An Algorithm to Choose Which Uncomplicated (Asymptomatic) Acute Type B Dissection Patients Should Undergo TEVAR

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Outline

• Uncomplicated type B dissection
• Randomized trials comparing TEVAR to best medical therapy
  - INSTEAD/INSTEAD XL trials (subacute)
  - ADSORB trial (acute)
• Subpopulations at risk for late complications
• VIRTUE registry (timing of TEVAR)
• Algorithm

Acute Type B Dissection

• Incidence: 0.5-2.1/100,000 person years
• Typical patient: male, age 60-65 years, history of hypertension
• Up to 30% will present with a complicated type B dissection
  - Rupture
  - Malperfusion
  - Unremitting pain
  - Uncontrolled hypertension
• TEVAR considered life-saving in complicated cases

Disclosures

• Royalties and research grant support from Cook Medical, Inc.
“Uncomplicated” Type B Dissection

- Medical therapy has been standard of care
  - Close ICU monitoring
  - Control of blood pressure, heart rate, and pain
  - β-blockers staple of optimal medical management

- Large databases: ~90% of patients can be successfully managed in-hospital with medical therapy alone

Why Intervene on “Uncomplicated” Type B Dissection?

- “Uncomplicated” is misnomer
  - 25% to 50% treated medically develop late aortic-related complications
    - Aneurysmal degeneration
    - Rupture
    - Malperfusion

- Difficult patient compliance with medical treatment

- Lower 5-year mortality in those treated surgically vs medical management alone

- Lose chance for favorable remodeling if not treated early
  - Especially important in subpopulations at higher risk

INSTEAD: The INvestigation of STEnt grafts in Aortic Dissection Trial

- First randomized trial to compare elective TEVAR to optimal medical therapy (OMT)
  - Uncomplicated type B dissection

- Randomized 140 patients to elective stent-graft placement + OMT (n=72) to OMT alone (n=68)
  - Stable clinical condition ≥ 2 weeks after index dissection
  - TALENT stent grafts (Medtronic, Inc.)

INSTEAD Trial: Results

- Favorable aortic remodeling in TEVAR group:
  - Significant increase in true lumen expansion at all follow-up time points
  - Decrease in false lumen diameter at all time points
  - More likely to have complete false lumen thrombosis at two years

- No significant difference between TEVAR and optimal medical therapy at two years:
  - All cause mortality
  - Aorta-related mortality
  - Progressive aortic disease
### INSTEAD Trial: Conclusions

- Elective TEVAR in clinically stable, low-risk patients does not improve 2-year survival, despite favorable aortic remodeling
  - Spinal injury in 2.8% of patients

- Trial results support complication-specific approach instead of TEVAR for all type B dissections

- Deferred endovascular therapy is feasible and safe in those who fail to respond to medical management

### INSTEAD XL Trial: Extended for Late Follow-up

- Performed to clarify late impact of TEVAR
  - Hypothesis: TEVAR may have long-term benefits, given increased rate of false lumen thrombosis

- Landmark statistical analysis of years 2-5 after index intervention
  - Primary end point: All-cause mortality
  - Secondary end points: Aorta-related death, Progression of disease

### INSTEAD XL: All Cause Mortality

- Landmark analysis at 2-year breakpoint
- Kaplan-Meier survival analysis

### INSTEAD XL: Aorta-Specific Mortality

- Landmark analysis at 2-year breakpoint
- Kaplan-Meier survival analysis

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Nienaber et al; Circ Cardiovasc Interv 2013;6:407-16
INSTEAD XL: Progression of Disease and Aorta-Specific Events

Landmark analysis at 2-year breakpoint

Kaplan-Meier survival analysis

Nienaber et al; Circ Cardiovasc Interv 2013;6:407-16

INSTEAD XL: Aortic Remodeling

Nienaber et al; Circ Cardiovasc Interv 2013;6:407-16

INSTEAD XL: Conclusions

• TEVAR in subacute phase of type B dissection:
  - Induces aortic remodeling
  - Reduces aorta-related mortality at 5 years

• Early hazard of TEVAR counterbalanced by prevention of late complications and crossover procedures

ADSORB: Acute Dissection: Stent graft OR Best medical therapy

• Randomized trial comparing best medical treatment (BMT) with BMT and Gore TAG stent graft
  - Uncomplicated acute dissection < 14 days
  - No connective tissue disease

• Combined one-year primary endpoint:
  - Incomplete/no false lumen thrombosis
  - Aortic dilation
  - Aortic rupture
ADSORB Trial: One Year Results

- 50% of TAG+BMT vs 100% of BMT patients had at least one endpoint event
- 43% of TAG+BMT vs 97% of BMT patients had incomplete false lumen thrombosis
- No difference in aortic dilation
- No ruptures in either group

Significant increase in true lumen expansion in BMT+TAG group (p<0.001)
Significant decrease in false lumen size in BMT+TAG group (p<0.001)

Uncomplicated acute aortic dissection can be safely treated with Gore TAG device
Better remodeling at one year, with increase in true lumen and decrease in false lumen in BMT+TAG group compared to BMT alone
Population at Risk: Location of Proximal Tear

Tear on Concavity more frequently associated with:
- Complicated dissections
- Retrograde extension (less "protection" from arch vessels)
- Need for intervention
- Larger false lumen in descending thoracic aorta

Weiss et al; Eur J Cardiothoracic Surg 2012;42:571-576

Tear on Convexity

Population at Risk: Size of Entry Tear

- Higher false lumen pressures with larger tears
- INSTEAD XL:
  - All patients in medical arm that ruptured during follow up had entry tear > 10mm
  - Patients who crossed over to TEVAR for critical expansion had entry tear > 10 mm
- Large (≥10mm) entry tear in proximal part of dissection
  - Rapid aortic expansion
  - Higher incidence of dissection-related events

Nienaber et al; Circ Cardiovasc Interv 2013;6:407-16
Evangelista et al; Circulation 2012;125:3133-41

Subpopulations at Risk for Late Complications: Partial False Lumen Thrombosis

Ng et al; Circ Cardiovasc Interv 2013;6:407-16
Evangelista et al; Circulation 2012;125:3133-41

IRAD Registry (n=201 patients)
Subpopulations at Risk for Late Complications:
Patent/Partially Thrombosed False Lumen

- Four single center trials (cumulative n=458)
  - False lumen patency associated with future aortic complications
  - HR/OR range from 2.6 to 7.6

Onitsuka et al; Ann Thorac Surg 2004;78:1268-73
Marui et al; J Thorac Cardiovasc Surg 2007;134:1163-70

Subpopulations at Risk for Late Complications:
Aortic Size

- Several studies have shown thoracic aortic diameter ≥ 40 mm or ≥ 45 mm:
  - Independently associated with future aortic complications in medically managed type B dissections
  - Risk factor for mortality
  - May be even more important than presence of patent false lumen

Onitsuka et al; Ann Thorac Surg 2004;78:1268-73
Takahashi et al; Ann Thorac Cardiovasc Surg 2008;14(5):303-10
Onitsuka et al; Ann Thorac Surg 2004;78:1268-73
Ueki et al; Ann Thorac Surg 2014;97:767-73

Subpopulations at Risk for Late Complications:
Large False Lumen

- Initial false lumen diameter > 15 mm associated with higher rate of dissection-related death
  - Most of the dissection-related deaths occurred within 3 months after onset

Ueki et al; Ann Thorac Surg 2014;97:767-73
Chang et al; J Am Coll Cardiol 2008;52:1170-76

Subpopulations at Risk for Late Complications:
Large False Lumen*

- Larger false lumen area associated with increased risk of in-hospital complications

*includes patients with type A dissection
Song JM et al; J Am Coll Cardiol 2007;50(8):799-804
Timing of TEVAR for Type B Dissection

- **VIRTUE Registry**
  - VALIANT Thoracic Stent Graft Evaluation For the Treatment of Descending Thoracic Aortic Dissections
  - Prospective registry type B dissection
- **Complicated acute (<15 days) (n=50)**
  - Rupture, malperfusion syndromes, persistent pain, refractory hypertension
- **Subacute (15-92 days) (n=24)**
  - Symptomatic, aorta>5.5 cm, aorta>4.0 cm with true and false lumens both patent
- **Chronic (>92 days) (n=26)**
  - Symptomatic, aorta>5.5 cm or expanding >0.5cm/year

VIRTUE Registry: False Lumen Area

- Acute and subacute groups had greater reduction in false lumen area than chronic group (p<0.001 for all locations)
- No difference between acute and subacute groups

VIRTUE Registry: False Lumen Thrombosis

- False lumen thrombosis increased over time
  - Greater the more proximal the anatomic location
- No difference in false lumen thrombosis rates between the three groups in the distal half of descending thoracic aorta

VIRTUE Registry: False Lumen Thrombosis at Celiac Axis

- Patients with chronic dissection had significantly lower rates of false lumen thrombosis than patients with subacute or acute dissection (p=0.035)
VIRTUE Registry: Freedom From Aortic Intervention

- No overall difference between three groups
- >30% with chronic dissection required re-intervention

The Virtue Registry Investigators, Eur J Vasc Endovasc Surg 2014

VIRTUE Registry

- Patients with subacute dissection show aortic remodeling analogous to acute group rather than chronic group
- Aorta retains plasticity to remodel for at least 92 days after index dissection

"Uncomplicated" Acute Type B Dissection: Algorithm