Long-term fish consumption is associated with protection against arrhythmia in healthy persons in a Mediterranean region—the ATTICA study[1–3]

Christina Chrysohoou, Demosthenes B Panagiotakos, Christos Pitsavos, John Skoumas, Xenofon Krinos, Yannis Chloptsios, Vassilios Nikolaou, and Christodoulos Stefanadis

ABSTRACT

Background: Dietary habits have long been associated with many manifestations of cardiovascular disease.

Objective: We sought to investigate whether a diet enriched with fish and n−3 fatty acid consumption are associated with changes in the potential duration of the electrical action, as represented by the QT duration on a resting electrocardiogram, in a population-based sample of Greek adults.

Design: During 2001 and 2002, we randomly enrolled 1514 men (18–87 y old) and 1528 women (18–89 y old) stratified by age and sex distribution (in the 2001 Greek census) from the Attica area, Greece. We studied several demographic, anthropometric, lifestyle, dietary, and bioclinical factors of the participants. Dietary habits (including fish consumption) were evaluated by using a validated food-frequency questionnaire. All subjects underwent electrocardiography with a 12-lead surface, in which, along with several other indexes, QT duration was measured, and the heart rate–corrected QT (QTc) was calculated (corrected by using Bazett's rate). The tested hypothesis was evaluated through multiple linear regression analysis, after control for physical activity status, sex, age, medication intake, and several other potential confounders.

Results: Compared with fish nonconsumers, those who consumed >300 g fish/wk had a mean 13.6% lower QTc ($P < 0.01$). These findings were confirmed after adjustment for age, sex, physical activity status, BMI, smoking habits, intake of nuts, and other confounders. Moreover, compared with fish nonconsumers, those who consumed ≥300 g fish/wk had a 29.2% lower likelihood of having QTc intervals >0.45 s ($P = 0.03$).

Conclusions: Long-term consumption of fish is associated with lower QTc interval in free-eating people without any evidence of cardiovascular disease. Thus, fish intake seems to provide antiarrhythmic protection at a population level. *Am J Clin Nutr* 2007;85:1385–91.

KEY WORDS Fish consumption, n−3 fatty acids, QTc interval, arrhythmia

INTRODUCTION

Diet has been proven to have a significant effect on the progression of cardiovascular diseases (1, 2). Fish is one of the main components of a healthy diet, and many epidemiologic studies and clinical trials have indicated its beneficial effects in primary and secondary prevention of coronary artery disease (CAD) (3–12). Furthermore, n−3 fatty acids, which make up the most important components of a diet high in fish, may protect against heart disease mortality, preventing fatal arrhythmias (13–15) by stabilizing ion transport through the heart's cellular membrane, which is essential for heart rhythm (16). In addition, animal experiments and clinical intervention studies indicate that n−3 fatty acids have antiinflammatory properties and, therefore, may be useful in the management of inflammatory and autoimmune diseases (17, 18).

The QT interval on the electrocardiogram (ECG) measures the duration of repolarization of the ventricular myocardium. Because the duration of QT and the heart rate are strongly correlated (19), a heart rate–corrected QT interval (QTc) on the ECG has been proposed as a more relevant measurement for arrhythmia risk than is maximum QT duration. Studies in the general population have revealed that a longer QTc interval correlates with a greater mortality risk (19–22). Moreover, QT lengthening has been reported in persons with diabetes (23) and in obese (24) and hypertensive (25) patients. Because fish intake, which is a main component of the Mediterranean type of diet along with olive oil, is rich in monounsaturated and polyunsaturated fat intakes, we hypothesized that the beneficial effect of this type of diet on cardiovascular mortality may be due to an additive profound effect on ECG characteristics and especially on QTc duration, which is related to life-threatening arrhythmias. Thus, we investigated the role of fish and dietary n−3 fatty acid intakes in the duration of the QTc interval in cardiovascular disease–free subjects from the general population of Greece.

[1] From the First Cardiology Clinic (CC, CP, JS, and CS) and the Unit of Nutrition, Department of Epidemiology (YC), School of Medicine, University of Athens, Athens, Greece; the Department of Nutrition–Dietetics, Harokopio University, Athens, Greece (DBP); and the First Cardiology Clinic, Red Cross Hospital, Athens, Greece (XK and VN).

[2] Supported by research grants from the Hellenic Cardiology Society and the Hellenic Atherosclerosis Society.

[3] Reprints not available. Address correspondence to C Chrysohoou, 46 Paleon Polemiston Street 16674, Athens, Greece. E-mail: chrysohoou@usa.net.

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SUBJECTS AND METHODS

Study population

The ATTICA epidemiologic study (26) has been carried out in the province of Attica (including 78% urban and 22% rural areas), where Athens is a major metropolis. From May 2001 to December 2002, 4056 inhabitants from the area were randomly selected and asked to enroll into the study. Of that group, 3042 agreed to participate (75% participation rate). All participants were interviewed by trained personnel (ie, cardiologists, general practitioners, dietitians, and nurses) who used a standard questionnaire. Five percent of men and 3% of women were excluded from the present study because they reported a history of cardiovascular or another atherosclerotic disease or chronic viral infection. Participants could not have a cold or flu, acute respiratory infection, dental and gout infections, or any type of surgery in the previous week. All people living in institutions were excluded from the sampling. Power analysis showed that the number of enrolled participants is adequate to evaluate 2-sided standardized differences >0.5 in mean QTc intervals between groups of fish intake, achieving statistical power >0.90 at a 5% probability level (*P* value).

All subjects were informed about the aims of the study and gave written informed consent. The study was approved by the Medical Research Ethics Committee of the First Cardiology Clinic, University of Athens, and was carried out in accordance with the Declaration of Helsinki (1989).

Electrocardiographic measurements

Complete ECG measurements at rest were available in 1822 participants, in whom electrocardiography with a standard 12-lead surface was conducted. The QT interval was measured from the beginning of the QRS complex to the end of the T wave; the last was defined as the intersection of the isoelectric line and the tangent of the maximal slope on the downward limb of the T wave (27). Bazett's formula ($QTc = QT/RR^{0.5}$) (RR = the interval between 3 consecutive R waves in the ECG) was used to correct QT duration for heart rate (28), whereas the mean QTc interval was calculated in each subject as the sum of QTc intervals from all measured leads divided by the number of measured intervals. A precision ruler (0.5-mm scale) was used to measure all intervals.

Dietary assessment

Dietary assessment was based on a food-frequency questionnaire (FFQ), which was validated by the Unit of Nutrition, University of Athens School of Medicine. Validation of the FFQ was based on 42 men and 38 women aged 25–67 y who completed 2 self-administered semiquantitative FFQ within 1 y and on an interviewer-administered 24-h dietary recall questionnaire (29). The FFQ also included validation for fish intake. Consumption of nonrefined cereals and cereal products, vegetables, legumes, fruit, olive oil, dairy products, fish, pulses, nuts, potatoes, eggs, sweets, poultry, red meat and meat products, coffee, and alcohol was measured as an average per week during the previous year. Frequency of consumption was quantified by the number of times per month that a food was consumed. On the basis of the FFQ, all participants were asked about their usual average frequency of fish consumption. We coded it as follows: 0, no or very rare intake; 1, rare intake (ie, <150 g/wk); 2, moderate intake (ie, 150–300 g/wk); and 3, frequent intake (ie, >300 g/wk). The consumption of alcohol (specifically wine, at 12% ethanol concentration) was recorded in 100-mL wineglasses.

Socioeconomic status and lifestyle variables

For proxies of social status, we recorded mean annual income during the previous 3 y and the educational level of the participants, calculated as the number of years of schooling. Current smokers were defined as those who smoked ≥1 cigarette/d, never smokers as those who have never smoked a cigarette, and former smokers as those who had stopped smoking for ≥1 y. Occasional smokers (<7 cigarettes/wk) were recorded and combined with current smokers because of their small sample size. For a more accurate evaluation of smoking habits, we calculated the pack-years (cigarette packs/d × y of smoking), adjusted for a nicotine content of 0.8 mg/cigarette. For the ascertainment of physical activity status, we developed an index of weekly energy expenditure by using frequency (times/wk), duration (in min/episode), and intensity of sports-related physical activity. Intensity was graded in qualitative terms, as light (expended calories <4 kcal/min: eg, walking slowly, stationary cycling, and light stretching), moderate (expended calories 4–7 kcal/min: eg, brisk walking, outdoor cycling, and swimming with moderate effort), and high (expended calories >7 kcal/min: eg, walking briskly uphill, long-distance running, cycling fast or racing, and swimming a fast crawl) intensity. Participants who did not report any physical activities were defined as sedentary. For the rest of the participants, we calculated a combined score by multiplying the weekly frequency, duration, and intensity of physical activity. Height and weight were recorded, and body mass index (BMI; in kg/m^2) was calculated.

Clinical and biochemical characteristics

Resting arterial blood pressure was measured 3 times in the right arm at the end of the physical examination with subject in sitting position. Fasting blood samples were collected from 0800 to 1000. All biochemical evaluations were carried out in the same laboratory, which followed the criteria of the World Health Organization Reference Laboratories. Blood lipid examinations (serum total and HDL cholesterol and triacylglycerols) were measured by using a chromatographic enzymic method in an automatic analyzer (Technicon RA-1000; Dade Behring, Marburg, Germany). LDL cholesterol was calculated by using the Friedewald formula: total cholesterol – HDL cholesterol – (1/5× triacylglycerols). The intraassay and interassay CVs of total and HDL-cholesterol concentrations and triacylglycerols did not exceed 3%, 4% and 4%, respectively. Patients whose average blood pressure levels were ≥140/90 mm Hg or who were taking antihypertensive medication were classified as having hypertension. Hypercholesterolemia was defined as a total serum cholesterol concentration >200 mg/dL or the use of lipid-lowering agents. Diabetes mellitus was defined as a fasting blood glucose >125 mg/dL or the use of antidiabetes medication.

Statistical analysis

Continuous variables are presented as means ± SDs or SEs, and categorical variables are presented as absolute and relative frequencies. Associations between categorical variables were tested by using contingency tables and a chi-square test. Correlations between ECG measurements and other continuous variables were evaluated by calculation of the Pearson correlation coefficient for the normally distributed variables and of the Spearman correlation coefficient for skewed variables. Comparisons of ECG interval variables between fish-consuming groups were performed with ANOVA or generalized linear regression models for fixed effects after adjustment for various potential confounders. Differences in ECG intervals between particular subgroups according to fish consumption were tested by using post hoc analysis after Bonferroni correction of the probability for multiple comparisons. Normality of residuals, homoscedacity, and multiple colinearity were evaluated by plotting standardized residuals against the predicted values. Because a significant interaction was observed between sex and various ECG measurements or covariates that may influence the investigated hypothesis, we stratified our analysis by sex when it was appropriate. Moreover, logistic regression analysis estimated the odds of a QTc interval >0.45 s by fish intake group and after control for other potential confounders. Deviance residuals evaluated goodness-of-fit. All reported *P* values were based on 2-sided tests. We used SPSS software (version 13.0; SPSS Inc, Chicago, IL) for all statistical calculations.

RESULTS

Demographic and clinical characteristics

During the survey, 88% of men and 91% of women reported that they typically consumed ≥1 serving (ie, 150 g) of fish/wk (> 80% of subjects reported that they consumed small lean fish, eg, sardines, goatfish, giltheads, and tope). In addition, most of the subjects (80%) reported that they have had the same dietary habits for at least a decade. Several demographic, clinical, and behavioral characteristics of the participants are presented in **Table 1**. In particular, a positive association was found between the amount of fish consumed and age, whereas an inverse relation was observed between fish intake and years of school, triacylglycerols, and systolic blood pressure levels, in men. Similarly, women who consumed fish ≥1 time/wk were older, less educated, more likely to be obese, and less likely to have hypertension and had lower triacylglycerol concentrations. No other significant associations were observed in men and women with respect to fish consumption, smoking habits, or the prevalence of diabetes, hypercholesterolemia, and blood lipid concentrations.

Fish consumption and electrocardiographic intervals

The age-adjusted mean values of ECG intervals by fish-consuming group are shown in **Table 2**. A significant decrease according to the amount of fish consumed was observed in the QTc interval in both men and women. Similarly, the QT interval was inversely associated with fish intake in men and less significantly so in women (*P* for interaction = 0.03). On the basis of the post hoc analysis, more prominent differences were observed when we compared moderate or high fish intake (ie, >150 g/wk) with no fish intake. In particular, when compared with fish nonconsumers, men who consumed >300 g fish/wk had mean 14% shorter QTc intervals, and women who consumed >300 g fish/wk had mean 13% shorter QTc intervals. No significant sex × fish-intake interaction was observed for the QTc intervals.

However, several potential confounders may influence the previous associations, especially other foods that are rich in n−3 fatty acids. Therefore, we also adjusted for physical activity status, BMI, smoking habits, annual income, years of school, intake of nuts (which are known as good sources of n−3 fatty acids), and the presence of hypertension, diabetes, and hypercholesterolemia. The QTc interval still was inversely associated with fish consumption after various adjustments were made (**Table 3**). In particular, a 2-serving (ie, 300-g) increase in weekly fish consumption was associated with 0.01-s shorter QTc intervals. Moreover, we included a variable that indicates high triacylglycerol concentrations (>150 mg/dL) in the model presented in Table 3, but it had no significant effect on QTc intervals (*P* = 0.78). We decided to retain the hypercholesterolemia variable because of the more significant effect and the high colinearity with high triacylglycerols that makes the model less robust.

Furthermore, stratified analysis showed that, compared with fish nonconsumers, persons who ate ≥300 g fish/wk had a 29.2% lower likelihood of having QTc intervals >0.45 s (*P* = 0.03). Finally, cutoff analysis showed that a fish intake of 300 g/wk was optimal for maximizing the likelihood of a QTc interval <0.45 s.

DISCUSSION

In the present study, we observed a strong inverse relation between fish consumption and QTc duration on resting ECG recording in cardiovascular disease–free subjects. These associations remained significant even after adjustments for intake of nuts that are rich in n−3 fatty acids, sex, age, BMI, smoking, diabetes mellitus, lipid concentrations, smoking, and physical status. In particular, consumption of 300 g fish/wk was associated with an ≈30% lower likelihood of an abnormal QTc interval. Two strengths of our findings are that the ATTICA project is a nutrition and health survey performed in a free-eating population and that the actual fish intake, rather than the consumption of fish supplements, was considered. Finally, we confirmed previous findings that suggested an inverse association between fish intake and triacylglycerol and glucose concentrations, BMI, and systolic blood pressure.

A prolonged QTc interval on electrocardiography with a 12-lead surface has been associated with an increased risk of ventricular arrhythmias, sudden death, and CAD (19–22). Few studies have been performed in general populations, and most of them (not the Framingham Heart study) have shown a correlation with cardiac and noncardiac mortality. Among those studies, the Rotterdam Study, reported by de Bruyne et al (19), found a positive linear association between Bazett's QTc interval and all-cause and cardiac mortality in both sexes. Those investigators concluded that the QTc interval is an independent predictor of cardiac and all-cause mortality in men and women and that the risk associated with QT prolongation is valid over the whole range of QT interval duration. The relation between a prolonged QTc interval and future cardiac mortality may be attributed to ventricular electrical instability and the dispersion of repolarization, which give rise to early after-depolarizations (ie, stimulations of the cellular membrane occurring early after the ventricular depolarization) that can lead to sudden death (13).

Many epidemiologic interventional studies have suggested that increased n−3 fatty acid intakes from fish or supplements decrease cardiovascular mortality and sudden cardiac death (6–8, 30, 31). In a recent study by Kottke et al (32), an increase in median blood concentrations of n−3 fatty acids led to a 6.4% reduction in total mortality, whereas implantation of cardioverter defibrillators led to a 3.3% reduction. Observational studies have

TABLE 1
Demographic, lifestyle, and clinical characteristics

	Fish consumption				
	None	<150 g/wk	150–300 g/wk	>300 g/wk	P[1]
Participants					
Men, $n = 1514$ (%)	12	55	24	9	
Women, $n = 1528$ (%)	9	58	25	8	
Age (y)					
Men	44 ± 12[2]	49 ± 11[3]	55 ± 12[4]	53 ± 12[4]	0.001
Women	44 ± 11	48 ± 12	53 ± 11[4]	53 ± 14[4]	
Education (y)					
Men	13 ± 4	12 ± 2	11 ± 4[3]	10 ± 4[4]	0.001
Women	12 ± 4	11 ± 3	11 ± 3[3]	9 ± 3[4]	
Nut intake (serving/wk)					
Men	1.5 ± 0.9	1.5 ± 1.2	1.7 ± 1.4	1.8 ± 1.4[4]	0.009
Women	1.1 ± 0.9	1.4 ± 1.2	1.4 ± 1.4	1.7 ± 1.2[4]	
Current smoker (%)					
Men	50	44	44	48	0.36
Women	35	38	31	30	0.09
Sedentary (%)					
Men	60	62	53	52	0.10
Women	73	65	63	58	0.30
Obese (%)					
Men	18	22	21	27[4]	0.02
Women	15	18	18	25[4]	
BMI (kg/m^2)					
Men	25.9 ± 4.6	26.5 ± 4.5	26.4 ± 4.9	27.8 ± 5.4	0.01
Women	23.9 ± 3.6	24.5 ± 4.1	24.4 ± 4.4	25.9 ± 4.4	
Hypertension (%)					
Men	41	43	37[3]	27[4]	0.02
Women	45	32	28[4]	21[4]	
Systolic blood pressure (mm Hg)					
Men	135 ± 21	128 ± 22[3]	125 ± 35[3]	124 ± 25[4]	0.001
Women	133 ± 20	125 ± 27[3]	124 ± 25[3]	121 ± 20[4]	
Diastolic blood pressure (mm Hg)					
Men	81 ± 18	83 ± 21	82 ± 18	79 ± 21	0.12
Women	79 ± 28	82 ± 22	84 ± 21	78 ± 22	0.21
Hypercholesterolemia (%)					
Men	34	37	33	31	0.29
Women	35	38	37	33	
Total cholesterol (mg/dL)					
Men	209 ± 41	197 ± 25	193 ± 32	189 ± 43	0.31
Women	211 ± 40	195 ± 22	190 ± 22	182 ± 33	
HDL cholesterol (mg/dL)					
Men	44 ± 11	48 ± 15	49 ± 22	49 ± 13	0.39
Women	53 ± 13	52 ± 11	51 ± 21	52 ± 16	
Triacylglycerol (mg/dL)					
Men	185 ± 41	168 ± 29	149 ± 32[3]	125 ± 33[4]	0.02
Women	188 ± 45	171 ± 32	145 ± 33[3]	131 ± 32[4]	
Diabetes mellitus (%)					
Men	6	10	10	9	0.19
Women	6	7	7	10	

[1] P values were derived from ANOVA for the comparisons between means or from z scores for the comparisons between percentages. Post hoc comparisons were performed by using the t test and the z test for continuous and binary variables, respectively. No significant sex × fish-intake interaction was found for age, education status, nut intake, obesity, BMI, hypertension, systolic blood pressure, hypercholesterolemia, total or HDL cholesterol, triacylglycerol, or diabetes. The sex × fish-intake interaction was significant for smoking habit, physical activity status, and diastolic blood pressure, $P < 0.05$.

[2] $\bar{x}$ ± SD (all such values).

[3] $P < 0.05$ (Bonferroni corrected) for the difference between fish consumption and no fish consumption.

[4] $P < 0.01$ (Bonferroni corrected) for the differences between the sexes combined when no significant interaction existed.

linked diets rich in n−3 fatty acids to increased heart rate variability (33), decreased heart rate (34), and improvements in endothelial function (17), inflammation response (18), lipid concentrations and blood pressure levels (25), and obesity (35). Furthermore, fatty fish and fish-oil intakes are associated with a lower risk of cardiac arrhythmias, cardiac sudden death, arrhythmic coronary heart disease death, and atrial fibrillation (6, 10, 36–39). Djousse et al (31) investigated the influence of dietary

TABLE 2
Electrocardiogram intervals and daily fish consumption[1]

	Fish consumption				
	None	<150 g/wk	150–300 g/wk	>300 g/wk	P^2
RR (s)					
Men	0.83 ± 0.01[3]	0.87 ± 0.01	0.88 ± 0.01	0.89 ± 0.03	0.13
Women	0.81 ± 0.01	0.82 ± 0.01	0.83 ± 0.01	0.85 ± 0.02	0.55
QT (s)					
Men	0.39 ± 0.01	0.37 ± 0.02	0.36 ± 0.03[4]	0.35 ± 0.02[4]	0.001
Women	0.38 ± 0.01	0.37 ± 0.02	0.37 ± 0.02	0.36 ± 0.02[5]	0.06
QTc					
Men	0.44 ± 0.01	0.42 ± 0.01	0.40 ± 0.01[5]	0.38 ± 0.02[4]	0.02
Women	0.45 ± 0.01	0.43 ± 0.01	0.42 ± 0.01[5]	0.39 ± 0.02[5]	0.03

[1] RR, interval between 2 consecutive R waves in an electrocardiogram; QTc, heart-rate corrected QT interval.
[2] P values for trend derived from the ANOVA for the comparisons of between-group means. Post hoc comparisons were performed with the t test.
[3] $\bar{x}$ ± SE (all such values).
[4] $P < 0.01$ and [5] $P < 0.05$ (Bonferroni corrected) for the differences between fish consumption group and no consumption. The sex × fish intake interaction for RR, QT, and QTc was significant, $P < 0.01$.

linolenic acid on the ventricular repolarization phase in humans, as measured by QTc and JTc intervals. They measured the dietary intake of linolenic acid in foods, where it occurs predominantly in α form in flaxseed, linseed, canola oil, soybean oil, green leafy vegetables, and fish, and they reported that higher intake of dietary total linolenic acid (in α and γ form) was inversely associated with QTc and JTc intervals in a dose-response manner in both sexes. In contrast, Geelen et al (13), in a clinical trial in which 1.5 g n−3 fatty acids or placebo was given daily for 14 wk, found no effect on QTc duration or other ECG characteristics.

The possible mechanisms by which n−3 fatty acids modify cardiovascular risk may be the modulation of L-type calcium channels in the sarcolemma of cardiac myocytes or the suppression of plasma concentrations of metabolites of linoleic acid, such as thromboxane A2, which stimulates vasoconstriction and platelet aggregation (40, 41). Another possibility is that the intake of fish that is rich in α-linoleic acid promotes the formation of prostaglandin I3, which acts as a vasodilator, and of thromboxane A3, which is less active. Thus, a limited amount of linolenic acid is converted to eicosapentaenoic fatty acid, which competes with arachidonic acid. The final result is the inhibition of the production of thromboxane A2 that causes vasoconstriction and platelet aggregation, reducing the risk for ventricular arrhythmia and cardiac arrest (42). In contrast, Leaf et al (36) showed that n−3 fatty acids can inhibit the fast, voltage-dependent sodium current and the L-type calcium currents in cultured myocardium.

TABLE 3
Results from the multiple linear regression analysis of the association between the heart rate–corrected QT interval (dependent outcome), fish consumption (main effect), and various other covariates

	β coefficient ± SEM	P
Fish intake (servings/wk)	−0.005 ± 0.002	0.04
Nut intake (servings/wk)	−0.006 ± 0.002	0.001
Age (y)	−0.001 ± 0.001	0.15
Male compared with female	−0.165 ± 0.006	0.007
BMI (kg/m^2)	0.001 ± 0.001	0.25
Very good or good compared with moderate or low income	0.002 ± 0.004	0.60
Years of school	0.001 ± 0.001	0.48
Current smoking (yes or no)	0.005 ± 0.005	0.38
High compared with moderate or low physical activity	−0.004 ± 0.006	0.46
Hypertension (yes or no)	0.028 ± 0.007	0.004
Hypercholesterolemia (yes or no)	0.007 ± 0.006	0.29
Diabetes (yes or no)	0.017 ± 0.016	0.53

In the present study, fish intake was inversely correlated with blood pressure levels, fasting glucose concentrations, BMI, and triacylglycerol concentrations. Furthermore, fish consumption of ≥300 g/wk seems to reduce the QTc duration, irrespective of other lifestyle and anthropometric factors in a free-eating Mediterranean population. That level of fish consumption is consistent with observational studies and randomized trials that indicate clinical benefits of fatty fish or fish-oil consumption at a relatively modest level—1–2 servings/wk or 500–1000 mg eicosapentaenoic acid and docasohexaenoic acid/d, respectively (43). In a meta-analysis by Mozaffarian et al (44), the lowest eicosapentaenoic acid and docasohexaenoic acid doses were 1 g/d, and it is possible that a dose-response effect may exist at lower (eg, dietary) intakes. A recent study from the same investigators in a large population-based sample found a beneficial effect of the consumption of tuna or other boiled or baked fish on ECG values related to arrhythmic risk, including a 46% lower likelihood of prolonged QT interval (45). The present study found a nearly 30% lower likelihood of having QTc > 0.45 s with consumption of >300 g fish/wk. This finding is modest compared with those of other studies, but the population we studied is free-eating persons in the Mediterranean region, where fish consumption mainly involves small, lean fish (2, 12, 17, 26), and we also took other natural sources of n−3 fatty acids (ie, nuts) into account in the analysis. Furthermore, the potential confounding effect of other habits of the studied Mediterranean sample, such as the method of cooking and serving fish—ie, with vegetables, legumes, fruit, and especially olive oil—may play a role in the different effect of fish consumption on the investigated ECG values.

Limitations

The present study has some limitations. For example, the design was cross-sectional, and therefore we cannot make assumptions about causal relations. Fish intake was evaluated by self-reports through FFQa, and, therefore, information about the amount of fish consumed could be overestimated or underestimated. Another limitation is the small number of subjects who consumed >300 g fish/wk. Blood sampling was performed at only one visit. We used resting and not ambulatory ECG measurements. We did not specify exactly the type of fish consumed (ie, small or large, lean or fat, fresh or frozen), but, in Greece, it is mainly small lean fish, which are inexpensive, that are consumed. We did not measure n−3 and n−6 fatty acids, and we were not able to measure serum concentrations of n−3 fatty acids.

Conclusion

The present study found that long-term intake of fish was associated with a shorter QTc interval in a free-eating Mediterranean population without any evidence of cardiovascular disease. Prolongation of QTc duration has been recognized as a major independent risk factor for cardiovascular death. Epidemiologic and interventional studies have shown the beneficial effect of n−3 fatty acid and fish-oil consumption on cardiovascular and overall survival and on the prevention of arrhythmic events through the modification of heart rate and QT duration and reductions in inflammatory markers. The present study shows the effect in a sample of CVD-free adults, independent from the other beneficial effects of a Mediterranean diet, of the consumption of mainly small, lean fish on the QTc interval in a resting ECG.

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