The Ratio of Serum Eicosapentaenoic Acid to Arachidonic Acid Is Associated With Renal Impairment and Diabetic Macroangiopathies in Elderly Patients With Type 2 Diabetes

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A low ratio of serum eicosapentaenoic acid to arachidonic acid (EPA/AA) has been reported to correlate with coronary heart disease (1–3), and no previous studies have investigated serum polyunsaturated fatty acid (PUFA) levels exclusively in patients with diabetes, in whom atherosclerotic diseases are commonly found. We therefore examined the association between serum EPA/AA ratio and the prevalence of diabetic angiopathies in patients with type 2 diabetes.

The serum levels of EPA and AA were determined in 744 Japanese patients with type 2 diabetes (aged 67 ± 12 years, 60% males, duration of diabetes 13 ± 11 years, estimated glomerular filtration rate [eGFR] 78 ± 32 mL/min/1.73 m^2, serum EPA 79.6 ± 52.6 μg/mL, serum AA 189.5 ± 55.0 μg/mL) and in 285 age- and sex-matched subjects without diabetes between October and December 2012. Individuals taking EPA capsules were excluded from the study.

The serum EPA/AA ratio was not significantly different between the diabetic (mean ± SD 0.45 ± 0.31, median 0.37) and nondiabetic (0.48 ± 0.31, 0.39) groups. The EPA/AA ratio correlated significantly with age in both the diabetic ($r = 0.25$, $P < 0.01$) and the nondiabetic ($r = 0.26$, $P < 0.01$) groups. A logistic regression analysis demonstrated that a lower EPA/AA ratio was associated with an eGFR <60 mL/min/1.73 m^2 (odds ratio 0.43 [95% CI 0.19–0.92], $P = 0.04$), coronary heart disease (0.43 [0.20–0.88], $P = 0.03$), and peripheral arterial disease (0.17 [0.03–0.70], $P = 0.03$) in diabetic patients when the EPA/AA ratio and known risk factors such as age, sex, smoking history, BMI, hypertension, and dyslipidemia were used as independent variables. Although the EPA/AA ratio was not significantly different between subjects with an eGFR ≥60 mL/min/1.73 m^2 and those with an eGFR <60 mL/min/1.73 m^2 among the total sample, the EPA/AA ratio was significantly lower in subjects with an eGFR <60 mL/min/1.73 m^2 (0.45 ± 0.25) than in those with an eGFR ≥60 mL/min/1.73 m^2 (0.56 ± 0.38) in the subgroup aged ≥75 years (Fig. 1*A*). The EPA/AA ratio was also significantly lower in subjects with coronary heart disease (0.44 ± 0.23) than in those without (0.57 ± 0.38) in the subgroup aged ≥75 years (Fig. 1*B*).

Several studies have demonstrated that the consumption of fish oil containing n-3 PUFAs reduces the risk of cardiovascular events and mortality (4,5). We found that a lower serum EPA/AA ratio is associated with coronary heart disease and renal impairment in the older patients with diabetes. Earlier intervention with EPA might be desirable in younger diabetic patients with lower EPA/AA levels if the administration of EPA is effective for preventing vascular events. Because the EPA/AA ratio was positively associated with age, it might be necessary to make separate reference values for different age-groups.

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References

1. Itakura H, Yokoyama M, Matsuzaki M, et al.; JELIS Investigators. Relationships between plasma fatty acid composition and coronary artery disease. J Atheroscler Thromb 2011; 18:99–107
2. Domei T, Yokoi H, Kuramitsu S, et al. Ratio of serum n-3 to n-6 polyunsaturated fatty acids and the incidence of major adverse cardiac events in patients undergoing percutaneous

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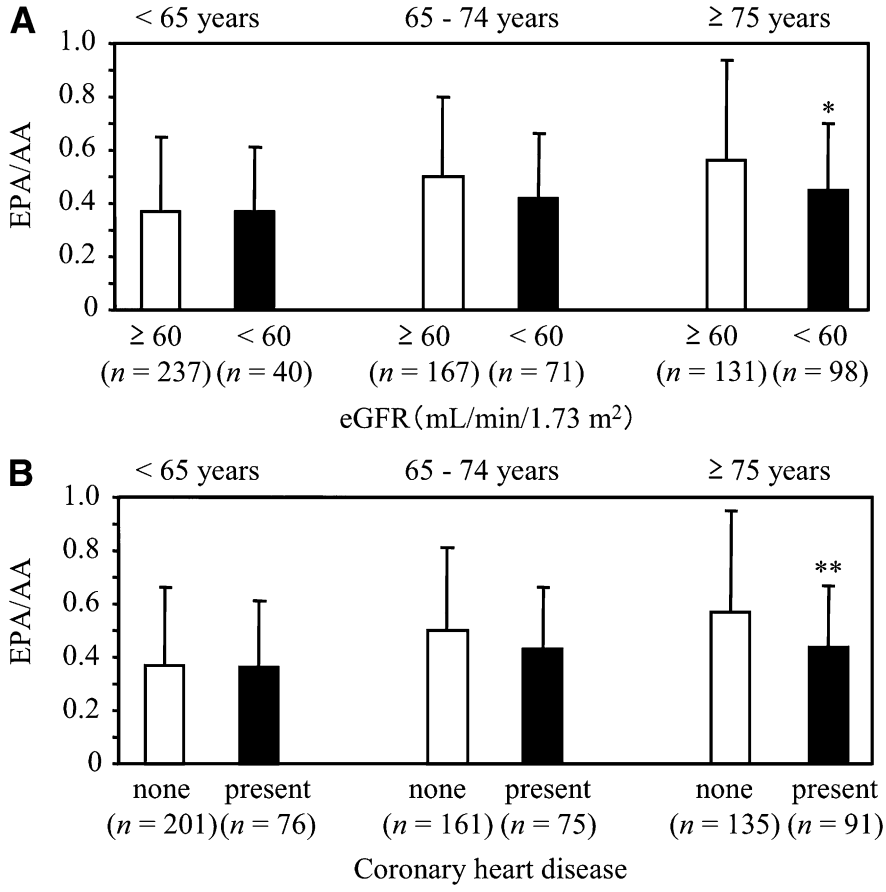

Figure 1—Serum EPA/AA ratios between diabetic subjects with an eGFR ≥60 mL/min/1.73 m^2 and those with an eGFR <60 mL/min/1.73 m^2 among age-groups (*A*) and between diabetic subjects with and without coronary heart disease among age-groups (*B*). *$P = 0.04$ vs. subjects with an eGFR ≥60 mL/min/1.73 m^2, **$P < 0.01$ vs. subjects without coronary heart disease (Wilcoxon signed rank test).

coronary intervention. Circ J 2012;76:423–429

3. Hayakawa S, Yoshikawa D, Ishii H, et al. Association of plasma ω-3 to ω-6 polyunsaturated fatty acid ratio with complexity of coronary artery lesion. Intern Med 2012;51:1009–1014
4. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Lancet 1999;354:447–455
5. Iso H, Kobayashi M, Ishihara J, et al.; JPHC Study Group. Intake of fish and n3 fatty acids and risk of coronary heart disease among Japanese: the Japan Public Health Center-Based (JPHC) Study Cohort I. Circulation 2006;113:195–202