for sensitivity. Of 2538 patients with acute aortic dissection, 2430 (95.7%) were identified by 1 or more of 12 proposed clinical risk markers. With the use of the ADD risk score, 108 patients (4.3%) were identified as low risk (ADD score 0), 927 patients (36.5%) were intermediate risk (ADD score 1), and 1503 patients (59.2%) were high risk (ADD score 2 or 3). Among 108 patients with no clinical risk markers present (ADD score 0), 72 had chest x-rays recorded, of which 35 (48.6%) demonstrated a widened mediastinum.

Conclusions—The clinical risk markers proposed in the 2010 thoracic aortic disease guidelines and their application as part of the ADD risk score comprise a highly sensitive clinical tool for the detection of acute aortic dissection. **(*Circulation*. 2011;123:2213-2218.)**

Key Words: aorta ■ aortic dissection ■ risk factors ■ risk score ■ screening

Acute aortic dissection (AD), among the most lethal of cardiovascular catastrophes, is suspected at initial evaluation in fewer than half of patients ultimately diagnosed with the disease.[1–5] Although multiple factors undoubtedly complicate early and accurate identification of the acute AD patient, principal among them is a signal-to-noise phenomenon.

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Clinical Perspective on p 2218

The incidence of acute AD in the United States is estimated at 10 000 cases annually, whereas emergency department visits are ≈100 000 000 during the same time period.[6–8] Accordingly, a single case of acute AD would be expected in only 1 in 10 000 emergency department presentations. This relatively weak signal is easily overwhelmed by the background noise of patients presenting with complaints that could, but do not, represent acute AD. To accurately identify all cases of acute AD, the clinician must consider the diagnosis in patients presenting not only with chest pain, but also with back pain, abdominal pain, syncope, or complaints related to a perfusion deficit including stroke, myocardial infarct, limb ischemia, and mesenteric ischemia.[9] Furthermore, accurate identification or exclusion of the disease requires an advanced imaging study. If every patient presenting with symptoms that might represent AD were imaged, the cost and radiation exposure would be prohibitive.

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Received September 14, 2010; accepted March 14, 2011.

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Guest Editor for this article was Robert O. Bonow, MD.

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Circulation **is available at http://circ.ahajournals.org** **DOI: 10.1161/CIRCULATIONAHA.110.988568**

Recently, the American Heart Association, American College of Cardiology, and other professional societies published guidelines for the diagnosis and management of thoracic aortic disease (TAD).[10] Included in the guidelines is a risk assessment tool that was developed on the basis of an extensive review of the literature on acute AD combined with the collective experience of the writing committee. The aortic dissection detection (ADD) risk score was adapted from this tool to provide clinicians with a simple, systematic method for screening large volumes of patients at the bedside. By focusing on specific high-risk predisposing conditions, pain features, and physical examination findings, patients are grouped into 1 of 3 categories on the basis of their pretest risk of acute AD. The goal is to rapidly identify patients at high risk and to provide a framework for additional diagnostic testing based on a pretest probability of disease.

Because this guideline-based tool has not been validated in a clinical setting, it is not known whether it will effectively identify patients with a high probability of acute AD. The purpose of the present study is to apply the ADD risk score to the International Registry of Acute Aortic Dissection (IRAD) database to determine the percentage of this group of patients with diagnosed AD that would have been identified.

Methods

The IRAD database is a multinational registry designed to provide a representative population of patients with acute AD. Treatment during the index hospitalization or in follow-up was not standardized, but at the discretion of each patient's treating physician. Full details of the IRAD methods have been published previously.[4] All sites have institutional review board approval to participate in IRAD.

Study Population

We examined data on all patients with acute AD enrolled in IRAD centers between January 1, 1996, and December 31, 2009 (24 centers). Acute AD was defined as any nontraumatic dissection within 14 days of symptom onset. Patients were identified prospectively at presentation or retrospectively via discharge diagnoses, imaging, and hospital databases. Diagnosis was based on imaging, surgical visualization, or autopsy.

Data Collection

Data on 290 variables were recorded on a standardized form that included information on patient demographics, history, clinical presentations, physical findings, imaging study results, details of medical and surgical treatment, and patient outcomes, including mortality. Data forms were reviewed for internal consistency and validity and then scanned electronically into a Microsoft Access database.

Imaging was interpreted at each patient's respective tertiary care center by specialized radiologists and echocardiographers and entered into the data form. Helical computed tomography, transesophageal echocardiography, magnetic resonance imaging, and/or angiography was obtained. Data contained in IRAD are identical to those reported to the physicians caring for the patients.

Statistical Analysis

We assessed the presenting characteristics of patients with confirmed acute AD to evaluate the sensitivity of the TAD guideline diagnostic algorithm. High-risk clinical markers that were tested include the following: history of Marfan syndrome, family history of aortic disease, history of known aortic valve disease, history of recent aortic manipulation, history of known thoracic aortic aneurysm, abrupt onset of pain, severe pain intensity, ripping or tearing pain, pulse deficit or systolic blood pressure differential between extremities, focal neurological deficit (in conjunction with pain), new murmur of aortic insufficiency (in conjunction with pain), and hypotension or shock state. After determining the frequency of each individual risk marker among patients with acute AD, we aggregated the risk markers into 3 categories (high-risk predisposing conditions, high-risk pain features, and high-risk examination features) on the basis of the algorithm proposed in the TAD guidelines (Figure 1). We assigned an ADD risk score of 0, 1, 2, or 3 to patients on the basis of the number of categories in which at least 1 risk marker was present. The sensitivity of each clinical risk marker, risk category, and ADD risk score was calculated.

In all cases, missing data were defaulted to negative, which should bias toward a conservative estimate of sensitivity. Bivariate analysis was performed with the use of χ^2 analysis or 2-sided Fisher exact tests where appropriate to identify clinical features more commonly present in patients not identified by the algorithm. PASW version 18.0.1 (SPSS Inc) was used for all analyses.

Results

Of 2538 patients with acute AD, 2430 (95.7%) were identified by 1 or more of 12 proposed clinical risk markers, whereas 2123 (83.6%) had at least 2 clinical risk markers present. A large percentage of patients (46.4%) had either 3 or 4 risk markers identified at the time of presentation (Table 1).

High-risk pain features, such as abrupt onset of pain (79.3%), severe intensity of pain (72.7%), and pain described as ripping or tearing (21.7%) were most frequently present in patients with acute AD. The most common high-risk predisposing conditions identified were known thoracic aortic aneurysm (14.7%) and known aortic valve disease (11.9%), whereas the most common high-risk examination features included a new murmur of aortic insufficiency in conjunction with pain (23.6%) and a pulse deficit or systolic blood pressure differential between extremities (20.3%) (Table 2).

Among the 3 risk categories, 713 patients (28.1%) had at least 1 of the high-risk predisposing conditions present, 2220 patients (87.5%) had at least 1 of the high-risk pain features present, and 1294 patients (51.0%) had at least 1 of the high-risk examination features present (Figure 2). With the use of an ADD risk score of 0 to 3 based on the number of risk categories for which criteria were met, 108 patients (4.3%) scored 0 and would have been considered low risk, 927 patients (36.5%) scored 1 and would have been considered intermediate risk, and 1503 patients (59.2%) scored 2 or 3 and would have been considered high risk (Figure 2).

Among 927 patients (36.5%) with an intermediate risk score of 1, high-risk pain features, including abrupt onset of pain (72.0%) and severe pain intensity (68.5%) were most commonly identified (Table 3). Cases of AD were identified with each of the 12 clinical risk markers present in isolation.

Of the 108 patients (4.3% of total population) with no clinical risk markers present (ADD risk score 0), 72 had chest x-rays recorded, of which 35 (48.6%) were noted to have a widened mediastinum (Figure 2). Compared with patients identified by the algorithm, those 108 not identified were more frequently of nonwhite race (23.5% versus 12.0%; $P=0.001$), had a history of diabetes mellitus (12.9% versus 5.9%; $P=0.006$), and presented as normotensive (49.4% versus 36.8%; $P=0.017$), whereas they less frequently presented with chest pain (40.5% versus 77.6%; $P<0.001$), back pain (24.1% versus 54.5%; $P<0.001$), head or neck pain (5.3% versus 18.1%; $P=0.001$), leg pain (3.8% versus 12.8%; $P=0.008$), radiating pain (12.7% versus 38.9%;

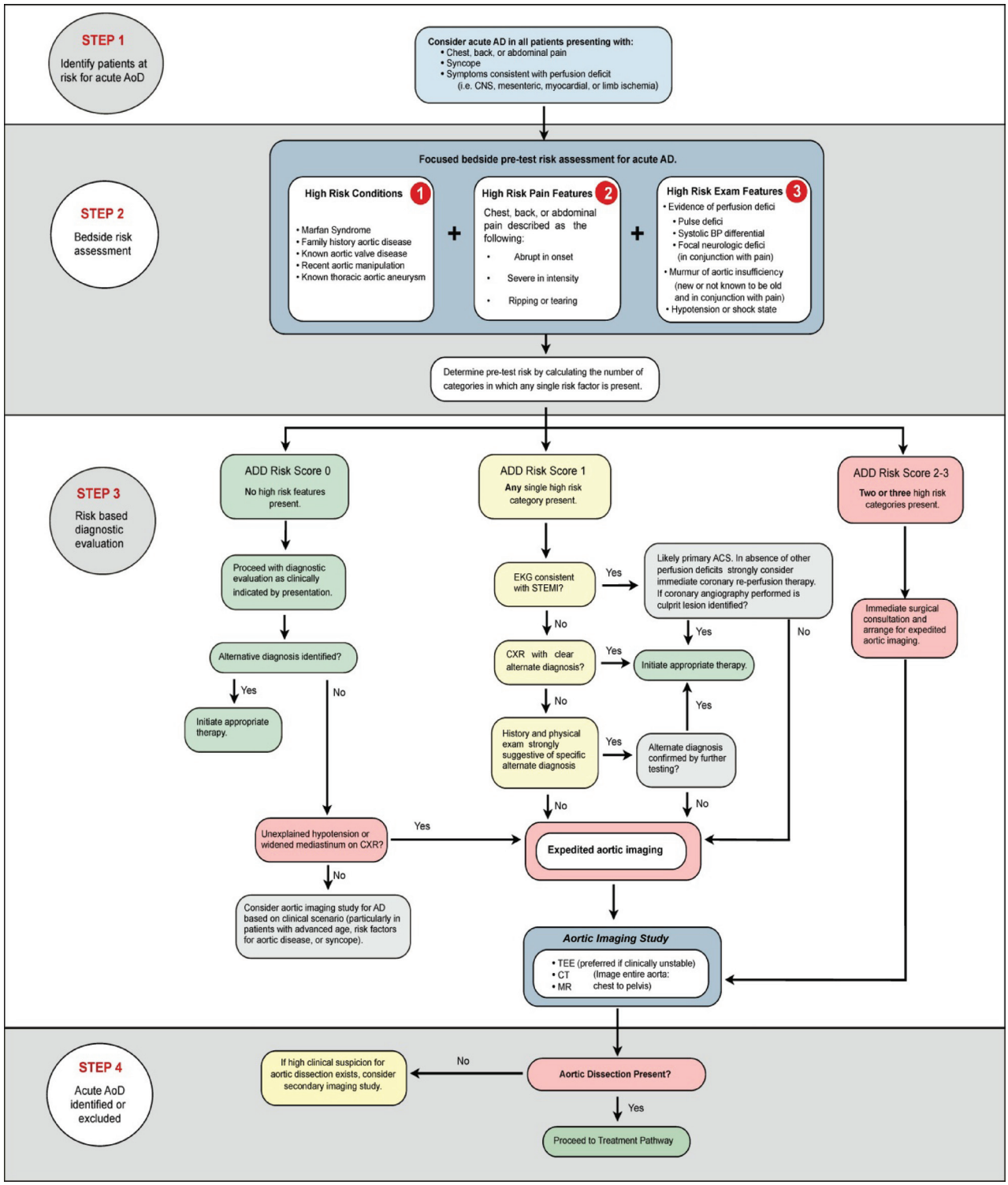

Figure 1. Aortic dissection (AoD, AD) evaluation pathway. ACS indicates acute coronary syndrome; ADD, aortic dissection detection; BP, blood pressure; CNS, central nervous system; CT, computed tomography; CXR, chest x-ray; MR, magnetic resonance imaging; STEMI, ST-segment elevation myocardial infarction; and TEE, transesophageal echocardiogram. Adapted from the 2010 American College of Cardiology/American Heart Association thoracic aortic disease guidelines.[10]

$P<0.001$), or with a history of prior cardiac surgery (8.4% versus 17.6%; $P=0.020$). Patients not identified by the algorithm were more frequently enrolled in the IRAD database from US hospitals compared with European hospitals (6.0% versus 2.5%; $P<0.001$).

Discussion

The diagnostic algorithm proposed in the TAD national guidelines is highly sensitive (95.7%) for the detection of acute AD at initial presentation.[10] The ADD risk score was adapted from this diagnostic algorithm to provide clinicians

Table 1. Number of Patients With Acute Aortic Dissection Presenting With 1 or More Clinical Risk Markers (n=2538)

No. of Risk Markers	No. of Patients	Percentage of Patients
0	108	4.3
1	307	12.1
2	666	26.2
3	750	29.6
4	426	16.8
5	187	7.4
6	79	3.1
7	15	0.6
Total	2538	100.0

with a simple, systematic method for screening large volumes of patients at the bedside. This novel score similarly classified 95.7% of patients diagnosed with acute AD in the IRAD database as either intermediate or high risk. Of the 2430 patients with any high-risk feature, 36.5% were categorized as intermediate risk (ADD score 1) and 59.2% were categorized as having a high risk of acute AD (ADD score 2 or 3) (Figure 2).

The clinical utility of the ADD risk score rests on its sensitivity and specificity as a diagnostic screening tool. The results from this study suggest that the ADD risk score, with the use of only information that is available at the bedside, offers adequate sensitivity to capture the vast majority of patients presenting with acute AD. Furthermore, 59% of those meeting criteria for the algorithm were categorized as high risk, in which the recommendation for expedited imaging has the potential to improve time to diagnosis of this acute life-threatening condition.[10,11] In the group categorized as intermediate risk (ADD score 1; 36.5% of study population), the diagnostic pathway proposed in the TAD guidelines provides specific clinical steps intended to promote prompt imaging in the appropriate subset of these patients (Figure 1). Given the relative infrequency of acute AD, which often leads to missed or delayed diagnosis, application of the ADD risk score has the potential to draw necessary clinical attention to the possibility of acute AD while ensuring that >95% of patients with true dissection meet criteria for further investigation.

Table 2. Number of Patients With Acute Aortic Dissection Identified by Each Clinical Risk Marker (n=2538)

	No. of Patients	Percentage of Patients
01: Marfan syndrome	110	4.3
02: Family history of aortic disease	48	1.9
03: Known aortic valve disease	303	11.9
04: Recent aortic manipulation	70	2.8
05: Known thoracic aortic aneurysm	374	14.7
06: Abrupt onset of pain	2012	79.3
07: Severe pain intensity	1845	72.7
08: Ripping or tearing pain	551	21.7
09: Pulse deficit or SBP differential	515	20.3
10: Focal neurological deficit (in conjunction with pain)	273	10.8
11: Murmur of aortic insufficiency (new in conjunction with pain)	599	23.6
12: Hypotension or shock state	407	16.0

SBP indicates systolic blood pressure.

Among the 4.3% of patients in IRAD categorized as low risk (ADD score 0), the clinical utility of the tool is less concrete, but still appears helpful. By guideline protocol, patients categorized as low risk should undergo diagnostic aortic imaging if a widened mediastinum is noted on chest x-ray, as was the case in nearly half (48.6%) of all low-risk IRAD patients who had a chest x-ray performed. With regard to the remainder of patients categorized as low risk by the ADD score (3% of all patients in IRAD), the pathway described in the guideline would recommend consideration of diagnostic aortic imaging if there was no identified source of the patient's presenting symptoms at the completion of the initial evaluation, potentially providing a mechanism to capture at least some of this group.[10]

Although the performance demonstrated by the ADD score in the present study is encouraging, there are specific limitations that warrant discussion. Because acute AD is a relatively rare disease process, testing the ADD score prospectively is not very feasible. We therefore used IRAD, the largest registry of acute AD, to test the clinical performance of the tool. There are inherent limitations to validating a tool in this manner. First, IRAD contains only patients in whom acute AD was identified at some point during their evaluation. Because patients with unrecognized acute AD do not appear in the database, and because these patients may in fact be unrecognized as a result of atypical presentations, we would anticipate that the risk score will not perform as well in an undifferentiated patient population.

Additionally, the present study does not allow for any estimation of the specificity of the ADD risk score. It is possible that a significant percentage of patients presenting with chest, abdominal, or back pain of a nonaortic pathogenesis would be classified as intermediate or high risk, leading to potential overtesting as an unintended consequence of widespread implementation of the proposed pathway. To address this issue, the original algorithm proposed in the TAD guidelines was modified when the ADD risk score was designed. Pain described as sharp or stabbing was not included as a stand-alone marker of risk; rather, high-risk pain features include pain described as ripping or tearing, abrupt in onset, or severe in intensity. Connective tissue disease was also excluded as a stand-alone high-risk predisposing condition, whereas patients with Marfan syndrome continue to meet criteria. Although we believe that these adjustments may help to increase the specificity of the ADD risk score, the present study does not offer clarity on this issue.

Further investigation is needed to corroborate the accuracy of the ADD risk score, and in particular to assess the specificity of this diagnostic screening tool. As is the case with most screening tools, specificity will likely prove to be significantly lower than sensitivity. One potential future strategy to address this issue might include the use of an

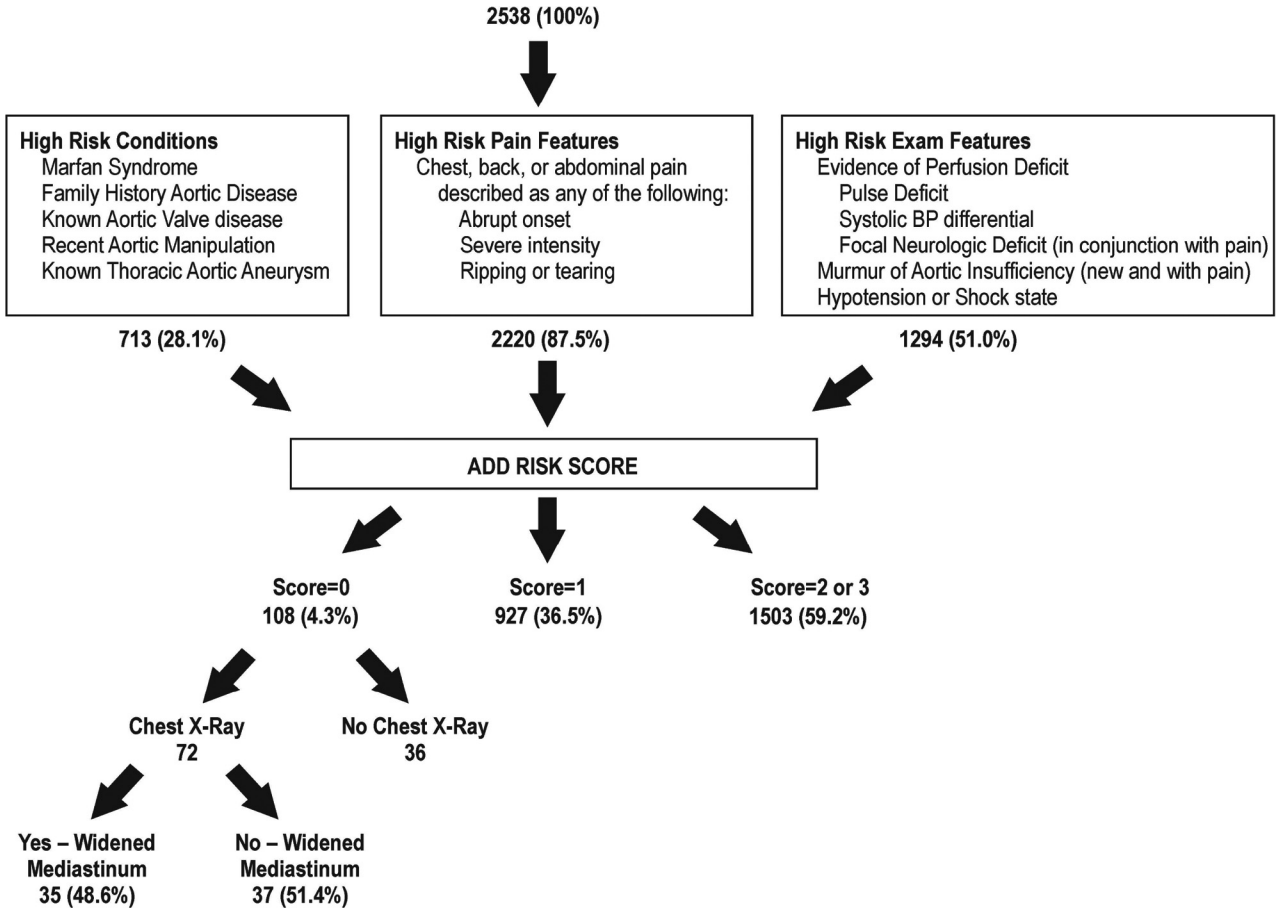

Figure 2. Evaluation of patients with known acute aortic dissection with the use of the aortic dissection detection (ADD) risk score. An ADD risk score of 0 is considered low risk, 1 is considered intermediate risk, and 2 or 3 is considered high risk. Further diagnostic workup should proceed according to the algorithm shown in Figure 1. Among patients with an ADD risk score of 0, the number of chest x-rays performed and the frequency of widened mediastinum on chest x-ray are depicted. BP indicates blood pressure.

existing or novel biomarker to further risk stratify patients identified as intermediate risk by the ADD risk score. Conceptually, this approach is somewhat analogous to the way in which Wells criteria and D-dimer testing combine to identify a low-risk population that does not require definitive radiological testing to rule out pulmonary embolism.[12,13] Analyses including the recent International Registry of Acute Aortic Dissection Substudy on Biomarkers (IRAD-Bio) offer preliminary evidence to suggest that D-dimer may have relevance in patients with acute AD as well.[14,15] Further study is warranted to investigate whether D-dimer or another biomarker could complement the ADD risk score in the initial triage of patients with suspected acute AD.

Table 3. Risk Factors Present in Patients With an Intermediate Aortic Dissection Detection Risk Score of 1 (n=927)

	No. of Patients	Percent of Patients
01: Marfan syndrome	6	0.6
02: Family history of aortic disease	3	0.3
03: Known aortic valve disease	50	5.4
04: Recent aortic manipulation	28	3.0
05: Known thoracic aortic aneurysm	44	4.7
06: Abrupt onset of pain	667	72.0
07: Severe pain intensity	635	68.5
08: Ripping or tearing pain	200	21.6
09: Pulse deficit or SBP differential	27	2.9
10: Focal neurological deficit (in conjunction with pain)	15	1.6
11: Murmur of aortic insufficiency (new in conjunction with pain)	22	2.4
12: Hypotension or shock state	29	3.1

SBP indicates systolic blood pressure.

Conclusion

The clinical risk markers proposed in the 2010 TAD guidelines and their application as part of the ADD risk score comprise a highly sensitive clinical tool for the detection of acute AD.

Sources of Funding

IRAD is supported by grants from the University of Michigan Health System, Varbedian Fund for Aortic Research, Hewlett Foundation, Mardigian Foundation, and Gore Inc.

Disclosures

Dr Froehlich reports the following conflicts: consultant: Pfizer, Sanofi-aventis; Speakers Bureau: Pfizer, Sanofi-aventis, Merck; contracted research: Blue Cross/Blue Shield of Michigan, Mardigian Foundation, Fibromuscular Disease Society of America. Dr Eagle

reports the following conflicts: grant/research support: Gore Inc, Hewlett Foundation, Mardigian Fund, Verbedian Fund; consultant: National Institutes of Health/National Heart, Lung, and Blood Institute. The other authors report no conflicts.

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CLINICAL PERSPECTIVE

Acute aortic dissection is known to be an underrecognized condition at presentation, yet the mortality associated with delayed or missed diagnosis is substantial. The American Heart Association, American College of Cardiology, and other professional societies recently published the 2010 thoracic aortic disease guidelines, which include recommendations for the initial bedside screening of at-risk patients. The goal of these recommendations is to improve physician recognition and facilitate prompt diagnostic testing in those at risk. In our study, we modified this guideline-based screening tool to define the aortic dissection detection risk score, which divides patients into low-, intermediate-, and high-risk groups on the basis of historical and examination features. We then tested the aortic dissection detection risk score for sensitivity among 2538 patients enrolled in the International Registry of Acute Aortic Dissection. Our results indicate that the aortic dissection detection risk score is 95.7% sensitive for the detection of acute aortic dissection and may help to facilitate prompt evaluation if applied at the bedside. Additional studies are needed to determine the specificity of the aortic dissection detection risk score and provide prospective validation.

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