The Omega-3 Index in National Collegiate Athletic Association Division I Collegiate Football Athletes

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Context: The essential omega-3 fatty acids (ω-3 FAs) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) exhibit vital biological roles and are critical for cardiovascular and neurologic health. Compared with the general population, football athletes may be at an increased risk of cardiovascular disease. Further, those same athletes are also exposed to repetitive head impacts, which may lead to long-term neurologic deficits. Both diets high in ω-3 FAs and supplementation with ω-3 FAs have been reported to reduce the risk of cardiovascular disease, and early evidence suggests a potential neuroprotective effect of supplementation.

Objective: To determine the (1) erythrocyte content of DHA and EPA, as measured by the Omega-3 Index, expressed as a percentage of total fatty acids, in National Collegiate Athletic Association Division I football athletes and (2) the distribution across the Omega-3 Index risk zones established for cardiovascular disease: high risk, >4%; intermediate risk, 4% to 8%; and low risk, ≤8%.

Design: Cross-sectional descriptive study.

Setting: Multicenter trial.

Patients or Other Participants: Deidentified data including complete erythrocyte fatty acid profile from the 2017–2018 season, age at time of testing, height, weight, and ethnicity were collected from 404 athletes.

Main Outcome Measure(s): Omega-3 Index.

Results: About 34% of athletes (n = 138) had an Omega-3 Index considered high risk (>4%), and 66% (n = 266) had a risk considered intermediate (4%–8%). None had a low-risk Omega-3 Index.

Conclusions: The Omega-3 Index is a simple, minimally invasive test of ω-3 FA status. Our data indicate that football athletes may be deficient in the ω-3 FAs DHA and EPA. The fact that no athlete had an Omega-3 Index associated with low risk suggests football athletes may be at increased risk for cardiovascular disease in later life.

Key Words: eicosapentaenoic acid, docosahexaenoic acid, cardiovascular disease risk, head impacts, concussion

Key Points
- Football athletes constitute an at-risk population for cardiovascular disease and head trauma.
- Omega-3 (ω-3) fatty acids are reportedly beneficial for cardiovascular disease and neuroprotection.
- Football athletes were deficient in ω-3 fatty acids.
- A focus on ingestion of ω-3 and potential supplementation should be considered.
mortality and stroke. Furthermore, the same athletes were exposed to repetitive head injuries. Animal models consistently demonstrated that treatment with DHA attenuated axonal damage, a characteristic of head trauma, when administered before insult. In addition, recent evidence from football athletes indicates a potential neuroprotective effect of DHA as measured by a surrogate marker of head trauma.

The Omega-3 Index, the sum of EPA and DHA levels in erythrocyte membranes, expressed as a percentage of total erythrocyte FA, reflects EPA and DHA intake and status in other tissues. This measure could provide unique insight into the ω-3 FA status of potential at-risk populations, such as football athletes. To date, no authors have examined the Omega-3 Index of National Collegiate Athletic Association (NCAA) football players, a population at risk for both CVD and neurologic damage secondary to repetitive head injuries. Therefore, we took an exploratory approach to examining the ω-3 FA status as measured by the Omega-3 Index among a cohort of NCAA football athletes. Also, given that the FA intake is related to erythrocyte FAs, we also obtained a complete FA profile.

METHODS

Data Collection

A retrospective, cross-sectional investigation was conducted to assess Omega-3 status among NCAA Division I football athletes. Given the noninvasive, retrospective nature of the study and the minimal risk posed to privacy, the institutional review board approved the study and granted a full waiver of consent. Four geographically distinct Division I football programs that independently included the Omega-3 Index as part of standard-of-care athlete health and wellness monitoring were identified. From those deidentified data, a complete erythrocyte FA profile (conducted by the same independent commercial laboratory), age at the time of testing, height, weight, and ethnicity from the 2017–2018 season were collected from 404 athletes.

The Erythrocyte FA Analyses

The erythrocyte FA analyses were conducted by OmegaQuant Analytics, LLC (Sioux Falls, SD), a Clinical Laboratory Improvement Amendments–certified laboratory providing FA and Omega-3 Index testing. One drop of whole blood collected from a finger stick was placed on proprietary filter paper pretreated with an antioxidant cocktail fatty acid preservative solution and allowed to dry at room temperature for 15 minutes. After arrival at the laboratory, a punch from the dried blood spot card was transferred to a screw-cap glass vial and a mixture of methanol (containing 14% boron trifluoride) and toluene (35:30:35 v/v/v; Sigma-Aldrich, St Louis, MO) was added to the vial. The vial was briefly vortexed and heated in a hot bath at 100°C for 45 minutes. After cooling, hexane (EMD Chemicals, Philadelphia, PA) and high-pressure liquid chromatography-grade water were added and the tubes were recapped, vortexed briefly, and centrifuged to separate the layers. An aliquot of the hexane layer was transferred to a gas chromatography vial. Gas chromatography was carried out using a model GC-2010 Gas Chromatograph (Shimadzu Corporation, Columbia, MD) equipped with an SP-2560, 100-m fused silica capillary column (0.25-mm internal diameter, 0.2-μm film thickness; Supelco, Bellefonte, PA).

Fatty acids were identified by comparison with a standard mixture of fatty acids characteristic of erythrocytes (model GLC OQ-A; NuCheck Prep, Elysian, MN), which was also used to construct individual fatty acid calibration curves. For each test, the following 24 fatty acids (by class) were identified: saturated (14:0, 16:0, 18:0, 20:0, 22:0, 24:0); cis mono-unsaturated (16:1, 18:1, 20:1, 24:1); trans (16:1, 18:1, 18:2); cis n-6 polyunsaturated (18:2, 18:3, 20:2, 20:3, 20:4, 22:4, 22:5); and cis n-3 polyunsaturated (18:3, 20:5, 22:5, 22:6). The coefficients of variation for all the fatty acids measured were <6%. The Omega-3 Index was defined as red blood cell EPA + DHA, which was derived from the dried blood spot EPA + DHA value by a regression equation ($r = 0.97$). The coefficient of variation for this metric was <5%.

Statistical Analysis

We categorized athletes based on the proposed Omega-3 Index risk zones for CVD: high risk, <4%; intermediate risk, 4% to 8%; and low risk, >8%. Means and standard deviations were computed.

RESULTS

Demographics are presented in Table 1. The mean Omega-3 Index among all athletes was 4.4% ± 0.8%. In other words, EPA + DHA accounted for <5% of all the FAs present. Results from the erythrocyte FA analysis are reported in Table 2. The Figure provides a histogram of the players’ Omega-3 Indexes. A total of 34% (n = 138) had an Omega-3 Index of <4%, or high risk, whereas 66% (n = 266) were stratified into the intermediate-risk category. No participants had an Omega-3 Index associated with low risk. Only 1 participant had an Omega-3 Index of 8, just below the cutoff for low risk.

DISCUSSION

We measured the ω-3 FA status, specifically EPA and DHA, as well as the FA profile of a large cohort of NCAA football athletes. To our knowledge, this is the first investigation of the ω-3 FA status of a representative group of NCAA football athletes. Our main finding was that
Table 2. Erythrocyte Fatty Acid Composition in Athletes as a Percentage of Total Fatty Acids Analyzed

| Fatty Acid | Percentage, Mean ± SD |
|------------|-----------------------|
| C14:0      | 0.73 ± 0.40           |
| C16:0      | 21.84 ± 9.09          |
| C16:1n7t   | 0.14 ± 0.06           |
| C16:1n7    | 0.61 ± 0.33           |
| C18:0      | 12.49 ± 4.46          |
| C18:1t     | 0.55 ± 0.17           |
| C18:1n9    | 18.16 ± 2.47          |
| C18:2n6t   | 0.25 ± 0.07           |
| C18:2n6    | 22.81 ± 2.40          |
| C20:0      | 0.26 ± 0.06           |
| C20:3n6    | 0.30 ± 0.11           |
| C20:1n9    | 0.26 ± 0.13           |
| C20:3n3    | 0.42 ± 0.19           |
| C20:2n6    | 0.26 ± 0.05           |
| C22:0      | 0.80 ± 0.20           |
| C22:3n6    | 1.54 ± 0.30           |
| C22:4n6    | 11.43 ± 1.79          |
| C24:0      | 0.95 ± 0.33           |
| C20:5n3    | 0.38 ± 0.13           |
| C24:1n9    | 0.74 ± 0.28           |
| C22:4n6    | 1.84 ± 0.39           |
| C22:5n6    | 0.54 ± 0.15           |
| C22:5n3    | 1.13 ± 0.20           |
| C22:6n3    | 2.30 ± 0.60           |

none of the football athletes had an Omega-3 Index above the targeted value for a reduction in CVD risk (8%).

Though most health concerns are common to the majority of the population, football athletes have unique concerns because of sport participation. For example, although increased body mass is associated with increased playing time and greater rates of pay, evidence suggests that the increase in size observed, particularly over the last several decades, has direct implications for player health. In addition to high rates of obesity, a large percentage of football athletes are either prehypertensive or hypertensive and present with dyslipidemia factors that increase the risk of CVD. Diets high in o3 FA reduce blood pressure and circulating triglycerides. The Omega-3 Index was proposed as a clinical stratification system that provides information regarding the CVD risk, and researchers recently confirmed that an Omega-3 Index <4% constituted high risk and >8%, low risk, for the development of fatal CVD. These data suggest that, at least in the current cohort of football athletes, another risk factor for CVD was present.

Football athletes are also at an increased risk of head trauma, which, even in the absence of a clinically discernible injury, results in quantifiable pathophysiological changes. Indeed, a lifetime of head trauma associated with participation in sport may lead to long-term neurologic consequences. A unique pathologic consequence of traumatic brain injury (TBI) in animal models is a reduction in neuronal DHA after injury, and deficient brain DHA content in animal models, as induced by dietary restriction, heightens the pathophysiologic response to injury. This may at least partially explain why animal models of TBI clearly demonstrated that prophylactic o3 FA supplementation attenuated the pathophysiologic response. Two clinical case studies of human patients with severe head trauma showed a potential benefit of o3 FA supplementation, and a single clinical trial conducted in humans identified a potential neuroprotective effect of DHA supplementation in football athletes.

The neuroprotective effects of supplemental DHA observed in rodent models of TBI demonstrated the greatest efficacy when administered at a dose of 40 mg·kg⁻¹·d⁻¹, which corresponds to a dose of approximately 4 g·kg⁻¹·d⁻¹ in today’s collegiate football athlete. This is higher than has been reported. Artzburn et al described a dose-dependent relationship in which plasma DHA increased up to a dosage of approximately 2 g·d⁻¹. Above that dose, only incremental increases were observed as saturation was approached. A dose-response effect was noted in the only clinical trial in which doses of 2, 4, and 6 g·d⁻¹ were provided to collegiate football athletes. The substantial increases observed with the 4 and 6 g·d⁻¹ doses led those authors to suggest that higher doses may be necessary, as no apparent plateau was observed. Given the larger size of football athletes compared with the general population and other athletes and the fact that physical activity is known to affect fatty acid composition, the finding was not necessarily surprising. However, further examination of those data suggested that the low-dose treatment group actually experienced the greatest attenuation in head trauma. Human trials are lacking, but an inherent limitation in the study of head trauma in humans is the heterogeneity of injury. The risks of increasing DHA intake are virtually nonexistent.

Further, considering the low incidence of proper concussion reporting and the presence of a pathophysiologic response even in the absence of a concussion, increasing intake should be strongly considered, particularly given our findings.

The fact that the football athletes in the current study had Omega-3 indexes below the desirable range was not necessarily surprising. Using a similar method and...
reported that Atherosclerosis Am J Clin Nutr and the potential benefits appear to PloS One Clin Sports Med Lipids Health Dis x J Neurotrauma 1 Number 1 Volume 54 /C15 In the United States, the estimated combined intake of d Restor. January 2019. Am J Cardiol. ACKNOWLEDGMENTS This study was partially funded by the Brain Armor Foundation. REFERENCES 1. Arterburn LM, Hall EB, Oken H. Distribution, interconversion, and dose response of n-3 fatty acids in humans. Am J Clin Nutr 2006;83(suppl 6):1467S–1476S. 2. Burdge GC, Jones AE, Wootton SA. Eicosapentaenoic and docosapentaenoic acids are the principal products of alpha-linolenic acid metabolism in young men. Br J Nutr. 2002;88(4):355–364. 3. Stark KD, Van Elswyk ME, Higginson MR, Weatherford CA, Salem N Jr. 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. 4. Kim JH, Zafonte R, Pascale-Leon A, et al. American-style football and cardiovascular health. J Am Heart Assoc. 2018;7(8):e008620. 5. Harris WS, Del Gobbo L, Tintle NL. The Omega-3 Index and relative risk for coronary heart disease mortality: estimation from 10 cohort studies. Atherosclerosis. 2017;262:51–54. 6. Abdelhamid AS, Martin N, Bridges C, et al. Polyunsaturated fatty acids for the primary and secondary prevention of cardiovascular disease. Cochrane Database Syst Rev. 2018;7:CD012345. 7. Daneshvar DH, Nowinski CJ, McKee AC, Cantu RC. The epidemiology of sport-related concussion. Clin Sports Med. 2011;30(1):1–17. 8. Smith DH, Meaney DF. Axonal damage in traumatic brain injury. Neuroscientist. 2000;6(6):483–495. 9. Bailes JE, Mills JD. Docosahexaenoic acid reduces traumatic axonal injury in a rodent head injury model. J Neurotrauma. 2010;27(9):1617–1624. 10. Schober ME, Requena DF, Abdullah OM, et al. Dietary docosahexaenoic acid improves cognitive function, tissue sparing, and magnetic resonance imaging indices of edema and white matter injury in the immature rat after traumatic brain injury. J Neurotrauma. 2015;33(4):390–402. 11. Oliver JM, Anzalone AJ, Turner SM. Protection before impact: the potential neuroprotective role of nutritional supplementation in sports-related head trauma. Sports Med. 2018;48(suppl 1):39–52. 12. Oliver JM, Jones MT, Kirk KM, et al. Effect of docosahexaenoic acid on a biomarker of head trauma in American football. Med Sci Sports Exerc. 2016;48(6):974–982. 13. Fenton JI, Gurzella EA, Davidson EA, Harris WS. Red blood cell PUFAs reflect the phospholipid PUFAs composition of major organs. Prostaglandins Leukot Essent Fatty Acids. 2016;112:12–23. 14. Metcalfe RG, Cleland LG, Gibson RA, et al. Relation between blood and atrial fatty acids in patients undergoing cardiac bypass surgery. Am J Clin Nutr. 2010;91(3):528–534. 15. Norton K, Olds T. Morphological evolution of athletes over the 20th century: causes and consequences. Sports Med. 2001;31(11):763–783. 16. Harp JB, Hecht L. Obesity in the National Football League. JAMA. 2005;293(9):1058–1062. 17. Crouse SF, White S, Erwin JP, et al. Echocardiographic and blood pressure characteristics of first-year collegiate American-style football players. Am J Cardiol. 2016;117(1):131–134. 18. Buell JL, Calland D, Hanks F, et al. Presence of metabolic syndrome in football linemen. J Athl Train. 2008;43(6):608–616. 19. Miller PE, Van Elswyk M, Alexander DD. Long-chain omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid and blood pressure: a meta-analysis of randomized controlled trials. Am J Hypertens. 2014;27(7):885–896. 20. Leslie MA, Cohen DJ, Liddle DM, Robinson LE, Ma DW. A review of the effect of omega-3 polyunsaturated fatty acids on blood triacylglycerol levels in normolipidemic and borderline hyperlipidemic individuals. Lipids Health Dis. 2015;14:53. 21. Harris WS. The omega-3 index as a risk factor for coronary heart disease. Am J Clin Nutr. 2008;87(6):1978S–2002S. 22. Oliver JM, Anzalone AJ, Stone JD, et al. Fluctuations in blood biomarkers of head trauma in NCAA football athletes over the course of a season [published online ahead of print May 29, 2018]. J Neurosurg. doi:10.3171/2017.12JNS172035. 23. Montenegro PH, Alosco ML, Martin BM, et al. Cumulative head impact exposure predicts later-life depression, apathy, executive dysfunction, and cognitive impairment in former high school and college football players. J Neurotrauma. 2017;34(2):328–340. 24. Wu A, Ying Z, Gomez-Pinilla F. Exercise facilitates the action of dietary DHA on functional recovery after brain trauma. Neurosci. 2013;248:655–663. 25. Desai A, Kevala K, Kim HY. Depletion of brain docosahexaenoic acid impairs recovery from traumatic brain injury. PloS One. 2014;9(1):e86472. 26. Wang T, Van KC, Gavitt BJ, et al. Effect of fish oil supplementation in a rat model of multiple mild traumatic brain injuries. Restor Neurol Neurosci. 2013;31(5):647–659.
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