In most uncomplicated Type B aortic Dissection
Patients TEVAR leads to false lumen thrombosis and stability

Observations and evidence

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Disclosure

Speaker name:

........Christoph A.Nienaber.............................................

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

- I do not have any potential conflict of interest
Why should stable type B aortic dissection be stented...?

Feasible
Safe
Quick recovery
Open surgery abandoned

Dake MD, et al. NEJM 1999; 340:1546-1552
...cause Type B aortic dissection is not a benign disease

Long-term survival requires FL thrombosis & remodeling...or ends in rupture

- FL open and no Isolation
- FL expansion
- TL compression
- Impending rupture
...and works in all parts of the aorta, even after type A dissection
...medical management alone does not prevent expansion of the aorta...

Medical management should prevent...

But fails to avoid rupture, aneurysm, and aortic repair.
only endovascular scaffolding is able to support the true lumen and induce remodeling

Completely reconstructed acute dissection

Progressive shrinkage of false lumen thrombus mass and aortic remodeling

Relief of infrarenal true lumen collapse
...but may require a PETTICOAT to facilitate false lumen remodeling
...or may require sealing of distal reentry tears for longterm stability

Stabilization of complicated type B aortic dissection STABLE trial JVS 2014
...or false lumen coils & occluder to facilitate thrombosis and aortic remodeling

Pre-TEVAR

55 d post-TEVAR

3 d post-repair

Complex, but uncomplicated case with secondary reperfusion of false lumen from proximal inflow caused by rupture of graft fabric. Retrograde coiling and an occluder turn procedural failure into a great success with additional procedures!
Impact of TEVAR on thrombosis and remodeling can be quantified.
thrombosis/remodeling in 84% in 2 years, but prognostic benefit later!

1 year crossover rate: 14% (p=0.02)
2 years crossover rate: 20% (p=0.02)
2 years: 84% versus 16% FL thrombosis (p<0.001)
Eventually remodeling shows prognostic benefit beyond 2 years!

(Definition: FL thrombosis & shrinkage, no progression)

<table>
<thead>
<tr>
<th></th>
<th>FLT</th>
<th>TLD</th>
<th>Remod.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>22%</td>
<td>18mm</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>91%*</td>
<td>33mm*</td>
<td>79%*</td>
</tr>
</tbody>
</table>

* p< 0.0001

Nienaber CA et al. Circulation CV Int 2013
The initial RCT showed a long-term advantage of an intervention (stent-grafting the TL), with two large registry-based analyses confirming the signal from the RCT; findings are supported by short-term F/U of an independent RCT. *On aggregate, all data are consistent! Very strong signal!*
2 predictors of long-term stability: FL thrombosis and Remodeling!

<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>Age</td>
<td>.030</td>
<td>.020</td>
<td>.134</td>
<td>1.031</td>
<td>.991-1.072</td>
</tr>
<tr>
<td>Female</td>
<td>-1.097</td>
<td>.649</td>
<td>.091</td>
<td>.334</td>
<td>.094-1.193</td>
</tr>
<tr>
<td>STJ diameter</td>
<td>-1.880</td>
<td>.637</td>
<td>.003</td>
<td>.153</td>
<td>.044-.532</td>
</tr>
<tr>
<td>Complete FLT</td>
<td>1.678</td>
<td>.751</td>
<td>.025</td>
<td>5.354</td>
<td>1.229-23.329</td>
</tr>
</tbody>
</table>

IRAD data on file

Suenaga H. et al. EJCTS 2016
remodeling is best in the acute and subacute phase of dissection!

Midterm outcomes and morphology are similar in acute and subacute type B dissection undergoing stent-graft treatment; the window of plasticity and for remodelling is open until 3 months.
Initiation of false lumen thrombosis to enhance remodeling

**Optimal endovascular management with false lumen isolation**

- Appropriate sizing/placing of stentgraft
- Use of the window of aortic plasticity for interventions
- Avoid type I and II endoleaks
- In case of retrograde FL flow consider adjunctive interventions:
  - PETTICOAT
  - Retrograde coiling
  - False lumen occluders
  - Focal stentgraft to seal distal reentry sites

- Interruption of anticoagulants for 4 weeks

**Optimal life-time medical management to minimize inflammation and wall stress to the aorta**
Most important: Always have a plan...
• “Dios creó la aorta con solo un canal...así debería quedarse...”

• Papa Francisco y Juan Parodi 2015
Local Inflammation in chronic TBAD, partial FL thrombosis

- Partial FL thrombosis
- Expanding FL
- Ongoing metabolic activity on FDG-PET
- Rupture?

No evidence of aortic remodelling!
Residual patent false lumen and long-term mortality

<table>
<thead>
<tr>
<th>Study ID</th>
<th>HR (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type A</td>
<td></td>
<td></td>
</tr>
<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>Type B</td>
<td></td>
<td></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>
<tr>
<td>Heterogeneity between groups: p = 0.102</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (I-squared = 12.6%, p = 0.330)</td>
<td>2.12 (1.58, 2.83)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

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Recommendations based on meta-analysis

Death Risk  Complete thrombosis  Patent  Partial thrombosis

- Type B AAD: 2.24
  - Extended arch resection
- Type A AAD: 1.75
  - Extended stent-graft placement
  - Extended arch resection

Partial thrombosis of false lumen
Residual patent false lumen

Dongze Li et al. J Am Heart Assoc 2016;5:e003172

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Acute/subacute dissection - Remodelling with shrinking FL

Figure 5. Change in false lumen area plotted for the three clinical groups over the course of the study. The data are given as the mean change in true lumen area from baseline preoperative scans at 10 cm distal to the left subclavian artery. Numbers analysed at each time point (months) are tabulated below the figure. Note. TEVR = thoracic endovascular repair; Post TEVR = number of patients at risk immediately after TEVR.
Conclusions

- Aortic Remodeling requires FLT and shrinkage, increasing TLD & no progression.
- Remodeling is associated with improved prognosis.
- Remodeling is facilitated during the window of aortic plasticity that may close at 3 – 6 months.
Future perspectives. 2

- Will we treat all B dissections with TEVAR?

- Which treatment?
Partial thrombosis of false lumen and long-term mortality in acute aortic dissection

Study ID | Type A | Larsen, 2013 | 0.78 (0.30, 1.99) | 17.65 | Song, 2010 | 6.48 (1.30, 32.35) | 6.12 | Song, 2011 | 3.21 (1.19, 14.38) | 10.18 | Subtotal (I-squared = 68.1%, p = 0.044) | 1.75 (0.88, 3.45) | 33.95 |

Type B | Tanaka, 2014 | 1.16 (0.41, 3.26) | 14.70 | Tsai, 2007 | 2.69 (1.45, 4.98) | 41.51 | Ueki, 2014 | 2.74 (0.77, 9.71) | 9.84 | Subtotal (I-squared = 0.0%, p = 0.371) | 2.24 (1.37, 3.65) | 66.05 |

Heterogeneity between groups: p = 0.563
Overall (I-squared = 41.7%, p = 0.127) | 2.06 (1.38, 3.06) | 100.00

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Figure. 2D and 3D volume rendered CT angiogram showing left subclavian artery aneurysm before (i,iii) and after (ii,iv) endovascular reconstruction. Note relationship to clavicle (C), first rib (R), vertebral artery (V), left internal mammary artery (L) and proximal stent edge (arrow).
Supplemental Figure 2c
Importance of strict blood pressure compliance

92% at 10 yrs
74% at 10 yrs
49% at 10 yrs

Textbook medicine: antihypertensive therapy of type B 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.
Current view on a new large trial for type B dissection

- RCT are rarely practical because of ethical issues when assigning patients to study arms.

- If one group receives treatment thought to be effective, while another does not, the ethics of a trial may forbid randomization.

- Very difficult: Who can define “uncomplicated aortic dissection”? 

- How to standardize the level of expertise and care in a multicenter RCT?

- How to avoid confounding impact of improving technology, skills and experience in a slow-recruiting trial?

- This would not be a (blinded) drug trial!
# Recommended treatment of aortic dissection

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In all patients with AD</strong>, medical therapy including pain relief and blood pressure control is recommended.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td><strong>In patients with type A AD</strong>, urgent surgery is recommended.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td><strong>In patients with acute type A AD and organ malperfusion</strong>, a hybrid approach (i.e. ascending aorta and/or arch replacement associated with any percutaneous aortic or branch artery procedure) should be considered.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td><strong>In uncomplicated type-B AD</strong>, medical therapy should always be recommended.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td><strong>In uncomplicated type-B AD</strong>, TEVAR should be considered.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td><strong>In complicated type-B AD</strong>, TEVAR is recommended.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td><strong>In complicated type-B AD</strong>, surgery may be considered.</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>
Therapy 2016

Patient with chest pain

Blood biomarkers, ECG

Urgent CT scan

Triple rule out CT if intermediate pretest probability of CAD

Pulmonary embolus

Aortic dissection

Acute coronary syndrome

Stanford type A

Stanford type B

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

Open surgery after initial risk assessment

Uncomplicated: Medical treatment

Complicated: Endovascular treatment

Nienaber CA, Clough RA, Lancet 2015
Supplemental Figure 2b
Remodeling with TEVAR...

Complete false lumen thrombosis in the descending thoracic aorta

Pre-procedure  Post-procedure  24 months
Complicated Type B dissection: Escalating complexity I-III

Simple Stentgraft  
PETTICOAT  
Complex branched
Secondary Effectiveness Endpoint Analysis – success?

**False Lumen Thrombosis Adjacent to Stent Graft (Last Available Follow-up)**

**Extent of Dissection**

- Complete Thrombosis
- Partial Thrombosis
- No Thrombosis
- Unknown

**False Lumen Thrombosis Distal to Stent Graft (Last Available Follow-up)**

**Extent of Dissection**

- Complete Thrombosis
- Partial Thrombosis
- No Thrombosis
- Unknown

- **Subjects with Core Lab False Lumen Thrombosis Result and Extent of Dissection Information**
  - Dissection stops at renal arteries (8)
  - Dissection extends past renal arteries (37)

- **Distal Re-entry Tears**
  - Dissection stops at renal arteries: Yes 1 (12.5%), No 5 (62.5%)
  - Dissection extends past renal arteries: Yes 30 (81.1%), No 3 (8.1%)
Actuarial overall survival and aortic event free on the thoracic aorta after the frozen elephant trunk technique in acute type A aortic dissection.

Overall survival

Aortic event free on the thoracic aorta

5 years: 90.1%
10 years: 76.1%
15 years: 45.1%

5 years: 92.7%
10 years: 89.8%
15 years: 73.6%

Akira Katayama et al. Eur J Cardiothorac Surg
2015;47:355-360
In most uncomplicated Type B aortic Dissection, Patients TEVAR leads to false lumen thrombosis and stability.

Observations and evidence

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