Open Thoracoabdominal Repair in Connective Tissue Disease Patient

Anthony L. Estrera, MD
Professor and Chief of Cardiac Surgery

Department of Cardiothoracic and Vascular Surgery
McGovern Medical School
The University of Texas Science Center at Houston
Memorial Hermann Heart & Vascular Institute
Disclosures

- A. Estrera Consultant Gore
Marfan Syndrome
*FBN1* Mutations

Skeletal
- Pectus deformities
- Reduced U/L segment
- Wrist and thumb sign
- Scoliosis

Ocular
- Ectopia Lentis
Thoracic Aortic Aneurysms and Dissections

20% of patients with TAAD have a first-degree relative with TAAD

Autosomal dominant inheritance
Decreased penetrance
Variable expression
R247C Variant Alters Myosin Function but Does Not Cause Aortic Disease

**In vitro**

- Baculovirus expression

<table>
<thead>
<tr>
<th>Myosin enzymatic activity</th>
<th>WT Myh11&lt;sup&gt;R247C&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

**In vivo**

- Aortic Ring Contraction

<table>
<thead>
<tr>
<th>Developed Force g/mg tissue</th>
<th>WT Myh11&lt;sup&gt;R247C&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

**H&E**

**Elastin**

In vitro assays- Sweeney lab (Penn), Aortic contractility- Stull lab (UTSW), Knockin model generation- Shao-Qing Kuang, PhD (UT Health)
ACTA2 Mutations

- Responsible for 10 - 14% familial TAAD
- No Marfan-like syndromic features
- PDA and other vascular diseases
- Type A and B aortic dissections
ACTA2 Mutations: Early Onset Coronary Artery Disease and Moyamoya Disease
TGFB2 and TGFB1 mutations: Variable spectrum of disease

Loeys-Dietz Syndrome

Marfan Syndrome
“Marfan syndrome type 2”

Familial TAAD
No syndromic features
National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC)

The GenTAC Registry was established in 2006 to collect information from eligible patients with genetic conditions that predispose them for thoracic aortic aneurysms to assist physicians and researchers in understanding the link between genes, aortic aneurysms, and heart disease. The Registry includes de-identified medical data, clinical images, and biological samples of about 3,700 patients and is available for research at no cost to qualified investigators worldwide. The GenTAC Registry concluded in 2016. Several new registries formed to continue longitudinal data collection on GenTAC cohort and to enroll additional patients. Information about these registries is available here.

If you wish to use GenTAC data, images or biological samples, apply here via the BioLINCC.
MAC Sites and Investigators

**United States**
DM Milewicz, MD, PhD
R Pyeritz, MD, PhD
A Braverman, MD
SA Morris, MD
RB Devereux, MD
J Grima, PhD
R Lacro, MD
SA LeMaire, MD
A Levin, MD
D Liang, MD, PhD
I Maumenee, MD
R Moran, MD
F Ramirez, PhD
P Robinson, MD
L Sakai, PhD
D Sallee, MD
S Shalhub, MD, MPH
A Yetman, MD
MN Singh, MD
ES Regalado, MS
MA Hofmann Bowman, MD, PhD
AM Crean, MD
J Bavaria, MD
A Psychogios, MD
V Kalahasti, MD
RF Ciampiota, MD, PhD

**Europe**
J De Backer, MD, PhD
A De Paepe, MD, PhD
B Callewaert, MD, PhD
M Renard, MSc, PhD
L Muiño-Mosquera, MD
G Jondeau, MD, PhD
C Boileau, PhD
F Labombarda, MD
L Faivre, MD, PhD
C Bouleti, MD, PhD
O Milleron, MD
Y von Kodolitsch
M Rybczynski, MD
Z Szabolcs, MD PhD
MSc
E Arbustini, MD
M Groenink, MD, PhD
A Evangelista, MD
G Teixido-Tura , MD, PhD
B Carlberg, MD, PhD

**Canada**
N Alvarez, BA, MD
I El-Hamamsy, MD, PhD
D Chitayat, MD
B Fernandez, MD
G Horne, MD, PhD
N Poirier, MD
D Reinhardt, PhD
G Sandor, MD
D Human BA, BM. BCh
M Ouzounian , MD PhD

**Australia**
L Ades, MD
R Jeremy, MB BS PhD

**Japan**
H Morisaki, MD, PhD
T Morisaki, MD, PhD

**MAC Houston Administrative Center**
Contact the Study Coordinator:
Ellen Hostetler
Tel 713 500 6843
Email ellen.m.hostetler@uth.tmc.edu

**Inclusion criteria:**
Any patient or family member with a pathogenic or non-benign variant in the known HTAD genes
MAC Aims: Evidence-based Diagnosis and Management of HTAD

- Establish a large cohort of patients with mutations in the HTAD genes and collect patient data
- Define the natural and clinical history of HTAD
- Characterize the disease risk associated with the HTAD genes and mutations
- Identify factors that modify risk
- Make the MAC resource available to investigators for further research and drug and device trials
- Address classification of disease genes
**HTAD Cases in MAC**

**N = 987**

<table>
<thead>
<tr>
<th>Gene</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTA2</td>
<td>319 (32%)</td>
</tr>
<tr>
<td>PRKG1</td>
<td>37 (4%)</td>
</tr>
<tr>
<td>SMAD3</td>
<td>190 (19%)</td>
</tr>
<tr>
<td>TGFBR1</td>
<td>176 (18%)</td>
</tr>
<tr>
<td>TGFBR2</td>
<td>265 (27%)</td>
</tr>
</tbody>
</table>
Systemic features associated with TGFBR1 and TGFBR2 mutations

<table>
<thead>
<tr>
<th>Feature</th>
<th>TGFBR1</th>
<th>TGFBR2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marfan systemic score mean (SD)</td>
<td>3.98 (3.44)</td>
<td>4.12 (2.94)</td>
<td>0.7</td>
</tr>
<tr>
<td>Systemic score &gt;=7</td>
<td>28/128 (21.9%)</td>
<td>34/183 (18.6%)</td>
<td>0.6</td>
</tr>
<tr>
<td>Hypertelorism</td>
<td>36/138 (26%)</td>
<td>62/199 (31%)</td>
<td>0.3</td>
</tr>
<tr>
<td>Broad or bifid uvula</td>
<td>36/139 (26%)</td>
<td>72/219 (33%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Arched palate</td>
<td>48/136 (35%)</td>
<td>109/229 (48%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Craniosynostosis</td>
<td>11/118 (9%)</td>
<td>20/190 (11%)</td>
<td>0.8</td>
</tr>
<tr>
<td>Translucent skin</td>
<td>63/144 (43%)</td>
<td>78/227 (34%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Wide scars</td>
<td>33/142 (23%)</td>
<td>62/218 (28%)</td>
<td>0.3</td>
</tr>
<tr>
<td>Head and neck arterial tortuosity</td>
<td>53/104 (51%)</td>
<td>72/133 (54%)</td>
<td>0.8</td>
</tr>
<tr>
<td>Cardiac defect (BAV, VSD, PDA)</td>
<td>13/154 (8.4%)</td>
<td>32/238 (21.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
<td>36/156 (23%)</td>
<td>65/244 (27%)</td>
<td>0.5</td>
</tr>
</tbody>
</table>
Aortic Root Diameter at Surgery or Dissection (UTH data)
## Does the Type of Aortic Event Differ Between Genes?

<table>
<thead>
<tr>
<th></th>
<th>FBN1</th>
<th>TGFBR1&lt;sup&gt;6&lt;/sup&gt;</th>
<th>TGFBR2</th>
<th>ACTA2&lt;sup&gt;7&lt;/sup&gt;</th>
<th>SMAD3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of individuals</strong></td>
<td>243</td>
<td>176</td>
<td>265</td>
<td>277</td>
<td>190</td>
</tr>
<tr>
<td><strong>Mean age (SD)</strong></td>
<td>30 (16)</td>
<td>38 (20)</td>
<td>41 (17)</td>
<td>48 (20)</td>
<td>41 (17)</td>
</tr>
<tr>
<td><strong>Aortic event</strong></td>
<td>30%</td>
<td>40%</td>
<td>45%</td>
<td>48%</td>
<td>37%</td>
</tr>
<tr>
<td><strong>Aortic dissection</strong></td>
<td>42%</td>
<td>50%</td>
<td>47%</td>
<td>88%</td>
<td>74%</td>
</tr>
<tr>
<td><strong>Type A&lt;sup&gt;‡&lt;/sup&gt;</strong></td>
<td>74%</td>
<td>89%</td>
<td>71%</td>
<td>61%</td>
<td>71%</td>
</tr>
<tr>
<td><strong>Mean Age</strong></td>
<td>39 ± 9</td>
<td>34 ± 17</td>
<td>36 ± 12</td>
<td>44 ± 16</td>
<td>53 yrs ± 15</td>
</tr>
<tr>
<td><strong>Type B</strong></td>
<td>26%</td>
<td>11%</td>
<td>29%</td>
<td>24%</td>
<td>12%</td>
</tr>
<tr>
<td><strong>Mean Age</strong></td>
<td>44 ± 10</td>
<td>38 ± 14</td>
<td>29 ± 12</td>
<td>53 yrs ± 15</td>
<td>46 ± 17</td>
</tr>
<tr>
<td><strong>Aneurysm repair</strong></td>
<td>58%</td>
<td>50%</td>
<td>53%</td>
<td>12%</td>
<td>26%</td>
</tr>
<tr>
<td><strong>Mean Age</strong></td>
<td>39 ± 13</td>
<td>33 ± 16</td>
<td>26 ± 16</td>
<td>33 ± 18</td>
<td>46 ± 17</td>
</tr>
<tr>
<td><strong>Cumulative risk of aortic event</strong></td>
<td>74% at 60 yrs</td>
<td>100% at 80 yrs</td>
<td>100% at 90 yrs</td>
<td>76% at 85 yrs</td>
<td>86% at 81 yrs</td>
</tr>
</tbody>
</table>
Connective Tissue Disorder

Genetically Triggered Aneurysm (GenTac)
Heritable Thoracic Aortic Disease (HTAD)
HTAD
25%

Sporadic Thoracic Aortic Disease
75%
TGF-β Pathway

Gene

ECM Genes

4.0-4.5
 TGFB1 (l)
 TGFB2 (l)
 SMAD3 (l)

≤ 5.0 cm
 FBN1 (MFS)
 COL3A1 (EDS)

4.5-5.0 cm
 ACTA2
 MYH11
 MYLK
 PRKG1

5.0-5.5 cm (Standard)

ECM Genes
 BGN
 A2
 A1
 A2
 P2

SMC Genes
 FLNA
 FOXE3
 MAT2A
 TGF-β Pathway
 SKI
 SLC2A10
 SMAD2
 SMAD4
 TGBF3
 NOTCH1

Other Genes

SMC Contractile Unit Genes

Asce

3.5

5.5 cm
Although we don’t own the patient, we should own the disease.
Differences in outcomes when repairing TAAA in HTAD?
# Marfan TAAA open surgical repair

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Dissection (acute)</th>
<th>Resp failure</th>
<th>Persist SCI</th>
<th>Bleeding reop</th>
<th>In-hospital mortality</th>
<th>8-yr survival</th>
<th>8-yr Freedom From reop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omura 2012 Japan</td>
<td>20</td>
<td></td>
<td>5%</td>
<td>0%</td>
<td>5%</td>
<td>0%</td>
<td>91%</td>
<td>86%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>100% (0%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coselli 2016 USA</td>
<td>127</td>
<td>100% (9%)</td>
<td>38%</td>
<td>2%</td>
<td>8%</td>
<td>4%</td>
<td>75%</td>
<td>86%</td>
</tr>
<tr>
<td>Mommertz 2008 Netherlands</td>
<td>22</td>
<td>100% (0%)</td>
<td>9%</td>
<td>0%</td>
<td>5%</td>
<td>0%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>UTH 2014 USA</td>
<td>78</td>
<td>100%</td>
<td>9%</td>
<td>4%</td>
<td>4%</td>
<td>5%</td>
<td>86%</td>
<td>88%</td>
</tr>
</tbody>
</table>
Approach

- CSFD
- DAP
- Moderate Hypothermia
- Sequential Clamp
- Reattach patent ICA 8-12
Motor

Stimulating Site (Motor Cortex)

Motor Response (Abductor Digiti Minimi)

Motor Response (Tibialis Anterior)

Motor Response (Adductor Hallucis)

[Graph showing neural responses on the left and right sides, labeled as Abductor Digiti Minimi, Tibialis Anterior, and Adductor Hallucis]
Paraplegia Prevention: OR

- Maintain CSF pressure <10 mmHg:
  - Intermittent manual gravity drainage
- Monitor SSEPs and MEPs
- Systolic BP >130 mmHg
- Maintain Spinal Cord Perfusion Pressure >120 mmHg
Conduct

- Proximal Anastomosis
- ICA reattachment
- Visceral/Renal
- Distal Anastomosis
Redo Thoracoabdominal Aortic Aneurysm Repair: A Single-Center Experience Over 25 Years

Rana O. Afifi, MD,* Harleen K. Sandhu, MD, MPH,* Amy. E. Trott, PhD, Tom C. Nguyen, MD, Charles C. Miller, PhD, Anthony L. Estrera, MD, and Hazim J. Safi, MD

Department of Cardiothoracic and Vascular Surgery, McGovern Medical School at The University of Texas Health Science Center at Houston (UTHealth), Memorial Hermann Heart & Vascular Institute, Houston, Texas

Background. Aortic disease is a lifelong, progressive illness that may require repeated intervention over time. We reviewed our 25-year experience with open redo thoracoabdominal aortic aneurysm (TAAA) and descending thoracic aortic aneurysm (DTAA) repair. Our objectives were to determine patient outcomes after redo repair of DTAA/TAAA and compare them with nonredo repair. We also attempted to identify the risk factors for poor outcome.

Methods. We reviewed all open redo TAAA and DTAA repairs between 1991 and 2014. Patient characteristics, preoperative, intraoperative variables, and postoperative outcomes were gathered. Data were analyzed by contingency table and by multiple logistic regression.

Results. We performed 1,900 open DTAA/TAAA repairs, with 266 (14%) being redos. Redos were associated with younger age (62 ± 16.4 years vs 64.5 ± 13.4 years, p < 0.02). Reasons for redo DTAA/TAAA were extension of the disease (86.8%), intercostal patch expansion (6.8%), visceral patch expansion (10.9%), infection (4.5%), anastomotic pseudoaneurysm (8.3%), and previous endovascular aortic repair complications (6.4%). Extent IV TAAA was predominantly involved in redos (42.8% redo vs 14.6% nonredo, p < 0.0001). The early mortality rate was significantly higher in redo (61 of 266 [23%]). Long-term survival was significantly lower among redo compared with nonredo DTAA/TAAAs. A multivariable analysis using the significant risk factors for early death from the risk factors on univariate analysis found four preoperative variables were significant (age >70 years, glomerular filtration rate <48 mL/min per 1.73m², extent III TAAA, and emergency presentation) for predicting early death. In the presence of all four risk factors in a redo patient, a maximal risk of 82% for early death was predicted.

Conclusions. The need for a redo operation in DTAA/TAAA repair is common and most often presents as an extension of the disease into an adjacent segment. A hybrid or completely endovascular treatment should be considered in high-risk patients.

Causes for Reoperation

- Aneurysmal Progression
- Intercostal Patch Enlargement
- Visceral Patch Enlargement
- TEVAR Complication
- Infective Pseudoaneurysm
- Pseudoaneurysm
Intercostal Reattachment with a Loop Graft  Intercostal Reattachment with an End Graft
Conduct

- Proximal Anastomosis
- Distal Anastomosis
- Visceral/Renal
- ICA reimplant
STAG Graft
Operative Outcomes Using a Side-branched Thoracoabdominal Aortic Graft (STAG) for Thoraco-abdominal Aortic Repair


\(^a\) Division of Vascular and Endovascular Surgery, University of Perugia, Ospedale S. Maria della Misericordia, Perugia, Italy
\(^b\) Cardiothoracic & Vascular Surgery, University of Texas Medical School, Houston, TX, USA
\(^c\) Department of Cardiovascular Surgery, Yonsei University College of Medicine, Seoul, South Korea
When to Use the STAG

- TAAA Extent II, III, IV with:
- HTAD (Heritable Thoracic Aortic Disease)
- Young patients (Age < 70 years)
- Displaced Visceral & Renal Vessels (>3 cm displacement)
Prophylactic Repair

- Age
- Comorbidities
- Added Risks
- Risk of Reoperation
- TEVAR
HTAD in TAAA

- Use bypasses for Reattachment
- Reversed Elephant trunk
- Frequently have chronic dissection
- Prophylactive repair
Conclusion

- Heritable Thoracic Aortic Disease: genetic specific management
- Open TAAA has good results in HTAD
- Technical considerations
- Although “we don’t own the patient”, we should own the disease.
Thank You