1. A Transition From Disease to Health
2. Heart – Brain Integration
3. Imaging / Omics / Regeneration / Life Style

Complex

CAD (5)
Valv. – CM

PVD-P
AF

Sub-Clinical

Arterial (2)

DBD/Frailty (2)

Health

Political (1)

Personal (3)

Evolving Understanding - TAA, TAD, AAA - 2014

- Definition, Imaging, ECM (3)
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  - Dysfunctional Structure (5)
  - Hemodynamics (3)
  - Approach to Hemodynamics (2)
  - Approach to Dysfunctional Structure (1)
- Principals of Management (TAA, TAD, AAA) (3)

1) Classification of Thoracic Aortic Dissection
(6 people per 100,000 per year)

**DeBakey**
- **Type I**: Originates in the ascending aorta, propagates at least to the aortic arch and often beyond it distally
- **Type II**: Originates in and is confined to the ascending aorta
- **Type III**: Originates in the descending aorta and extends distally down the aorta or rarely retrograde into the aortic arch and ascending aorta

**Stanford**
- **Type A**: All dissections involving the ascending aorta, regardless of the site of origin
- **Type B**: All dissections not involving the ascending aorta

A 14-day Mortality In 645 Pts From IRAD Stratified By Medical And Surgical Treatment In TAD Type A & B

IRAD (TT Tsai et. al.) Eur J Vasc Endov Surg 2009;37:149-Av 9h to Surgery
PG Hagan et. al. JAMA 2000;283:897
## Imaging Modalities In The Diagnosis Of AAS

<table>
<thead>
<tr>
<th>Feature of imaging modality</th>
<th>Angio</th>
<th>CT</th>
<th>MRI</th>
<th>TEE</th>
<th>TTE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Readily available</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Quickly performed</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Performed at bedside</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Noninvasive</td>
<td>—</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>No iodinated contrast</td>
<td>—</td>
<td>—</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>No ionizing radiation</td>
<td>—</td>
<td>—</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Low cost</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Diagnostic performance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Specificity</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Detection of intramural haematoma</td>
<td>—</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>–</td>
</tr>
<tr>
<td>Detection of site of intimal tear</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Detection of aortic regurgitation</td>
<td>+++</td>
<td>−/+*</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Detection of coronary artery involvement</td>
<td>+++</td>
<td>+/+*</td>
<td>+</td>
<td>++</td>
<td>–</td>
</tr>
<tr>
<td>Detection of pericardial effusion</td>
<td>—</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Detection of branch vessel involvement</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Detection of periaortic haemorrhage</td>
<td>—</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>–</td>
</tr>
</tbody>
</table>
3) **Pathophysiological Features of Marfan’s & Bicuspid Aortopathy**

Evolving Understanding - TAA, TAD, AAA - 2014

- Definition, Imaging, ECM (3)
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- Etiology and Pathogenesis (TAA, TAD, AAA) (11)

  Dysfunctional Structure (5)
  Hemodynamics (3)
  Approach to Hemodynamics (2)
  Approach to Dysfunctional Structure (1)

- Principals of Management (TAA, TAD, AAA) (3)

<table>
<thead>
<tr>
<th>TAA, Marfan's &amp; AAA</th>
<th>Prevalence</th>
<th>Risk Factors</th>
<th>Histology</th>
<th>Rupt./Disect.</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAA</td>
<td>1.25%</td>
<td>Genetic Predisposition</td>
<td>Cystic medial Necrosis</td>
<td>+</td>
</tr>
<tr>
<td>1. Marfan Syndrome</td>
<td>1 in 10,000</td>
<td>2. Bicuspid Valve</td>
<td>Inflammatory Infiltrate, VSMC Apoptosis</td>
<td>+++</td>
</tr>
<tr>
<td>5. AAA,</td>
<td>5%</td>
<td>Genetic Predisposition</td>
<td>Cystic medial Necrosis</td>
<td>++</td>
</tr>
</tbody>
</table>

Evolving Understanding - TAA, TAD, AAA - 2014

- Definition, Imaging, ECM (3)
- Types and Demographics (TAA, TAD, AAA) (5)
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  - Approach to Hemodynamics (2)
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The Structural and Functional Effects of Normal and Mutant Fibrillin 1 in the Regulation of Aorta Homeostasis

1) AORTIC ANEURYSM - MFS

Structure:
- Internal elastic lamina
- Tunica media
- Tunica adventitia
- Endothelium
- Small blood vessels

Dysfunction:
- Fibrillin
- TGF
- MMPs
- Elastin
- SMC
- Collagen
- Mucoid

1,2) TAA/TAD – MARFAN’S / BIC. VALVE – 3,4) HYPERT. / ATER

- FBN1 Mutation → ▼ Fibrillin → ▼ TGF-β → ▼ TIMP, ▲ MMP
- Rupture → ▼ Collagen
- Aneurysm Formation → ▲ Stiffness → ▼ Elastin, ▲ Collagen
- ▲ dp/dt, ▲ Aortic diameter, ▲ BP
- CMD → ▲ Proteases
- Degenerative Diseases → ▲ VSMC

1). Marfan’s Type of Syndromes

DIAGNOSTIC CRITERIA FOR MARFAN SYNDROME

Ghent Nosology

FBN1/TGFB2 MUTATIONS

Consider other diseases
MRA, Biochemical diagnosis, Genetic testing

MARFAN SYNDROME

LOEYS-DIETZ TYPE I

Aortic aneurysm, arterial tortuosity, hypertelorism, cleft palate, bifid uvula

TAAD1, TAAD2 and FAA MUTATIONS

LOEYS-DIETZ TYPE II

Normal synthesis of type III procollagen

EHLERS-DANLOS TYPE IV

Abnormal synthesis of type III procollagen

COLA31 MUTATIONS

Visceral rupture, easy bruising,
Thin translucent skin,
Characteristic facial appearance

FAAD†

First-degree relatives with aortic aneurysms or dissection or aneurysms in other localizations

TGFBR1 and TGFBR2 MUTATIONS
2) Biologic Features Of The Aorta And The Three Types Of Bicuspid Aortopathy

2) Morphologic Features of the Bicuspid Aortic Valve That Influence the Pattern of Aortopathy

1-4) Pathways Implicated In TAA – Fibrillin, TGF-β

1. Marfan, 2,3,4 Loeys-Dietz, 12 Ehlers-Danlos

5) Imaging Aortic Aneurysm Mouse Model With MRI and Nanoparticle PET-CT


M Nahrendorf, Rweissleder et al. ATVB. 2011;31:750

A Klink, V Fuster, ZA Fayad et al. J Am Coll Cardiol 2011;58:2522
### Evolving Understanding - TAA, TAD, AAA - 2014

- **Definition, Imaging, ECM** (3)
- **Types and Demographics (TAA, TAD, AAA)** (5)
- **Etiology and Pathogenesis (TAA, TAD, AAA)** (11)
  - **Dysfunctional Structure** (5)
  - **Hemodynamics** (3)
  - **Approach to Hemodynamics** (2)
  - **Approach to Dysfunctional Structure** (1)
- **Principals of Management (TAA, TAD, AAA)** (3)

**TAA:** Thor. Aort. Aneur.  – **TAD:** Thor. Aort. Dissect.  – **AAA:** Abd. Aort. Aneur.
Hemodynamic Factors - Dilatation To Dissection

1. Arterial Diameter

2. BP

3. \( \frac{dp}{dt_{\text{max}}} \)

Evolving Understanding - TAA, TAD, AAA - 2014

• Definition, Imaging, ECM (3)
• Types and Demographics (TAA, TAD, AAA) (5)
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  Dysfunctional Structure (5)
  Hemodynamics (3)
  Approach to Hemodynamics (2)
  Approach to Dysfunctional Structure (1)
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1) **TAD – Hemodynamic Approach**

**Baseline**

2) Vasodilator  
   *(i.e., Nitroprusside)*  
3) Beta blockade

---

2) MFS - IMPACT OF \( \beta \) BLOCKERS ON AORTIC ROOT DIAMETER - THE REGRESSION CURVES OF DIAMETER 2 (SINUSES OF VALSALVA) ACCORDING TO AGE (\( N=77 \) vs 78)

M Ladouceur et al., AJC 2007; 99:406 (Paris)
Evolving Understanding - TAA, TAD, AAA - 2014

- Definition, Imaging, ECM (3)
- Types and Demographics (TAA, TAD, AAA) (5)
- Etiology and Pathogenesis (TAA, TAD, AAA) (11)
  - Dysfunctional Structure (5)
  - Hemodynamics (3)
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We conducted a randomized trial comparing losartan with atenolol in children and young adults with Marfan’s syndrome. The primary outcome was the rate of aortic-root enlargement, over a 3-year period. Secondary outcomes included the rate of change in the absolute diameter of the aortic root; the rate of change in aortic regurgitation; the time to aortic dissection, aortic-root surgery, or death; somatic growth; and the incidence of adverse events. A total of 21 clinical centers enrolled 608 participants, 6 months to 25 years of age (mean [±SD] age, 11.5±6 years. We found no significant difference in the rate of aortic-root dilatation between the two treatment groups over a 3-year period.

RV Lacro et al., NEJM 2014; 371:2061
Atenolol versus Losartan in Children and Young Adults with Marfan’s Syndrome

Change in Aortic-Root $z$ Score and Aortic-Root Diameter

Atenolol vs. Losartan in Children and Young Adults with Marfan’s Syndrome

Freedom from Adverse Clinical Outcomes

Evolving Understanding - TAA, TAD, AAA - 2014

- Definition, Imaging, ECM (3)
- Types and Demographics (TAA, TAD, AAA) (5)
- Etiology and Pathogenesis (TAA, TAD, AAA) (11)
  - Dysfunctional Structure (5)
  - Hemodynamics (3)
  - Approach to Hemodynamics (2)
  - Approach to Dysfunctional Structure (1)
- Principals of Management (TAA, TAD, AAA) (3)

1). TAA - INDICATIONS FOR SURGERY

- $\geq 40 \text{ mm}$ with indication for elective AVR (BAV etc)
- $\geq 45 \text{ mm}$ in MFS
- $\geq 50 \text{ mm}$ in BAV (?)
- $\geq 55 \text{ mm}$ for an ascending aortic aneurysm,
- $\geq 60 \text{ mm}$ for a descending aortic aneurysm;
- $\geq 70 \text{ mm}$ in high-risk comorbidities;
- Growth rate $\geq 10 \text{ mm per year}$ in <55 mm diameter
- Recurrent symptoms, Evidence of proximal dissect.

L Cozijnsen et al., Circ 2011; 123:924
2). **Acute Aortic Syndromes - TAD**

- Aortic Dissection
- Aortic Intramural Hematoma
- Penetrating Atherosclerotic Ulcer

RR Baliga et al. J Am Coll Cardiol Img 2014;7:406

6-15% - CT / MR Diameter 16 mm, Rupture within 10 days
3). Annual Risk of Rupture of Abdominal Aortic Aneurysms

<table>
<thead>
<tr>
<th>Aneurysm Size</th>
<th>1-yr Incidence of Rupture</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5.5 cm</td>
<td>≤1.0</td>
</tr>
<tr>
<td>5.5–5.9 cm</td>
<td>9.4</td>
</tr>
<tr>
<td>6.0–6.9 cm</td>
<td>10.2</td>
</tr>
<tr>
<td>≥7.0 cm</td>
<td>32.5</td>
</tr>
</tbody>
</table>

Screening for AAA: U.S. Preventive Services Task Force Recommendation Statement

- The USPSTF recommends 1-time screening for AAA with ultrasonography in men aged 65 to 75 years who have ever smoked. (B recommendation)
- The USPSTF recommends that clinicians selectively offer screening for AAA in men aged 65 to 75 years who have never smoked (C recommendation)
- The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for AAA in women aged 65 to 75 years who have ever smoked. (1 statement)
- The USPSTF recommends against routine screening for AAA in women who have never smoked. (D recommendation)

ML LeFevre et al., Ann Intern Med 2014; 161:281
Small AAAs (3.0 cm – 5.4 cm in diameter) are monitored by ultrasound surveillance. The intervals between surveillance scans should be chosen to detect an expanding aneurysm prior to rupture. Studies were identified for inclusion through a systematic literature search through December 2010. Study authors were contacted, which yielded 18 data sets providing repeated ultrasound measurements of AAA diameter over time in 15,471 patients. Predictions of the risk of exceeding 5.5-cm diameter and of rupture within given time intervals were estimated. Growth rates increased on average by 0.59 mm per year. In contrast to the commonly adopted surveillance intervals in current AAA screening programs, surveillance intervals of several years may be clinically acceptable for the majority of patients with small AAA.
Techniques Available for Repair of Abdominal Aortic Aneurysms

Annual Proportion of Elective Endovascular & Open Repairs for Abdominal Aortic Aneurysms in the US

1. **A Transition From Disease to Health**
   - **Heart – Brain Integration**
   - **Imaging / Omics / Regeneration / Life Style**

<table>
<thead>
<tr>
<th>Health</th>
<th>Political (1)</th>
<th>Personal (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1980</strong></td>
<td>1990</td>
<td>2000</td>
</tr>
<tr>
<td><strong>1990</strong></td>
<td>2000</td>
<td>2010</td>
</tr>
<tr>
<td><strong>2000</strong></td>
<td>2010</td>
<td>2015</td>
</tr>
<tr>
<td><strong>2010</strong></td>
<td>2015</td>
<td>2020</td>
</tr>
</tbody>
</table>

- **Complex**
  - CAD (5)
  - Valv. – CM
  - PVD-P AF

- **Sub-Clinical**
  - Arterial (2)
  - DBD/Frailty (2)
ACEI postop, valve-sparing root replacement, and mitral valve repair have low reoperative risk.
1b). Risk of Aortic Surgery After Definite Bicuspid Aortic Valve Diagnosis (n=416)

HI Michelena et. al. JAMA 2011;306:1104.
**1c). SURGICAL OPTIONS FOR AV & TAA REPAIR**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bentall</strong></td>
<td>Total aortic root replacement with a composite valve graft consisting of a Dacron aortic root and a prosthetic aortic valve with re-implantation of the coronary arteries.</td>
</tr>
<tr>
<td><strong>Yacoub (Root Rem.)</strong></td>
<td>Dacron aortic root with a scalloped design.</td>
</tr>
<tr>
<td><strong>David (Valve Spar.)</strong></td>
<td>Native aortic valve is re-implanted into a Dacron aortic graft and coronary arteries are re-attached.</td>
</tr>
<tr>
<td><strong>Ross Procedure</strong></td>
<td>Pulmonary valve autograft is placed in the aortic valve position, and a homograft valve replaces the pulm. valve.</td>
</tr>
<tr>
<td><strong>Aortic Homograft</strong></td>
<td>Consists of aortic valve and ascending aorta.</td>
</tr>
</tbody>
</table>
1d). Arch Aneurysm - Branched Thoracic Endograft Hybrid With / Without Supra-Aortic Bypass

MG Davies et. al. Methodist DeBakey Cardiovasc J. 2011;7:35.
L-W Chen et. al. Circulation 2010;122:1373 (Fujian, China)
L-W Chen et. al. Circulation 2010;122:1373 (Fujian, China)
2). Acute Aortic Syndromes

Aortic Dissection  
Aortic Intramural Hematoma  
Penetrating Atherosclerotic Ulcer

RR Baliga et. al. J Am Coll Cardiol Img 2014;7:406
Hospital mortality decreased (1979-2003) from 21% to 4% and to late survival.

**2a) TAD TYPE A - SURVIVAL CURVE & REOPERATION (N=303)**

**Survival after surgical intervention for all hospital survivors (n=195)**

**Freedom from Aortic Reoperation on the Aorta or Aortic Valve – (n=195)**

L-M Stevens et al., JTCS 2009; 138:1349 (MGH, Boston)
2b) Transapical Endovascular Ascending Repair for Inoperable Acute Type A Dissection

Pre-Operative Imaging of Acute Ascend. Aortic Dissection

EE Roselli et. al. JACC Cardiovasc Intv. 2013;6:425
2c) **TEVAR For Traumatic Aortic Injury**

Immediate endovascular treatment is indicated in patients with complete transsection of the aortic wall and free bleeding into the mediastinum or pseudocoarctation syndrome, whereas delayed treatment can be suggested when limited disruption of the aorta is present but media and adventitia are intact.

_EACTS, ESC, EAPCI – (M Grabenwöger et al.) EHJ 2012; 33:1558_
3). Acute Aortic Syndromes

Aortic Dissection

Aortic Intramural Hematoma

Penetrating Atherosclerotic Ulcer

RR Baliga et. al. J Am Coll Cardiol Img 2014;7:406
3). Acute Aortic Syndromes and Thoracic Aortic Aneurysm

IRAD (A Evangelista et al.) Circulation 2005; 111:1063 - IMH
3) Cases of Small Intimal Defects Detected With Longitudinal Multiplanar Reformation (MPR) Images

T Kitai et. al. Circulation. 2011;124[suppl 1]:S174
3). Acute Aortic Syndromes

Penetrating Ulcer

Intramural Hematoma

RR Baliga et. al. J Am Coll Cardiol Img 2014;7:406
3) Acute Type A Intramural Hematoma
Analysis of Current Management Strategy

Best cutoff to Predict Events: 16 mm (Hematoma) - Often Type A

A Estrera et al., Circ. 2009; 120 [suppl 1]:S287 (Houston) – n=33
T Kitai et al., Circ. 2009; 120[suppl 1]:S292 (Kobe, Japan) – n=66,20y
J-K Song et al., Circ. 2009; 120:2040 (Seoul, S. Korea) – n=101
IRAD – TYPE B DISSECTION – SURVIVAL CURVE (N=300)

Hospital Mortality
- Surgical (11%)
- Endovascular (11%)
- Medical (18%)

Survival rate (%)
- 29%
- 10%
- 10%

Log rank $P = .61$

Days
0 300 600 900 1200

Worst Prognosis: Hypotension, Pleural Effusion, Renal Failure
Refractory Pain & Hypertension

IRAD (Tsai TT et al.) Circulation 2006; 114:2226 –
IRAD (S Trimarchi et al.) Circulation 2010; 122:1283
4a) Interdisciplinary Expert Consensus Document on Management of TAD Type B – No Complications

A Medical therapy vs. TEVAR for acute type B dissections: early mortality

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Medical Therapy</th>
<th>TEVAR</th>
<th>Weight</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemelli-Steinbrugger 2010</td>
<td>3 Events 50</td>
<td>58</td>
<td>38</td>
<td>0.42 [0.09, 1.89]</td>
</tr>
<tr>
<td>Fattori, IRAD 2008</td>
<td>34 Events 390</td>
<td>54</td>
<td>33</td>
<td>0.73 [0.27, 1.97]</td>
</tr>
<tr>
<td>Garbade 2010</td>
<td>7 Events 84</td>
<td>9</td>
<td>46</td>
<td>0.37 [0.13, 1.08]</td>
</tr>
</tbody>
</table>

Total (95% CI) 

Heterogeneity: Chi² = 0.87, df = 2 (P = 0.65); I² = 0%

Test for overall effect: Z = 2.11 (P = 0.03)

B Medical therapy vs. TEVAR for acute type B dissections: early neurologic complications

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Medical Therapy</th>
<th>TEVAR</th>
<th>Weight</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemelli-Steinbrugger 2010</td>
<td>1 Events 50</td>
<td>18</td>
<td>38</td>
<td>0.76 [0.05, 12.47]</td>
</tr>
<tr>
<td>Garbade 2010</td>
<td>12 Events 84</td>
<td>11</td>
<td>46</td>
<td>0.53 [0.21, 1.32]</td>
</tr>
</tbody>
</table>

Total (95% CI) 

Heterogeneity: Chi² = 0.06, df = 1 (P = 0.81); I² = 0%

Test for overall effect: Z = 1.35 (P = 0.18)

Medical Rx 1548, Surgical Rx 1706, TEVAR 3457
R Fattori et. al. J Am Coll Cardiol 2013;61:1661
### 4b) Interdisciplinary Expert Consensus Document on Management of TAD Type B - Complications

#### A. Open surgery vs. TEVAR for acute type B dissections: early mortality

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>open surgery Events</th>
<th>Total</th>
<th>TEVAR Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brunst, elective NIS 2011</td>
<td>16</td>
<td>282</td>
<td>9</td>
<td>262</td>
<td>29.2%</td>
<td>1.82 [0.79, 4.20]</td>
<td></td>
</tr>
<tr>
<td>Brunst, emergent NIS 2011</td>
<td>173</td>
<td>991</td>
<td>137</td>
<td>951</td>
<td>41.7%</td>
<td>1.75 [1.35, 2.26]</td>
<td></td>
</tr>
<tr>
<td>Fattori, IRAD 2009</td>
<td>20</td>
<td>59</td>
<td>5</td>
<td>43</td>
<td>20.9%</td>
<td>3.90 [1.33, 11.44]</td>
<td></td>
</tr>
<tr>
<td>Zeeshan, 2010</td>
<td>8</td>
<td>20</td>
<td>2</td>
<td>45</td>
<td>11.9%</td>
<td>14.33 [2.68, 76.63]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 1352

Heterogeneity: Tau^2 = 0.26; Chi^2 = 7.71, df = 3 (p = 0.05); I^2 = 61%

Test for overall effect: Z = 2.88 (p = 0.004)

#### B. Open surgery vs. TEVAR for acute type B dissections: early stroke

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>open surgery Events</th>
<th>Total</th>
<th>TEVAR Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brunst, elective NIS 2011</td>
<td>6</td>
<td>282</td>
<td>10</td>
<td>262</td>
<td>36.4%</td>
<td>0.49 [0.17, 1.44]</td>
<td></td>
</tr>
<tr>
<td>Brunst, emergent NIS 2011</td>
<td>61</td>
<td>991</td>
<td>37</td>
<td>951</td>
<td>53.9%</td>
<td>1.69 [1.11, 2.57]</td>
<td></td>
</tr>
<tr>
<td>Zeeshan, 2010</td>
<td>0</td>
<td>20</td>
<td>3</td>
<td>45</td>
<td>10.8%</td>
<td>0.30 [0.01, 6.01]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 1293

Heterogeneity: Tau^2 = 0.53; Chi^2 = 5.39, df = 2 (p = 0.07); I^2 = 63%

Test for overall effect: Z = 2.29 (p = 0.04)

#### C. Open surgery vs. TEVAR for acute type B dissections: early spinal cord ischemia

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>open surgery Events</th>
<th>Total</th>
<th>TEVAR Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brunst, elective NIS 2011</td>
<td>0</td>
<td>292</td>
<td>0</td>
<td>292</td>
<td>Not estimable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brunst, emergent NIS 2011</td>
<td>25</td>
<td>991</td>
<td>32</td>
<td>991</td>
<td>87.6%</td>
<td>0.78 [0.46, 1.32]</td>
<td></td>
</tr>
<tr>
<td>Fattori, IRAD 2009</td>
<td>3</td>
<td>59</td>
<td>1</td>
<td>43</td>
<td>3.1%</td>
<td>2.25 [0.23, 22.40]</td>
<td></td>
</tr>
<tr>
<td>Zeeshan, 2010</td>
<td>7</td>
<td>20</td>
<td>6</td>
<td>45</td>
<td>9.3%</td>
<td>0.72 [0.13, 3.93]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 1352

Heterogeneity: Chi^2 = 0.80, df = 2 (p = 0.67), I^2 = 0%

Test for overall effect: Z = 0.81 (p = 0.42)

---

Medical Rx 1548, Surgical Rx 1706, TEVAR 3457

R Fattori et. al. J Am Coll Cardiol 2013;61:1661
5) Long-Term Comparison of Endovascular and Open Repair of AAA

Cumulative Probability of Death or Secondary Procedure

Endovascular (n=444)

Open (n=437)

P=0.57

OVER (FA Lederle et al.) NEJM 2012; 367; 2
Small AAAs (3.0 cm – 5.4 cm in diameter) are monitored by ultrasound surveillance. The intervals between surveillance scans should be chosen to detect an expanding aneurysm prior to rupture. Studies were identified for inclusion through a systematic literature search through December 2010. Study authors were contacted, which yielded 18 data sets providing repeated ultrasound measurements of AAA diameter over time in 15,471 patients. Predictions of the risk of exceeding 5.5-cm diameter and of rupture within given time intervals were estimated. Growth rates increased on average by 0.59 mm per year. In contrast to the commonly adopted surveillance intervals in current AAA screening programs, surveillance intervals of several years may be clinically acceptable for the majority of patients with small AAA.
Reviews of 4 RCTs involving 137,214 participants. One-time invitation for AAA screening in men aged 65 years or older was associated with decreased AAA rupture and AAA-related mortality rates but had little or no effect on all-cause mortality rates. One RCT involving 9342 women showed that screening had no benefit on AAA-related or all-cause mortality rates.

Aortic Dissection Evaluation Pathway

**STEP 1**
Identify patients at risk for acute AoA.

**STEP 2**
Evaluate patient with acute AoA.
- High Risk Conditions
  - Marked hypertension
  - Connective tissue disease
  - Family history of aortic dissection
  - Recent aortic manipulation
  - Known thoracic aortic aneurysm

High Risk Pain Features
- Chest, back, or abdominal pain described as the following:
  - Sharp or tearing in severity
  - Ripping tearing chest or tearing back

High Risk Exam Features
- Evidence of perfusion deficit
- Pulse deficits
- Symptomatic arterial wall defect
- Abnormal noncoronary arterial signs
- Evidence of aortic insufficiency

**STEP 3**
Risk based diagnostic evaluation.
- Low Risk
  - No high risk features present.

- Intermediate Risk
  - Any single high risk feature present.

- High Risk
  - Two or more high risk features present.

**STEP 4**
Acute AoA identified or excluded.

Consider acute AoA in all patients presenting with:
- Chest, back, or abdominal pain
- Symptoms of abdominal compartment syndrome
- Symptoms of aortic dissection with pericardial effusion

Begin aortic imaging study for T2A.
- Chest x-ray
- ECG
- CTA
- MRI
- ARDI

Contraindication to any test?

Aortic Dissection Present?
- Yes
  - Proceed to Treatment Pathway

- No
  - Proceed to secondary imaging study.
1) **Blood TGF-β1 Concentrations are elevated in MFS and Decreased After Administration of Losartan, β-blocker Therapy, or Both**

A Prognostic and Therapeutic Marker in MFS

Aortic aneurysm and dissection are manifestations of Marfan syndrome (MFS), a disorder caused by mutations in the gene that encodes fibrillin-1. Aortic aneurysm in a mouse model of MFS is associated with increased TGF-β signaling and can be prevented by TGF-β antagonists such as TGF-β-neutralizing antibody or the angiotensin II type-1 receptor (AT1) blocker, losartan. Losartan merits investigation as a therapeutic strategy for patients with MFS.

HC Dietz et al., Science 2006; 312:117 (Johns Hopkins)
D McLoughlin et al., Circn 2011; 124[suppl 1]:S168 - Pravastatin
COMPARE: evaluated the effect of losartan on aortic dilatation rate in adults with Marfan syndrome (MFS). Patients with MFS have an increased risk of life-threatening aortic complications, mostly preceded by aortic dilatation. A total of 233 patients (47% female) underwent randomization to losartan 50-100mg/d (n=116) or no additional treatment (n=117). Follow-up was 3.1 ± 0.4 years.

<table>
<thead>
<tr>
<th>End Points</th>
<th>Losartan</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Aortic-root enlargement (mm)</td>
<td>0.77</td>
<td>1.35</td>
<td>0.014</td>
</tr>
<tr>
<td>No aortic-root growth (%)</td>
<td>50</td>
<td>31</td>
<td>0.022</td>
</tr>
<tr>
<td>2. Previous root replacement:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>significant lower aortic arch</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>expansion</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MARFAN SARTAN: 300 patients, 1ary EP-root diameter, 2ary EP-clinical

M Groenink et al., EHJ 2013; Aug 21 (Netherlands)
Trends in Aortic Dissection
Medicare Beneficiaries in the United States, 2000–2011