TREATING ANGULATED NECKS & TORTUOUS ILIACS WITH EVAR

SERIOUS CLINICAL CHALLENGE?

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Cardiovascular Institute of the South
Opelousas, LA
ANGLED NECK ANATOMY
Challenges With High Neck Angulation
-Increased Type 1 endoleaks*
-Increased Migration*

* eurostar date: J Endovasc Ther 2007
Challenges with High Iliac Angulations

Iliac limb kinking
Iliac limb occlusions (up to 7%)*

*EJVS 34:59-65 2007

Post adjunctive stent
2 days post op

*EJVS 34:59-65 2007
The influence of gender and aortic aneurysm size on eligibility for endovascular abdominal aortic aneurysm repair

Matthew P. Sweet, MD, Mark F. Fillinger, MD, Tina M. Morrison, PhD, and Dorothy Abel, BSME, Lebanon, NH; and Rockville, Md

Objectives: The purpose of this study was to compare the eligibility of men and women with infrarenal abdominal aortic aneurysms (IAAs) for on-label endovascular aneurysm repair (EVAR) to that of the clinician-Food & Drug Administration (FDA) postmarketing surveillance studies (CHART).
Non Compliance with IFU results in sac enlargement and inferior medium term results
Clinical evidence
EVAR in challenging anatomy

- 238 patients S/P EVAR between 2000-2008

<table>
<thead>
<tr>
<th>outcome</th>
<th>&lt;45°</th>
<th>45-60°</th>
<th>&gt;60°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-op Type 1a Els (p&lt;.0001)</td>
<td>9%</td>
<td>33%</td>
<td>38%</td>
</tr>
<tr>
<td>Intra-op Ao cuff (p&lt;.0001)</td>
<td>7%</td>
<td>28%</td>
<td>33%</td>
</tr>
<tr>
<td>AAA shrinkage (p&lt;.015)</td>
<td>97%</td>
<td>95%</td>
<td>84%</td>
</tr>
<tr>
<td>3-yr Type 1a EL (p&lt;.001)</td>
<td>15%</td>
<td>32%</td>
<td>47%</td>
</tr>
</tbody>
</table>

- All outcomes significantly worsen with neck angulation >60°
Clinical Evidence
EVAR In Challenging Anatomy

Influence of Severe Infrarenal Aortic Neck Angulation on Complications at the Proximal Neck Following Endovascular AAA Repair: A EUROSTAR Study

Roel Hobo, MSc; Jur Kievit, MD; Lina J. Leurs, MSc; and Jacob Buth, MD, PhD, FRCS on behalf of the EUROSTAR Collaborators

EUROSTAR Data Registry Centre, Catharina Hospital, Eindhoven, The Netherlands.
EUROSTAR
Impact of neck angulation on EVAR outcomes

TABLE 2
Multivariate Analysis of Short-term Outcomes (30 Days) According to the Presence/Absence of Severe Neck Angulation (>60°)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Presence of Neck Angulation &gt;60°</th>
<th>Absence of Neck Angulation ≤60°</th>
</tr>
</thead>
<tbody>
<tr>
<td>22% of cases had neck Angulation &gt;60</td>
<td>5% endoleak rate at 30 days</td>
<td>Odds ratio+ 2.3 times worse</td>
</tr>
</tbody>
</table>

Categorical data are given as the percentage.
CI: confidence interval, NS: not significant.
* Odds ratio adjusted for age, gender, risk factors, morphological factors, and experience.
**Off label usage significantly increases the odds of endoleaks**

**TABLE 4**
Multivariate Analysis of Device-Specific Outcome (Significant Associations)

<table>
<thead>
<tr>
<th></th>
<th>Severe Anomaly</th>
<th>Short-term</th>
<th>Long-term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eurorstar*</td>
<td>2.62</td>
<td>1.49 to 4.63</td>
<td>0.0009</td>
</tr>
<tr>
<td>Proximal endoleak</td>
<td>2.34</td>
<td>1.06 to 5.19</td>
<td>0.0353</td>
</tr>
</tbody>
</table>

Categorical data are given as the percentage. OR: odds ratio, HR: hazard ratio, CI: confidence interval. * Odds and hazard ratios adjusted for age, gender, risk factors, morphological factors, and experience.
### AAA Device IFU

<table>
<thead>
<tr>
<th>Company</th>
<th>AAA stent graft</th>
<th>Indication Neck angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lombard Medical</td>
<td>Aorfix™</td>
<td>≤ 90°</td>
</tr>
<tr>
<td>Medtronic</td>
<td>Endurant</td>
<td>≤ 60°</td>
</tr>
<tr>
<td>COOK</td>
<td>Zenith</td>
<td>≤ 60°</td>
</tr>
<tr>
<td>Gore</td>
<td>Excluder</td>
<td>≤ 60°</td>
</tr>
<tr>
<td>Endologix</td>
<td>Powerlink</td>
<td>≤ 60°</td>
</tr>
</tbody>
</table>

Aorfix™ is the only AAA stent graft approved in the US to treat neck angulations up to 90° on label.
IFU INDICATIONS
Off label use

IFU indications are determined by

- Design specification
- Regulatory body approval
- Preclinical vitro and in vivo engineering studies
- Clinical study/trial results

Risks
- Potential for increased complications and MAEs
- Potential for device failure
- Done at clinician’s own risk, manufacturer not liable
- Difficult to defend, especially if on label alternative is available
Pythagoras

STUDY OVERVIEW

Pythagoras IDE study – the largest prospective, controlled and multi-center study of highly angulated necks (0° - 90°)

How is the Pythagoras different to all other PMA studies?

• The unique study parameters

• Patient selection & demographics

• Gender distribution

• Consistent results in both low and high angle groups
STUDY PARAMETERS

• Multicenter trial (45 centers) – no prior practice with Aorfix™ before performing cases

• 218 patients enrolled on intent to treat

• Primary Study Group: UP to 150 EVARs, neck angles 60° - 90° (and higher)

• ‘Roll-in’ low angle practice group: Up to 65 EVARs, neck angle <60°

• The US trial enrolled 218 patients on intent to treat, 67 <60°, 151 ≥ 60°
CONTROL ARMS FOR COMPARISON

- SVS Registry meta-analysis of control patients from prior PMA US EVAR clinical trials (n=323)
- Concurrently enrolled Open Surgical controls (n=76) for neck angulation and other variables not in SVS

Why comparison against OR and not another AAA device?
- On FDA's suggestion
- Comprehensive data on competitor devices is not available so control against another EVAR is only possible if company owns the data itself
- Off label use is not permitted (all US commercially available grafts have indication up to 60° only)
- Goals set in 2006 and remained unchanged – the study achieved what it set out to do
GENDER DISTRIBUTION

• Female patients are very much more prevalent among those with high angle necks
  • More challenging to treat
  • Small access vessels, high neck angulations

• Females do represent about 10% of patients with neck angles <60°
  • Hence previous EVAR trials have had such biased gender distribution

35% of Aorfix™ high angle patients were females vs. 20% in the open group and vs. approximately 10% in other EVAR trials
## Results

<table>
<thead>
<tr>
<th></th>
<th>Aorfix™ &lt;60° N=67</th>
<th>Aorfix™ 60-133° N=151</th>
<th>Aorfix™ All N=218</th>
<th>SVS control group N=323</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedom from SVS MAE (30 d)</td>
<td>92.5%</td>
<td>81.5%</td>
<td>84.9%</td>
<td>56.4%</td>
</tr>
<tr>
<td>Mortality (30 d)</td>
<td>1.5%</td>
<td>2.0%</td>
<td>1.8%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Mortality (1 yr)</td>
<td>4.5%</td>
<td>7.9%</td>
<td>6.9%</td>
<td>6.5%</td>
</tr>
<tr>
<td>Sac diameter shrinkage (5mm 1yr)</td>
<td>36.7%</td>
<td>44.1%</td>
<td>41.9%</td>
<td>-</td>
</tr>
<tr>
<td>Sac diameter expansion (5mm 1yr)</td>
<td>0%</td>
<td>1.8%</td>
<td>1.1%</td>
<td>-</td>
</tr>
<tr>
<td>Type I/III leak (1yr)</td>
<td>0%</td>
<td>1.9%</td>
<td>1.3%</td>
<td>-</td>
</tr>
<tr>
<td>Migration (10mm 1yr)</td>
<td>0%</td>
<td>1.7%</td>
<td>1.2%</td>
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Performance of Aorfix™ is almost uniform in all angles.
## RESULTS

**Aorfix™ vs. other AAA grafts**

<table>
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<tr>
<th></th>
<th>Aorfix™ (n=218)</th>
<th>Talent</th>
<th>Endurant</th>
<th>Endologix</th>
<th>Gore Excluder</th>
<th>Cook Zenith</th>
<th>Cook Zenith (Hi Risk)</th>
</tr>
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<tr>
<td>Freedom from SVS MAE (30 d)</td>
<td>84.9%</td>
<td>96%</td>
<td>89%</td>
<td>Not Comparable</td>
<td>Not Comparable</td>
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</tr>
<tr>
<td>Mortality (30 d)</td>
<td>1.8%</td>
<td>1.8%</td>
<td>0%</td>
<td>1%</td>
<td>1.3%</td>
<td>0.5%</td>
<td>2%</td>
</tr>
<tr>
<td>Mortality (1 yr)</td>
<td>6.9%</td>
<td>6.5%</td>
<td>4%</td>
<td>6.8%</td>
<td>7.2%</td>
<td>3.5%</td>
<td>9%</td>
</tr>
<tr>
<td>Sac diameter shrinkage (5mm 1yr)</td>
<td>43.9%</td>
<td>33.6%</td>
<td>49.6%</td>
<td>35.7%</td>
<td>14.3%</td>
<td>67.5%</td>
<td>62.9%</td>
</tr>
<tr>
<td>Sac diameter expansion (5mm 1yr)</td>
<td>1.4%</td>
<td>2.3%</td>
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Pythagoras data from Fillinger et al, SVS presentation, Washington DC June 9, 2012
Competitor data from Summaries of Safety and Effectiveness filed with FDA
DATA COMPARISON

- Only Pythagoras low angle data can be compared like for like with competitors’ FDA results - no other high angle FDA trials

- Low angles were not the focus of Pythagoras - fewer patients were treated

- Pythagoras results can be compared with competitors, consider:
  - Sac expansion
  - Migration
  - Endoleaks

“Performance is equivalent to or better than competitors despite the more challenging angulated anatomy and sicker patient cohort”

Dr Fillinger (Washington DC, 2012)
Mortality rates

EVAR 1 VS. PYTHAGORAS AT 4 YEARS

- Data comparing the mortality rates of OR vs. EVAR\(^{(1)}\)
- Aorfix™ AAA related mortality ≈ EVAR 1\(^{(1,2)}\)
- Aorfix™ all cause mortality – marginally higher potentially due to treating sicker patients\(^{(1,2)}\)

This analysis adds Confidence that Aorfix™ in High angulations delivers Similar results to competitor grafts in straightforward anatomy

1. Jean-Noel Albertini, Prof Vascular Surgery, CHU Saint-Etienne
2. Initial Analysis of 4 Year Outcomes of Pythagoras Study
## CONCLUSIONS

- Results indicative that performance of Aorfix™ is comparable to competitors’ grafts despite treating sicker patients and higher neck angulations.
- Performance of Aorfix™ in Pythagoras is almost uniform in all angles.

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STUDY SUMMARY

- The US Pythagoras Clinical Trial of the Aorfix™ is the largest prospective, controlled, multi-center IDE study of highly angulated necks (0°- 90°)

- “Despite significant predictors of worse short and long-term outcomes (age, female, CHF, neck angle), MAEs and other pertinent outcomes were either better or similar to open repair, and similar to EVAR trials and competitor graft performance with much less severe anatomy”

- Dr Fillinger (Washington DC, 2012)

- “These results suggest a potential for a less invasive option for patients with highly angulated neck anatomy who would otherwise have no endovascular options”

- Dr Fillinger (Washington DC, 2012)

- FDA Approval for the following indications received Feb 14, 2013:
  - Adequate iliac or femoral access that is compatible with vascular access techniques, implants, and accessories
  - Aortic neck landing zone diameters with a range of 19mm to 29mm
  - Non aneurysmal proximal neck center-line length of ≥ 15mm
  - Infrarenal aortic neck angulations including those up to and including 90°
  - Common iliac landing zone diameters with a range of 9mm to 19mm
  - Distal fixation length of ≥ 15mm
Pre Operative

Courtesy of Dr Hanif, Mr Browne and Mr Prionidis,
Broomfield Hospital - Mid Essex Hospital Services NHS Trust, 2013

6 month follow-up
Pre-operative 6 week follow up
Pre-operative

6 month follow up

Photo courtesy Musgrove Hospital, Taunton 2011
Pre-operative

12 month follow up

Courtesy of Musgrove Park Hospital Taunton 2011
Pre operative
Courtesy of Royal Devon and Exeter NHS Trust 2010

6 weeks follow up
Closing Remarks / Thank You
TREATING ANGULATED NECKS & TORTUOUS ILIACS WITH EVAR

SERIOUS CLINICAL CHALLENGE?

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