The role of fish oil in the natural history of abdominal aortic aneurysms

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On behalf of
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Disclosure of Interest

Speaker name: Jes S. Lindholt

I have the following potential conflicts of interest to report:
- Consulting
- Employment in industry
- Shareholder in a healthcare company
- Owner of a healthcare company
- Other(s)

X I do not have any potential conflict of interest
Main mechanisms of AAA are inflammation, proteolysis and oxidative stress.

Oxidative stress and particularly inflammation are inhibited by the fish-derived omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).
Hypothesis

• This prompted the notion that dietary omega-3 might protect against AAA.

• Such hypothesis was confirmed in experimental models (angiotensin II-infused Apolipoprotein E-knockout mice [2-4])

• - but to date clinical data are lacking, as reviewed (1).
Lack of human data

The genetic similarity between a **human** and a **mouse** is...

85%
Material from VIVA trial*

Baseline sampled RCB from 498 AAA patients and 199 controls

Annual aneurysmal control ultrasound scan

Median follow-up of 4.85 y

141 patients had repair (AAA ≥55 mm) within 5 yrs

Methods

• Although the fatty acid profile of adipose tissue is the best surrogate of long-term fat intake, circulating fatty acids are a convenient and accepted alternative (6).

• The turnover of red blood cells (RBC) (120-day lifespan) makes RBCs suitable for objective assessment of omega-3 fatty acid status (7).


Methods II

- **Gas-chromatography:**
  - Omega-3 eicosapentaenoic acid (EPA)
  - Omega-3-docosahexaenoic acid (DHA)
  - Omega-3 index (EPA+DHA)
  - Arachidonic acid (AA).

- The association of their *upper tertiles* with
  1. the risk of having an AAA
  2. the need for later AAA repair
Results: EPA, DHA and Omega-3-index

- Mean omega-3 index = 7.6% (= participants were high consumers of omega-3).
- Only 4.9% < 4.0% (Threshold for high CVD risk)
- No significant associations: Omega-3 index, EPA, DHA with risk of AAA or need for AAA repair
Results: Arachidonic acid (AA) - the bad proinflammatory fatty oil

AA in AAA vs Controls:
15.90% ± 2.58 vs 15.06% ± 2.33, P < 0.001
Results: Arachidonic acid (AA) - the bad proinflammatory fatty oil

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper tertile of AA</td>
<td>1.31 (1.02 to 1.68)</td>
<td>0.033</td>
</tr>
<tr>
<td>Smoking</td>
<td>4.11 (2.53 to 6.68)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.06 (0.70 to 1.61)</td>
<td>0.5333</td>
</tr>
<tr>
<td>Antiplatelets</td>
<td>2.95 (1.81 to 4.81)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Statins</td>
<td>1.19 (0.75 to 1.90)</td>
<td>0.3152</td>
</tr>
<tr>
<td>PAD</td>
<td>9.33 (3.59 to 24.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>1.09 (1.03 to 1.16)</td>
<td>0.005</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>1.08 (1.06 to 1.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Constant</td>
<td>0.02</td>
<td>&lt;0.001</td>
</tr>
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</table>

Diagram:
- Arachidonic acid
- Omega-3-index

<table>
<thead>
<tr>
<th></th>
<th>Area</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omega-3- index</td>
<td>0.50 (0.45, 0.56)</td>
<td>0.946</td>
</tr>
<tr>
<td>Arachidonic acid</td>
<td>0.58 (0.54; 0.62)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Results: Arachidonic acid (AA) - Need for later preventive repair

Variable | Hazard Ratio (95% CI) | P
---|---|---
**Upper tertile** | 1.544 (1.127 to 2.114) | 0.007
Smoking | 1.097 (0.797 to 1.510) | 0.395
Hypertension | 1.570 (1.117 to 2.207) | 0.009
Antiplatelet | 0.799 (0.550 to 1.160) | 0.554
Statin | 1.166 (0.805 to 1.689) | 0.290
PAD | 0.821 (0.547 to 1.234) | 0.238
BMI | 0.973 (0.930 to 1.017) | 0.152
Diabetes | 0.959 (0.554 to 1.658) | 0.611
Betablocker | 0.730 (0.494 to 1.079) | 0.506
Hs-CRP | 1.000 (0.985 to 1.014) | 0.661
Aortic size | 1.087 (1.076 to 1.097) | <0.001

<table>
<thead>
<tr>
<th>N at entry</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper tertile</td>
<td>229</td>
<td>195</td>
<td>177</td>
<td>156</td>
<td>137</td>
<td>67</td>
</tr>
<tr>
<td>Lower tertiles</td>
<td>463</td>
<td>416</td>
<td>388</td>
<td>352</td>
<td>326</td>
<td>109</td>
</tr>
</tbody>
</table>
Further downstream

- Arachidonic acid-derived metabolites, such as leukotriene B4 (LTB4), has been previously observed in human AAA tissue, potentially contributing to neutrophil recruitment.

- Individuals in the upper tertile of LTB4 at baseline had higher probability of having AAA (Odds Ratio=8.3, 95% CI 4.2;16.5, P<0.001).

- AAA patients at the upper tertile of LTB4 at baseline had a 60% higher risk of needing surgical repair during the follow-up (Hazard Ratio=1.6, 95% CI, 1.2;2.3, P=0.003).

See poster in hall: Leukotriene B4 plasma levels are associated to AAA prevalence and progression.
Monica Torres-Fonseca ¹*, Jes S Lindholt²*, Raquel Roldan-Montero¹, Diego Martinez-Lopez¹, Luis M Blanco-Colio¹, Jose L Martin-Ventura¹.
Conclusion

• Surprisingly, omega-3-fatty acids didn´t influence the risk of AAA or need for AAA repair.

• In contrast, arachidonic acid increased the risk of having an AAA and need for AAA repair.

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