Reduction in cardiovascular related adverse events following active sac management with Nellix vs. EVAR: Are there biological advantages?

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Disclosure

Speaker name:
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I have the following potential conflicts of interest to report:

- [x] 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
Purpose of the Study

• to evaluate the risk of post-implantation syndrome (PIS) with endovascular aneurysm sealing (EVAS) and endovascular aneurysm repair (EVAR) in patients with abdominal aortic aneurysm (AAA).
• to evaluate CVAE
Methods

• retrospective single-center study

• patients with AAA electively treated with EVAS or EVAR over a 5-year period (January 2011 to December 2015).

• Exclusion criteria: suspected infection, ruptured AAA, prior EVAR, complex endovascular procedures, need for concomitant open surgical procedures (e.g. vascular reconstruction), or use of non-steroidal anti-inflammatory drugs, cyclo-oxygenase-2 inhibitors, or corticosteroids.
Methods

• preoperative computed tomography scans to determine aortoiliac morphology and suitability for endovascular treatment.

• measurements of aneurysm volume and thrombus volume
Methods

• Main outcomes included:
  – body temperature,
  – white blood cell (WBC) count,
  – CRP concentration
  – platelet counts.

• The maximum value for each outcome during the 72-hour post-procedural period was used for data analysis.

• Post-implant syndrome was defined as temperature >38°C and WBC count >12,000 / μl
Methods

- Clinical outcomes included major adverse events (MAEs), cardiovascular MAEs, mortality, and endoleak through 30-day follow-up.
Results

• Five-year period: 210 EVAR/EVAS procedures

01.01.11 - 31.12.15
endovascular aortic procedures: 290
AAA incl. criteria 104
AAA excl. criteria 106
PAOD 80

AAA excl. criteria
AAA+vascular reconstruction 46
F-EVAR 17
Chimney procedures 15
Symptomatic/ruptured AAA 14
Iliac side branch 8
EVAR-Repair 3
TAA 2
Multi-Branch 1

• 104 patients electively treated were included in the study.
  – EVAR: n=63
  – EVAS: n=41
Stent devices

<table>
<thead>
<tr>
<th>Type</th>
<th>Devices</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAR-Polyester</td>
<td>Anaconda, Vascutek</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>Endurant, Medtronic</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Zenith, Cook</td>
<td>2</td>
</tr>
<tr>
<td>EVAR-PTFE</td>
<td>AFX, ELGX</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Excluder, Gore</td>
<td>14</td>
</tr>
<tr>
<td>EVAS</td>
<td>Nellix</td>
<td>41</td>
</tr>
</tbody>
</table>

cut-down: 86%
percutaneous: 14%
Propensity Score-Matched Analysis

• 2 matched groups 39 pat. (asymptomatic infrarenal AAA)
• EVAS vs. EVAR
• No difference in aortoiliac anatomy, thrombus burden, AAA volume
• incidences of postimplantation syndrome (p=0.07), mean body temperature (p=0.05), mean leukocyte count (p=0.003), and mean hs-CRP (p<0.001) were proportionally lower with EVAS vs EVAR.
• Serious adverse events (0% vs 12.8%, p=0.05) and endoleaks (0% vs 10.3%, p=0.13) through 30 days were less frequent with EVAS

Major adverse events

Non-cardiac MAEs

**EVAS: 6 MAEs in 5 patients**
- access site complications (5)
- lower extremity paresthesia (1).

**EVAR: 10 MAEs in 7 patients**
- access site complications (5)
- type I endoleak (2)
- abdominal pain (1)
- dementia (1)
- hematuria (1)

Cardiac MAEs

**EVAS: 0 cMAEs**
- No cardiac MAEs

**EVAR: 8 cMAEs in 8 patients**
- cardiac decompensation (6)
- coronary heart disease (1)
- myocardial infarction (1)
  (1 post-op death)
Relationship of perioperative CRP concentration and 30-day MAE
Why might EVAS carry a lower PIS compared to EVAR?

- **EVAR:** Passive Sac Management
  - Thrombosis of aneurysm sac
  - Type 2 endoleak and sac growth
  - Sac remains biologically active and may trigger inflammatory response

- **EVAS:** Active Sac Management
  - Eradicate space in aneurysm sac
  - Prevent Type 2 endoleak and sac growth
  - Change biological response to endovascular AAA intervention
Role of intraluminal thrombus?

- disturbance of intraluminal thrombus during EVAR stimulates a pro-inflammatory cytokine release
- presence of type II endoleaks may provide a sustained pathway for signaling proteins to reach the systemic circulation
## EVAR and Post-Implantation Syndrome

### First Post-Operative Month
- Fever
- Elevated heart rate, respiratory rate
- Elevated WBC (Leukocytosis)
- Elevated C-reactive protein
- Coagulation disturbances
- Prolonged hospitalization

### Within First Year
- Serious Adverse Events, including *Cardiovascular Events* (CAD, MI, Stroke)
- Inflammatory Markers (Cytokines) remain elevated in patients with no sac regression

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“The inflammatory response after EVAR is attenuated after the first post-op month, as shown by the kinetics of several inflammatory biomarkers. However, **PIS seems to correlate with the presence of a cardiovascular or any other adverse event** during the first year after EVAR.”

Arnaoutoglou 2009, Arnaoutoglou 2016, Ridker NEJM 2017
Inflammatory Response and CV Events

Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease


CONCLUSIONS

Antiinflammatory therapy targeting the interleukin-1β innate immunity pathway with canakinumab at a dose of 150 mg every 3 months led to a significantly lower rate of recurrent cardiovascular events than placebo, independent of lipid-level lowering. (Funded by Novartis; CANTOS ClinicalTrials.gov number, NCT01327846.)

Inflammation and Hypertension

• immune system, inflammation and hypertension are related to each other.

• increase in cytokines release and reactive oxygen species (ROS) production are hallmarks which are always found in hypertension.

• In our study, 6 cardiac decompensations secondary to dysregulation of hypertension

Agita et al, 2017
Possible long-term consequences of PIS

**3 Year Survival**

<table>
<thead>
<tr>
<th></th>
<th><strong>EVAS</strong>&lt;sup&gt;1&lt;/sup&gt;</th>
<th><strong>EVAR</strong>&lt;sup&gt;2,3,4&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Cause Mortality</td>
<td>88%</td>
<td>≈80%</td>
</tr>
<tr>
<td>Cardiovascular Mortality</td>
<td>99%</td>
<td>≈90%</td>
</tr>
</tbody>
</table>

1. EVAS FORWARD IDE and Global Registry. Endologix Inc. Data on file
3. Bahia et al, EJVES 2015 (n=107,814) / EVAR 1 HTA Report (n=626)
4. Van Sambeek. 4-Year Results, ENGAGE Registry. Presented at the 2015 VEITHsymposium, New York, NY.
Conclusion

- EVAR durability is limited
  - Sac growth, all-cause and cardiovascular mortality
- Post-implantation syndrome linked to EVAR
  - Increased risk of cardiovascular adverse events
- Polyester stent-grafts induce the greatest periprocedural inflammatory response
- Active Sac Management with EVAS is associated with a blunted systematic inflammatory response
- EVAS yields lower than expected all cause and cardiovascular mortality rates
- Further studies needed to explain possible mortality benefits with EVAS
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