Influence of patient selection and IFU compliance on outcomes following EVAS

LUNCH SYMPOSIUM

LINC 2017

Jan MM Heyligers, MD, PhD, FEBVS
Consultant Vascular Surgeon
Elisabeth TweeSteden Hospital Tilburg,
The Netherlands
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Disclosure

Speaker name:

.............Jan Heyligers..........................................

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

- I do not have any potential conflict of interest
What was The Primary motive of EVAS?

To overcome EVAR issues
EVAR has an early survival benefit but an inferior late survival compared with open repair, which needs to be addressed by lifelong surveillance of EVAR and prompt re-intervention if necessary.
Propensity-score matched cohorts of Medicare beneficiaries undergoing aneurysm repair

39,966 matched pairs of patients

Early survival advantage for EVAR but significantly higher late rupture rate

Is EVAR the AAA Therapy of the Future?

The Nellix® EndoVascular Aneurysm Sealing System approved to treat infrarenal abdominal aortic aneurysms and is not approved for any other intended use in any geography.
Concept of **EndoVascular Aneurysm Sealing (EVAS)**

Constrained liquid polymer seal at attachment sites

- Designed to treat a range of anatomies while maintaining seal

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Concept of **EndoVascular Aneurysm Sealing (EVAS)**

Active aneurysm sac management

- Designed to mitigate endoleak of any type
- May prevent acute sac thrombosis – reduced PIS
- Analogous to open surgical repair with sac ablation

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Validating EVAS with Clinical Data

- US FDA Trial
- Enrollment 2014
- 150 patients, 29 sites
  - 26 US, 3 EU
- Core lab adjudicated
- 5 year follow-up

- Post-market registry
- Enrollment 2013-2014
- 300 patients, 30 sites
  - EU, NZ
- Real world, all comers
- Core lab adjudicated
- 5 year follow-up

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Validating EVAS

- At 1 year, 50% reduction in endoleaks and reinterventions compared to EVAR

<table>
<thead>
<tr>
<th>Device</th>
<th>Mortality</th>
<th>Endoleaks (%)</th>
<th>Reintervention (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAS FORWARD</td>
<td>3.4%</td>
<td>3.1%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Zenith IDE</td>
<td>3.0%</td>
<td>6.1%</td>
<td>11.0%</td>
</tr>
<tr>
<td>Excluder IDE</td>
<td>7.0%</td>
<td>9.2%</td>
<td>11.5%</td>
</tr>
<tr>
<td>Endurant IDE</td>
<td>4.3%</td>
<td>9.8%</td>
<td>6.7%</td>
</tr>
</tbody>
</table>

1-Yr results for commercially available devices shown per the respective US FDA Summary of Safety and Effectiveness Data (SSED) and peer-reviewed publications of trial results. Mortality rates for days 31-365.

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Global Registry: 2 Year Clinical Results

- **98% freedom** from persistent endoleaks
- **No secondary interventions** for Type II endoleaks
- **97% freedom** from aneurysm-related mortality
- **98.5% freedom** from cardiovascular mortality

These data continue to support positive outcomes in a real world patient population that had no screening or anatomical restrictions at enrollment, and constitute the broadest range of aortic anatomies for any prospective endovascular AAA study.

**37% complex**

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Global Registry: Designed to Test the Boundaries of EVAR

37% of all treated patients has complex anatomy outside of the Nellix IFU*


* Based on previous IFU

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Global Registry: Freedom from All Persistent Endoleak at 2 Years

98.1%

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### Global Registry: Persistent Endoleak through Last Follow-Up

<table>
<thead>
<tr>
<th>All Endoleak</th>
<th>1.8% (5) (N = 277)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type Ia</td>
<td>0.4% (1)</td>
</tr>
<tr>
<td>Type Ib</td>
<td>0.4% (1)</td>
</tr>
<tr>
<td>Type II</td>
<td>0.7% (2)</td>
</tr>
<tr>
<td>Type III</td>
<td>-</td>
</tr>
<tr>
<td>Type Unknown</td>
<td>0.4% (1)</td>
</tr>
</tbody>
</table>

Mean follow-up 25 mo (0-35 mo)

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Global Registry: Freedom from Type Ia Endoleak -- On- and Off-IFU

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Complex Proximal Neck Anatomy

Large proximal necks
>28mm
Thrombus-laden necks

Based on previous IFU

On-IFU
Off-IFU

p-value = 0.0008

96.9%
85.6%

On-label
Off-label

Month

0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30

102 93 85 82 82 80 78 77 77 77 68 48 25 30
Global Registry: Freedom from Secondary Intervention: On- and Off-IFU

Based on previous IFU

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Global Registry: Freedom from Secondary Intervention: On- and Off-IFU

99.6% Freedom from Persistent Type 1A Endoleaks, demonstrated by successful secondary repair

Transcatheter Embolization: Coils & Glue


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Global Registry: Limb Occlusion -- Freedom from Secondary Intervention

- Prevalence higher early in learning curve
- Directly influenced by Nellix stent lumen diameters
- Strategies to optimize stent lumen include angioplasty balloons up during polymer cure and post-ballooning after device removal

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Global Registry: Freedom from Mortality at 2 Years

Cardiovascular Mortality 98.5%
Aneurysm-Related Mortality 97.4%
All Cause Mortality 89.1%

98.5% Freedom from Cardiovascular Mortality through 2 Years

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Global Registry: Freedom from Mortality at 2 Years

\[ \text{Survival Estimates: At Risk} \]

\[
\begin{array}{cccccccc}
\text{Month} & 277 & 271 & 267 & 265 & 261 & 257 & 256 & 253 & 261 & 249 & 246 & 212 \\
1.063 & 1.240 & 1.146 & 265 & 263 & 261 & 249 & 246 & 212 \\
\end{array}
\]


2ENGAGE Registry: Verhagen et al. *LINC Symposium* 2014

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Nellix EVAS: A Procedure in Evolution

- We thought it to be a ‘one size fits all’ device, for every anatomy
- What did we learn in the past years?
Nellix EVAS: A Procedure in Evolution

- We need proximal landing zone

SHORT NECK AND PROXIMAL ENDOLEAK

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Nellix EVAS: A Procedure in Evolution

- Device Migration: Impact of Small Flow Lumen Relative to Thrombus Burden

**INADEQUATE POLYMER DISTRIBUTION**

**CAUDAL MIGRATION AT 2 YEARS**

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Nellix EVAS: A Procedure in Evolution

- Partial Common Iliac Artery Exclusion Can Lead to Aneurysm Growth

Post-Op

Partial CIA Exclusion

Sac Change
52.6mm to 59.6

Complete seal
No endoleak

Coil embolization and covered stent ext.
Nellix EVAS: A Procedure in Evolution

- Increasing Seal Zone Reduces Reintervention Risk

LOW

CORRECT

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Global Registry: Lessons Learned

The ‘sealing the entire aneurysm’ idea...quite simply represents a very seductive concept that seems to lure the vascular surgeon beyond the IFU.”

“Little to no neck?” Angulated necks? Large necks?....All not a problem, the endobags will take care of it....the sky seems the limit.”

BEST PRACTICES

- Realistic patient selection
- Precise stent placement
- Good endobag filling
- Adequate proximal and distal seal in parallel sided artery
Nellix EVAS: A Procedure in Evolution

- Nellix 3.5

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Nellix EVAS: A Procedure in Evolution

2016

Selection  Position  Seal

EVAS Procedure Evolved and Improved

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Nellix EVAS: A Procedure in Evolution

- Stents deployed slowly
- Angioplasty balloons left inflated
- Pre-fill with dilute contrast
- Polymer fill volume matches pre-fill

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Nellix EVAS: A Procedure in Evolution

- Establishing Seal during EVAS Procedure
  - Optimal seal requires precise management of *Pressure AND Volume*
  - Inflate Nellix balloons to nominal pressure (7 Atm) for 30 seconds
  - Leave balloons up during polymer fill

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Preliminary analysis shows migration and aneurysm enlargement in limited number of patients with up to 2 year follow-up;

Comprehensive engineering evaluation, statistical analysis, and clinical assessment completed;

Result: Decision to update the Nellix indications to ensure excellent patient outcomes

1. Type 1A Endoleak
2. Migration
3. Aneurysm Enlargement
In IDE patients (Nellix 3SQ+) with refined Nellix 3.5 IFU

1. **Proximal Neck Diameter**
   - From: 18-32mm
   - To: 18-28mm

2. **Neck Diameter Change**
   - From: ≤20%
   - To: ≤10%

3. **Iliac Artery Luminal Diameter - Unchanged**
   - 9-35mm

4. **Distal Seal Zone**
   - ≥10mm
   - Length: 9-25mm

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Refined Nellix IFU

Aneurysm Ratio

Max aortic aneurysm dia < 1.4
Max aortic blood lumen dia

In IDE patients (Nellix 3SQ+) with refined Nellix 3.5 IFU
Let me stress what IFU means

- IFU starts with **Selection**
- IFU continues during the procedure: **Positioning** is key
- **Seal** is the goal of treatment

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So, if we stay within IFU: SPS

- Your patients could benefit from outstanding results
So, if we stay within IFU: SPS

- Your patients could benefit from outstanding results

Freedom from Core Lab-Reported
- Migration >5mm
- Type Ia Endoleak
- Sac Enlargement >5mm

Based on redefined IFU
Influence of patient selection and IFU compliance on outcomes following EVAS

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