Nellix EVAS: Key Learnings from the Global Registry and Personal Experience

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Auckland, New Zealand
Disclosure

Speaker name:
Andrew Holden

I have the following potential conflicts of interest to report:
- [x] Consulting – Medical Advisory Board Member for Endologix Inc
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)
EndoVascular Aneurysm Sealing (EVAS) with Nellix

- Designed to seal entire aneurysm with contained biostable polymer
- Non-modular design with complete fixation
- Expands endovascular patient eligibility
- May overcome issues associated conventional endografts
VALIDATING EVAS with Clinical Data

**Nellix CE Study**
- **2008-2012**: N=69
- **2013**: CE Marking EU Launch Feb 2013
- **2014-2017**: Over 50 Independent EVAS Studies and Publications

**EVAS FORWARD GLOBAL REGISTRY**
- **2013**: N=300
  - 30 Centers (29 EU, 1 NZ)
  - Enrollment Completed Sept, 2014
- **2014-2017**: Over 3000 EU Commercial Cases to Date as of 12/1/2015
- **2015-2017**: Over 50 Independent EVAS Studies and Publications

**EVAS FORWARD IDE**
- **2014-2015**: N=180
  - 29 Centers (26 US, 3 EU)
  - Enrollment Completed Nov, 2014
- **2015-2017**: Over 50 Independent EVAS Studies and Publications

**US Commercial Launch**
- **2016-2017**: N=300
  - 30 Centers (29 EU, 1 NZ)
  - 1 YR FU
  - 2 YR FU
  - 3 YR FU

**Over 3000 EU Commercial Cases to Date as of 12/1/2015**

**Over 50 Independent EVAS Studies and Publications**
EVAS FORWARD Global Registry: Design and Status

- **Principal Investigators**
  - Andrew Holden, MBChB, Auckland, NZ
  - Matt Thompson, MD, London, UK

- 300 patients, 30 centers with five year follow-up

- Real-world experience; no prospective screening of patients

- CT scan core lab analysis (Cleveland Clinic Core Lab)

- Independent adverse events adjudication

- Primary outcomes typical of EVAR therapy

**Mean time in study:** 425d; 14mo (0-21mo)

**Median time in study:** 434d (Min=0, Max=643, 25%ile 369 75%ile 490)

*One (1) consented patient did not receive implant*
Cohorts

Cohort 1
- N=200
- Neck Length ≥ 10mm
- Infrarenal Angle ≤ 60°

Cohort 2
- N=39
- Neck Length 5 -10mm
- Infrarenal Angle 61 - 90°

Cohort 3
- N=38
- Neck Length < 5mm
- Infrarenal Angle > 90°
- Juxtarenal / Pararenal

Cohort 4
- N=22
- rAAA; EVAR revision;
- AUI; Isolated iliac aneurysm

6
AAA Complexity across All-Comer Registries

- **EVAS Global Registry (n=300)**
- **ENGAGE Registry (n=1262)**
- **GREAT Registry (n=400)**

<table>
<thead>
<tr>
<th>Criterion</th>
<th>EVAS</th>
<th>ENGAGE</th>
<th>GREAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck Length &lt;10mm</td>
<td>17%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Conical Neck</td>
<td>46%</td>
<td>n/r</td>
<td>0%</td>
</tr>
<tr>
<td>Neck Angle &gt;60°</td>
<td>8%</td>
<td>6%</td>
<td>0%</td>
</tr>
<tr>
<td>Chimney Procedure</td>
<td>5%</td>
<td>0.1%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Iliac diameters &gt;25mm</td>
<td>13%</td>
<td>0.6% n/r</td>
<td>0%</td>
</tr>
</tbody>
</table>
## Major Adverse Events

<table>
<thead>
<tr>
<th>Classification</th>
<th>≤30 days n=277</th>
<th>31d – 1yr n=272</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Cause Death</strong></td>
<td>3 (1.1%)</td>
<td>11 (4.0%)</td>
</tr>
<tr>
<td><strong>Peri-operative mortality</strong></td>
<td>3 (1.1%)</td>
<td>-</td>
</tr>
<tr>
<td><strong>AAA-related mortality</strong></td>
<td>-</td>
<td>1 (0.4%)*</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>0</td>
<td>2 (0.7%)</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>2 (0.7%)</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>Bowel Ischemia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory Failure</td>
<td>2 (0.7%)</td>
<td>2 (0.7%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (0.4%)</td>
<td>3 (1.1%)</td>
</tr>
<tr>
<td>Blood loss &gt;1000 mL</td>
<td>2 (0.7%)</td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Patients with one or more MAE</strong></td>
<td>8 (2.9%)</td>
<td>16 (5.9%)</td>
</tr>
</tbody>
</table>

Peri-operative mortality ≤30d:
- Day 5: Hospital-acquired pneumonia
- Day 15: Gastrointestinal hemorrhage
- Day 19: Aspiration pneumonia

*One late AAA-related death due to aorto-duodenal fistula at day 148
Freedom from All Endoleak

Through 1 yr 94.5%
Type Ia Endoleak – Most Common Causes

- Low stent deployment
- Stent Misalignment
Transcatheter Embolization Of Type IA Endoleak

Type IB Endoleak

- Procedural issues
- Inadequate Nellix stent length to seal in the iliac artery
- Easily treated with covered stent extension
Type II Endoleak

- Very low incidence of Core Laboratory reported Type II Endoleak
- All are small
- Vast majority spontaneously resolve by 6 months
## Persistent Endoleaks

<table>
<thead>
<tr>
<th>Endoleak (Total)</th>
<th>At 30 Days N=277</th>
<th>At 1 Year N=269</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoleak (Total)</td>
<td>1.4% (4)</td>
<td>0.7% (2)</td>
</tr>
<tr>
<td>Type IA</td>
<td>1.1% (3)</td>
<td>0.4% (1)</td>
</tr>
<tr>
<td>Type IB</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Type II</td>
<td>0.4% (1)</td>
<td>0.4% (1)</td>
</tr>
<tr>
<td>Type III</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Endoleaks at 1 Year

EVAS

ENGAGE

Type 1A, 1B  Type II  Type III  Type IV  Undetermined

Endoleaks at 1 Year

9.8%

0.7%

ENGAGE Registry: Verhagen et al. LINC Symposium 2014
Conclusions from Endoleak Data

- The incidence of ≤ 30 day and 1 year endoleak remains very low
- The root causes are attributed to procedural factors
- Type 1A and 1B endoleak can be effectively treated
- Low incidence of ≤ 30 day Core Laboratory reported type 2 endoleak but these are small and most resolve without intervention
Freedom from Secondary Intervention

Occlusion
1Yr 98.2%

Endoleak
1Yr 96.3%

All
1Yr 92.3%

Plot
- All Interventions
- Intervention for Endoleak
- Intervention for Occlusion
Patients with Secondary Interventions through 1 Yr

- **EVAS:**
  - ≤30d: 3.2%
  - 31d-1yr: 4.5%

- **ENGAGE:**
  - ≤30d: 1.6%
  - 31d-1yr: 5.6%

- **GREAT:**
  - ≤30d: 1.0%
  - 31d-1yr: 6.5%

**OFF IFU**

ENGAGE Registry: Verhagen H. LINC Symposium 2014
GREAT Registry: Verhoeven E. et al. *EJVES* 2014;48:131-37
Freedom from Aneurysm-Related and All-Cause Mortality

![Survival Probability Graph]

<table>
<thead>
<tr>
<th>Month</th>
<th>EVAS FORWARD Global Registry - ARM</th>
<th>EVAS FORWARD Global Registry - ACM</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>2</td>
<td>0.99</td>
<td>0.99</td>
</tr>
<tr>
<td>4</td>
<td>0.98</td>
<td>0.98</td>
</tr>
<tr>
<td>6</td>
<td>0.97</td>
<td>0.97</td>
</tr>
<tr>
<td>8</td>
<td>0.96</td>
<td>0.96</td>
</tr>
<tr>
<td>10</td>
<td>0.95</td>
<td>0.95</td>
</tr>
<tr>
<td>12</td>
<td>0.94</td>
<td>0.94</td>
</tr>
<tr>
<td>14</td>
<td>0.93</td>
<td>0.93</td>
</tr>
<tr>
<td>16</td>
<td>0.92</td>
<td>0.92</td>
</tr>
<tr>
<td>18</td>
<td>0.91</td>
<td>0.91</td>
</tr>
</tbody>
</table>

1 Yr ARM: 98.2%
1 Yr ACM: 94.8%
Mortality and Cardiac Morbidity at 1 Year

<table>
<thead>
<tr>
<th></th>
<th>EVAS</th>
<th>ENGAGE</th>
<th>GREAT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASA Class III/IV</strong></td>
<td>64%</td>
<td>52%</td>
<td>63%</td>
</tr>
<tr>
<td><strong>Cardiac History</strong></td>
<td>55%</td>
<td>53%</td>
<td>39%</td>
</tr>
<tr>
<td><strong>All Cause Death</strong></td>
<td>5.1%</td>
<td>7.4%</td>
<td>7.0%</td>
</tr>
<tr>
<td><strong>AAA-related mortality</strong></td>
<td>1.4%</td>
<td>1.5%</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Myocardial Infarction</strong></td>
<td>1.1%</td>
<td>1.8%</td>
<td></td>
</tr>
</tbody>
</table>

- Lower mortality despite higher comorbidities
- Cardiac events trending lower

GREAT: Verhoeven et al. *EJVES* 2014
All-Cause and Aneurysm-Related Mortality
EVAS and ENGAGE

ENGAGE: Stokmans et al. *EJVES* 2012;44:369-75
Conclusions – Global Registry at 1 Year

- Impressive results in first-ever prospective, EVAS all-comers clinical study showing durability of repair
- Low endoleak and reintervention rates in a complex patient population
- Excellent one year aneurysm related and overall survival outcomes
Personal Experience

- 220 cases from "first in man" to advanced clinical applications
- Important lessons through the learning curve
Lessons Learnt

- Case Selection Important – not all anatomies are suited to standard Nellix
- Care with the Implant Procedure – there are a number of bail outs and redundancies with Nellix EVAS and they should be used
- Understand the normal and abnormal post-implant imaging appearances
Case Selection

- Need a length of healthy aorta for proximal/distal seal
- Conical necks with an adequate neck length are ideal
- “No necked” and very short necked aneurysms are better treated with Ch-EVAS
- Avoid very angulated necks
Juxta-renal AAA - ChEVAS

- Principal Investigators
  - Matt Thompson, MD, London, UK
  - Andrew Holden, MBChB, Auckland, NZ
- Open-label, single-arm, real-world study
- 200 patients, up to 10 international centers
- Retrospective and prospective arms
Case Selection

- Ideal device for concomitant and isolated iliac artery aneurysms
- Ideal device for short iliac arteries
Implant Procedure

- Slow and careful deployment of Nellix stents
- Usual issues with parallax (centering, angulation)
- Angioplasty balloons inflated – provides added stability
Implant Procedure

- Pre-fill step most important (pressure – volume curve)
- Contrast in pre-fill may be helpful
- Secondary fill option
- Quality completion angiography before device removal
Post-Implant Imaging Appearances

Imaging After Nellix Endovascular Aneurysm Sealing: A Consensus Document

Andrew Holden, MBChB, FRANZCR, EBIR¹, Janis Savlovskis, MD, PhD², Andrew Winterbottom, MD, FRCR³, Leo H. van den Ham, MD⁴, Andrew Hill, MBChB, FRACS⁵, Dainis Krievis, MD, PhD⁶, Paul D. Hayes, MD, FRCS⁷, Michel M. P. J. Reijnen, MD, PhD⁸, Dittmar Böckler, MD, PhD⁹, Jean-Paul P. M. de Vries, MD, PhD¹⁰, Jeffrey P. Carpenter, MD¹¹, and Matt M. Thompson, MD, FRCS¹²

Normal Early CT Appearances

- Endobags demonstrate radiodensity due to contrast incorporation in polymer
- Other evident components are mural thrombus, chromium cobalt stents and stent lumens
CT Appearances Change with Time

- Polymer radiodensity within the endobag decreases with time
- Precipitation of contrast may appear at endobag inner edge

1 month
Uniform radiodensity throughout endobags

6 months
Density loss within endobags; contrast migration to endobag edge

1 year
Minimal change from 6-month CT
Normal US Appearances

- Correlates with CT but does not change with time
Type 1 Endoleak

- Crescenteric shaped contrast rim between endobag and thrombus or aortic wall
- May see outflow via lumbar arteries, IMA etc
Type 1 Endoleak

- May be subtle and difficult to differentiate from calcium or contrast within the endobags
- Non-contrast CT important

CT at 1 month

CT at 6 months

Non-contrast

Arterial phase
Subtle endoleak between 2 areas of calcified plaque

Arterial phase
Endoleak is larger
Conclusions

- Nellix EVAS is a very different technology to treat AAAs that provides unique opportunities but also challenges.
- Lessons learnt include care with case selection and implant procedure as well as post-procedural imaging.
- Evidence to support Nellix EVAS is rapidly growing and demonstrates the procedure can be performed safely with a high level of technical success and very low endoleak and re-intervention rate at 1 year.
- Longer term follow up is required to demonstrate long term durability.
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