Arachidonic Acid, but Not Omega-3 Index, Relates to the Prevalence and Progression of Abdominal Aortic Aneurysm in a Population-Based Study of Danish Men

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Background—Animal models support dietary omega-3 fatty acids protection against abdominal aortic aneurysm (AAA), but clinical data are scarce. The sum of red blood cell proportions of the omega-3 eicosapentaenoic and docosahexaenoic acids, known as omega-3 index, is a valid surrogate for long-term omega-3 intake. We investigated the association between the omega-3 index and the prevalence and progression of AAA. We also investigated associations between AAA and arachidonic acid, an omega-6 fatty acid that is a substrate for proinflammatory lipid mediators.

Methods and Results—We obtained blood samples from 498 AAA patients (maximal aortic diameter ≥30 mm) within a population-based ultrasound-screening trial in men and from 199 age-matched controls who screened negative. We determined the fatty acids of red blood cells by gas chromatography. During a median follow-up of 4.85 years, 141 AAA patients reached criteria for vascular surgical repair. Participants were high consumers of omega-3 (average omega-3 index: 7.6%). No significant associations were found for omega-3 index. In contrast, arachidonic acid in AAA patients was higher than in controls (P<0.001), and individuals in the upper tertile of arachidonic acid at baseline had higher probability of having AAA (odds ratio: 1.309; 95% confidence interval, 1.021–1.678; P=0.033). AAA patients at the upper tertile of arachidonic acid at baseline had a 54% higher risk of needing surgical repair during follow-up (hazard ratio: 1.544; 95% confidence interval, 1.127–2.114; P=0.007).

Conclusions—Omega-3 index is unrelated to men with AAA from a country in which fish consumption is customarily high. Arachidonic acid is associated with AAA presence and progression.

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Key Words: abdominal aortic aneurysm • diet • inflammation

Abdominal aortic aneurysm (AAA) is characterized by a focal dilation of the aortic diameter ≥30 mm. AAA is asymptomatic until aortic rupture, which is fatal in ≈90% of cases. Main mechanisms of AAA are proteolysis and oxidative stress, which triggers the inflammatory response of the aortic wall, contributing to the AAA continuum. Oxidative stress and particularly inflammation are inhibited by the fish-derived omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). This prompted the notion that dietary omega-3 might protect against AAA.¹ Such a hypothesis was confirmed in experimental models (angiotensin II–infused apolipoprotein E–knockout mice²–⁴). To date, however, clinical data are limited to a recent study conducted in a small Japanese population that reported a low proportion of EPA in serum related to AAA growth and size.⁵

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In the frame of a population-based ultrasound-screening trial for AAA in Danish men aged 65 to 74 years (VIVA [Viborg Vascular] trial6), we conducted an observational study that aimed to test whether long-term intake of omega-3 related to decreased prevalence and progression of AAA. In observational studies, the optimal approach to address this issue is by using the fatty acid composition of body tissues, given the difficulties of accurately measuring fat intake from the diet records.7 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.7 The turnover of red blood cells (RBCs; 120-day life span) makes RBCs more suitable for objective assessment of omega-3 fatty acid status than serum or plasma.8 We focused on the sum of proportions of EPA and DHA in RBCs, known as the omega-3 index, because it is a valid surrogate for long-term omega-3 intake9 and has been proposed as a risk factor for cardiovascular diseases, particularly sudden cardiac death.10 We also determined the RBC proportion of arachidonic acid, an omega-6 fatty acid that is a substrate for the synthesis of proinflammatory lipid mediators once released from cell membranes.

Materials and Methods

Data Availability

The authors confirm that, for approved reasons, some access restrictions apply to the data underlying the findings. Access to the data can be requested by applying for permission from the Danish Data Protection Agency and Statistics Denmark.
RBC Membrane Fatty Acid Analysis

Overnight fasting-period (>10 hours) blood samples were obtained by venipuncture and stored at −80°C until fatty acid analysis. The RBC fatty acid profile was determined, as described.9 In brief, cells contained in a 100-µL aliquot of EDTA-collected blood were hemolyzed and spun. The pellet (>99% RBC membranes) was dissolved in 1 mL BF3 methanol solution and heated to hydrolyze and methylate glycerophospholipid fatty acids. The fatty acid methyl esters were isolated by adding n-hexane and were separated by gas chromatography using an Agilent HP 7890 gas chromatograph equipped with a 30 m×0.25 µm×0.25 mm SupraWAX-280 capillary column (Teknokroma), an autosampler, and a flame ionization detector. The amount of each fatty acid was expressed as a percentage of the total identified fatty acids in the sample. The omega-3 index was calculated as the sum of the percentages of EPA and DHA. As reported,9 the fatty analysis method has been cross-validated against the method used in the original definition of the omega-3 index, with a coefficient of variance of 3% for EPA and DHA.12

Statistical Analyses

When the sampling occurred, the hypothesis about an association between AAA and fatty acids had not yet been formulated. To our knowledge, there is a single report of association between AAA and fatty acids had not yet been made. To our knowledge, there is a single report of association between AAA and fatty acids in Denmark.13 Given that no data on RBC fatty acids in Denmark.13 Given that no data concerning need for later repair. To address this issue, we obtained a Kaplan–Meier curve for cumulative freedom by constructing a multivariate Cox proportional hazards model, adjusted for active smoking, hypertension, use of low-dose aspirin, use of statins, peripheral arterial disease at screening, body mass index, diabetes mellitus, use of beta blockers, C-reactive protein, and baseline maximal aortic diameter.

Results

The Student t test revealed expected differences in clinical characteristics between AAA patients and controls (Table 1). No significant differences were found between AAA patients and controls for omega-3 index. The average omega-3 index was 7.6% and was <4% (the proposed cutoff for high cardiovascular risk10) in only 4.9% of the study population (Figure 1A). Arachidonic acid proportion in AAA patients was higher than in controls (mean±SD: 15.90%±2.58 versus 15.06%±2.33, respectively; P<0.001; Figure 1B). Participants in the upper tertile of arachidonic acid at baseline consistently had significantly higher prevalence of AAA, independent of potential confounding factors (adjusted odds ratio: 1.309; 95% confidence interval [CI], 1.021–1.678; P=0.033; Table 2). In AAA patients, the proportion of arachidonic acid in RBCs directly correlated with maximal aortic diameter (R=0.091, P=0.042; Figure 2A) but not with aneurysmal growth rate (R=−0.020, P=0.702). No correlation was noted concerning maximal aortic diameter and aneurysmal growth rate for omega-3 index (R=−0.037, P=0.476, and R=0.001, P=0.979, respectively), EPA (R=−0.06, P=0.117, and R=−0.02, P=0.967, respectively), or DHA (R=−0.08, P=0.872, and R=0.01, P=0.816, respectively). Finally, after a median follow-up of 4.85 years, AAA patients in the upper tertile of arachidonic acid at baseline showed a 54% higher risk of needing surgical repair (adjusted hazard ratio: 1.544; 95% CI, 1.127–2.114; P=0.007; Figure 2B), independent of potential confounding factors, including aortic diameter (Table 3). No significant associations were found in AAA patients in the upper tertile of EPA (hazard ratio: 0.957; 95% CI, 0.709–1.292; P=0.773), DHA (hazard ratio: 0.832; 95% CI, 0.613–1.130; P=0.239), or omega-3 index (hazard ratio: 0.906; 95% CI, 0.669–1.227; P=0.520). Finally, C-reactive protein levels inversely correlated with EPA (R=−0.112, P=0.015), DHA (R=−0.148, P=0.001), and the omega-3 index (R=−0.147, P=0.001), but no significant correlation was found for arachidonic acid levels (R=0.052, P=0.261).
Discussion

The main conclusion of our study is that in a population with a high intake of omega-3, the omega-3 index was unrelated to AAA. In contrast, the RBC proportion of arachidonic acid, a substrate for generation of lipid mediators with proinflammatory properties, related to an increased prevalence of AAA and, in those diagnosed with AAA, an increased risk of needing surgical repair.

Although the role of EPA and DHA in primary prevention of coronary heart disease has long been explored, clinical research on omega-3 and AAA is limited to a recent study conducted in 67 Japanese participants with AAA. Aikawa et al reported that the proportion of EPA in serum, a surrogate marker for EPA intake, inversely related to AAA size and growth after a mean follow-up of 30.6 months. In conflict with this finding, we found that in our population, omega-3 in RBC membranes was unrelated to both AAA prevalence and progression. This discrepancy could underlie several issues. First, the use of fatty acid composition of total serum, which does not reflect long-term intake as accurately as adipose tissue or RBC do, precludes the adscription of observed

![Figure 1](http://jaha.ahajournals.org/)

**Figure 1.** Red blood cell proportions (percentage of total fatty acids) of (A) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)/(EPA+DHA=omega-3 index) and (B) arachidonic acid in 498 patients with abdominal aortic aneurysm (AAA) and 199 age-matched controls who screened negative. Dots are individual participant data, and bars represent mean±SD. P obtained by Student t test. In panel (A), discontinuous lines at 8% and 4% indicate proposed low- and high-risk cutoffs for cardiovascular risk, respectively.10

**Table 1.** Clinical Baseline Characteristics of the Study Population

|                          | AAA (n=498) | Age-Matched Controls (n=199) | P Value* | AAA, Vascular Repair (n=141) | AAA, No Repair (n=357) | P Value† |
|--------------------------|-------------|-----------------------------|----------|-----------------------------|-----------------------|----------|
| Baseline aortic size, mm | 40.8 (11.8) | 18.3 (3.0)                  | <0.001   | 47.7 (13.7)                 | 35.6 (6.4)            | <0.001   |
| PAD, n (%)               | 130 (26.1)  | 0‡                          | <0.001   | 27 (19.1)                   | 103 (28.9)            | 0.013    |
| BMI, kg/m²               | 27.4 (3.6)  | 26.2 (3.3)                  | <0.001   | 27.4 (3.5)                  | 27.3 (3.7)            | 0.640    |
| Current smoking, n (%)   | 203 (40.8)  | 39 (19.6)                   | <0.001   | 57 (40.4)                   | 146 (40.9)            | 0.878    |
| Diabetes mellitus, n (%) | 54 (10.8)   | 29 (14.6)                   | 0.181    | 15 (10.6)                   | 39 (10.9)             | 0.608    |
| Hypertension, n (%)      | 266 (53.3)  | 91 (45.7)                   | 0.030    | 80 (56.7)                   | 186 (52.1)            | 0.305    |
| Diastolic blood pressure, mm Hg | 87.9 (12.1) | 81.1 (10.2)               | <0.001   | 89.1 (12.5)                 | 87.0 (11.8)           | 0.064    |
| Use of statins, n (%)    | 260 (52.1)  | 73 (36.7)                   | <0.001   | 74 (52.5)                   | 186 (52.1)            | 0.972    |
| Use of low-dose aspirin, n (%) | 247 (49.5) | 54 (27.1)                | <0.001   | 64 (45.4)                   | 183 (51.3)            | 0.199    |
| Use of bronchodilators, n (%) | 39 (7.8)   | 11 (5.5)                   | 0.260    | 8 (5.7)                     | 31 (8.7)             | 0.289    |
| Use of beta blockers, n (%) | 150 (30.1) | 46 (23.1)                  | 0.053    | 35 (24.8)                   | 115 (32.2)            | 0.079    |

Data are expressed as mean (SD), except for quantitative variables, expressed as %. AAA indicates abdominal aortic aneurysm; BMI, body mass index; PAD, peripheral artery disease.

*Comparison between AAA and controls. P obtained by Student t test.
†Comparison between AAA needing vascular repair vs not. P obtained by Student t test.
‡Controls were free of PAD by definition.
effects to membrane changes with long-term omega-3 intake. In contrast, the omega-3 fatty acid status in RBCs has stability documented over a 6-week period\textsuperscript{8}; the use of RBCs also allowed us to examine the omega-3 index, defined as the sum of the percentages of EPA and DHA in RBC membranes, and its role as a risk marker for cardiovascular disease is emerging. Second, the number of AAA patients in our study was noticeably larger and had longer follow-up. Third, white race is a well-defined risk factor associated with the development of AAA, thus hampering direct comparisons regarding the influence of environmental risk factors for AAA between Asian and Western populations.

A plausible explanation for our neutral findings on omega-3 and AAA could be the existence of a threshold of protection of EPA and DHA against AAA in non-Asian individuals, largely exceeded by both controls and AAA patients in our study (given the average omega-3 index of 7.6\% in our population). This value resembles those described in other Scandinavian populations,\textsuperscript{14} resulting from the customarily high consumption of fatty fish in this area.\textsuperscript{15,16} Future research should confirm or dispel whether the benefits of increasing dietary EPA and DHA on AAA would be observed only with a low background intake of omega-3. This would be similar to prevention of coronary heart disease, for which few benefits

### Table 2. Independent Determinants of AAA by Multivariate Logistic Regression

| Variable                                      | B     | SE   | OR (95\% CI)       | \( P \) Value |
|-----------------------------------------------|-------|------|-------------------|-----------|
| Being at the upper tertile of arachidonic acid at baseline, yes | 0.269 | 0.127 | 1.309 (1.021–1.678) | 0.033 |
| Current smoking, yes                          | 1.413 | 0.248 | 4.110 (2.528–6.682) | <0.001 |
| Hypertension, yes                             | 0.062 | 0.211 | 1.064 (0.703–1.610) | 0.768 |
| Use of low-dose aspirin, yes                  | 1.082 | 0.249 | 2.951 (1.809–4.812) | <0.001 |
| Use of statin, yes                            | 0.178 | 0.238 | 1.194 (0.750–1.903) | 0.454 |
| PAD, yes                                      | 2.233 | 0.486 | 9.331 (3.598–24.197) | <0.001 |
| BMI, increase by 1 kg/m\(^2\)                | 0.088 | 0.032 | 1.092 (1.026–1.162) | 0.005 |
| DBP, increase by 1 mm Hg                      | 0.074 | 0.010 | 1.077 (1.056–1.099) | <0.001 |
| Constant                                      | -9.144 | 1.184 | 0.0002            | <0.001 |

AAA indicates abdominal aortic aneurysm; BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; OR, odds ratio; PAD, peripheral artery disease.

### Figure 2.

In 498 patients with abdominal aortic aneurysm (AAA), (A) a scatter plot shows the red blood cell proportion of arachidonic acid and the maximal aneurysm diameter, and (B) the Kaplan–Meier curve shows cumulative freedom from needing vascular repair, stratified by being in the upper tertile of red blood cell proportion of arachidonic acid at baseline vs not. Data were obtained using a multivariate Cox proportional hazards model adjusted for active smoking, hypertension, use of low-dose aspirin, use of statins, peripheral arterial disease at screening, body mass index, diabetes mellitus, use of beta blockers, C-reactive protein, and baseline maximal aortic diameter.

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are observed beyond intakes of 500 mg/d, an amount easily achievable through 2 weekly servings of fatty fish. Of particular interest are cohorts in the United States, a country with low omega-3 index and high AAA prevalence.

We observed increased levels of arachidonic acid in AAA patients. Although EPA and DHA act by generating anti-inflammatory and vasoprotective compounds (eg, lipoxins, protectins, maresins), arachidonic acid mostly generates proinflammatory molecules on release of cell membranes. Arachidonic acid levels at baseline were associated with increased need of surgical repair independent of C-reactive protein. Interestingly, C-reactive protein showed no association with arachidonic acid, whereas significant inverse associations were observed for omega-3 fatty acids. These findings support the view that the association of arachidonic acid with AAA presence and progression is not simply a reflection of increased systemic inflammation. However, the absence of correlation with C-reactive protein does not preclude the potential contribution of arachidonic acid to vascular (local) inflammatory response. In this regard, increased levels of leukotriene B4 (an arachidonic acid-derived compound) have been observed in tissues of AAA patients. Moreover, protection against experimental AAA was afforded by blockade of enzymes involved in arachidonic acid metabolism, such as lipooxygenase. Further research is needed to identify determinants of arachidonic acid in cell membranes and to elucidate the role of this fatty acid, particularly regarding its lipid-derived mediators, on AAA progression.

The main limitation of our study is its observational design. A cause–effect relationship would be established only by a randomized controlled trial involving a nutritional intervention in a large population, ideally, with low background omega-3 intake and high risk of AAA, followed for several years. In addition, cumulative average estimates of arachidonic acid would provide a more robust association with AAA progression than a single baseline measurement. The study also has strengths. Selection bias seems unlikely because the study group members were participants in a population-based screening trial with an attendance rate of 74%. Information bias also seems unlikely because ultrasound-based measurement of the aorta was performed by a validated method showing high position, and information on the need for later AAA repair was based on nationwide registry data in which all AAA repair procedures are recorded by law and for reimbursement. Consequently, all participants had follow-up without missing data. Finally, the analyses were adjusted for known potential risk factors for AAA.

In conclusion, we found that omega-3 index, an objective marker of omega-3 intake, was unrelated to AAA in men from a country in which fish consumption is customarily high. In contrast, the content of arachidonic acid was related to prevalence and progression of AAA.

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Disclosures

None.

References

1. Meital LT, Sandow SL, Calder PC, Russell FD. Abdominal aortic aneurysm and omega-3 polyunsaturated fatty acids: mechanisms, animal models, and potential treatment. Prostaglandins Leukot Essent Fatty Acids. 2017;118:1–9.

2. Wang JH, Eguchi K, Matsumoto S, Fujiu K, Komuro I, Nagai R, Manabe I. The ω-3 polyunsaturated fatty acid, eicosapentaenoic acid, attenuates abdominal aortic aneurysm development via suppression of tissue remodeling. PLoS One. 2014;9:e96286.

3. Yoshihara T, Shimada K, Fukao K, Sai E, Sato-Okabayashi Y, Matsumori R, Shiozawa T, Aishahi H, Miyazaki T, Tada N, Daida H. Omega 3 polyunsaturated fatty acids suppress the development of aortic aneurysms through the inhibition of macrophage-mediated inflammation. Circ J. 2015;79:1470–1478.

4. Kavazos K, Nataaatmadja M, Wales KM, Hartland E, Williams C, Russell FD. Dietary supplementation with omega-3 polyunsaturated fatty acids modulate matrix metalloproteinase immunoreactivity in a mouse model of pre-abdominal aortic aneurysm. Heart Lung Circ. 2015;24:377–385.

5. Aikawa T, Miyazaki T, Shimada K, Sugita Y, Shimizu M, Ouchi S, Kadoguchi T, Yokoyama Y, Shiozawa T, Hiki M, Takahashi S, Alshahi H, Miyazaki T, Tada N, Daida H. Low serum levels of EPA are associated with the size and growth rate of abdominal aortic aneurysm. J Atheroscler Thromb. 2017;24:912–920.

6. Grøndal N, Søgaard R, Henneberg EW, Lindholt JS. The Viborg Vascular (VIVA) screening trial of 65–74 year old men in the central region of Denmark: study protocol. Trials. 2010;11:67.

7. Hodson L, Skeaff CM, Fielding BA. Fatty acid composition of adipose tissue and blood in humans and its use as a biomarker of dietary intake. Prog Lipid Res. 2008;47:348–380.

8. Harris WS, Thomas RM. Biological variability of blood omega-3 biomarkers. Clin Biochem. 2010;43:338–340.

9. Sala-Vila A, Harris WS, Cofan M, Pérez-Heras AM, Pintó X, Lamuela-Raventós RM, Covas MI, Estruch R, Ros E. Determinants of the omega-3 index in a Mediterranean population at increased risk for CHD. Br J Nutr. 2011;106:425–431.

10. Harris WS. The omega-3 index: from biomarker to risk marker to risk factor. Curr Atheroscler Rep. 2009;11:411–417.

11. Grandal N, Branssen MB, Thomsen MD, Rasmussen CB, Lindholt JS. The cardiac cycle is a major contributor to variability in size measurements of abdominal aortic aneurysms by ultrasound. Eur J Vasc Endovasc Surg. 2012;43:30–33.

12. Harris WS, Pottala JV, Vasan RS, Larson MG, Robins SJ. Changes in erythrocyte membrane trans and marine fatty acids between 1999 and 2006 in older Americans. J Nutr. 2012;142:1297–1303.

13. Launizten L, Harlaft J, Hellgren U, Pedersen MH, Melgaard C, Michaelsen KF. Fish intake, erythrocyte n-3 fatty acid status and metabolic health in Danish adolescent girls and boys. Br J Nutr. 2012;107:697–704.

14. Stark KD, Van Elswyk ME, Higgins MR, Weatherford CA, Salem N J. Global survey of the omega-3 fatty acids, docosahexaenoic acid and eicosapentaenoic acid in the blood stream of healthy adults. Prog Lipid Res. 2016;63:132–152.

15. Micha R, Khatrizbadeh S, Shi P, Fahimi S, Lim S, Andrews KG, Engell RE, Powles J, Ezzati M, Mozaffarian D; Global Burden of Diseases Nutrition and Chronic Diseases Expert Group NutriCoDE. Global, regional, and national consumption levels of dietary fats and oils in 1990 and 2010: a systematic analysis including 266 country-specific nutrition surveys. BMJ. 2014;348:g2272.

16. Welch AA, Lund E, Amiano P, Dorrorsoro M, Brustad M, Kumle M, Rodriguez M, Lasheras C, Janzon L, Jansson J, Luben R, Spencer EA, Overvad K, Tjønneland A, Averod K, Nansen D, Jensen PB; Diet, Cancer and Collaborative Groups (DCAG). Fish intake, erythrocyte n-3 fatty acid status and metabolic health in Danish adolescent girls and boys. Br J Nutr. 2012;107:697–704.

17. Mozaffarian D, Rimm EB. Fish intake, contaminants, and human health: evaluating the risks and the benefits. JAMA. 2006;296:1885–1899.

18. Li X, Zhao G, Zhang J, Duan Z, Xin S. Prevalence and trends of the abdominal aortic aneurysms epidemic in general population-a meta-analysis. PLoS One. 2013;8:e81280.

19. Houard X, Ollivier V, Louedec L, Michel JB, Berruget X, Zavitsanos X, Turnino R, Galasso R, Bueno-De-Mesquita HB, Ocké MC, Charrondière UR, Slimani N. Variability of fish consumption within the 10 European countries participating in the European Investigation into Cancer and Nutrition (EPIC) study. Public Health Nutr. 2002;5:1273–1285.

20. Bhamidipati CM, Whatling CA, Mehta GS, Meher AK, Hajzus VA, Su G, Salmon M, Upchurch GR Jr, Owens GK, Alawadi G. S-Lipoxygenase pathway in experimental abdominal aortic aneurysms. Arterioscler Thromb Vasc Biol. 2014;34:2669–2678.

21. Grandal N, Søgaard R, Lindholt JS. Baseline prevalence of abdominal aortic aneurysm, peripheral arterial disease and hypertension in men aged 65–74 years from a population screening study (VIVA trial). Br J Surg. 2015;102:902–906.

22. Laustsen J, Jensen LP, Hansen AK; Danish National Vascular Registry. Accuracy of clinical data in a population based vascular registry. Eur J Vasc Endovasc Surg. 2004;27:216–219.
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