CURRENT TREATMENT OPTIONS FOR HOSTILE NECK ANATOMY

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Anatomic Limitations of EVAR

Adverse anatomic characteristics of the infrarenal aortic neck in particular have restricted the widespread applicability of EVAR and constitute the “Achilles’ heel” of the procedure\(^1,2\)

Proximal neck adequacy and endograft seal zone have also been identified as key predictors of long-term outcomes and success after EVAR

Current anatomic limitations include:

Current Treatment Strategies

According to literature\textsuperscript{3,4}, in two-thirds of the patients with this challenging anatomy, the proximal neck is less than the required 10-15mm or is unsuitable as a proximal landing zone.

To address these limitations, physicians have adopted a number of strategies in recent years to safely expand the treatment options for these patients.

Treatment strategies include:

- Hybrid By-pass
- Fenestration/Branch
- Chimney/Snorkel

Endograft Evolution

Since the 1\textsuperscript{st} generation grafts of the late-1990’s entered the market, endograft development has sought to achieve an “out of the box solution” to address the hostile neck presentation.

And while the outcomes for both fenestration and snorkeling/chimney show some promise for the future, significant limitations still exist for these treatment techniques\textsuperscript{5}

- Radiation Exposure
- Resource Utilization
- Cost
- Anatomic applicability
- Graft availability
- Technical demand

<table>
<thead>
<tr>
<th></th>
<th>Fenestrated (N=631)</th>
<th>Snorkeling/Chimney (N=123)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>1.17% p=0.645</td>
<td>.58%</td>
</tr>
<tr>
<td>Renal Impairment</td>
<td>9.67</td>
<td>12.43%</td>
</tr>
<tr>
<td>Dialysis</td>
<td>1.33% p=0.567</td>
<td>0.57%</td>
</tr>
<tr>
<td>Type I</td>
<td>2.06% p=0.939</td>
<td>1.93%</td>
</tr>
</tbody>
</table>

Current Endograft Options

Of the current commercially available endograft designs, the Medtronic Endurant endograft was specifically designed to treat many of these hostile neck conditions.

**Proximal Design Characteristics:**

1. Suprarenal stents with hooks provide high level active fixation for migration resistance

2. One piece laser cut stent with anchoring pins designed for better structural integrity and durability.

3. Lower amplitude stent provides better sealing with short necks

4. M-shaped stents provide high conformability

5. Engineered and tested to treat 1cm necks at up to 60° neck angulation

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6. Medtronic IFU; 75° angulation indicated to treat OUS; Medtronic Endurant IFU in US is 60°
Patient Applicability – Real World Results

As with any device design, the hallmark of success is always gauged by the “real world” application of a device to a range of patient presentation states.

The ENGAGE registry (Endurant Stent Graft Natural Selection Global Postmarket Registry) was specifically designed to track, collect and analyze outcomes of a wide variety of patients worldwide.

**ENGAGE Registry**
- N=1,200+ patients
- Prospective, Multi-Center, Non-randomized
- N=79 Centers Worldwide

1st Patient Treated March 2009
1° Endpoint: 12M Treatment Success
Follow-up: 30D, 12M & annually through 10Y
100% independent monitoring of protocol endpoints

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7. Treatment Success - successful technical delivery and deployment of the stent graft as well as freedom from aneurysm diameter increase, endoleaks Type I & III, aneurysm rupture, conversion to surgery, stent migration >10mm and graft occlusion.
Registry evaluated the Endurant Stent Graft System.
ENGAGE – Patient Demographics

Patient Baseline Characteristics n=1263

- **AAA >7cm**: 15.2%
- **Outside IFU**: 17.8%
- **Female**: 10.5%
- **Symptomatic AAA**: 16.0%
- **SVS 3**: 35.3%
- **ASA IV**: 10.6%
- **Proximal Neck <15mm**: 12.0%
- **Infrarenal Neck >60°**: 10.2%

**Mean (mm)**: 60.3 ± 11.6

**Anatomic factors associated with worse EVAR outcomes**
ENGAGE Outcomes – Short Neck

With the limited restrictions of ENGAGE enrollment criteria, a wealth of device performance information has been gained on a sub-group of patients that would be otherwise identified to have potentially “hostile” neck anatomy (8-15mm)

<table>
<thead>
<tr>
<th>Endoleak Type I (both Type IA and IB)</th>
<th>8-15 mm</th>
<th>≥15 mm</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 1 yr</td>
<td>0.0% (0/113)</td>
<td>0.4% (4/942)</td>
<td>0.49</td>
</tr>
<tr>
<td>At 2 yr</td>
<td>0.0% (0/97)</td>
<td>0.9% (7/784)</td>
<td>0.35</td>
</tr>
<tr>
<td>At 3 yr</td>
<td>3.1% (2/64)</td>
<td>1.2% (8/652)</td>
<td>0.22</td>
</tr>
<tr>
<td>At 4 yr</td>
<td>3.8% (1/26)</td>
<td>2.4% (6/246)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

NO SIGNIFICANT DIFFERENCE
## ENGAGE 3-year Outcomes

<table>
<thead>
<tr>
<th></th>
<th>ENGAGE n=1263</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migration*</td>
<td>0%</td>
</tr>
<tr>
<td>Endoleak (All)</td>
<td>10.0%</td>
</tr>
<tr>
<td>• Type I/III</td>
<td>1.5%</td>
</tr>
<tr>
<td>AAA Rupture</td>
<td>0.2%</td>
</tr>
<tr>
<td>Freedom From 2\textsuperscript{nd} Procedures</td>
<td>90.9%</td>
</tr>
</tbody>
</table>

### ENGAGE Registry at 3 Years
- 98.5% freedom from aneurysm-related mortality
- 90.9% freedom from secondary procedure
- 58.4% of aneurysm sacs decreased >5mm\textsuperscript{1}
- Low 1.5% Type I/III endoleak rate

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D. Bockler. VEITH 2013. Data on File at Medtronic
3Y US IDE Data on file at Medtronic.
Supporting Technologies - Aptus

The Heli-FX Aortic Securement System by Aptus has helped to further the repair options available to physicians to treat patients with hostile neck anatomy.

There may be an opportunity to utilize the Heli-FX technology in combination with one or more of the existing endovascular techniques to treat more of these hostile neck presentations both safely and effectively.
Major Studies Show Higher 2nd Interventions in EVAR vs. Open Repair

- Late ruptures in EVAR, none in open surgery
- Unlike open repair, endoleaks and migration are major complications of EVAR
  - Predictors for rupture, and risks increase with time
- Open surgery remains a ‘more durable option’
  - In ACE, 16% re-interventions in EVAR vs. 2.4% for open repair at 3 yr median f/u
Literature Review

Meta-Analysis of 7 major studies in EVAR by Antoniou et al\(^1\) compared outcomes in hostile vs. friendly neck anatomies (total patients N = 1559)

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Endografts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Torsello et al, 2011</td>
<td>177</td>
<td>Endurant</td>
</tr>
<tr>
<td>AbuRahma et al, 2010</td>
<td>238</td>
<td>AneuRx, Excluder, Zenith, Talent</td>
</tr>
<tr>
<td>Hoshina et al, 2010</td>
<td>129</td>
<td>Excluder, Zenith</td>
</tr>
<tr>
<td>Abbruzzese et al, 2008</td>
<td>565</td>
<td>AneuRx, Excluder, Zenith</td>
</tr>
<tr>
<td>Choke et al, 2006</td>
<td>147</td>
<td>Talent, Zenith, Excluder, AneuRx</td>
</tr>
<tr>
<td>Fulton et al, 2006</td>
<td>84</td>
<td>AneuRx</td>
</tr>
<tr>
<td>Fairman et al, 2004</td>
<td>219</td>
<td>Talent</td>
</tr>
</tbody>
</table>

- **Type I endoleaks 4.5x more likely at 1-year** after endograft implantation in hostile proximal aortic neck anatomy \((P = .010)\)

- **Aneurysm-related mortality risk 9x greater** in hostile neck anatomy \((P= .013)\)

# Managing EVAR with Aptus

## PROPHYLAXIS

### Hostile Anatomy

**Overcoming concerns for implant stability**

- Challenging neck anatomies (e.g. wide, short, conical, angulated)
- Difficult landing (e.g. birdbeaking, close to branched vessels)

## TREATMENT

### Normal Anatomy

**Mitigating risk of re-interventions**

- Severe comorbidities that preclude safe re-intervention
- Patients potentially lost during F/U
- Long remaining life expectancy (young pts)

### Resolve proximal seal failures

- Targeted sealing of acute type I endoleaks
- Targeted sealing of late type I endoleaks
- Augmented stability in migrated grafts

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*Case image from Gandhi RT, Katzen BT Treating a Type 1A Endoleak Using EndoAnchors. Endovascular Today March 2012 23:26.*
ANCHOR Registry

Similar to the ENGAGE Registry, the objective of the ANCHOR registry is to gain a greater understanding as to the application and performance of the Heli-FX Anchor System in a “real world” scenarios for hostile neck anatomy.

Indications for EndoAnchoring in Primary n=307

- Acute Type I endoleak 25%
- Concern for late failure 75%

Outcome-based anatomic criteria for defining the hostile aortic neck

William D. Jordan Jr, MD, Kenneth Ouard, MD, Manish Mehta, MD, MPH, David Varnagy, MD, William M. Moore Jr, MD, Frank R. Arko, MD, James Joyce, DO, and Jean-Paul M. de Vries, MD, Birmingham, Ala; New York and Albany, NY; Orlando, Fla; West Columbia, SC; Charlotte, NC; Mountain View, Calif; and Nieuwegein, The Netherlands

Objective: There is abundant evidence linking hostile proximal aortic neck anatomy to poor outcome after endovascular aortic aneurysm repair (EVAR), yet the definition of hostile anatomy varies from study to study. This current analysis was undertaken to identify anatomic criteria that are most predictive of success or failure at the aortic neck after EVAR.

Methods: The study group comprised 221 patients in the Aneurysm Treatment Using the Heli-FX Aortic Sequestration System Global Registry (ANCHOR) clinical trial, a population enriched with patients with challenging aortic neck anatomy and failure of sealing. Imaging protocols were not protocol specified but were performed according to the institution’s standard of care. Core laboratory analysis assessed the three-dimensional centerline-reformatted computed tomography scans. Failure at the aortic neck was defined by type Ia endoleak occurring at the time of the initial endograft implantation or during follow-up. Receiver operating characteristic curve analysis was used to assess the value of each anatomic measure in the classification of aortic neck success and failure and to identify optimal thresholds of discrimination. Binary logistic regression was performed after excluding highly intercorrelated variables, creating a final model with significant predictors of outcome after EVAR.

Results: Among the 221 patients, 121 (54.8%) remained free of type Ia endoleak and 100 (45.2%) did not. Type Ia endoleaks presented immediately after endograft deployment in 58 (58.0%) and during follow-up in 42 (42.0%). Receiver operating characteristic curve analysis identified 12 variables where the classification of patients with type Ia endoleak was significantly more accurate than chance alone. Increased aortic neck diameter at the lowest renal artery (P = .013) and at 5 mm (P = .008), 10 mm (P = .008), and 15 mm (P = .010) distally, aneurysm sac diameter (P = .001), common iliac artery diameters (right, P = .012; left, P = .002), and a conical (P = .049) neck configuration were predictive of endoleak. By contrast, increased aortic neck length (P = .050), a funnel-shaped aortic neck (P = .036), and neck mural thrombus content, as measured by average thickness (P = .044) or degrees of circumferential coverage (P = .029), were protective against endoleak. Binary logistic regression identified three variables independently predictive of type Ia endoleak. Neck diameter at the lowest renal artery (P = .002, cutpoint 26 mm) and neck length (P = .017, cutpoint 17 mm) were associated with endoleak, whereas some mural neck thrombus content was protective (P = .001, cutpoint 11° of circumferential coverage).

Conclusions: A limited number of independent anatomic variables are predictive of type Ia endoleak after EVAR, including aortic neck diameter and aortic neck length, whereas mural thrombus in the neck is protective. This study suggests that anatomic measures with identifiable threshold cutpoints should be considered when defining the hostile aortic neck and assessing the risk of complications after EVAR. (J Vasc Surg 2015;1:1-8.)
### High Ratio Hostile Neck Anatomy in ANCHOR

<table>
<thead>
<tr>
<th>Proximal Neck Anatomical Characteristics (based on Corelab)</th>
<th>Primary n=242*</th>
<th>Revision n=77*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max Aneurysm Diameter [mm], mean (± SD)</td>
<td>56 ± 11</td>
<td>65 ± 13</td>
</tr>
<tr>
<td>Neck Length [mm], mean (± SD)</td>
<td>17 ± 13</td>
<td>15 ± 12</td>
</tr>
<tr>
<td>Necks ≤ 10mm Length, N (%)</td>
<td>101 (41.7%)</td>
<td>36 (46.5%)</td>
</tr>
<tr>
<td>Necks ≤ 15mm Length, N (%)</td>
<td>141 (58.3%)</td>
<td>47 (60.5%)</td>
</tr>
<tr>
<td>Neck Diameter(^1) [mm], mean (± SD)</td>
<td>26 ± 4</td>
<td>29 ± 5</td>
</tr>
<tr>
<td>Conical Necks(^2), %</td>
<td>41.7%</td>
<td>46.5%</td>
</tr>
<tr>
<td>Neck Thrombus ≥ 2mm</td>
<td>37%</td>
<td>21%</td>
</tr>
<tr>
<td>Neck Calcium ≥ 2mm</td>
<td>48%</td>
<td>12%</td>
</tr>
<tr>
<td>Hostile Neck(^3)</td>
<td>53%</td>
<td>63%</td>
</tr>
</tbody>
</table>

(1) At most distal renal artery
(2) ≥10% diameter change over 10mm length
(3) As determined by the investigator

*Note: Corelab sample sizes is different from total patients in ANCHOR. Corelab for all patients is still in-process. All above data is per Corelab except the ‘Hostile Neck’ line item which is investigator reported.

High success in treating type I endoleaks
- 83% for acute T1 ELs in primary
- 80% for late T1 ELs in revision

In majority of persisting type I endoleaks, standard adjuncts failed to treat or could not be administered
- Reflect high ability for EndoAnchors to treat difficult endoleaks

<table>
<thead>
<tr>
<th>Arm</th>
<th>N</th>
<th>Success</th>
<th>% Successful</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>242</td>
<td>223</td>
<td>92.1%</td>
</tr>
<tr>
<td>Revision</td>
<td>77</td>
<td>67</td>
<td>87.0%</td>
</tr>
</tbody>
</table>

Procedure Success w/Freedom from Type Ia Endoleak at Final Angio Remains Excellent

... Despite Hostile Proximal Neck Anatomy

Excellent Outcomes as Prophylaxis in ANCHOR

- Strong acute results
  - Zero type I endoleaks (0/178) at final angio

- Favorable early follow-up (7-month mean)
  - Zero re-interventions for type Ia endoleak or endograft migration (0/186)
  - High early sac regression, 47% (20/43)

Seal Durability in F/U Compares Favorably

**ANCHOR Results vs. Antoniou et al. Meta-Analysis**

<table>
<thead>
<tr>
<th>Studies</th>
<th>Median Follow-Up</th>
<th>Type 1 Endoleaks in Hostile Necks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta-analysis, Antoniou et al&lt;sup&gt;1&lt;/sup&gt;</td>
<td>12-Months</td>
<td>20/205* (9.8%)</td>
</tr>
<tr>
<td>ANCHOR Registry&lt;sup&gt;2&lt;/sup&gt;</td>
<td>14.3-Months</td>
<td>2/178** (1.1%)</td>
</tr>
</tbody>
</table>


* Hostile neck criteria: neck length <15 mm and neck angulation > 60 degrees
** Hostile as determined by physician in Primary Arm

No EndoAnchor Related SAEs or Re-Interventions Reported To-Date
Patient H/P

- 70 year-old male referred from outside institution with a 6cm juxta-renal AAA on routine follow-up
- Previous open AAA repair () with standard tube graft
- Right renal nephrectomy ()
- History of cirrhosis, COPD, CVA and previous MI
- Current smoker
Pre-case Imaging
Device Creation

10mm Gore Viabahn cut into (3) equal 3.25cm sections

Viabahn sewn together using Ethibond suture and attached to the contralateral limb of a Medtronic Endurant 32x16x124

Graft is re-constrained into the 20F Xcelerant delivery system for insertion to the patient
Access Sites

Right Axillary conduit with 10mm Maquet Dacron graft

Modified 24F Gore Dry Seal sheath inserted into end of conduit and (2) 7F sheaths are inserted into the end

A single 7F sheath accessed from the right brachial artery

Standard bilateral femoral access
Deployment

**Left Renal Artery**: 6x100 Gore Viabahn w/ (2) 7x59 Atrium iCast Stents

**SMA**: (2) 7x59 Atrium iCast Stents

**Celiac**: (2) 8x59 Atrium iCast Stents

All junctions were then ballooned with (3) 7x80mm balloons
A Medtronic Endurant 16x24x156 contralateral limb was then landed into the distal aorta at the aortic bifurcation.

(2) Medtronic Endurant 16x10x82 limbs were then placed into the common iliac arteries bilaterally, ballooned and then a final angiogram was taken.
30-day Follow-up
Patient H&P

- 59 y/o male
- Tobacco use, mild PAD and pvs CABG
- ASA Type II Classification
- Juxtarenal AAA with 2-4mm infrarenal seal zone
- Accessory Left renal artery – planned embolization
- Pararenal seal zone ~ 11mm
- Iliac and access arteries normal caliber bilaterally
Initial Angiogram

Neck: 14mm
Left Renal Cannulation/Device Placement
Final Angiogram
Conclusion

Considerable advancements have been made to more effectively treat patients with “hostile” neck morphology.

The creation, monitoring and analysis of more post-market registries such as ENGAGE and ANCHOR help to better understand the performance and outcomes of “real world” device use.

Data from these registries would indicate that with careful patient selection and case planning that some patients with hostile necks can be treated both safely and effectively without more advanced endograft techniques.

Continued evaluation of acute outcomes and long-term patient follow-up are critical in determining the future direction of EVAR.
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