The ongoing need to establish proof of benefit from intervention for uncomplicated Type B aortic dissection

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Disclosure

Speaker name: MICHEL MAKAROUN, M.D.

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- WL Gore: Scientific Advisory Board / Research Grants
- Medtronic: Study PI and Research Grants
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Two Main Options in 2015

- Agressive Medical Management limiting Interventions until After complications develop

- Prophylactic TEVAR Before any complications develop
  - In All Patients ?
  - Only In High Risk Patients ?
  - Timing ?
Uncomplicated Acute Type B Aortic Dissection

Argument for Early Intervention

1. TEVAR has lower Mortality and Morbidity than Traditional Surgery
Medical vs Open Surgery for type B Aortic Dissection

14 Day Mortality by Type and Management

Cumulative Mortality, %

Days Following Presentation

Circulation 2003; 108 [Suppl II]: II312-II317
Updated IRAD Data
Mortality in 550 Patients with Type B Dissection

- **Uncomplicated Dissection**
  - Medical Management: 6.1%

- **Complicated Dissection**
  - Open Surgery: 28.6%
  - TEVAR: 10.1%
Use of TEVAR for dissection continues to increase

2010 0.8/100,000 in Medicare Population
Uncomplicated Acute Type B Aortic Dissection

Argument for Early Intervention

2. Medically treated Type B has a high rate of late Aortic M&M that can be reduced by prophylactic TEVAR
Late Follow up of The INSTEAD Trial
68 Patients Intent to treat by Medical Rx
66 Patients followed per protocol
14 late interventions by 5 years
26.7% Late Aortic Interventions

Aortic Related Mortality of Medical Rx from Randomization
~ 20% @ 6 years
IRAD: International Multicenter Prospective Registry

The Journal of Cardiovascular Surgery 2012 April;53(2):161-8

Advances in the management of diseases of the thoracic aorta

Influence of clinical presentation on the outcome of acute B aortic dissection: evidences from IRAD

Trimarchi S. 1, Tolenaar J. L. 1, Tsai T. T. 2, Froehlich J. 3, Pegorer M. 1, Upchurch G. R. Jr. 4, Fattori R. 5, Sundt III T. M. 6,

IRAD
All Cause Survival

Medical Rx (434 pts) vs
TEVAR (146 Pts)

\[ P = 0.018 \]
Uncomplicated Acute Type B Aortic Dissection

Argument for Early Intervention

3. Minimally invasive TEVAR should be done EARLY to be effective in remodeling the aorta !!
Mid-term Outcomes and Aortic Remodelling After Thoracic Endovascular Repair for Acute, Subacute, and Chronic Aortic Dissection: The VIRTUE Registry

The VIRTUE Registry Investigators *

FL Thrombosis at celiac
Chronic << Subacute or Acute TEVAR

FL Thrombosis at celiac
Chronic << Subacute or Acute TEVAR
Aortic Remodeling has no demonstrated clinical benefit. It is used as a surrogate for long term stability of the aorta.
Uncomplicated Acute Type B Aortic Dissection

Argument for Early Intervention

4. Even if not all patients benefit from early TEVAR, some high risk patients will.
Small Number of patients Expand Fast > 1 cm/yr
By now you should all be convinced that prophylactic TEVAR for uncomplicated dissection is a great idea whose time has come!

I. Akin · S. Kische · T.C. Rehders · H. Schneider · H. Ince · C.A. Nienaber
Heart Center Rostock, Department of Internal Medicine I,
University Hospital Rostock, Rostock

TEVAR

The solution to all aortic problems

*Herz* 2011;36:539-547
NOT SO FAST!

Why we do not have enough evidence to change practice yet

1. Rate of aortic expansion in medically treated patients is small, and most are stable or remodel spontaneously!
Many Patients Simply Heal their Dissection
MW 51 year old woman Oct 2004

Other Patients Remain Completely Stable
Uncomplicated type B can be stable for a long time.

PY (53 F) CTA for PE

12/2/2006

2/4/2013

37x41 mm

6 years

37x41 mm
PW 63 year old man. March 2010

Type B dissection
Uncomplicated
PW: 28 Months later. July 2012

Completely Unchanged
No dilatation Anywhere
NOT SO FAST!

Why we do not have enough evidence to change practice yet

2. The rate of late aortic complications is not really well known, and there is no clear benefit yet for early TEVAR!
A Prospective Study of Medically Treated Acute Type B Aortic Dissection

A. Winnerkvist, U. Lockowandt, E. Rasmussen and K. Rådegran

66 pts Rx medically. Mean FU of 79 months (>6yrs) Compared to Age and Sex Matched Swedish Population

- No Mortality Difference from General Population
- Freedom from dissection related death: 82% @ 10 yrs

Eur J Vasc Endovasc Surg 2006;32:349-355

15% Late aneurysm development
Endovascular Repair of Type B Aortic Dissection: Long-term Results of the Randomized Investigation of Stent Grafts in Aortic Dissection Trial
Christoph A. Nienaber, Stephan Kische, Hervé Rousseau, Holger Eggebrecht, Tim C. Rehders, Guenther Kundt, Aenne Glass, Dierk Scheinert, Martin Czerny, Tilo Kleinfeldt, Burkhart Zipfel, Louis Labrousse, Rossella Fattori and Hüseyin Ince
for the INSTEAD-XL trial

- Small Study 66 pts
- Prospective only for 2 years
- Late FU done retrospectively
- Medical therapy better First 2 years

CONVERSION FROM TYPE B TO A

05/18/01

Courtesy of M. Dake MD
NOT SO FAST!

Why we do not have enough evidence to change practice yet

3. Remodeling and good results can be obtained after complications set in.
PS: 55 year old Baggage Handler

Initial aortic diameter 38 mm (Patent False Lumen)

Proximal DTA Celiac SMA Renals

✓ No abdominal pain
✓ Good urine output
✓ Good femoral pulses

Medical Therapy
PS: Follow-up over 3 Months

Rapid Aneurysmal Degeneration

TEVAR
PS: TEVAR 5 months later after Complication Develops

Jan 30, 07 / Pre

Jan 30, 07 / Post
PS: TEVAR 5 months later after Complication Develops

TEVAR can be effective AFTER Complications develop in the chronic stage
Actually INSTEAD was carried out in the Chronic Stage.
NOT SO FAST!

Why we do not have enough evidence to change practice yet.

4. Best timing for intervention is not clear if we want maximal protection from Aortic related mortality.
TEVAR may be safer if delayed at least 2 weeks from presentation

Impact of timing on major complications after thoracic endovascular aortic repair for acute type B aortic dissection

Nimesh D. Desai, MD, PhD, a,b Jean-Paul Gottret, MD, b Wilson Y. Szeto, MD, b Fenton McCarthy, MD, a,b Patrick Moeller, BS, b Rohan Menon, BS, b Benjamin Jackson, MD, c Prashanth Vallabhajosyula, MD, b Grace J. Wang, MD, c Ronald Fairman, MD, c and Joseph E. Bavaria, MD b

J Thorac Cardiovasc Surg 2014;in Press. E-pub

132 TEVAR for Type B dissection

Mid-term Outcomes and Aortic Remodelling After Thoracic Endovascular Repair for Acute, Subacute, and Chronic Aortic Dissection: The VIRTUE Registry

The VIRTUE Registry Investigators *

Eur J Vasc Endovasc Surg 2014;48:363-371

100 TEVAR for Type B dissection
Should prophylactic TEVAR be done at presentation?

9.4% develop complications and die in <2 weeks.

IRAD Registry

The IRAD Classification System for Characterizing Survival after Aortic Dissection

Anna M. Booher, MD, a Eric M. Isselbacher, MD, b Christoph A. Nienaber, MD, c Santi Trimarchi, MD, d
Arturo Evangelista, MD, e Daniel G. Montgomery, BS, f James B. Froehlich, MD, MPH, g Marek P. Ehrlich, MD, h
Jae K. Oh, MD, i James L. Januzzi, MD, b Patrick O’Gara, MD, h Thoralf M. Sundt, MD, b Kevin M. Harris, MD, i
Eduardo Bossone, MD, PhD, j Reed E. Pyeritz, MD, PhD, k Kim A. Eagle, MD; a IRAD Investigators

- 440 Medically Treated Type B Dissection
  - In Hospital Mortality  
    - Stroke: 1 (2.9%)  
    - Tamponade: 1 (2.9%)  
    - Visceral Ischemia: 7 (20.0%)  
    - Rupture: 20 (57.1%)  
    - Other: 6 (17.1%)
- Initial goal of 150 patients not reached
- 61 highly selected patients randomized early < 14 days

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mortality</th>
<th>1 year Deaths</th>
<th>False Lumen Thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEVAR (TAG)</td>
<td>30</td>
<td>0%</td>
<td>1</td>
<td>57%</td>
</tr>
<tr>
<td>Best Medical RX</td>
<td>31</td>
<td>0%</td>
<td>0</td>
<td>3%</td>
</tr>
</tbody>
</table>

- 3 cross overs to TEVAR because of early expansion
- 2 failures in BMT by 1 year: malperfusion and aneurysm

Mortality 1 year

Deaths

TEVAR (TAG) 30 0%
Best Medical RX 31 0%
NOT SO FAST!

Why we do not have enough evidence to change practice yet

5. No standardized way of identifying patients at high risk to target TEVAR
Type-Selective Benefits of Medications in Treatment of Acute Aortic Dissection (from the International Registry of Acute Aortic Dissection [IRAD])

Toru Suzuki, MD\textsuperscript{a,*}, Eric M. Isselbacher, MD\textsuperscript{b}, Christoph A. Nienaber, MD\textsuperscript{c}, Reed E. Pyeritz, MD\textsuperscript{d}, Kim A. Eagle, MD\textsuperscript{e}, Thomas T. Tsai, MD\textsuperscript{f}, Jeanna V. Cooper, MS\textsuperscript{g}, James L. Januzzi, Jr., MD\textsuperscript{b}, Alan C. Braverman, MD\textsuperscript{h}, Daniel G. Montgomery, BS\textsuperscript{e}, Rossella Fattori, MD\textsuperscript{b}, Linda Pape, MD\textsuperscript{i}, Kevin M. Harris, MD\textsuperscript{i}, Anna Booher, MD\textsuperscript{e}, Jae K. Oh, MD\textsuperscript{i}, Mark Peterson, MD\textsuperscript{i}.

- Size of Aorta
- Size of False Lumen
- Use of Calcium Channel Blockers
- Gender
- Age
- Location of Entry Tear on curvature of Aorta
- Size of Entry tears
- Re-entry Tears
- Ulcer like projections
100 Dissection patients

False lumen diameter >22 mm predicted late aneurysm formation

Sensitivity 100%  Specificity 76%

Other predictors

- Marfan’s Syndrome
- Aortic Diameter
117 patients. Cox Regression

Maximal diameter $> 40$ mm Most Predictive of later Aortic Dissection Related Events. $P = .003$

Ulcer like projections also Highly Predictive. 5 year event free rate 36%. $P = .016$
191 patients with Type B dissection

Predictors of Faster Expansion:
- White race
- Initial aortic diameter < 4.0 cm

Predictors of Slower expansion:
- Female gender / IMH / Ca Channel Blockers

NOT SO FAST!

Why we do not have enough evidence to change practice yet

5. No Cost effectiveness data
6. No Quality of Life data
7. Medical Rx outcomes are Improving
8. Early complications of TEVAR
9. Late Re-Interventions with
Summary

- Early Intervention with TEVAR may be of benefit in acute uncomplicated type B dissection.
- The premise however has NOT been proven yet and many uncertainties remain.

Conclusion

- There is an ongoing need to establish proof of benefit from intervention for uncomplicated Type B aortic dissection.