Thoracic aorta – acute type B dissection and AAS

What is the role of medical management?

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Algorithm

Patient with chest pain
Blood biomarkers, ECG
Urgent CT scan

Triple rule out CT if intermediate pre-test probability of CAD
Negative initial imaging, high clinical suspicion – add TTE

Pulmonary embolus
Aortic dissection
Acute Coronary Syndrome

Stanford type A
Open surgery after initial risk assessment

Stanford type B

Complications:
- Aortic rupture
- End-organ ischaemia
- On-going pain and hypertension despite full medical therapy
- Early false lumen expansion
- Large single entry

Uncomplicated
Medical treatment

Complicated
Endovascular treatment
**TEVAR in complex complicated type B dissection (IC)**

Malperfusion syndrome treated with endovascular stent-graft and PETTICOAT; a) angiography of lower body malperfusion; b) reperfusion after proximal stent-graft; c) 3D CT reconstruction of acute complicated dissection with malperfusion; d) reconstructed aorta and abolished malperfusion after stent-graft and PETTICOAT.
PETTICOAT for malperfusion resolution
Dual stent-graft procedure in type A aortic dissection
INSTEAD-XL: Landmark analysis

CV death (2nd EP)

Overall
HR=0.35 (0.13 - 0.98)
p=0.045

HR=2.46 (0.48 - 12.7)
p=0.283
p(Log-Rank) <0.001

HR=0.142 (0.032 - 0.625)
p=0.01

Nienaber CA et al, Circulation CV Int 2013
Longterm outcomes in IRAD

TEVAR versus medical management of type B dissection

Fattori R, JACC CV Int 2013
Algorithm...role of medical management?

1. Patient with chest pain
   - Blood biomarkers, ECG
   - Urgent CT scan
     - Triple rule out CT if intermediate pre-test probability of CAD
     - Negative initial imaging, high clinical suspicion – add TTE

2. Pulmonary embolus
3. Aortic dissection
   - Stanford type A
     - Open surgery after initial risk assessment
   - Stanford type B
     - Complications:
       - Aortic rupture
       - End-organ ischaemia
       - On-going pain and hypertension despite full medical therapy
       - Early false lumen expansion
       - Large single entry
     - Uncomplicated Medical treatment
     - Complicated Endovascular treatment
4. Acute Coronary Syndrome
Patients with aortic dissection are at risk for late aortic events

Medical management to prevent ...
rupture, aneurysm, aortic repair
Shear stresses on the aortic wall are highest at sites of increased dilatation.

dP/dt, which is affected by wave reflections, is greatest in areas of aortic dilatation

Association between residual patent FL and long-term mortality in AAS

<table>
<thead>
<tr>
<th>Study ID</th>
<th>HR (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kimura, 2015</td>
<td>1.71 (1.12, 2.59)</td>
<td>48.18</td>
</tr>
<tr>
<td>Bernard, 2001</td>
<td>1.70 (0.60, 4.80)</td>
<td>7.83</td>
</tr>
<tr>
<td>Subtotal (I-squared = 0.0%, p = 0.992)</td>
<td>1.71 (1.16, 2.52)</td>
<td>56.02</td>
</tr>
<tr>
<td>Akutsu, 2004</td>
<td>5.57 (1.10, 28.30)</td>
<td>3.21</td>
</tr>
<tr>
<td>Marui, 2007</td>
<td>2.64 (1.62, 4.03)</td>
<td>40.77</td>
</tr>
<tr>
<td>Subtotal (I-squared = 0.0%, p = 0.386)</td>
<td>2.79 (1.80, 4.32)</td>
<td>43.98</td>
</tr>
</tbody>
</table>

Heterogeneity between groups: p = 0.102
Overall (I-squared = 12.6%, p = 0.330) | 2.12 (1.58, 2.83) | 100.00 |
Association between partial FL thrombosis of and long-term mortality

**Study ID**

<table>
<thead>
<tr>
<th>Type A</th>
<th>HR (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Larsen,2013</td>
<td>0.78 (0.30, 1.99)</td>
<td>17.65</td>
</tr>
<tr>
<td>Song,2010</td>
<td>6.48 (1.30, 32.35)</td>
<td>6.12</td>
</tr>
<tr>
<td>Song,2011</td>
<td>3.21 (1.19, 14.38)</td>
<td>10.18</td>
</tr>
<tr>
<td>Subtotal</td>
<td>1.75 (0.88, 3.45)</td>
<td>33.95</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type B</th>
<th>HR (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tanaka,2014</td>
<td>1.16 (0.41, 3.26)</td>
<td>14.70</td>
</tr>
<tr>
<td>Tsai,2007</td>
<td>2.69 (1.45, 4.98)</td>
<td>41.51</td>
</tr>
<tr>
<td>Ueki,2014</td>
<td>2.74 (0.77, 9.71)</td>
<td>9.84</td>
</tr>
<tr>
<td>Subtotal</td>
<td>2.24 (1.37, 3.65)</td>
<td>66.05</td>
</tr>
</tbody>
</table>

Heterogeneity between groups: p = 0.563
Overall (I-squared = 41.7%, p = 0.127) 2.06 (1.38, 3.06) 100.00
**Predictors of long-term stability**

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>SE</th>
<th>p-value</th>
<th>OR</th>
<th>95.0% CI for Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>.030</td>
<td>.020</td>
<td>.134</td>
<td>1.031</td>
<td>.991-1.072</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>-1.097</td>
<td>.649</td>
<td>.091</td>
<td>.334</td>
<td>.094-1.193</td>
</tr>
<tr>
<td><strong>STJ diameter</strong></td>
<td>-1.880</td>
<td>.637</td>
<td>.003</td>
<td>.153</td>
<td>.044-.532</td>
</tr>
<tr>
<td><strong>Complete FLT</strong></td>
<td>1.678</td>
<td>.751</td>
<td>.025</td>
<td>5.354</td>
<td></td>
</tr>
</tbody>
</table>
Medical Management of Thoracic Aortic Dissection

1. Diagnosis of underlying disease
2. Pharmacologic therapy
3. Lifestyle modification
4. Long term surveillance
5. Referral for prophylactic aortic repair
20% of individuals with a Thoracic Aortic Aneurysm disease will have an affected 1st degree relative

Risk Factors for Aortic Dissection:
Bicuspid Aortic Valve Disease

Genes associated with BAV and TAA Disease:

NOTCH1, TGFB1, TGFB2, TGFB3, ACTA2, MAT2A, GATA5, SMAD6, LOX
Medical Management of Thoracic Aortic Dissection

1. Diagnosis of underlying disease
2. Pharmacologic therapy
3. Lifestyle modification
4. Long-term surveillance
5. Timing of prophylactic aortic repair
**Antihypertensive Therapy after Aortic Dissection**

**Multiple guidelines:** IV beta-blockers as first-line therapy based on theoretical ability to decrease aortic wall shear stress.

- HR <60 bpm
- Systolic BP of 100-120 mm Hg or as tolerated while maintaining adequate end-organ perfusion

CCB (diltiazem, verapamil) suggested as alternatives if intolerance to beta-blockers.

If BP remains over target, ACE-inhibitors and other IV vasodilators can be used.

Once stable, transition to oral medications and continue long-term. Beta-blockers are recommended long-term.
What are the data on antihypertensive therapy after aortic dissection?

RCT: none
Non-randomized studies of antihypertensive medications in aortic dissection


2. Takeshita 2008. ACE-inhibitor treatment may reduce the risk of long-term aortic events after type B aortic dissection.

3. Sakakura K 2009. CCB use at discharge is associated with increased survival in type B aortic dissection.


Chronic beta-blocker therapy improves outcome and reduces treatment costs in chronic type B dissection


Increasing diameter of the aorta was the most important indication for surgery in both groups.

<table>
<thead>
<tr>
<th>Indication for aortic surgery</th>
<th>Beta-blocker use (n=51)</th>
<th>Other anti-hypertensive use (n=20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic diameter</td>
<td>6 (12%)</td>
<td>8 (40%)</td>
<td>P=0.002</td>
</tr>
<tr>
<td>Persistent pain</td>
<td>2 (4%)</td>
<td>1 (5%)</td>
<td></td>
</tr>
<tr>
<td>Rupture</td>
<td>0</td>
<td>1 (5%)</td>
<td></td>
</tr>
<tr>
<td>Malperfusion</td>
<td>1 (2%)</td>
<td>1 (5%)</td>
<td></td>
</tr>
</tbody>
</table>
ACE-Inhibitors Reduce Longterm Aortic Events in Patients with Acute Type B Aortic Dissection


2000-2006 78 type B AD admitted within 48 hours of symptom onset to the National Cardiovascular Center, Suita, Japan.

All patients treated with “anti-impulse medications”

73/78 survived hospitalization. Average follow-up of 2.5 ± 1.5 years.

Dissection-related aortic events occurred in 13 of 73 (18%) of medically-treated type B aortic dissection.

Events:
Aortic rupture in 2 (3%)
Aneurysmal enlargement ≥ 60 mm in 7 (10%)
Rapid enlargement of the dissected aorta in 3 (4%)
Visceral/limb ischemia in 1 (1%)
Angiotensin-Converting Enzyme Inhibitors Reduce Long-Term Aortic Events in Patients With Acute Type B Aortic Dissection


Patients receiving ACEI had a significantly lower incidence of dissection-related aortic events than those not receiving ACEI (6% vs 28%, p=0.02)

**Events:**
- Aortic rupture in 3%
- Aneurysmal enlargement ≥ 60 mm in 10%
- Rapid enlargement of the dissected aorta in 4%
- Visceral/limb ischemia in 1%

![Kaplan-Meier curve showing dissection-related aortic event free survival during the follow-up. ACEI, angiotensin-converting enzyme inhibitor.](image)
Determinants of Long-Term Mortality in Patients with Type B Acute Aortic Dissection


1991-2006 202 hospital survivors of acute type B AD treated medically. Median follow-up 55 months:

44 post-DC deaths:
   21/44 CV deaths (9 complications from AD, 5 sudden death, 7 cardiac cause).
   1-, 3-, and 5-year survival: 96%, 92%, and 88%, respectively.

Multivariate analysis predicting all cause mortality:

Use of beta blocker at DC (80%): HR 0.6 (95% CI, 0.29-1.24), p = 0.17
Use of CCB at DC (93%): HR 0.38 (95% CI 0.15-0.97), p = 0.04
No anti-hypertensive meds at DC (2%): HR 9.5 (95% CI 1.85-48.8), p <0.007
Type-Selective Benefits of Medications in Treatment of Acute Aortic Dissection (from IRAD)


1301 pts who survived acute AD with information about medications at discharge.

Median f/u: 26 months (interquartile range 12-48)

At DC, most patients normotensive (124 + 18/71 + 11 mm Hg)

Meds upon DC:

- Beta-blockers 89%
- CCB 50% [not specified by type or dose]
- ACE-i 47%
- diuretics 29%
- vasodilators 22%
- ARBs 8%
Type-Selective Benefits of Medications in Treatment of Acute Aortic Dissection (from IRAD)


Kaplan-Meier survival curves for effects of medications on mortality. β Blockers in patients with (A) type A dissection and (B) type B dissection; and calcium channel blockers in those with (C) type A and (D) type B.

Survival in surgically treated type A AD

Survival in medically treated type B AD
**Type-Selective Benefits of Medications in Treatment of Acute Aortic Dissection (from IRAD)**


Effects of medications on outcomes. (A) Patients with type A who underwent surgery; and (B) those with type B treated medically. ACE = angiotensin-converting enzyme; BB = β blocker; CCB = calcium channel blocker

Study not powered to examine which combinations of drugs showed most benefit.
Importance of Blood Pressure Control After Repair of Acute Type A Aortic Dissection: 25-Year Follow-Up in 252 Patients


1984-2009, 252 patients underwent repair of type A AD at Washington University

Operative mortality 16%
Mean f/u for reoperation or death 6.9 ± 5.9 years

For operative survivors:
5-, 10-, and 20 year survival was 78%, 59%, and 24%, respectively.

Risk factors for late reoperation:
- male sex (OR 2.9)
- Marfan syndrome (OR 7.8)
- SBP >120 at late f/u (OR 8.9)
- Absence of beta-blocker therapy (OR 6.1)
Freedom from reoperation after type A AD was much greater in beta-blocker treated patients


40/188 (21%) of patients were not receiving beta-blockers at late follow-up.

Reoperation was performed in 12/148 (8%) on beta blockers and 14/40 (35%) not taking beta blockers (p<0.001).
Importance of Blood Pressure Control After Repair of Acute Type A Aortic Dissection: 25-Year Follow-Up in 252 Patients


Reoperation rates:
- SBP <120 mm Hg: 3/85 (4%)
- SBP 120-140 mm Hg: 13/63 (21%)
- SBP >140 mm Hg: 10/30 (33%)

92% at 10 yrs
74% at 10 yrs
49% at 10 yrs
Figure 3

Aortic Dissection – inflammatory process?
A, Thoracic aortic dilations in interleukin-1β (IL-1β) knockout (KO) and IL-1 receptor (IL-1R) KO mice exposed to elastase were significantly less than wild-type (WT) thoracic aortic aneurysm (TAA) mice. *P<0.0001, †P<0.001. B, By immunohistochemistry, representative samples demonstrated increased staining of elastin fibers (black) and smooth muscle cells (brown) in IL-1β KO and IL-1R KO mice compared with WT TAAs. IL-1β KO and IL-1R KO aortas also had decreased macrophage staining and neutrophil staining (brown). Scale bar, 100 μm.
1. Diagnosis of underlying disease

2. Pharmacologic therapy

3. **Lifestyle modification**

4. Long term surveillance

5. Referral for prophylactic aortic repair
Physical activity and work guidelines and recommendations:

Individuals with aortic dissection are restricted from participation in most competitive athletics.

One must inquire about job requirements and isometric activity.

Advocate for your patients to modify and adopt appropriate work loads.
**Post aortic dissection: Gap between activity recommendation and real life patients aerobic capacities**

Delsart P et al. CHU Lille Cardiology Hospital. Int J Cardiol 2016;219:271-6

Blood pressure at maximal exercise (while on meds): $\frac{151 \pm 20}{77 \pm 13}$

Average METS $5.5 \pm 1.5$

<table>
<thead>
<tr>
<th>Activity</th>
<th>METS</th>
</tr>
</thead>
<tbody>
<tr>
<td>General house cleaning</td>
<td>3.0</td>
</tr>
<tr>
<td>Loading/unloading car</td>
<td>3.0</td>
</tr>
<tr>
<td>Walking the dog</td>
<td>3.0</td>
</tr>
<tr>
<td>Walking briskly, 3 mph</td>
<td>3.3</td>
</tr>
<tr>
<td>Mopping the floor</td>
<td>3.5</td>
</tr>
<tr>
<td>Vacuuming</td>
<td>3.5</td>
</tr>
<tr>
<td>Household tasks requiring moderate effort</td>
<td>3.5</td>
</tr>
<tr>
<td>Heavy yard work or gardening</td>
<td>4.0</td>
</tr>
<tr>
<td>Climbing stairs</td>
<td>4.0</td>
</tr>
<tr>
<td>Bicycling, casual, &lt;10 mph</td>
<td>4.0</td>
</tr>
<tr>
<td>Raking lawn</td>
<td>4.0</td>
</tr>
<tr>
<td>Golf (without cart, carrying heavy bag of clubs)</td>
<td>4.4</td>
</tr>
<tr>
<td>Swimming at a slow pace</td>
<td>4.5</td>
</tr>
<tr>
<td>Dancing (ballet or modern)</td>
<td>4.8</td>
</tr>
<tr>
<td>Chopping wood</td>
<td>4.9</td>
</tr>
<tr>
<td>Snorkeling</td>
<td>5.0</td>
</tr>
<tr>
<td>Tennis (doubles)</td>
<td>5.0</td>
</tr>
<tr>
<td>Competitive ballroom dancing, fast</td>
<td>5.5</td>
</tr>
<tr>
<td>Square dancing</td>
<td>5.5</td>
</tr>
<tr>
<td>Ice skating</td>
<td>5.5</td>
</tr>
<tr>
<td>Mowing the lawn with hand mower</td>
<td>5.5-6.0</td>
</tr>
</tbody>
</table>
314 survivors of acute aortic dissection surveyed regarding lifestyle modifications, exercise practice and emotional state.

Response rate was 42%.

32% with new-onset depression
32% with new onset anxiety
24% no longer engaged in any exercise
Majority of patients no longer sexually active after aortic dissection

Those who exercised routinely had less depression and lower BP.
Medical Management of Thoracic Aortic Dissection

1. Diagnosis of underlying disease
2. Pharmacologic therapy
3. Lifestyle modification
4. Long term surveillance
5. Referral for prophylactic aortic repair
“Medical” Management after Aortic Dissection

E-A-S-Y-T-I-P

Establish the underlying diagnosis
Achieve normal blood pressure
Stop cigarette smoking
Yearn to exercise moderately
Test 1st degree relatives for TAA disease
Image the aorta over time
Perform aortic repair when appropriate
Remodeling with TEVAR…

Complete false lumen thrombosis in the descending thoracic aorta

Pre-procedure  Post-procedure  24 months