etables, and fish; daily fruit; less meat, with red meat replaced by poultry; and butter and cream replaced by a canola-oil–based margarine. The canola-oil–based margarine used in the study was higher in linoleic acid (16.4% vs 8.6%) and alpha-linolenic acid (4.8% vs 0.6%) than olive oil, which is typically used in the Mediterranean diet.

The trial was ended early after finding a 70% reduction in cardiac events with 27 months of follow-up. The report was criticized by some and mostly ignored by the medical community. This final article reports on the results after an average of approximately 4 years of study.

Population studied This study enrolled 605 patients younger than 70 years (mean age 53.5 years, 91% men) who had suffered a first heart attack within 6 months of enrollment. Subjects were recruited from a cardiovascular hospital in France. Patients were excluded if they had overt heart failure, recurrent angina, ventricular arrhythmias, atrioventricular block, or severe uncontrolled hypertension.

Study design and validity This was a 4-year randomized controlled trial comparing the Mediterranean diet with the usual postinfarction diet. The 303 subjects in the control group were prescribed a "prudent Western diet" by their attending physicians. It is unclear how close the control group diet approximates the typical postinfarction diet in the United States and other western countries. Subjects in the treatment group attended a 1-hour class during which a dietitian and cardiologist explained the Mediterranean diet. Both groups returned at 8 weeks and annually for follow-up, but only the treatment group received dietary advice from investigators. Clinical end points were assessed blindly at annual visits. Analysis was by intention to treat. Although the trial was terminated after 2 years and participants were notified of the findings, most continued to follow the diet originally assigned to them.

The investigators did not control for multiple comparisons; it may be that at least some of the differences were due to chance. Another report noted that only 42% of the control group (compared with 92% of the experimental group) changed their diet during the study.[1]

Outcomes measured The primary outcome was the incidence of combined cardiac death and nonfatal heart attack. This outcome plus major secondary end points (including unstable angina, heart failure, stroke, and embolism) constituted composite outcome 2. The preceding outcomes plus minor secondary events, such as recurrent stable angina, surgical intervention for heart disease, and thrombophlebitis, made up composite outcome 3.

Results There were significantly fewer deaths and nonfatal heart attacks in the treatment group, 1.24 per 100 patients per year of follow-up compared with 4.07 in the control group (adjusted risk ratio [ARR] = 0.28; 95% confidence interval [CI], 0.15 - 0.53). Thirty-five patients would have to be treated for 4 years to prevent 1 cardiac death or nonfatal heart attack (number needed to treat [NNT] = 35). For composite outcome 2, the rates were 2.59 compared with 9.03 (ARR = 0.33; 95% CI, 0.21 - 0.52; NNT = 16). For composite outcome 3, the rates were 18.74 compared with 9.63 (ARR = 0.53; 95% CI, 0.38 - 0.74; NNT = 11).

Recommendations for clinical practice **This French study found that the Mediterranean diet is effective in reducing mortality and recurrence of cardiovascular events following a heart attack. The diet, which is high in alpha-linolenic acid, is a significant departure from the step 1 and step 2 diet recommended by the American Heart Association. The dietary manipulations of the Mediterranean diet are simple, but this study should be repeated in other countries before it is used to replace the typical cardiac diet.**

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Amiodarone for the Treatment of Persistent Atrial Fibrillation

Kochiadakis GE, Igoumenidis NE, Solomou MC, et al. Efficacy of amiodarone for the termination of persistent atrial fibrillation. Am J Cardiol 1999; 83:58-61.

Clinical question **Is amiodarone superior to placebo for the restoration of sinus rhythm in patients with persistent atrial fibrillation?**

Background Chemical cardioversion is very effective for the treatment of atrial fibrillation (AF) lasting less than 48 hours. For AF of greater duration, chemical cardioversion has been shown to have limited value. A Class III anti-arrhythmic drug, amiodarone has been shown in previous studies to have potential efficacy in the treatment of AF of longer duration. In most cases, however, amiodarone was only used when AF was refractory to other agents, and no studies used a placebo control group.

Population studied The study included 67 consecutive adult patients (32 men, 35 women) with a mean age of 64 years. All had AF of greater than 48 hours'

duration and presented either to an emergency department or to the authors' clinic. Exclusion criteria included patients with unstable angina, acute myocarditis, acute pericarditis, a recent myocardial infarction, heart surgery in the previous 6 months, severe uncontrolled heart failure (ejection fraction <30%), sick sinus syndrome, a history of second- or third-degree atrioventricular block, use of any anti-arrhythmic drug other than digoxin within a period of 5 half-lives of the drug before the study, cardiogenic shock, significant chronic obstructive pulmonary disease, pulmonary embolism, pneumonia, liver or kidney failure, thyroid disease, electrolyte disturbances, pregnancy, or lactation.

Study design and validity This was a prospective randomized single-blind clinical trial. Patients randomized to the amiodarone group received 300 mg intravenously for 1 hour followed by 20 mg per kg for 24 hours. Simultaneously, they were given 600 mg per day orally, 3 times a day for 1 week, followed by 400 mg per day for 3 weeks. Patients in the placebo group received saline and placebo tablets at a similar frequency. All patients were given digoxin if they had not previously received it. Acenocoumarol (warfarin) adjusted to an international normalized ratio of 3 was given to all patients not already taking anticoagulant medication for at least 21 days before cardioversion was attempted. Patients were observed in a coronary care unit or in the cardiology department for the first 72 hours and evaluated in the clinic at 30 days. The mean duration of AF was 58 and 69 days for the placebo and amiodarone groups, respectively. The relatively long duration of AF may have influenced the findings, since the conversion rate for AF of more than 3 days' duration falls dramatically compared with the conversion of AF of shorter duration.[1] Ideally, the study should have been double-blinded to prevent bias in the interpretation of diagnostic findings.

Outcomes measured The primary outcome was conversion to sinus rhythm within the 1-month study period.

Results At the end of the study period, 16 of 33 patients in the amiodarone group (48.5%) and none of the patients in the placebo group converted to sinus rhythm (P <.001). No patient converted in the first 24 hours. Beta-blockers were added to the treatment regimen to better control the heart rate in 7 patients (3 in the amiodarone group and 4 in the placebo group). Of these, 2 in the amiodarone group converted. No adverse drug effects necessitated discontinuation of amiodarone, and there were no pro-arrhythmic effects. No side effects were observed in the placebo group.

Recommendations for clinical practice **This study lends support for the use of amiodarone for the restoration of sinus rhythm among patients with persistent AF. The extent that these findings can be generalized is limited by the above exclusion criteria. Amiodarone has generally been used as the drug of last resort for the treatment of AF. This is in part because of potentially serious side effects, although studies have shown that these side effects are rare. Consistent with these findings, the present study reported no adverse effects that caused discontinuation of the drug. Further studies are warranted that directly compare oral amiodarone with other oral drugs such as flecainide or propranolol, that measure longer-term outcomes, and that define the duration of therapy.**

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Incorporating Right Precordial Leads in Exercise Electrocardiography

Michaelides AP, Psomadaki ZD, Dilaveris PE, et al. Improving detection of coronary artery disease by exercise electrocardiography with the use of right precordial leads. N Engl J Med 1999; 340:340-5.

Clinical question **Does the addition of right precordial leads to the standard 12-lead exercise electrocardiogram improve detection of coronary artery disease?**

Background Coronary artery disease (CAD) is one of the leading causes of morbidity and mortality in the United States. Exercise electrocardiographic treadmill testing (ETT) is a frequently employed screening test. However, its sensitivity for the detection of single-vessel CAD is only 35% to 61% in various studies. This study evaluates the incorporation of right precordial leads as a noninvasive method for improving the sensitivity of ETT.

Population studied Participants of this study included 245 adults (218 men, 27 women) who were referred to a cardiology department with symptoms suggestive of angina. Exclusion criteria included left or right bundle branch block; left or right ventricular hypertrophy; ventricular pre-excitation; valvular or congenital heart disease; history of bypass surgery, coro-