Why TEVAR for Uncomplicated Thoracic Dissections is Rarely Indicated

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Disclosures
None

IRAD
- Registry established 1996
- 30 centers in 11 countries

Aortic Dissections
Surgical Therapy
Medical Therapy

Figure 4. Thirty-day mortality in 464 patients from the IRAD registry stratified by medical and surgical treatment in both type A and type B aortic dissections. Adapted from reference 3.

JAMA 2000 vol. 283 (7) pp 897-903
Medical Therapy

- Concept of anti-impulse therapy proposed by Wheat et al in 1965
  - 100% 1 year survival in 6 patients (2 ascending & 4 descending)
- Daily reported 5 year series of 35 dissections
  - Proposed classification scheme of ascending (type A) and descending (type B) to guide treatment
  - Surgery reserved for type A and medical therapy for type B
- Optimal medical therapy today
  - Goal SBP < 120
  - HR < 60
  - β-blocker are first line agent as they decrease aortic wall shear stress
- 90% of patients w/ type B dissections can be managed with medical therapy alone

Natural History of Type B Dissection

- Long term results are not ideal
  - Mortality of 25% at 3 years
    - May be as high as 50% over 5 years
  - Up to 25% will have late aortic related complications
  - Large fraction of mortality may be related to comorbid conditions
- A vulnerable aorta

Adjunctive Treatment to Prevent Late Events

- Continued pressurization of thin, weak false lumen wall
  - Aneurysmal degeneration and potentially rupture
- Does a patent false lumen affect the long term outcome in type B dissection?
- Does false lumen thrombosis have a better long term prognosis?
- Hypothesis
  - TEVAR as adjunctive treatment early in the course of uncomplicated aortic dissection can promote remodeling and subsequent healing of the aorta
  - Can it change the long term mortality related to chronic aortic dissections?

Consequences of a Patent False Lumen

- Single institution retrospective review
- Nippon medical school series
- 110 patients with medically managed type B dissection
  - Treated from 1981 - 2000
- CT scans reviewed for up to 10 years of follow up
  - 87 censored cases and 11 lost to follow up at 10 years
- All cause mortality, dissection related morbidity and mortality

Consequences of a Patent False Lumen

- Univariate analysis failed to identify variables leading to false lumen thrombosis
- Multivariable modeling identified patent false lumen as independent factor for dissection related events
  - HR 7.6 (95% CI 2.7 - 22) p = <0.01

- Single institution retrospective review
- Kurume University, Japan
- 76 patients with medically managed type B dissection
  - Treated from 1990 - 2000
- Mean follow up 53 +/- 35 months
  - 2 lost to follow up
Consequences of a Patent False Lumen

Predictors of Aneurysmal Change

- Single institution retrospective review
- University of Ulsan, South Korea
- 100 patients with acute aortic dissection
  - Mix of type A and type B
  - Excluded patients with in-hospital mortality during initial admission
  - 6 patients with Marfans
- Mean follow up 53 +/- 26 months
- Complete healing of aorta in 6 patients

Predictors of Aneurysmal Change

- Table 3: Multivariate Analysis (Performed Using Logistic Regression) for Event Predictors

<table>
<thead>
<tr>
<th>Event Predictors</th>
<th>p</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atherosclerotic factors</td>
<td>0.089</td>
<td>3.27</td>
</tr>
<tr>
<td>Blood status in the false lumen,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>initial false lumen</td>
<td>0.001</td>
<td>9.00</td>
</tr>
<tr>
<td>Maximum aortic diameter, initial</td>
<td>0.064</td>
<td>3.86</td>
</tr>
<tr>
<td>40 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean systolic BP = 140 mm Hg</td>
<td>0.089</td>
<td>5.79</td>
</tr>
<tr>
<td>Mean diastolic BP = 90 mm Hg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


J Am Coll Cardiol 2007 vol. 50 (8) pp. 799-804

Predictors of Aneurysmal Change

- Graph showing incidence of aneurysm (%) by location:
  - Arch
  - Upper
  - Mid
  - Lower
  - Abdominal

J Am Coll Cardiol 2007 vol. 50 (8) pp. 799-804
Predictors of Aneurysmal Change

- Presenting false lumen diameter correlated with upper thoracic aortic aneurysm formation
  - Total aortic diameter did not
  - OR 1.5 (95% CI 1.15 - 1.95) p < 0.01

- Upper thoracic false lumen diameter > 22 mm
  - Predicts late aneurysm formation with sensitivity of 100% and specificity of 76%

J Am Coll Cardiol 2007 vol. 50 (8) pp. 799-804

TEVAR as Adjunct in Uncomplicated Dissections

- Cover principle false lumen entry tear
- Promotes false lumen thrombosis
- Subsequent remodeling decreases late risk of rupture
- Risk unstable landing zones with possible retrograde dissection
- Potentially greater risk of spinal ischemia as more intercostals will be covered

INSTEAD Trial

- Investigation of Stent Grafts in Aortic Dissection
- Prospective multicenter randomized trial
  - 7 European centers
- Optimal medical therapy (OMT) vs OMT + TEVAR
- Sponsor: Medtronic

**INSTEAD Trial: Patient Population**

- **Type B Aortic Dissections**
  - No intramural hematoma or penetrating ulcers
- **Subacute or Chronic**
  - Randomization between 2 or 52 weeks of dissection
  - To exclude patients with early complications or spontaneous thrombosis

**Circulation (2009) vol. 120 (25) pp. 2519-28**

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**INSTEAD Trial: Study Design**

- 140 patients enrolled
  - 597 patients evaluated over 2 year period (2003 - 2005)
- Randomized 1:1
- Follow up for 2 years
- Endpoints
  - All cause mortality
  - Aortic related mortality
  - Aortic remodeling
  - Progressive aortic pathology
    - Composite end point
      - Crossover
      - Any open or endovascular intervention
      - Expansion

**Circulation (2009) vol. 120 (25) pp. 2519-28**

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**INSTEAD Trial: Anatomy**

- Coverage of < 20 cm of aorta
- Seal major entry tears
- Coverage of L subclavian and revascularization left to discretion of surgeon
- TEVAR with Talent (Medtronic)

**Circulation (2009) vol. 120 (25) pp. 2519-28**

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**INSTEAD Trial: Results**

- Ave time from dissection to randomization 40 days
- Ave time from randomization to TEVAR 12 days

**Table 3. Peri-procedural Outcomes After TEVAR (48 Days)**

<table>
<thead>
<tr>
<th>Event</th>
<th>n (%)</th>
<th>2/28 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>2 (2.8)</td>
<td></td>
</tr>
<tr>
<td>Peri-procedural events, n (%)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Retrograde type A dissection</td>
<td>1 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Rupture of iliac access vessel</td>
<td>1 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Conversion to open surgery</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Ancillary procedures/lesions</td>
<td>3 (4.5)</td>
<td></td>
</tr>
<tr>
<td>Stenting of iliac artery</td>
<td>1 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Aortic stent-graft extension</td>
<td>1 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Aortic stent-graft extension</td>
<td>1 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Peri-procedural neurological</td>
<td>2 (2.8)</td>
<td></td>
</tr>
<tr>
<td>events, n (%)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Paraplegia/paraparesis</td>
<td>1 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Major stroke</td>
<td>1 (1.5)</td>
<td></td>
</tr>
</tbody>
</table>

**Circulation (2009) vol. 120 (25) pp. 2519-28**
INSTEAD Trial: Remodeling

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>OMT (n=68)</th>
<th>OMT + TEVAR (n=72)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>False lumen thrombus at 2 y; n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>13 (19.4)</td>
<td>63 (91.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Incomplete</td>
<td>6 (9.1)</td>
<td>6 (8.7)</td>
<td>0.79</td>
</tr>
</tbody>
</table>

INSTEAD Trial: Results

- Crossovers
  - 11 in OMT group to TEVAR
    - Expansion to > 6 cm
  - All patients that crossed over did well
    - Uneventful follow up
    - Remodeling despite late intervention

INSTEAD Trial: Mortality

A Cumulative survival within 36 months after randomization
**INSTEAD Trial: Mortality**

![Graph showing freedom from progressive aortic disease](image)

**INSTEAD Trial: Interpretation**

- TEVAR for uncomplicated aortic dissection failed to improve 2 year survival rate
  - Exposure to procedurally related complications (neurological, access related)
  - Study effect: excellent survival with OMT
- OMT group had timely crossover to TEVAR while under surveillance
  - Observation is feasible and safe

**INSTEAD Trial: Criticisms**

- Underpowered
  - Expected 28 deaths
  - Power calculation based on “real world” registry data
  - Observed 11 deaths
  - Optimal medical therapy and surveillance in setting of prospective trial
  - Will conclusions change after 5 years of follow up?
- 4 deaths in TEVAR group later identified as randomized despite protocol violations
  - Evidence of malperfusion or impending rupture
  - No report of how many patients were randomized to OMT with similar findings

**ADSORB Trial**

- Acute Dissection: Stent Graft or Best Medical Therapy
- Randomized trial of OMT vs. OMT + TEVAR
- 17 European centers
- Sponsor: Gore

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Eur J Vasc Endovasc Surg. 2012 Jul;44(1):31-6
ADSORB Trial: Patient Population

- Type B dissection only
  - No intramural hematoma or penetrating ulcers
  - Entry tear distal to the left subclavian
- Acute
  - Time from symptom onset to treatment < 14 days
- Uncomplicated
  - Freedom from
    - End organ ischemia
    - Paraplegia
    - Rupture
    - Uncontrolled pain

ADSORB Trial: Study Design

- Total 250 patients
- Randomized 1:1
  - Control arm optimal medical therapy
  - Treatment arm optimal medical therapy + TEVAR
- Follow up for 3 years
- Exclusion criteria
  - Connective tissue disorders
  - Need for other surgical procedures
- Inclusion criteria
  - Maximal diameter of thoracic aorta < 5.5 cm
- End points
  - Incomplete false lumen thrombosis
  - Aortic dilation at 1 year
  - Aortic rupture at 1 year

ADSORB Trial: Anatomy

- Proximal neck diameter 23 - 42 mm
- Proximal neck length > 2 cm
  - Coverage of left subclavian OK
- Distal coverage > 10 cm beyond primary entry tear
- TEVAR with TAG device (Gore)

ADSORB Trial: Interim Results

- One year interim results presented in May 2012
- Randomized 61 patients
  - OMT + TEVAR 30 patients
  - OMT 31 patients
- One year outcome data on 43 patients
  - Two crossovers from TEVAR to OMT
    - Withdrew consent
    - Inadequate proximal neck on additional imaging
  - Three crossovers from OMT to TEVAR
    - Acute aortic dilation 2 days after randomization
    - Mesenteric malperfusion 1 day after randomization
    - Retrograde dissection 3 days post randomization

17th Annual Critical Issues in Aortic Endografting 2012
ADSORB Trial: Core Lab Measurements

- Core lab adjudication of aortic measurements
- Maximum true lumen diameter
- Minimum true lumen diameter
- Maximum false lumen diameter
- Overall transverse aortic diameter

ADSORB Trial: Aortic Remodeling

- Maximum true lumen significantly different at first post procedure imaging

ADSORB Trial: Aortic Remodeling

- Minimum false lumen significantly different at first post procedure imaging
ADSORB Trial: Aortic Remodeling

- Overall transverse aorta not different between groups

17th Annual Critical Issues in Aortic Endografting 2012

ADSORB Trial: Mortality

- Overall mortality not different between groups

17th Annual Critical Issues in Aortic Endografting 2012

Conclusions

- Survivors of acute type B dissection have up to 25% mortality 3 years after event
  - Optimal medical therapy can improve survival
  - Close surveillance for timely interventions is safe and effective

- TEVAR uncomplicated aortic dissection improves surrogate markers of aortic pathology (false lumen flow, diameter) but has not been shown to improve mortality over OMT with a complication specific approach to intervention