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Circulating Omega-3 Fatty Acids and Incident Adverse Events in Patients With Acute Myocardial Infarction

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ABSTRACT

BACKGROUND Dietary omega-3 eicosapentaenoic acid (EPA) has multiple cardioprotective properties. The proportion of EPA in serum phosphatidylcholine (PC) mirrors dietary EPA intake during previous weeks. Circulating EPA in ST-segment elevation myocardial infarction (STEMI) relates to smaller infarct size and preserved long-term ventricular function.

OBJECTIVES The authors investigated whether serum-PC EPA (proxy for marine omega-3 consumption) levels at the time of STEMI were associated with a lower incidence of major adverse cardiovascular events (MACE), all-cause mortality, and readmission for cardiovascular (CV) causes at 3 years' follow-up. We also explored the association of alpha-linolenic acid (ALA, proxy for vegetable omega-3 intake) with all-cause mortality and MACE.

METHODS The authors prospectively included 944 consecutive patients with STEMI (mean age 61 years, 209 women) undergoing primary percutaneous coronary intervention. We determined serum-PC fatty acids with gas chromatography.

RESULTS During follow-up, 211 patients had MACE, 108 died, and 130 were readmitted for CV causes. A Cox proportional hazards model adjusted for known clinical predictors showed that serum-PC EPA at the time of STEMI was inversely associated with both incident MACE and CV readmission (hazard ratio [HR]: 0.76; 95% confidence interval [CI]: 0.62 to 0.94, and HR: 0.74; 95% CI: 0.58 to 0.95, respectively, for a 1-standard deviation [SD] increase). Serum-PC ALA was inversely related to all-cause mortality (HR: 0.65; 95% CI: 0.44 to 0.96, for a 1-SD increase).

CONCLUSIONS Elevated serum-PC EPA and ALA levels at the time of STEMI were associated with a lower risk of clinical adverse events. Consumption of foods rich in these fatty acids might improve the prognosis of STEMI.

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ABBREVIATIONS AND ACRONYMS

AA = arachidonic acid

ALA = alpha-linolenic acid

CAD = coronary artery disease

CI = confidence interval

EPA = eicosapentaenoic acid

HR = hazard ratio

MACE = major adverse cardiovascular events

MI = myocardial infarction

PC = phosphatidylcholine

PPCI = primary percutaneous coronary intervention

SD = standard deviation

STEMI = ST-segment-elevation myocardial infarction

Coronary artery disease (CAD) is the leading cause of mortality worldwide (1). Advances in prompt reperfusion methods have reduced the acute mortality associated with myocardial infarction (MI); however, secondary cardiovascular (CV) events continue to pose a significant burden beyond the acute-care time period for MI survivors (2). Therefore, developing strategies to improve the prognosis after an MI is a major issue in clinical and public health settings.

Diets high in seafood have been strongly associated with a lower risk of fatal CV events, particularly sudden cardiac death (3). Fatty fish is the main source of omega-3 eicosapentaenoic acid (C20:5n-3, EPA). Dietary EPA is readily incorporated into the phospholipids of cardiomyocyte membranes, where it partially displaces omega-6 arachidonic acid (C20:4n-6, AA) (4). Membrane accretion of EPA is believed to underlie most salutary cardiac effects associated with long-term consumption of fatty fish and fish oils (5). In addition to promoting more efficient myocardial oxygen consumption, membrane EPA protects against a variety of heart stressors. Of note, cardiac ischemia triggers fatty acid cleavage from cardiomyocyte membranes; these fatty acids can be converted to lipid mediators by cyclooxygenase, lipoxygenase, and cytochrome P450. Released AA mostly generates proinflammatory eicosanoids that amplify ischemic myocardial damage. In contrast, cleaved EPA is converted to anti-inflammatory eicosanoids (6). This observation gave rise to the notion that EPA enrichment in cardiac membranes, due to sustained consumption of fatty fish or fish oils, might limit the degree of myocardial damage in the event of an MI, which has been repeatedly confirmed in animal models (7–10). Two small-sized clinical reports in MI survivors showed an inverse association between blood EPA levels, which mirrors previous dietary EPA intake (11), and infarct size on cardiac magnetic resonance imaging (12) and CV events (13).

We hypothesized that regular consumers of fatty fish would have a better long-term prognosis after a ST-segment elevation MI (STEMI) than nonconsumers. Accordingly, the present study aimed to bridge this gap by testing associations between the EPA in serum phosphatidylcholine (PC) at hospital admission and the occurrences of major adverse CV events (MACE), all-cause mortality, and CV-related hospital readmission at 3 years' follow-up in a large cohort of patients treated for STEMI. In addition, given that alpha-linolenic acid (C18:3n-3, ALA, the vegetable omega-3) was found to be inversely associated with all-cause mortality in high vascular risk individuals (14), we also examined the predictive value (incident all-cause mortality and MACE) of the serum-PC status of ALA in STEMI.

SEE PAGE 2098

METHODS

STUDY DESIGN AND POPULATION. This prospective observational study included 955 consecutive patients with STEMI who were admitted to a tertiary university center within a primary percutaneous coronary intervention (PPCI) network between February 23, 2011, and June 30, 2016. The hospital served a population of approximately 850,000 inhabitants, mainly distributed among 4 urban areas, located 2, 7, 20, or 45 km from the PPCI-capable unit. The STEMI diagnosis was established according to the current universal definition of MI at the time of the study (15), which included chest pain and the electrocardiogram showing ST-segment elevation in 2 or more contiguous leads (a minimum of 0.1 mV in the frontal leads and 0.2 mV in the precordial leads) or with new-onset left bundle branch block (16). Baseline demographics and clinical data were recorded during hospital admission. The study conducted in accordance with the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee. Participants provided informed consent.

OUTCOMES. This study aimed to analyze the composite of MACE at 3 years, which was identified as all-cause mortality and readmission due to CV causes, including nonfatal MI, unstable angina, heart failure, or stroke. The secondary outcomes were 3-year all-cause mortality and CV readmissions. For patients with recurrent events, the time to the first event was recorded. Mortality was determined from patient health records and/or by directly contacting patients or relatives by phone.

LABORATORY MEASUREMENTS. Blood samples were obtained from venipuncture soon after admission and within 12 h after symptoms onset. Samples were processed in a central laboratory for biomarker measurements. Serum was stored at −80°C until we performed a fatty acid analysis.

Fatty acid methyl-esters were extracted from serum-PC as described previously (17). Different types were separated with gas chromatography on an Agilent HP 7890 Gas Chromatograph equipped with a 30 m × 0.25 μm × 0.25 mm SupraWAX-280 capillary column (Teknokroma, Barcelona, Spain), an autosampler, and flame ionization detection. The amount

of each fatty acid is expressed as a percentage of the total amount of fatty acids.

STATISTICAL ANALYSES. Categorical variables are expressed as a number (percentage); continuous variables are expressed as the median (interquartile range). Comparisons of categorical variables were performed with the chi-square test. Comparisons of continuous variables were performed with the Wilcoxon rank sum test.

Associations of serum-PC EPA with clinical outcomes were determined using Cox proportional hazard regression modeling. For each outcome, in addition to the univariate model (model 1) we created a second model (model 2), adjusting for variables that were significantly associated with the primary outcome with a $p < 0.05$ in the univariate analysis or constituted confounding factors. Those variables were age, sex, history of arterial hypertension, diabetes, cerebrovascular disease, heart failure and MI, hemoglobin, estimated glomerular filtration rate, triglycerides, total cholesterol, Killip-Kimball Class III to IV and left ventricular ejection fraction. For analyses concerning mortality (all-cause mortality, and MACE) we created an additional model including reciprocal adjustment for EPA, ALA, and AA (model 3). Hazard ratios (HRs) reflecting a 1-standard deviation (SD) change in a given fatty acid and the 95% confidence intervals (CIs) are reported. The satisfaction of the proportional hazards assumption of Cox regression models was confirmed by assessing Schoenfeld residuals. The same analyses were repeated only considering first-STEMI patients ($n = 859$). Finally, survival curves were generated from the full model using tertiles of EPA and ALA, adjusting for the variables previously listed. Differences were considered statistically significant at $p < 0.05$. All analyses were performed with STATA version 13.0 (StataCorp, College Station, Texas).

RESULTS

Of 955 consecutive patients enrolled, 944 (98.8%) had available samples and were included in the final analysis. **Table 1** summarizes the baseline demographics, clinical characteristics, and laboratory measurements of the study population by the incident MACE. The median age was 61 years (interquartile range:, 52 to 72 years) and 209 patients (22.1%) were women. **Table 2** displays the clinical endpoints documented over the follow-up. The baseline characteristics of the study population categorized by all-cause mortality and hospital readmission due to CV cause are shown in Supplemental Tables 1 and 2, respectively. The distribution of the serum-PC proportion of EPA and ALA (and the cutoffs to create their respective tertiles) is depicted in Supplemental Figure 1. Serum-PC EPA and ALA average proportions were 0.58 ± 0.46 and 0.25 ± 0.22, respectively.

Table 3 shows the HRs for the risk of incident endpoints associated with EPA, both in unadjusted and adjusted models. The unadjusted model (model 1) showed that each 1-SD increase in the proportion of serum-PC EPA was related to a borderline significant 16% reduction in the incident MACE risk ($p = 0.053$) and a significant 20% reduction in the CV readmission risk ($p = 0.038$). The inclusion of confounders (model 2) showed that the proportion of PC-EPA was significantly related to both incident MACE (HR: 0.76; 95% CI: 0.62 to 0.94) and CV readmission (HR: 0.74; 95% CI: 0.58 to 0.95). We also explored whether EPA associations with outcomes concerning mortality (all-cause mortality and MACE) changed after including reciprocal adjustment for EPA, ALA, and AA (model 3) (Supplemental Table 3). For both outcomes, the associations observed for EPA remained essentially unchanged. Of note, for all-cause mortality, we observed a significant 35% reduction in mortality risk for each 1-SD increase in the proportion of serum-PC ALA (HR: 0.65; 95% CI: 0.44 to 0.96) (model 3) (Supplemental Table 3).

Statistical significance remained for serum-PC EPA associations when only patients with first-STEMI were considered; borderline statistical significance was observed for serum-PC ALA and mortality-related outcomes (Supplemental Table 4).

We constructed Kaplan-Meier curves (**Figure 1**) to analyze how the occurrences of selected endpoints were related to the tertiles of serum-PC EPA (**Figures 1A and 1B**) and ALA (**Figure 1C**). Compared with subjects in the lowest tertile of EPA (cutoff <0.366% of all the fatty acids in serum-PC), those in the highest EPA tertile (≥0.592% of all the fatty acids in the serum-PC) had significantly reduced risks of incident CV readmission (**Figure 1A**) and incident MACE (**Figure 1B**). When we explored ALA as exposure, subjects in the lowest ALA tertile (<0.134% of all the fatty acids in serum-PC) had a significantly increased risk of incident all-cause mortality (**Figure 1C**), compared with those in the intermediate and highest ALA tertiles.

DISCUSSION

This prospective longitudinal study with a large cohort of patients with STEMI showed that elevated proportions of serum-PC EPA (a marine omega-3) at the time of a STEMI were inversely related to the risks of incident MACE and CV-hospital readmission during follow-up. In addition, the proportion of serum-PC ALA (the vegetable omega-3) was inversely

TABLE 1 Baseline Characteristics of the Study Population by 3-Year MACEs

	All Patients (N = 944)	No MACE (n = 733)	MACE (n = 211)	p Value
Demographics				
Age, yrs	61 (52–72)	59 (51–69)	72 (59–81)	<0.001
Female	209 (22.1)	147 (20.1)	62 (29.4)	0.004
History				
Smoking	720 (76.3)	571 (77.9)	149 (70.6)	0.028
Hypertension	505 (53.5)	365 (49.8)	140 (66.4)	<0.001
Diabetes mellitus	221 (23.4)	144 (19.7)	77 (36.5)	<0.001
Dyslipidemia	542 (57.4)	415 (56.6)	127 (60.2)	0.355
Cerebrovascular disease	55 (5.8)	27 (3.7)	28 (13.3)	<0.001
Peripheral arterial disease	64 (6.8)	40 (5.5)	24 (11.4)	0.003
Heart failure	14 (1.5)	3 (0.4)	11 (5.2)	<0.001
Coronary artery disease	202 (21.4)	142 (19.4)	60 (28.4)	0.005
Myocardial infarction	85 (9.0)	58 (7.9)	27 (12.8)	0.029
PCI	76 (8.1)	49 (6.7)	27 (12.8)	0.004
CABG	9 (1.0)	5 (0.7)	4 (0.4)	0.119
Physical examination				
Killip-Kimball class III to IV	61 (6.5)	21 (2.9)	40 (19.0)	<0.001
BMI, kg/m^2	27.0 (24.7–29.9)	27.0 (24.8–29.8)	27.2 (24.2–30.0)	0.976
Anterior infarct location	393 (41.6)	299 (40.8)	94 (44.6)	0.342
Coronary angiography	935 (99.0)	732 (99.9)	203 (96.2)	<0.001
Main epicardial coronary arteries ≥70% stenosis				
0	8 (0.9)	6 (0.8)	2 (1.0)	0.821
1	485 (51.9)	399 (54.5)	86 (42.4)	0.002
2	259 (27.7)	197 (26.9)	62 (30.5)	0.307
3	183 (19.6)	130 (17.8)	53 (26.1)	0.008
Left main ≥50% stenosis	38 (4.1)	22 (3.0)	16 (7.9)	0.002
Successful primary PCI	881 (93.3)	697 (95.1)	184 (87.2)	<0.001
Symptom onset-to-balloon, min	183 (127–288)	176 (123–270)	224 (144–347)	<0.001
Laboratory results				
Hemoglobin, g/dl	13.2 (12–14.3)	13.3 (12.2–14.4)	12.7 (11.1–14.0)	<0.001
eGFR, ml/min/1.73 m^2	83.7 (60.3–107.6)	87.8 (68.6–110.9)	60.1 (43.5–90.3)	<0.001
Total cholesterol, mg/dl	174 (151–203)	178 (154–205)	166 (139–189)	<0.001
Triglycerides, mg/dl	116 (87–158)	119 (90–161)	103 (77–136)	<0.001
CK-MB peak, ng/ml	169.4 (69.7–335.0)	166.9 (69.5–282.8)	180.2 (69.7–475.8)	<0.017
LVEF, %	53 (45–59)	54 (47–59)	48 (40–55)	<0.001
In-hospital mortality	45 (4.8)	0	45 (21.3)	<0.001
Fatty acids in serum phosphatidylcholine, % of total identified fatty acids				
C20:5n-3	0.47 (0.32–0.68)	0.47 (0.33–0.70)	0.43 (0.29–0.63)	0.123
C20:4n-6	8.45 (5.97–10.72)	8.61 (6.08–10.77)	8.10 (5.89–10.34)	0.081
C18:3n-3	0.19 (0.12–0.34)	0.18 (0.11–0.33)	0.21 (0.13–0.36)	0.029

Values are median (interquartile range) or n (%). The p values were obtained by the chi-square test (categorical variables) or the Wilcoxon rank sum test (continuous variables).

BMI = body mass index; CABG = coronary artery bypass grafting; CK-MB = creatine kinase-MB; eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; MACE = major adverse cardiovascular events; PCI = percutaneous coronary intervention.

related to all-cause mortality. Therefore, dietary ALA and EPA appeared to be partners, rather than competitors, in improving the long-term prognosis of a STEMI. These findings support the notion that regular consumption of foods rich in these fatty acids could serve as a preventive strategy for individuals at risk of STEMI (**Central Illustration**).

Two aspects of our results merit highlighting. First, at a mechanistic level, consistent with previous studies, our findings confirmed the notion that phospholipid enrichment in omega-3 fatty acids, which results from sustained consumption of parent foods, might be beneficial in the event of an MI, by improving the long-term vital and functional CV prognosis. This result strengthened the hypothesis that several dietary omega-3 fatty acids have a preconditioning-like effect on the heart. Second, at a nutritional level, we also explored ALA, the vegetable

omega-3, as a fatty acid of interest. Previous studies have largely investigated the role of omega-3 fatty acids supplied by fatty fish and fish oils on cardioprotection. In contrast, to date, clinical research on ALA has received much less attention. This is a relevant point, given the low customary fish consumption in most Western societies and the unsustainability of fishing.

EPA, A MARINE OMEGA 3, AND OUTCOMES. Our results on EPA were consistent with a previous study on the topic, conducted in Japanese patients with MI who underwent PPCI. That study showed that the proportion of EPA in total serum fatty acids at hospital admission was inversely associated with the long-term incidence of MACE (13). A similar result was observed, although it did not reach statistical significance ($p = 0.079$), in Japanese patients who underwent an elective PPCI due to angina pectoris (18). In contrast to those studies, we analyzed serum phospholipids instead of total serum. Our approach was based on 2 observations. First, compared with total serum (or plasma), serum phospholipids more accurately reflect the long-term intake of both essential polyunsaturated fatty acids (C18:2n-6 [linoleic acid] and ALA) and polyunsaturated fatty acids that are endogenously synthesized at a low rate (i.e., EPA). In contrast, total serum (or plasma) is an effective short-term marker of polyunsaturated fatty acid status (11). In addition, the proportion of EPA in plasma phospholipids is a suitable biomarker of long-term seafood intake (19). This explains why plasma phospholipids have been repeatedly used in large epidemiologic studies that evaluated omega-3 fatty acid effects on CV health, such as the Cardiovascular Health Study (20), the Atherosclerosis Risk In Communities Study (21), and the Multi-Ethnic Study of Atherosclerosis (22). Second, we used circulating EPA as a surrogate marker of EPA status in cardiomyocyte membranes, which is virtually all in phospholipids. Therefore, in the absence of available red blood cells (the best circulating surrogate marker [23]), when only plasma is available, it would be preferable to determine fatty acid levels in the phospholipid fractions, rather than whole plasma, to achieve a better assessment of tissue fatty acid composition.

The notion that circulating EPA might relate to a better prognosis after MI has only been investigated in populations from Japan and Spain, 2 countries with paradoxical low rates of fatal CAD (24), despite the high prevalence of CV risk factors (25,26). The lower-than-predicted fatal CAD rates in these countries might be attributable, in part, to regional dietary factors. This hypothesis was supported by the fact that Japanese immigrants to the United States showed increased CAD mortality after adopting local dietary habits (27). A common characteristic of both the Japanese and Spanish diets that might partly explain this paradox is the high dietary intake of EPA (28). This observation provided evidence that consumption of seafood, a simple and easy to implement lifestyle modification, might help reduce the increasing burden of post-STEMI management (29).

TABLE 2 Clinical Endpoints After 3-Year Follow-Up

All-cause mortality	108 (11.4)
CV readmission	130 (13.8)
Myocardial infarction	32/130 (24.6)
Angina	45/130 (34.6)
Heart failure	43/130 (33.1)
Stroke	10/130 (7.7)
MACE	211 (22.4)

Values are n/N (%).
CV = cardiovascular; MACE = major adverse cardiovascular events.

ALA, THE VEGETABLE OMEGA-3, AND OUTCOMES. In addition to fish-derived EPA, we also uncovered a beneficial effect of ALA, an inexpensive omega-3 fatty acid that is readily available in plant sources, mainly flaxseed, walnuts, soy products, and canola oil. In contrast to its longer-chain marine omega-3 counterpart, no observational studies have related ALA to the prognosis of STEMI survivors. However, a meta-analysis conducted in 19 cohort studies reported that ALA in plasma phospholipids was inversely associated with fatal CAD (relative risk [RR]: 0.85; 95% CI: 0.74 to 0.97) (30). However, because most cohorts were from the United States, a country

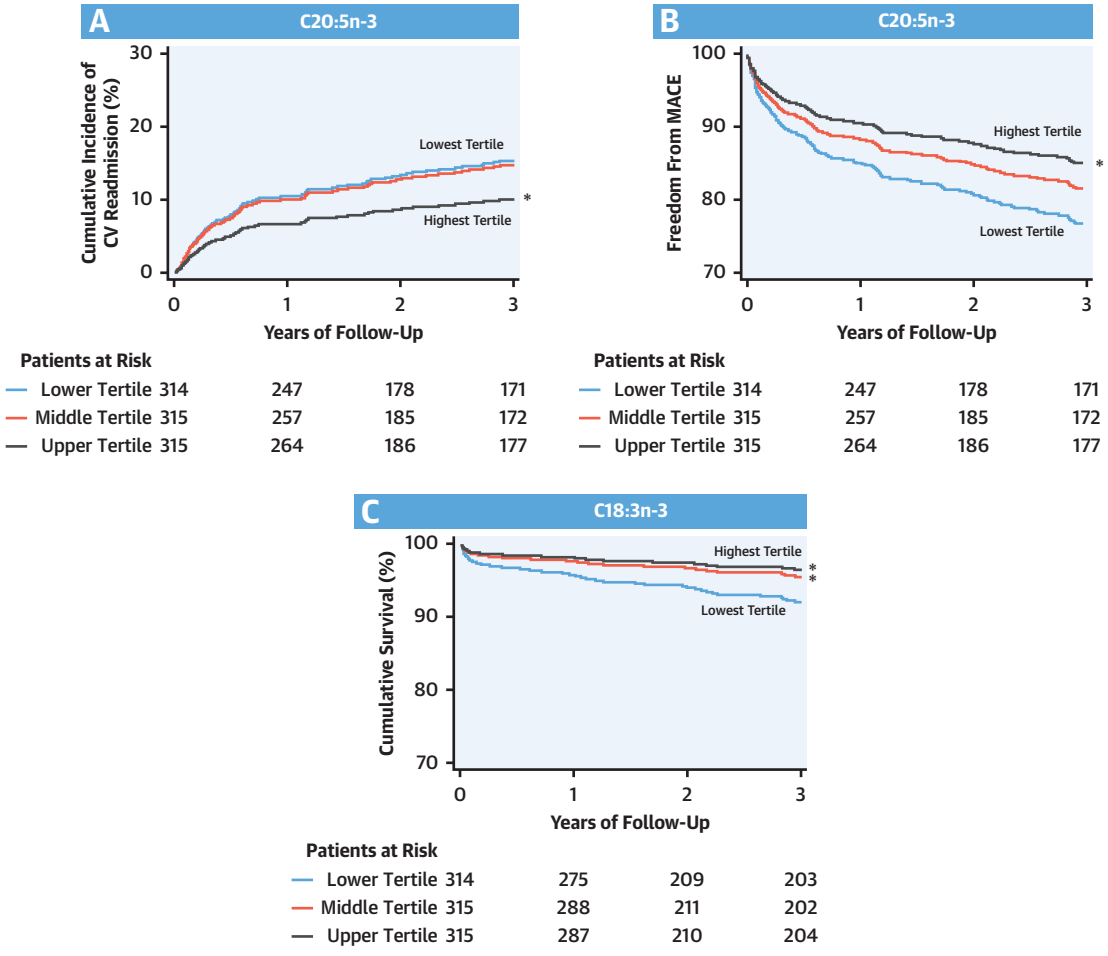
TABLE 3 HRs for Selected Serum-PC Omega-3 Fatty Acids on Clinical Endpoints

Fatty Acid	MACE (211 yes/723 no)	All-Cause Mortality (108 dead/836 alive)	CV Readmission (130 yes/814 no)
C20:5n-3 (EPA)			
Model 1	0.84 (0.71–1.00)	0.90 (0.72–1.12)	0.80 (0.65–0.99)
Model 2	0.76 (0.62–0.94)	0.88 (0.65–1.18)	0.74 (0.58–0.95)
Model 3	0.77 (0.62–0.96)	0.91 (0.68–1.22)	–
C18:3n-3 (ALA)			
Model 1	–	–	–
Model 2	–	–	–
Model 3	0.81 (0.64–1.03)	0.65 (0.44–0.96)	–

Values are HR (95% CI). All HRs reflect a 1-standard deviation change in the indicated fatty acid. Model 1, univariate Cox regression model. Model 2, multivariable Cox regression model, adjusted for age, sex, history of arterial hypertension, diabetes, cerebrovascular disease, heart failure and myocardial infarction, hemoglobin, estimated glomerular filtration rate, triglycerides, total cholesterol, Killip-Kimball Class III to IV, and left ventricular ejection fraction. For outcomes concerning mortality, we constructed a third model (Model 3), with further adjustments for C18:3n-3 and C20:4n-6.

ALA = alpha-linolenic acid; EPA = eicosapentaenoic acid; HR = hazard ratio; PC = phosphatidylcholine; other abbreviations as in Table 2.

FIGURE 1 Adjusted Kaplan-Meier Curves Showing Selected Relationships Between Tertiles of Fatty Acids at the Time of STEMI and Incident Endpoints

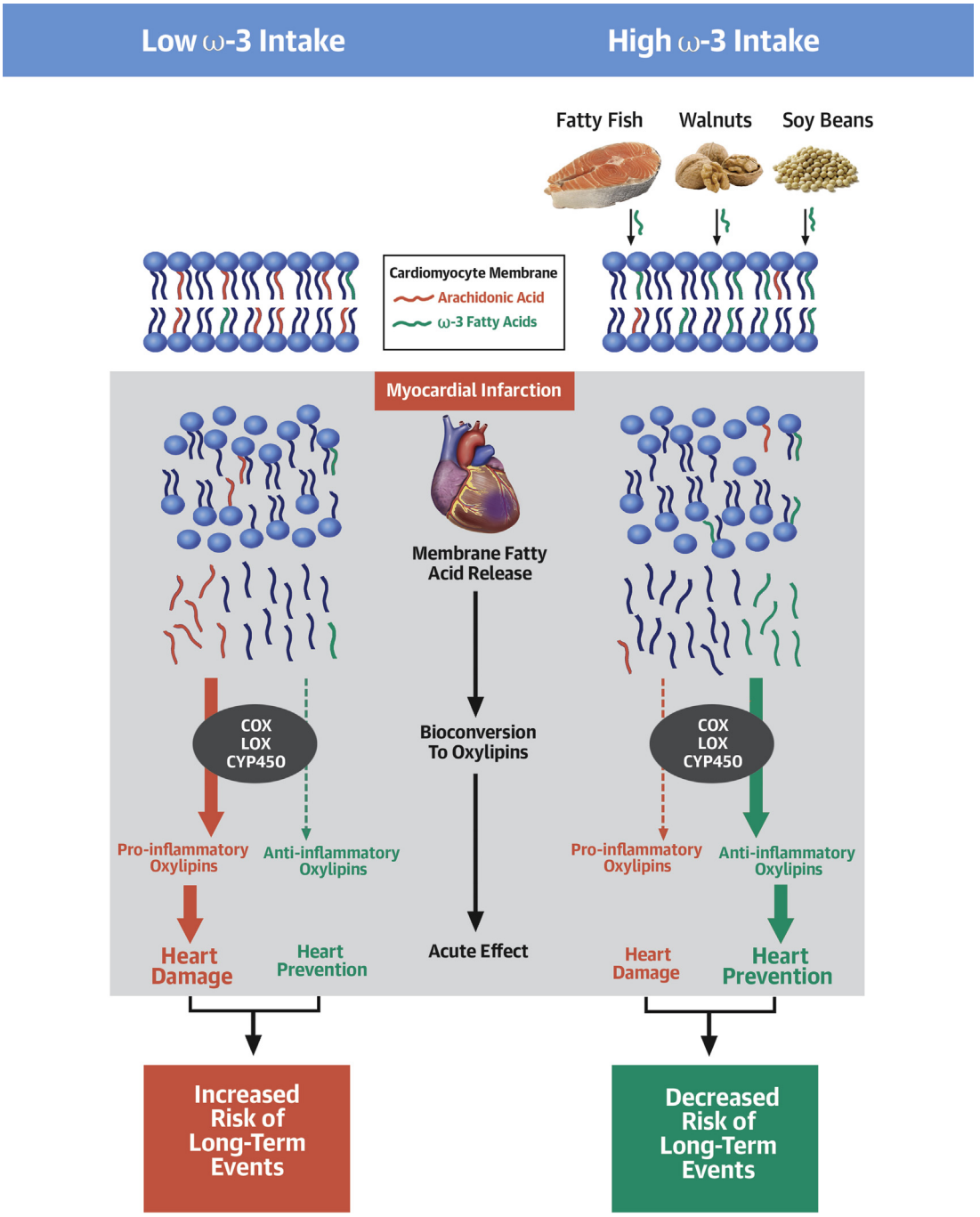


(A) Eicosapentaenoic acid (EPA) and cardiovascular (CV) hospital readmission; **(B)** EPA and major adverse cardiovascular events (MACE); **(C)** alpha-linolenic acid (ALA) and all-cause mortality. Models were adjusted for age, sex, history of arterial hypertension, diabetes, cerebrovascular disease, heart failure and myocardial infarction, hemoglobin, estimated glomerular filtration rate, triglycerides, total cholesterol, Killip-Kimball Class III to IV, and left ventricular ejection fraction. For **B and C**, models included reciprocal adjustments for the 3 fatty acids examined (EPA, ALA, and arachidonic acid). *Significantly different from the lowest tertile. STEMI = ST-segment elevation myocardial infarction.

characterized by a low fish consumption (28), the issue of whether ALA would be cardioprotective in a setting of high fish consumption remains controversial. In the present study, we found a trend for an association between ALA and a lower risk of incident MACE ($p = 0.093$) and a significant association between ALA and all-cause mortality, the only endpoint that was actually not related to EPA. Therefore, we have provided evidence that ALA might be protective, even when the background diet is high in marine omega-3 fatty acids, a notion suggested in a former paper conducted in a population at high vascular risk but free of CV disease (14). This finding reinforces that marine and vegetable omega-3 fatty acids act as partners in prevention.

STUDY STRENGTHS AND LIMITATIONS. The strengths of the present study include the precise clinical characterization of the participants, the large sample size, and the long-term follow-up. In addition, we used lipidomic-based objective biomarkers of long-term dietary fatty acid intake, which allowed us to circumvent the disadvantages of self-reported dietary data, assessed by either methods of real-time recording (i.e., food diaries) and methods of recall (i.e., food frequency questionnaires) widely used in

CENTRAL ILLUSTRATION **Suggested Cardioprotective Mechanism of Omega-3 Fatty Acids**



Lázaro, I. et al. J Am Coll Cardiol. 2020;76(18):2089-97.

When dietary intake of omega-3 is low, phospholipids of cardiomyocyte membranes contain a high proportion of omega-6 arachidonic acid. A sustained consumption of foods rich in omega-3 fatty acids (i.e., fatty fish, walnuts, or soybean products) enriches cardiomyocyte membranes with these fatty acids, partially displacing arachidonic acid. When myocardial infarction occurs, cardiac ischemia triggers fatty acid cleavage from cardiomyocyte membranes. Released fatty acids can be converted to lipid mediators (oxylipins) by the action of cyclooxygenase, lipoxygenase, and cytochrome P450. Released arachidonic acid generates proinflammatory eicosanoids that amplify ischemic myocardial damage. In contrast, cleaved omega-3 fatty acids are converted to anti-inflammatory eicosanoids, hence limiting ischemic-associated myocardial damage. This translates into a decreased risk of long-term cardiac events. ω-3, omega-3; COX, cyclooxygenase; LOX, lipoxygenase; CYP450, cytochrome P450.

nutritional epidemiology (11). Our study also had several limitations. First, it was observational in nature; therefore, we could not determine whether the consumption of dietary EPA and ALA intakes before STEMI actually improve the long-term prognosis. This issue could be established only in a randomized controlled clinical trial involving a nutritional intervention before the occurrence of the STEMI. Second, the fatty acids in serum-PC do not reflect long-term intake as accurately as the fatty acids harbored in adipose tissue or red blood cells. Finally, dietary data other than fatty acids and some potential confounding variables like socioeconomic status, education, and pharmacologic treatments at baseline and during follow-up were not available; therefore, we could not exclude the possibility that health-related variables that may covary with omega-3 fatty acids might have affected the studied outcomes.

CONCLUSIONS

We found that elevated EPA and ALA levels in serum-PC at the time of STEMI related to a lower risk of incident adverse clinical outcomes during a long-term follow-up. Our results support the notion that, for cardiac patients or patients with CV risk factors, consuming sources of marine and vegetable omega-3 fatty acids might serve as an integrative strategy for improving the quality of life and life expectancy in the event they experience a MI. These results might also explain, in part, the paradoxical observation that countries with customarily high seafood intake, such as Japan and Spain, have lower CAD mortality rates, despite a high prevalence of CV risk factors.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE: In patients with acute MI, higher blood levels of EPA and ALA, which reflect dietary intake of omega-3 fatty acids, are associated with a more favorable prognosis.

TRANSLATIONAL OUTLOOK: Further research is needed to establish dietary approaches to optimizing EPA and ALA intake for individuals at risk of developing acute MI as well as for survivors of MI.

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APPENDIX For supplemental tables and a figure, please see the online version of this paper.