46M with acute severe chest pain and diaphoresis
Advances in the Diagnosis and Treatment of Acute Aortic Dissection

Keith A. Marill, M.D.
Massachusetts General Hospital
Harvard Affiliated Emergency Medical Residency
Contents

- Acute Aortic Dissection: Description
- Emergency Diagnosis
  - Differential Diagnosis
  - History and Physical Exam
  - ECG, Chest X-ray
  - Lab Studies: D-Dimer?
  - Echocardiography, Chest CTA and MRA
- Treatment
  - Emergent
  - Definitive
    - Type A
    - Type B
Aortic Dissection

- Acute = symptoms for less than 2 weeks
- Dissection of the wall of the aorta most commonly due to a tear of the inner surface
  - Also atherosclerotic ulcer, intramural hematoma
- Approximately 3 cases/100,000/year or more than 7,000 annual U.S. cases
- High mortality: up to 1% per hour if untreated, and 27% overall mortality with treatment

Aortic Dissection: Anatomy

Normal Dissection

Stanford Classification

"A" "B"
Aortic Dissection: Anatomy

Location distribution:
- Ascending 65%
- Descending 20%
- Aortic arch 10%
- Abdominal aorta 5%
Aortic Dissection Pathophysiology

- Weakened aortic connective tissue
  - Cystic medial necrosis
  - Advanced age (~1/3 > 70 years), Marfans, Ehlers-Danlos IV, Osteogenesis imperfecta, hypertension (~2/3), aortitis (Takayasu), bicuspid aortic valve (Turner’s syndrome), late pregnancy
  - Other undiscovered genetic abnormalities
- Local trauma (iatrogenic)
- Increased sheer forces
  - Abnormal anatomy: bicuspid aortic valve, coarctation of the aorta
  - Hypertension
  - Late pregnancy
  - Cocaine (rare)
  - Sudden isometric exercise/weight lifting (?)
- Male gender (2/3)
- Atherosclerosis (~1/3)
- Prior cardiovascular/aortic surgery
Aortic Dissection Pathophysiology

- Variants
  - Intramural hematoma without intimal flap
  - Penetrating atherosclerotic ulcer (type B)
Aortic Dissection Complications

- Aortic valve failure
- Pericardial tamponade
- Myocardial Infarction
- Aortic rupture
ED Diagnosis: History of Present Illness

- Chest, back, or upper abdominal pain (90-95% sensitive)
  Classically:
  - sudden, severe, sharp, stabbing, tearing, ripping
  - maximal intensity at onset
  - radiation/migration to interscapular region and elsewhere reflecting anatomy of disease
- Neurologic complaints
  - approx 10%-syncope (hemopericardium), CVA, paraplegia
- Acute CHF (acute aortic regurgitation)
- Trauma

New York City, July 1999
ED Diagnosis: Past Medical History

- Hypertension (65-75%)
- Aortic valve disease (5% bicuspid)
- Connective tissue disease (5% Marfan’s Syndrome)
- Aortitis (syphilitic, giant cell)
- Advanced age (most common 6th, 7th decades of life)
- Pregnancy (<1% of dissections: 3rd trimester, postpartum)
- Iatrogenic (5%: left side catheterization, balloon pump)
- Previous cardiac/aortic surgery (~15%)
Marfan Syndrome - Review

Fig. 1
This person with Marfan syndrome is tall and thin and has an arm span that exceeds her height.

Fig. 2

Fig. 3
Scoliosis
Kyphoscoliosis
Kyphosis

Normal
Marfan Syndrome

Normal chest
ED Diagnosis: Physical Exam

- Blood pressure
  - elevated (50%) (type B)
  - low blood pressure (20%) (type A)
    (aortic regurg, pericardial tamponade, rupture)
- Variably asymmetric blood pressure/pulses (30%)
- Aortic regurgitation murmur (30%)
  - Acute CHF
- Neurologic deficits (10-20%)
  - CVA, altered mental status, paraplegia
- Acute MI (predominately RCA/inferior MI) (2-5%)
ED Diagnosis: Bedside Ultrasound

- 72F with CC chest pain radiating to back and neck
- HR 86 BP 180/84

ED Diagnosis: Bedside Ultrasound

- LVH (35%)
- Acute MI (Inferior most common) (2-7%)
46M with acute severe chest pain and diaphoresis

Acute ascending aortic dissection complicated by retrograde dissection to the left main coronary artery with occluding flap.
Chest X-Ray

- Overall sensitivity ~90% at best (range 50-90%)
- Widened aortic silhouette or mediastinum (80-90%)
- Separation of intimal calcification from external aorta (10%)
- Pleural effusion, L>R, (15%)
Chest X-Ray: A Recent Study of 216 Suspected AAD Patients with 2 Blinded Radiologists

- Consensus decision based on all findings:
  - Sensitivity 64% (70/109) (Proximal 47%, Distal 77%)
  - Specificity 86% (92/107)

Table 3. Radiographic Features of Aortic Disease on Chest Radiography

<table>
<thead>
<tr>
<th>Radiographic Feature</th>
<th>Aortic Disease (n = 109)</th>
<th>No Aortic Disease (n = 107)</th>
<th>Likelihood Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number (%)</td>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td>Widened aortic contour</td>
<td>75 (69)</td>
<td>23 (21)</td>
<td>3.2 (2.2–4.7)</td>
</tr>
<tr>
<td>Widened mediastinum</td>
<td>63 (58)</td>
<td>28 (26)</td>
<td>2.2 (1.5–3.7)</td>
</tr>
<tr>
<td>Tracheal displacement</td>
<td>28 (26)</td>
<td>32 (30)</td>
<td>0.9 (0.6–1.3)</td>
</tr>
<tr>
<td>Displaced calcification</td>
<td>17 (16)</td>
<td>3 (3)</td>
<td>5.6 (1.7–18.4)</td>
</tr>
<tr>
<td>Aortic kinking</td>
<td>52 (48)</td>
<td>5 (5)</td>
<td>10.2 (4.2–24.6)</td>
</tr>
<tr>
<td>Opacified pulmonary window</td>
<td>40 (37)</td>
<td>17 (16)</td>
<td>2.3 (1.4–3.8)</td>
</tr>
<tr>
<td>Blurred aortic contour</td>
<td>11 (10)</td>
<td>4 (4)</td>
<td>2.7 (0.9–8.2)</td>
</tr>
</tbody>
</table>

Sens.     1 – Spec.

CXR – Intimal Calcification

“Double aortic knob” sign

“Calcium” sign
CXR – Widened Aortic Knob

**Figure 1.** Type B dissection in a patient with acute chest pain. Previously obtained radiographs were not available for prospective comparison. (a) Chest radiograph shows a widened aortic knob and displaced intimal calcifications (arrows), which were interpreted as suggestive of aortic dissection at both prospective and retrospective evaluation. (b) Radiograph obtained 18 months before a shows a normal aortic knob and peripheral intimal calcifications (arrows). Aortic dissection was diagnosed by means of CT on the day of admission.

CXR – Normal Aortic Contour

Other AAD CXR Examples

Courtesy of EMedicine
14M with acute ascending dissection

Courtesy of U. of Hawaii Dept Pediatrics
CXR Summary

- Approximate 90% sensitivity
  - aortic or mediastinal widening most important
- Reliability of findings fair, and not clearly effected by portable vs PA/lat technique
- Indicates further imaging if suspicious
- CANNOT be used to rule out disease in patients with moderate or high pretest probability
Laboratory Studies

- Hematocrit
- Urinalysis
- Biomarkers
  - Smooth muscle myosin
  - Elastin fragments
  - D-dimer
Serum D-Dimer to evaluate for Acute Aortic Dissection

- **The Good**
  - D-dimer reflects intravascular clot destruction
  - Readily available, inexpensive test
  - Variably fast to perform

- **The Bad**
  - Multiple test methodologies
  - Likely poor specificity
  - May be elevated in acute MI
Serum D-Dimer Is a Sensitive Test for the Detection of Acute Aortic Dissection: A Pooled Meta-Analysis

- 11 studies from around the globe
- Pooled meta-analytic method
- Sensitivity = 327/349, 94% (95% CI 91 to 96)
- Specificity: control groups inhomogeneous and not combined

D-Dimer for Acute Aortic Dissection Diagnosis
Sensitivity and Specificity Forest Plots

Figure 2. Forest plots with individual studies listed by reference number in chronological order. Point estimates along with 95% confidence intervals are listed for each study. Square size represents study sample size for each plot. (A) Sensitivity forest plot. The diamond represents the pooled sensitivity estimate. (B) Specificity forest plot. Specificity for chronic aortic dissection control groups is not shown. Specificity was not pooled due to heterogeneous control groups.
D-Dimer for Acute Aortic Dissection Diagnosis Potential Utility

- Low pretest probability patient based on H and P, with negative CXR and serum d-dimer would be “ruled out”
- Remaining patients at higher risk receive advanced imaging (CT, TEE, MR)
  - CT protocol for multiple diagnoses (AAD, PE, ?ACS)
- More efficient use of advanced imaging for higher risk population
- More rapid and accurate diagnosis of acute aortic dissection
  - Less inappropriate anticoagulation
  - More rapid surgical repair and medical therapy
  - Decreased mortality
D-Dimer for Acute Aortic Dissection Diagnosis

- **Study limitations**
  - Limited, often retrospective data
  - Potential sampling and publication bias
  - Non-standardized d-dimer test methodology with a possibly suboptimal test threshold for acute aortic dissection.

- **Remaining Questions**
  - Optimal test methodology and threshold
  - Test specificity
  - Time dependence of the test as suggested by the single study with poor sensitivity
  - Independence from other clinical and radiologic predictors of disease
  - Utility of the quantitative value to distinguish from PE or MI
Figure 1: Funnel Plot of Study Size Versus D-Dimer Test Sensitivity. Individual studies are represented by squares where square size represents study sample size. The unbroken line represents the pooled sensitivity estimate of 94%. The dotted lines suggest the expected area of distribution in the absence of publication bias. Smaller studies should be distributed symmetrically, but with more widely variable sensitivity, around larger studies. The expected distribution has the shape of an inverted funnel.
D-Dimer and Acute Aortic Dissection
The Latest Word

Diagnosis of Acute Aortic Dissection by D-Dimer
The International Registry of Acute Aortic Dissection Substudy on Biomarkers (IRAD-Bio) Experience

Toru Suzuki, MD; Alessandro Distante, MD; Antonella Zizza, MS; Santi Trimarchi, MD; Massimo Villani, MD; Jorge Antonio Salerno Uriarte, MD; Luigi De Luca Tuppiti Schinosa, MD; Attilio Renzulli, MD; Federico Sabino, MD; Richard Nowak, MD; Robert Birkhahn, MD; Judd E. Hollander, MD; Francis Counselman, MD; Ravi Vijayendran, PhD; Eduardo Bossone, MD; Kim Eagle, MD; for the IRAD-Bio Investigators

Background—D-dimer has been reported to be elevated in acute aortic dissection. Potential use as a “rule-out” marker has been suggested, but concerns remain given that it is elevated in other acute chest diseases, including pulmonary embolism and ischemic heart disease. We evaluated the diagnostic performance of D-dimer testing in a study population of patients with suspected aortic dissection.

Methods and Results—In this prospective multicenter study, 220 patients with initial suspicion of having acute aortic dissection were enrolled, of whom 87 were diagnosed with acute aortic dissection and 133 with other final diagnoses, including myocardial infarction, angina, pulmonary embolism, and other uncertain diagnoses. D-dimer was markedly elevated in patients with acute aortic dissection. Analysis according to control disease, type of dissection, and time course showed that the widely used cutoff level of 500 ng/mL for ruling out pulmonary embolism also can reliably rule out aortic dissection, with a negative likelihood ratio of 0.07 throughout the first 24 hours.

Conclusion—D-dimer levels may be useful in risk stratifying patients with suspected aortic dissection to rule out aortic dissection if used within the first 24 hours after symptom onset. (Circulation. 2009;119:000-000.)

Sensitivity point estimate 96% with Triage D-Dimer Test (Biosite).
D-Dimer and Acute Aortic Dissection
Time Course Data

Figure 2. Time course box plots for D-dimer levels in patients according to time from onset.
Summary: Contrasting Type A and B Dissections

- **Type A**
  - Anterior chest pain radiating to neck, jaw, throat
  - Neurovascular symptoms
  - Acute aortic regurgitation/diastolic murmur/CHF
  - Acute MI (inferior)
  - Variable blood pressure

- **Type B**
  - Chest or epigastric pain radiating to interscapular area
  - Hypertensive
Abbreviated Differential Diagnosis

- **Cardiovascular**
  - Myocardial Infarction
  - Valvular disease/failure (aortic)
  - Pericarditis
  - Thoracic or abdominal aneurysm
  - Acute CHF

- Pulmonary embolism
- Mediastinal tumor
- Upper gastrointestinal disease
The Challenge of Emergency Diagnosis

- EP’s correctly suspect disease in 40-60% patients
- 50% type B dissections not suspected
- Major pitfalls:
  - 10% patients have NO pain
    - CHF, CVA, syncope, paraplegia, abnl CXR
  - 20-30% patients with pain in abdomen (epigastric)
    - Majority were missed

Definitive Diagnosis: Advanced Imaging

- Echo (TEE, TTE)
- CT angiogram
- MR angiogram
- Angiography
Desired Imaging Information

- Detect acute dissection
- Secondary goals
  - Dissection location (ascending, descending, arch)
  - Extent/size
  - Site of intimal tear
  - Aortic regurgitation
  - Branch vessel or coronary artery involvement
  - Pericardial effusion
Imaging Considerations

- Diagnostic accuracy
- Safety
- Speed
- Convenience
- Contraindications
- Identification of alternative diagnoses
## Diagnostic Test Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiography</td>
<td>88%</td>
<td>94%</td>
</tr>
<tr>
<td>CTA</td>
<td>96-100%</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>MRA</td>
<td>98%</td>
<td>98%</td>
</tr>
<tr>
<td>TTE</td>
<td>59-85%</td>
<td>63-96%</td>
</tr>
<tr>
<td>TEE</td>
<td>98-99%</td>
<td>94-97%</td>
</tr>
</tbody>
</table>
International Registry of Acute Aortic Dissection (IRAD) Initial Diagnostic Choices

- CT (63%)
- TEE (32%)
- Aortography (4%)
- MRI (1%)

64 Slice Multidetector CT Angiography
The “Triple Rule Out” Protocol

- CT protocol with ECG gating and timed contrast bolus designed to assess for:
  - Aortic dissection
  - Coronary artery disease
  - Pulmonary embolism

The “Triple Rule Out” Protocol

- Advantages
  - Fast
  - Highly accurate for all 3 conditions
  - Broad spectrum of other chest and upper abdominal diseases identified
  - ECG gating freezes cardiac motion allowing evaluation of perivalvular area and coronary arteries for patients with Type A aortic dissection

The “Triple Rule Out” Protocol

- **Challenges**
  - Acquisition time (~20 seconds)
  - Limitations: coronary calcifications/stents, obesity, renal insufficiency, atrial fibrillation, heart rate control, contrast allergy
  - Indication: how often do clinicians seriously consider all 3 diagnoses?
    (~3% of chest pain evaluations at present)
  - Cost
  - Contrast dose (~125 cc)
  - Radiation
    - Radionuclide stress test 8-16 mSv
    - Angiography 5-13 mSv
    - Coronary CTA 8-22 mSv
    - “Triple rule-out” scan ~12-30 mSv
      (minimize: tube current modulation, slice thickness variation)

60M with acute CP

- Vital signs stable
- Nonspecific ECG changes
- ASA, heparin, beta blocker administered
- Cardiology consulted in ED
- ED TTE performed
  - Normal flow across aortic valve
  - Pericardial effusion without tamponade
- Consider acute pericarditis
- Patient codes with PEA and dies a short time later
60M with acute CP
Management of Acute Aortic Dissection

- Acute management
  - Initial suspicion: hold ACS antiplatelet and anticoagulant therapies
  - BP/Heart rate control
    - Hypertension
    - Hypotension
  - Analgesia
  - Cardiac tamponade
  - Definitive diagnostic imaging
  - Surgical preparation
Blood Pressure Control

- Hypertension
  - Goal: SBP 100-120 mm Hg
  - Lower absolute blood pressure and dP/dt (change in pressure per time)

- Agents
  - Beta blockade: propanolol, labetalol, metoprolol, esmolol
  - Alternative: calcium channel blockade with diltiazem, verapamil
  - Nitroprusside
  - ACE inhibitor: enalaprilat (particularly if renal artery compromise)

- Arterial catheter for monitoring
- Heart rate control (<60 BPM) may also be protective

Blood Pressure Control

- Hypotension
  - Prefer primary vasoconstrictor over positive inotropy
    - Norepinephrine (Levophed)
    - Phenylephrine (Neo-Synephrine)

- Analgesia - morphine
Cardiac Tamponade

- Complicates up to 18% of acute aortic dissections
- Associated with syncope and altered consciousness
- 50% mortality
- Stable versus unstable
- Pericardiocentesis
  - May increase risk of PEA in stable patient
  - Increased aortic pressure leads to renewed or increased bleeding into pericardium

Emergent Surgery - Indications

- Majority of acute type A dissections
  - 30 day mortality >50% for those treated medically
- Complicated acute type B dissection
  - Vital organ or limb ischemia
  - Expanding hematoma
  - Retrograde extension to ascending aorta
  - Marfans Syndrome
  - Uncontrolled hypertension or pain
Emergent Surgery

- Repair of intimal tear and closure of false lumen
- Aortic graft replacement
- Aortic valve repair or replacement
Endovascular Surgical Repair
Goals/Location/Type

Transfemoral intraluminal covered stent-graft
(type B dissection)
(distal portion of type A dissection)

Goals:
Halt flow of blood into false lumen and promote thrombosis
Keep true lumen open
Further Endovascular Techniques

- Balloon or scissors techniques to widen the reentry site
- Branch artery bare metal stenting for static or dynamic obstruction

Prognosis

- 30-day survival post surgery
  - Proximal: 74%
  - Distal: 69%

- 30-day survival with medical treatment of Type B dissection: 92%

- 5-year survival for all groups discharged from the hospital: 75-82%

Long-term Complications and Care

- Most common within the first 2 years
  - Aortic regurgitation
  - Recurrent dissection (esp. Marfans)
  - Aneurysm formation and rupture
    - Dilatation at site of distal residual false lumen
- Serial imaging (CT or MRI) for monitoring
- Lifelong aggressive blood pressure control for ALL patients
  - Late aneurysm rupture 10x more common in patients with poorly controlled HTN
  - Angiotensin II blockers (losartan) may have some advantage particularly for Marfan’s independent of blood pressure via transforming growth factor (TGF-beta) antagonism

Questions?
Keith Marill, M.D.
kmorill@partners.org