Diagnostic Delay in Acute Aortic Syndromes: How Sensitive and Specific are Clinical Features in Disease Recognition

7

Kevin M. Harris and Craig Strauss

Abstract

Aortic dissection presents a diagnostic challenge. The history and pain characteristics of aortic dissection overlap significantly with those of acute coronary syndrome (ACS), a condition that is more common by several orders of magnitude. A careful interview focused on high risk conditions (connective tissue diseases, recent aortic manipulation, gene mutations, aortic aneurysm and aortic valve disease), high risk pain characteristics (abrupt, severe or ripping/tearing) and high risk examination features (pulse deficit, focal neurologic deficit or murmur of aortic regurgitation) is critical. High risk pain characteristics are particularly sensitive for detection of aortic dissection. By combining these clinical features, the clinician can identify a patient in whom aortic dissection is more likely and proceed to further aortic imaging. Delays in recognition of dissection are common. Symptoms at presentation, especially in the elderly may be atypical and may include syncope, heart failure, or a lack of pain. Abnormalities on the electrocardiogram, which are common, may lead clinicians to suspect and treat ACS. Additionally, it is not widely recognized that patients with recent aortic manipulation are at risk for dissection, leading to delays in recognition. Clinicians can improve the accuracy and speed with which they diagnose aortic dissection by integrating known risk factors into a careful history and physical exam. One must remain mindful that atypical presentation occur and are associated with delayed diagnosis and increased mortality.

Keywords

Aortic Dissection • Diagnosis • History • Physical Examination • Imaging

Introduction

The diagnosis of acute aortic syndromes is challenging and delays in reaching a definitive diagnosis are frequent. The challenge of chest pain evaluation in the emergency department (ED) is increased by its great frequency in the United

K.M. Harris, MD (✉) • C. Strauss, MD, MPH
Minneapolis Heart Institute, Abbott Northwestern Hospital, 920 E. 28th St., Suite 300, Minneapolis, MN 55407, USA
e-mail: kevin.harris@allina.com

R.S. Bonser et al. (eds.), *Controversies in Aortic Dissection and Aneurysmal Disease*,
DOI 10.1007/978-1-4471-5622-2_7,

States; approximately 4.6 million visits annually [1]. Performing diagnostic imaging on every patient presenting to the ED with chest pain for the purpose of excluding acute aortic syndrome would be an irrational use of limited healthcare resources. Furthermore, it would unnecessarily subject patients to the risk of intravenous contrast and radiation. In current practice, ED evaluation of patients with chest pain emphasizes the exclusion of more common clinical conditions, principally acute coronary syndromes (ACS). It is imperative that clinicians recognize the appropriate cues from a patient's history, physical exam, laboratory findings, and chest x-ray to decide which patients require further diagnostic imaging to exclude acute aortic pathology [1]. Only 0.003 % of patients presenting to the ED with acute chest, back or abdominal pain will ultimately be diagnosed with an aortic dissection [2], and it is estimated that one in every 10,000 patients presenting to EDs will have aortic dissection [3].

Improved survival requires timely diagnosis and rapid access to definitive treatment. In one large series, 38 % of cases were missed on initial diagnosis and 28 % were diagnosed at autopsy [4]. The diagnosis is correctly suspected in only 15–43 % of patients at the time of original presentation [1]. Delayed diagnosis often begins in the ED, where atypical symptoms can lead to misdiagnosis and, in some cases, exposure to antithrombotic agents [5].

The American College of Cardiology (ACC), American Heart Association (AHA) and other professional societies have published an inaugural set of guidelines for the diagnosis and management of patients with aortic disease [6]. These guidelines identify three groupings of high risk clinical markers; *high risk clinical conditions* (Marfan syndrome, family history of aortic disease, known aortic valve disease, recent aortic manipulation, known thoracic aortic aneurysm), *high risk pain features* (chest, back or abdominal pain that is abrupt in onset, severe and/or ripping or tearing) and *high risk exam findings* (pulse deficit, systolic BP differential, focal neurologic deficit with pain, murmur of aortic insufficiency, hypotension or shock state) (Table 7.1).

Table 7.1 Percentage of patients with acute aortic dissection identified by each clinical risk marker (n = 2,538)

	Risk marker	Percentage of patients
High risk clinical conditions		
1	Marfan syndrome	4.3
2	Family history of aortic disease	1.9
3	Known aortic valve disease	11.9
4	Recent aortic manipulation	2.8
5	Known thoracic aortic aneurysm	14.7
High risk pain characteristics		
6	Abrupt onset of pain	79.3
7	Severe pain intensity	72.7
8	Ripping or tearing pain	21.7
High risk physical exam characteristics		
9	Pulse deficit or SBP differential	20.3
10	Focal neurological deficit (in conjunction with pain)	10.8
11	Murmur of aortic insufficiency (new in conjunction with pain)	23.6
12	Hypotension or shock state	16.0

Adapted from: Rogers et al. [3] used with permission
Prevalence of clinical markers suggested in the AHA/ACC guidelines for diagnosis of acute aortic dissection. When patients could be assigned a maximum of one point from each category (clinical conditions, pain features and exam findings), investigators found that only 4 % of patients in IRAD scored 0, 37 % scored 1 and 59 % scored 2 or 3, identifying the latter group as high risk. The investigators concluded that the scoring system was unlikely to perform as well in an undifferentiated patient population. Specificity cannot be assessed, but it was felt that the specificity would be significantly less than the sensitivity

In the guidelines, much of the data is driven by the large International Registry of Acute Aortic Dissection (IRAD) registry. This large registry was established in 1996 and currently has over 30 sites in 11 countries and has collected data on over 3,800 cases [7–9]. As aortic dissection does not lend itself to randomized studies, and single institution studies are often small in number, the IRAD registry offers the best opportunity to evaluate this condition. In the original IRAD series of 464 patients, the typical patient with aortic dissection was male (65 %) with a mean age of 63 years and 62 % had a type A dissection [8]. The term acute aortic syndrome includes not only acute aortic dissection but aortic intramural hematoma [9] as well as penetrating aortic ulcers [6, 10].

Predisposing (High-Risk Clinical) Conditions

The majority of patients with aortic dissection will have a history of hypertension, but several other predisposing conditions should trigger the clinician to consider the diagnosis of aortic dissection. These conditions include a history of a bicuspid aortic valve, connective tissue diseases, such as Marfan syndrome or Ehlers-Danlos syndrome and a history of recent cardiac surgery [6] Rogers et al. examined the sensitivity of the proposed AHA/ACC diagnostic algorithm for diagnosis of acute aortic dissection in IRAD. In their analysis, only 28 % of patients with a proven aortic dissection had one of these predisposing conditions [3]. Few studies have evaluated the sensitivity of individual clinical markers for the diagnosis of aortic dissection. In the most thorough review of this topic, Klompas identified 274 potential sources through a comprehensive MEDLINE review. Among the 21 studies that met inclusion criteria, the majority of patients with aortic dissection had a history of hypertension (pooled sensitivity of 64 % and a positive likelihood ratio (LR) of 1.6) [1]. Marfan syndrome is rare, with a prevalence of 5 %, but when present is more strongly predictive of dissection (LR 4.1) [1]. Interestingly, prior cardiac surgery is one of the more common predisposing conditions with a prevalence of 18 % in cases of type A dissection in the IRAD registry [11, 12].

Classic Symptoms (High Risk Pain Features)

The vast majority of patients with aortic dissection have chest pain that is severe and abrupt in onset (Table 7.2). The presence of pain, severe pain and abrupt-onset pain are highly sensitivity markers, 90, 90 and 84 % respectively [1] 87.5 % of patients in the IRAD registry have high risk pain features, as defined by the inaugural ACC/AHA aortic guidelines [3]. The sudden onset of pain, for example, has a positive LR of 1.6. Its absence argues against aortic dissection with a negative LR of only 0.3 [1]. Classic pain descriptors include a "tearing" or "ripping" sensation in the chest and back, but these descriptors are less frequently noted (31–39 %) [1]. When present, the specificity of a "tearing" or "ripping" sensation is 94–95 % and LR of 1.2–10.8 have been reported [1]. However, the specificity of other pain characteristics, particularly chest pain of a severe nature, is unknown as it may frequently be the presenting symptom of the more common acute coronary syndromes. The specific location of pain is a less valuable predictor, with only moderate sensitivity, as aortic dissection related pain can be migratory and occur is a variety of locations (chest, back, abdomen) [1]. In general, anterior chest pain is more typical of a dissection involving the ascending aorta or arch whereas back pain is more typical in type B dissection, which involves the descending aorta [8]. In the IRAD registry, patients with classic symptoms including "worst pain ever" and back pain were diagnosed nearly twice as quickly as those without classic presenting symptoms [11].

High Risk Physical Exam Findings

The classic physical exam findings of aortic dissection such as a pulse deficit or murmur consistent with aortic insufficiency can be useful in the emergent triage of patients with acute chest pain [1, 6] (Table 7.2). High risk exam findings, as defined by ACC/AHA guidelines, are found in approximately half of patients with proven aortic dissection [1, 3]. However, if physical exam findings are present, they can be highly predictive of aortic dissection [1]. For example, although a pulse differential is uncommon (31 %), the presence of this finding is highly suggestive of aortic dissection with a positive LR of 5.7 [1]. Similarly, neurologic findings, even more uncommon (17 %), greatly increase the odds of aortic dissection when present with a positive LR of 6.6. The absence of these findings, however, does not decrease the likelihood of aortic dissection [1]. The presence or absence

Table 7.2 Accuracy of clinical findings for thoracic aortic dissection in consecutive patients preselected for high clinical suspicion of dissection referred for advanced imaging

Symptom or sign	Source, year of publication	Positive likelihood ratio (95 % CI[a])	Negative likelihood ratio (95 % CI[a])
History of hypertension	Chan [21][b]	1.5 (0.8–3.0)	0.7 (0.4–1.3)
	Enia et al. [22][c]	1.1 (0.7–1.6)	0.7 (0.4–2.4)
	Von Kodolitsch et al. 2000[d]	1.8 (1.4–2.3)	0.4 (0.3–0.6)
	Summary	1.6 (1.2–2.0)	0.5 (0.3–0.7)
Sudden chest pain	Chan [21][b]	1.0 (0.7–1.4)	0.98 (0.3–3.1)
	Armstrong et al. [23][e]	1.5 (1.1–1.9)	0.3 (0.1–0.8)
	Von Kodolitsch et al. 2000[d]	2.6 (2.0–3.5)	0.3 (0.2–0.4)
	Summary	1.6 (1.0–2.4)	0.3 (0.2–0.5)
"Tearing" or "ripping" pain	Armstrong et al. [23][e]	1.2 (0.2–8.1)	0.99 (0.9–1.1)
	Von Kodolitsch et al. 2000[d]	10.8 (5.2–22.0)	0.4 (0.3–0.5)
Migrating pain	Chan [21][b]	1.1 (0.5–2.4)	0.97 (0.6–1.6)
	Von Kodolitsch et al. 2000[d]	7.6 (3.6–16.0)	0.6 (0.5–0.7)
Pulse deficit	Armstrong et al. [23][e]	2.4 (0.5–12.0)	0.93 (0.8–1.1)
	Enia et al. [22][c]	2.7 (0.7–9.8)	0.63 (0.4–1.0)
	Von Kodolitsch et al. 2000[d]	47.0 (6.6–333.0)	0.62 (0.5–0.7)
	Summary	5.7 (1.4–23.0)	0.7 (0.6–0.9)
Focal neurological deficit	Armstrong et al. [23][e]	6.6 (1.6–28.0)	0.71 (0.6–0.9)
	Von Kodolitsch et al. 2000[d]	33.0 (2.0–549.0)	0.87 (0.8–0.9)
Diastolic murmur	Chan [21][b]	4.9 (0.6–40.0)	0.8 (0.6–1.1)
	Armstrong et al. [23][e]	1.2 (0.4–3.8)	0.97 (0.8–1.2)
	Enia et al. [22][c]	0.9 (0.5–1.7)	1.1 (0.6–1.7)
	Von Kodolitsch et al. 2000[d]	1.7 (1.1–2.5)	0.79 (0.6–0.9)
	Summary	1.4 (1.0–2.0)	0.9 (0.8–1.0)
Enlarged aorta or wide mediastinum	Chan [21][b]	1.6 (1.1–2.3)	0.13 (0.02–1.00)
	Armstrong et al. [23][e]	1.6 (1.1–2.2)	0.42 (0.2–0.9)
	Von Kodolitsch et al. 2000[d]	0.31 (0.2–0.4)	3.4 (2.4–4.8)
	Summary	2.0 (1.4–3.1)	0.3 (0.2–0.4)
Left ventricular hypertrophy on admission electrocardiogram	Chan [21][b]	0.2 (0.03–1.9)	1.2 (0.9–1.6)
	Von Kodolitsch et al. 2000[d]	3.2 (1.5–6.8)	0.84 (0.7–0.9)

Adapted from: Klompas [1] used with permission
[a]CI indicates confidence interval
[b]A total of 18 (n = 40) patients with thoracic aortic dissection
[c]A total of 35 (n = 46) patients with thoracic aortic dissection
[d]A total of 128 (n = 250) patients with thoracic aortic dissection
[e]A total of 34 (n = 75) patients with thoracic aortic dissection

of a diastolic murmur does not aid in the diagnosis of aortic dissection (positive LR 1.4, negative LR 0.9, respectively) [1].

In a cohort of IRAD cases, patients with classic physical exam findings, including hypotension, were diagnosed more quickly than those without

these features [11]. In contrast, the diagnosis of aortic dissection was delayed by greater than 23 h in patients who were normotensive or had signs of heart failure on presentation [11].

Diagnostic Imaging and Biomarkers

Diagnostic imaging is essential to confirm the presence or absence of an acute aortic syndrome. The most common imaging modalities include chest X-ray (CXR), computed tomography (CT), magnetic resonance imaging (MRI), transesophageal echocardiography (TEE) and aortographyA normal appearing aorta and mediastinum on chest x-ray can help to exclude the diagnosis of aortic dissection with a negative LR of 0.3 [95 % CI 0.2—0.4], but a chest x-ray is insufficient to diagnose acute aortic pathology [1]. The sensitivity and specificity of CT, MRI, and TEE are comparable, therefore selection should be dictated by availability and access to clinicians trained in the interpretation of these studies at each institution. 24-h access to CT scanners is now widespread, from small regional emergency departments to large tertiary care hospitals. This development has led in recent years to a decrease of 0.3 h in the median time from presentation to diagnosis [11]. In the IRAD registry, CT scan of the chest as the initial imaging modality was associated with the quickest time to diagnosis [11].

D-dimer has been evaluated as diagnostic test for acute aortic syndrome (as discussed in Chap. 10). Since it is frequently done in the ED to exclude acute pulmonary embolism, it would be ideal, if it could exclude both conditions. It has been evaluated and found at a level of 0.5 μg ml^{-1} to have a pooled sensitivity of 94–100 % and specificity of 40–100 % [6, 13, 14]. However, it is a less sensitive and specific marker in cases of intramural hematoma and thrombus of the false lumen. Therefore, while highly sensitive, the d-dimer test may help lead patients towards definitive imaging but is not appropriate as a standalone test to exclude aortic dissection in patients with a suspicion of acute aortic syndrome [6, 13].

Putting the Clinical Clues Together to Diagnose Aortic Dissection

Aortic dissection is diagnosed most effectively when the clinician is able to identify and integrate high-risk clinical markers as well as common and uncommon presentations [1, 2]. The ACC/AHA guidelines suggest that a combination of two or more high risk features, as discussed above (high risk conditions, high risk pain characteristics and high risk exam features), should prompt an immediate search for dissection with expedited aortic imaging and surgical consultation [6]. If a single high risk feature is present, then the pathway dictates an initial evaluation by electrocardiogram (ECG) and CXR [6]. Further evaluation, typically imaging, for possible aortic etiology of pain is appropriate if these studies are not suggestive of ACS or alternative diagnosis [6].

The presence of sudden onset tearing or ripping pain that reaches maximal intensity at onset is suggestive of aortic dissection with a positive LR of 2.6. When combined with a blood pressure differential identified on physical exam, the positive LR climbs to 10.5 [1]. The addition of a third suggestive finding, an abnormal chest X-ray with mediastinal widening, is strongly suggestive of aortic dissection with a positive LR of 66 [1]. Similarly, the absence of any of these three findings makes the diagnosis of aortic dissection less likely with a negative LR of 0.7 [1]. In the absence of classic symptoms, a search for dissection may be appropriate in patients without a clear alternative diagnosis and one or more of the following risk factors; advanced age, syncope, focal neurologic deficit or recent aortic manipulation by surgery or catheter [6]. Apart from ACS, acute aortic syndromes must be distinguished from other life threatening emergencies including acute pulmonary embolus as well as intra-abdominal processes including bowel perforations, peripheral embolic events and cerebrovascular accidents [6].

Presentation of variants of acute aortic syndromes: Patients with acute aortic intramural hematoma (discussed in greater detail in Chaps. 28 and 35) present in a similar fashion to those with acute

dissection, though tend to be older and the majority of IMH are type B [6, 9]. Patients with IMH are less likely to have a murmur of aortic insufficiency or pulse deficits [6, 9]. Furthermore, patients with penetrating aortic ulcers (discussed in Chap. 51) tend to be elderly and present with severe sudden chest or back pain but do not tend to have neurologic deficits, the murmur of aortic insufficiency or pulse deficits [10].

Delays in Clinical Recognition

The delay in clinical recognition of aortic dissection has been examined through the IRAD registry. Factors associated with delay include initial presentation to a non-tertiary hospital, which may relate to unfamiliarity with the diagnosis of aortic dissection among treating physicians [11]. Clinicians unfamiliar with the clinical risk markers suggesting aortic dissection may be less likely to consider the diagnosis and direct their examination accordingly. The quality of the original history obtained by the ED physician has been found to correlate with diagnostic accuracy. If the patient was asked about the quality, location and onset of pain, the diagnosis of aortic dissection was correctly suspected in 91 % of patients, versus only 24 % of patients if the ED physician asked one or none of these questions [15].

Among demographic characteristics, female gender is associated with delays in clinical recognition of aortic dissection [11, 16]. Women present more frequently in an atypical manner, e.g. altered mental status or congestive heart failure, are less likely to report symptoms of abrupt pain, and pulse deficits are less frequently discovered on exam [16].

Atypical Presentations

Approximately 6–10 % of patients with aortic dissection will present without pain [4, 17]. Patients presenting without pain often have symptoms suggestive of acute systolic heart failure (secondary to severe aortic insufficiency), neurologic deficits (present in up to 20 % of cases), or syncope [4, 17]. This patient population has been shown to have increased mortality (Table 7.3) [17]. While the majority of patients present with some component of pain, usually in the chest or back, the absence of typical pain symptoms may lessen clinical suspicion of aortic dissection. IRAD data suggests that lack of typical features is associated with prolonged time to diagnosis, including absence of abrupt pain (24 h), absence of any pain (24 h), and mild pain (17 h) [11].

Table 7.3 Features associated with diagnostic delay in aortic dissection

Presentation to non-tertiary hospital [11]
Prior aortic manipulation (cardiac surgery or catheter based) [11, 12]
Female gender [11, 16]
Absence of pain [11, 17]
ACS like syndrome [5, 11, 19]
Congestive heart failure or dyspnea [11, 18]

Patients who present with a constellation of symptoms that suggests an alternative diagnosis can mislead diagnosing clinicians and delay the diagnosis of aortic dissection. Those patients presenting with symptoms suggestive of congestive heart failure, as manifested by dyspnea and pleural effusion [11, 18] may undergo a different diagnostic and treatment algorithm. Among IRAD patients presenting with congestive heart failure, the mean time to diagnosis of aortic dissection was greater than 23 h from the time of presentation [11].

Given that the annual volume of ACS patients greatly outnumbers that of acute aortic dissection, there is an appropriate tendency for ED physicians to focus on ACS in patients presenting with acute chest or even back pain. Patients with ACS and aortic dissection share common risk factors. Acute aortic pathology can be associated with positive troponin levels and an ECG resembling an ACS [19]. The ECG is normal in less than 20 % of acute aortic dissections and in 27 % may resemble an ACS [19]. Patients in whom ACS is initially suspected have both delayed diagnosis and exposure to anticoagulants, which increases the risk of bleeding [5]. Suspicion of ACS is the most common reason for a missed or delayed diagnosis of dissection [6]. In the IRAD cohort, several features suggestive of coronary artery disease; including prior coronary catheterization, coronary artery bypass surgery, a

history of atherosclerosis, and ECG findings suggestive of infarction, were associated with longer diagnostic times [11]. It is suspected that delays arose in these cases due to excess emphasis on ACS without consideration of alternative diagnoses. It should again be emphasized that cardiac surgery is itself an important risk factor for aortic dissection, as one in six dissection patients have undergone prior cardiac surgery [12].

Improving the Overall Recognition of Dissection

The median time from presentation to diagnosis for aortic dissection patients in the IRAD registry is 4.3 h. An additional 4.3 h required to reach definitive surgical treatment [11]. Given the reported 1 % hourly mortality, during its early hours, there is significant incentive to minimize the time from presentation to diagnosis of acute aortic syndromes. Educational efforts across a network of hospitals have successfully achieved significant improvements in the time from presentation to diagnosis and to definitive treatment [20]. These efforts focused on recognition of common and uncommon aortic presentations, risk factors and imaging caveats. Site-specific feedback was provided to referring physicians, hospitals and transport teams. These efforts led to a 43 % reduction in the time to diagnosis of acute aortic dissection, which translates to a reduction of 4.5 h in local community hospitals [20].

Acknowledgement The authors appreciate the helpful suggestions of Lou Kohl, MD and Lori Boland, MPH.

References

1. Klompas M. Does this patient have an acute thoracic aortic dissection? JAMA. 2002;287:2262–72.
2. von Kodolitsch Y, Schwartz AG, Nienaber CA. Clinical prediction of acute aortic dissection. Arch Intern Med. 2000;160:2977–82.
3. Rogers AM, Hermann LK, Booher AM, et al. Sensitivity of the National Thoracic Aortic Disease Guideline Diagnostic Algorithm for identification of acute aortic dissection at initial presentation: results from the International Registry of Acute Aortic Dissection (IRAD). Circulation. 2011;123:2213–8.
4. Spittell PC, Spittell JA, Joyce Jr JW, et al. Clinical features and differential diagnosis of aortic dissection: experience with 236 cases (1980 through 1990). Mayo Clin Proc. 1993;68:642–51.
5. Hansen MS, Nogareda GJ, Hutchison SJ. Frequency of and inappropriate treatment of misdiagnosis of acute aortic dissection. Am J Cardiol. 2007;99:852–6.
6. Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. Circulation. 2010;121:e266–369.
7. http://www.iradonline.org/irad.html. Accessed 13 Oct 2012.
8. Hagan PG, Nienaber CA, Isselbacher EM, et al. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. JAMA. 2000;283:897–903.
9. Harris KM, Braverman AC, Eagle KA, et al. Acute aortic intramural hematoma: an analysis from the international registry of acute aortic dissection. Circulation. 2012;126:S91–6.
10. Movsowitz HD, Lampert C, Jacobs LE, Kotler MN. Penetrating atherosclerotic aortic ulcers. Am Heart J. 1994;128:1210–7.
11. Harris KM, Strauss CE, Eagle KA, et al. Correlates of delayed recognition and treatment of acute type A aortic dissection: the International Registry of Acute Aortic Dissection (IRAD). Circulation. 2011;124:1911–8.
12. Collins JS, Evangelista A, Nienaber CA, et al. Differences in clinical presentation, management, and outcomes of acute type A aortic dissection in patients with and without previous cardiac surgery. Circulation. 2004;110:II237–42.
13. Ranasinghe AM, Bonser RS. Biomarkers in acute aortic dissection and other aortic syndromes. J Am Coll Cardiol. 2010;56:1535–41.
14. Weber T, Hogler S, Auer J, et al. D-dimer in acute aortic dissection. Chest. 2003;123:1375–8.
15. Rosman HS, Patel S, Borzak S, et al. Quality of history taking in patients with aortic dissection. Chest. 1998;114:793–5.
16. Nienaber CA, Fattori R, Mehta RH, For the International Registry of Acute Aortic Dissection, et al. Gender-related differences in acute aortic dissection. Circulation. 2004;109:3014–21.
17. Park SW, Hutchison S, Mehta RH, et al. Association of painless acute aortic dissection with increased mortality. Mayo Clin Proc. 2004;79:1252–7.

18. Rapezzi C, Longhi S, Graziosi M, et al. Risk factors for diagnostic delay in acute aortic dissection. Am J Cardiol. 2008;102:1399–406.
19. Biagini E, Lofiego C, Ferlito M, et al. Frequency, determinants, and clinical relevance of acute coronary syndrome-like electrocardiographic findings in patients with acute aortic syndrome. Am J Cardiol. 2007;100:1013–9.
20. Harris KM, Strauss CE, Duval S, et al. Multidisciplinary standardized care for acute aortic dissection: design and initial outcomes of a regional care model. Circ Cardiovasc Qual Outcomes. 2010;3:424–30.
21. Chan KL. Usefulness of transesoophageal echocardiography in the diagnosis of conditions mimicking aortic dissection. Am Heart J. 1991;122:495–504.
22. Enia F, Ledda G, LoMauro R et al. Utility of echocardiography in the diagnosis of aortic dissection involving the ascending aorta. Chest. 1989;95:124–129.
23. Amastrong Wf, Bach Ds, Carey LM et al. Clinical, and echocardographic finings in patients with suspected acute aortic dissection. Am Heart J. 1998; 136:1051–1060.