CARDIOLOGY Rounds®

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Diet and Cardiovascular Disease: A Complex Relationship

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It is well known that diet has an impact on cardiovascular disease (CVD); however, it is unclear whether the effect of diet is solely due to its influence on underlying cardiac risk factors or to other mechanisms. This issue of *Cardiology Rounds* explores the complex relationship between dietary intake and overall CV risk. Initially, the association of diet and overall CV health is discussed on the scale of populations through the use of epidemiological data. Subsequently, meta-analyses and randomized controlled trials are reviewed to determine the role of dietary intervention on the prevention of CVD. Finally, to understand the pathophysiological factors associating diet and CV risk, several studies are examined to illustrate the effect of diet on the underlying CV risk factors.

Epidemiological studies

INTERHEART study

In 2004, Yusuf et al published a large, case-control, cohort study spanning 52 countries and examining the modifiable risk factors of acute myocardial infarction (MI).[1] The study included patients admitted with a first-time MI to the coronary care unit or cardiology ward in their respective hospitals, and control patients selected from the community or from admitted in-hospital noncardiac patients. Any patient was excluded if he or she had a history of coronary artery disease (CAD). Each patient and control subject completed a standardized questionnaire detailing cardiac risk factors, diet, and psychosocial factors. Baseline waist-to-hip ratio and blood pressure (BP) were measured and standardized laboratory measures investigated, including apolipoprotein (apo)B, apoA1, high-density lipoprotein cholesterol (HDL-C), and glycated hemoglobin (HbA_{1c}).

This study found a synergistic association between the numbers of modifiable cardiac risk factors found in this patient population with the risk for MI (Figure 1). On the other hand, there appeared to be a pronounced decrease in the risk for MI associated with healthier lifestyle choices. The population-attributable risk (PAR) for all 9 coronary risk factors (current and former smoking, dyslipidemia, hypertension, abdominal obesity, diabetes, psychosocial stress, exercise, diet, and alcohol consumption) accounted for approximately 90% of all first-time MI. This calculation was adjusted for age, sex, region, and all other factors. The authors concluded that approximately 90% of all CV disease potentially could be preventable. Given that this study examined CV risk on the level of aggregate population, the results may or may not be applicable to the individual patient. In addition, the only CV outcome assessed in INTERHEART was the risk of first MI and, therefore, other modes of CAD presentation, such as stable angina, cardiovascular mortality, and sudden cardiac death, were not included.

INTERHEART study: diet subgroup analysis

A subgroup analysis of the INTERHEART study, was performed to determine whether diet had an independent association with the risk of MI.[2] To minimize confounding effects, all patients enrolled with a history of dyslipidemia, hypertension, and diabetes were excluded in the analysis. Patients completed questionnaires regarding the frequency of consumed food groups; further statistical analysis converted the frequency to consumption per day. Out of 5764 patients admitted after a first MI, and 10 646 control subjects, 3 major dietary patterns were observed: prudent, Oriental, and Western. The prudent diet consisted of a diet rich in fresh fruits and vegetables, nuts, and fibre and the Oriental diet was associated with a high intake of soya and tofu. The Western diet involved high intakes of deep-fried and salty foods, and meat.

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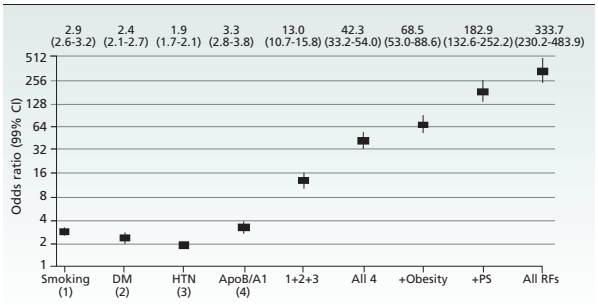
Figure 1: Risk of acute myocardial infarction (MI) with exposure to multiple risk factors[1]



Note the doubling scale on the Y axis. The odds ratios are based on current versus never smoking, top versus lowest tertile for abdominal obesity, and top versus lowest quintile for ApoB/ApoA1, then the odds ratio for the combined risk factors is 333.7 (99% CI 230.2 – 483.9).
DM = diabetes mellitus; HTN = hypertension; Apo=apolipoprotein; PS=psychosocial; RF=risk factors; CI=confidence interval.
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In addition to dietary patterns, the authors devised a dietary risk score (DRS), which consisted of the consumption ratio of healthy versus harmful foods. A higher DRS indicated increased patient consumption of harmful foods such as meat and salty foods. DRS and dietary pattern adherence were divided into quartiles for statistical analysis. For the Western dietary pattern in the control subjects (Table 1), no relation between quartiles and apoB/A1 ratio or HbA_{1c} was observed, but there was a significant trend towards lower waist-to-hip ratios (WHR) and systolic blood pressure (SBP) in the higher quartiles. Interestingly, there was a trend towards lower apoB/A1 ratios, SBP, and WHR, in the higher (ie, more harmful) quartiles of the Oriental diet pattern. Similar trends were found in the upper quartiles of the DRS, except for a small but significantly higher WHR. On the other hand, there was a statistically significant but mild increase in apoB/A1 ratios and SBP in the higher quartiles of the prudent diet.

Despite the counterintuitive trends of dietary patterns and DRS on measured coronary risk factors, there was a statistically significant increased risk of MI in the fourth quartile of the Western diet pattern. The odds ratio (OR) of the third and fourth quartiles compared to the first were 1.12 (95% confidence interval [CI], 1.00 to 1.25) and 1.35 (95% CI, 1.21 to 1.51), respectively. This association remained after adjusting for age, sex, obesity, and other risk factors. There was a statistically significant inverse association of the prudent diet with risk of MI: the adjusted ORs were 0.76 (95% CI, 0.68 to 0.85) for the second quartile, 0.66 (95% CI, 0.59 to 0.74) for the third quartile, and 0.67 (95% CI, 0.59 to 0.76) for the fourth quartile. There were no significant associations between Oriental diet and MI when all regions were combined.

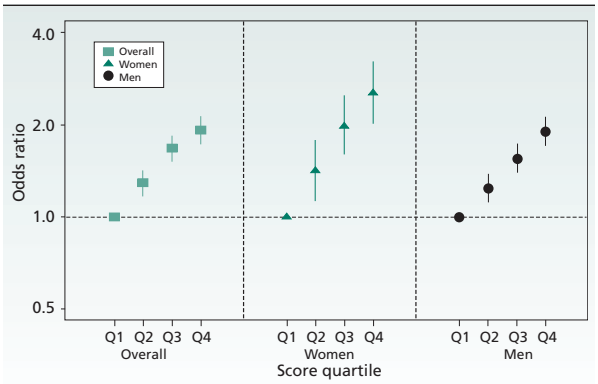
There was a graded associated risk of MI with increasing quartiles of the DRS. The second quartile of DRS had an OR adjusted for age, sex, and region of 1.29 (95% CI, 1.17 to 1.42), the third quartile had an OR of 1.67 (95% CI, 1.51 to 1.83), and the fourth quartile had an OR of 1.92 (95% CI, 1.74 to 2.11; Figure 2). The PAR for DRS and acute MI was 0.3 for all regions. Finally, this study demonstrated that, on a global population scale, diet may be attributable to 30% of all MI and, furthermore, this association may be independent of all other measured risk factors.

Table 1: Mean (SD) plasma concentrations of biomarkers of CVD, SBP, and WHR by quartiles of dietary pattern and DRSs for control subjects[2]

Dietary	Patterns	ApoB/A1, mmol/L	% Hba_{1c}	Mean SBP, mm Hg	WHR
Oriental					
Quartile	1 (lowest quartile)	0.84 (0.33)	5.73 (0.59)	125.41 (15.18)	0.92 (0.08)
Quartile	2	0.82 (0.34)	5.72 (0.62)	126.36 (15.44)	0.91 (0.08)
Quartile	3	0.81 (0.46)	5.77 (0.76)	125.48 (14.68)	0.91 (0.08)
Quartile	4 (highest quartile)	0.71 (0.28)	5.80 (0.80)	124.73 (14.51)	0.88 (0.08)
P for trend		<0.0001	0.0004	0.03	<0.0001
Western					
Quartile	1	0.80 (0.41)	5.78 (0.76)	125.99 (14.96)	0.91 (0.08)
Quartile	2	0.77 (0.35)	5.73 (0.68)	125.63 (15.31)	0.91 (0.08)
Quartile	3	0.80 (0.36)	5.75 (0.69)	125.09 (14.75)	0.91 (0.08)
Quartile	4	0.78 (0.31)	5.77 (0.68)	125.20 (14.75)	0.90 (0.09)
P for trend		0.48	0.82	0.03	<0.0001
Prudent					
Quartile	1	0.78 (0.33)	5.72 (0.71)	124.06 (14.59)	0.91 (0.08)
Quartile	2	0.78 (0.33)	5.76 (0.76)	125.42 (14.58)	0.91 (0.08)
Quartile	3	0.80 (0.37)	5.77 (0.69)	125.64 (14.66)	0.91 (0.08)
Quartile	4	0.80 (0.41)	5.77 (0.64)	126.52 (15.74)	0.90 (0.09)
P for trend		0.02	0.03	<0.0001	0.0003
Dietary risk scores					
Quartile	1	0.80 (0.43)	5.78 (0.68)	125.94 (15.37)	0.90 (0.08)
Quartile	2	0.79 (0.35)	5.78 (0.75)	125.24 (15.10)	0.91 (0.08)
Quartile	3	0.78 (0.34)	5.73 (0.69)	125.46 (14.68)	0.91 (0.09)
Quartile	4	0.78 (0.29)	5.73 (0.67)	125.12 (14.48)	0.91 (0.08)

ApoB/A1 = apolipoprotein B/A1 ratio; HbA_{1c}= glycated hemoglobin; SBP= systolic blood pressure; WHR = waist-to-hip ratio.

Figure 2: Risk of MI and dietary risk score (DRS)[2]



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Nurses' Health Study

Other population studies, such as the Nurses' Health Study (NHS), demonstrated similar results to the INTERHEART study. The NHS was a prospective population cohort study determining risk factors for certain diseases, including CVD disease. This study was initiated in 1976, and included 176 000 healthy nurses ranging in age from 30 to 55 years. Patients were followed with biennial questionnaires; in 1984, investigators began to distribute food-frequency questionnaires to the study patients. Patients with a history of CAD, diabetes, stroke, and cancer were excluded. Of the 72 113 patients, a cardioprotective association was found with the prudent diet, in addition to a statistically significant harmful effect of the Western diet.[3] The relative risk of CV mortality (adjusted for age, sex, and other coronary risk factors) in the highest quintile was 0.72 (95% CI, 0.6-0.87) and 1.22 (95% CI, 1.01-1.48) for the prudent and Western diets, respectively.

Mediterranean diet studies

The Mediterranean diet, which is rich in vegetables, legumes, nuts, fish, and seafood, has also been well studied. This diet contains low to moderate levels of dairy products, a moderate use of olive oil and less use of saturated fats. There is moderate alcohol intake, such as wine with meals, and low intakes of meat and poultry.

One prospective cohort study examined 28 572 subjects in Greece, ranging in age from 20 to 86 years, who had no history of CAD, cancer, or diabetes.[4] All patients completed a detailed questionnaire regarding food-group frequency and portion sizes. A Mediterranean diet scale was devised to assess the adherence of each subject to a Mediterranean diet. Researchers found a statistically significantly lower risk of cardiac mortality, all-cause mortality, and death from cancer in patients with greater adherence to the Mediterranean diet. The hazard ratio (HR) for CV mortality associated with a 2-point increment in the Mediterranean diet scale, fully adjusted for all other cardiac risk factors, was 0.67 (95% CI, 0.47-0.94). The fully adjusted HRs for all-cause mortality and cancer death were 0.75 (95% CI, 0.64-0.87) and 0.76 (95% CI, 0.59-0.98), respectively. A meta-analysis that combined population cohort studies of the Mediterranean diet found similar results. There was a statistically significant 9% RR reduction in CV mortality (95% CI, 0.87-0.95) and 9% RR reduction in all-cause death (95% CI, 0.89-0.94).[5]

The *Prevención con Dieta Mediterránea* (PREDIMED) study[6] was a randomized controlled trial involving 722 patients at high risk of CV, that compared those on a low-fat diet to those on the Mediterranean diet with enhanced consumption of either olive oil or nuts. Although this study did not assess hard outcomes such as coronary events, it did find significant reductions in plasma glucose, systolic BP, total cholesterol/HDL-C ratios, as well as C-reactive protein (CRP) levels in patients on the Mediterranean diets compared with low-fat diets. This study suggests that the Mediterranean diet may improve underlying cardiac risk factors more than a traditional low-fat diet, which may lead to improved CV outcomes.

Randomized controlled trials of low-fat diets

There have been numerous randomized controlled trials on diet and CV risk with inconsistent results. The Mediterranean α-linolenic acid-rich diet in secondary prevention of coronary heart disease, called the Lyon Diet Heart study,[7] was a single-blind, prospective, randomized study of 605 patients after their first MI. Patients in the experimental arm received specific dietary advice from a research dietician or cardiologist. The experimental diet consisted of a high intake of fruits and vegetables, less meat, less butter, more margarine, and more fish. Over a follow-up of approximately 4 years, daily caloric intake was significantly reduced in the experimental arm. In addition, there was a significant increase in daily polyunsaturated fat intake and a decrease in saturated fat and cholesterol intake in the experimental group. There was a significant decrease in CV deaths, nonfatal MIs, and overall mortality after 4 years of follow-up. Despite the reduction in cardiac endpoints, it is unknown whether this was independent of other cardiac risk factors. Although there was no statistical difference, there was a trend towards a decrease in BP, weight, and triglycerides, and an increase in low-density lipoprotein cholesterol (LDL-C) in the experimental diet group. Although the Lyon study demonstrated the efficacy of a cardiac healthy diet, this study was conducted before the advent of statin therapy and other efficacious secondary-prevention medications. Therefore, in addition to standard medical therapy, it is unknown whether there would be additional CV benefits with this dietary intervention.

A meta-analysis[8] performed on 27 randomized controlled trials examining the effect of low-fat diets in healthy adults found a nonsignificant 9% decreased risk in CV mortality (OR 0.91; 95% CI, 0.77 to 1.07). However, there was a statistically significant decrease in combined CV events (OR 0.84; 95% CI, 0.72 to 0.99), for example: CV death, nonfatal MI, congestive heart failure, angioplasty, coronary artery bypass graft (CABG) surgery, stroke, peripheral vascular disease, and angina. This effect appeared to be independent of the changes in serum lipids, dietary fat, and cholesterol intake.

Effect of diet on coronary risk factors

The aforementioned studies demonstrate how diet can impact CV health. The following section briefly reviews some studies illustrating the impact of diet on underlying coronary risk factors, which may explain the potential benefit of heart-healthy eating to improved CV outcomes.

Diet and hypertension

Salt intake has long been known to be associated with high BP, primarily due to its effect on fluid balance. Sacks et al[9] assessed the relationship between different degrees of salt intake and BP; 412 patients with normal or mildly elevated BP were randomly assigned to a control diet or to the Dietary Approaches to Stop Hypertension (DASH) diet, which is rich in fruit, vegetables, and low-fat dairy products. Within each assigned group, patients were subdivided to either high salt intake (>150 mmol/ day), intermediate (100 mmol/day), and low salt intake (50 mmol/day).[9] After 30 consecutive days, the patients in the DASH diet group had significantly lower systolic BP compared with the control diet group, in all levels of sodium intake. The mean systolic BP was 7.1 mm Hg less in the DASH diet group with low sodium intake compared with those in the control-diet group with high sodium intake and no history of hypertension. The difference was greater in patients with a history of hypertension, 11.5 mm Hg; however, both diet groups benefited from reduced salt intake, leading to lower BP. CV outcomes were not assessed in this trial.

Dark chocolate intake has been studied to determine its effect on BP. Cocoa contains flavanols that may exert antihypertensive effects by facilitating endothelial cell production of nitric oxide (NO), which causes vasodilatation and, hence, lowers BP. A randomized controlled trial[10] of 44 patients with stage 1 hypertension found that 6.3 g of dark chocolate per day significantly reduced BP by a mean of 2.9/1.9 mm Hg. This effect was accompanied by increased levels of NO activity.[10]

Garlic has also been well studied in the treatment of hypertension. A recent meta-analysis[11] of 11 randomized controlled trials with true placebo groups found that garlic significantly reduced systolic BP by a mean of 4.6 ± 2.8 mm Hg. However, in the subset of patients with a history of hypertension, garlic reduced BP by a mean of 8.4 ± 2.8 for systolic BP, and 7.3 ±1.5 mm Hg in diastolic BP.

Diet and risk of diabetes mellitus

It is recognized that poor dietary habits exacerbate glucose control in diabetic patients; however, the aspect of diet and an unhealthy lifestyle increasing the risk of developing diabetes was demonstrated in the Nurses' Health Study.[12] This study followed 84 941 nurses for 16 years, using serial questionnaires about diet and lifestyle. Patients with a history of diabetes, CAD, and cancer were excluded. Multivariate analysis found that poor diet, obesity, and abstinence from alcohol significantly increased the risk of developing diabetes. The highest risk group were the subjects with a body-mass index (BMI) of >35 kg/m^2; their relative risk for developing diabetes was 38.8 (95% CI, 31.9 - 47.2).[12]

Diet and dyslipidemia

Multiple studies and animal data have demonstrated that high intakes of saturated fats and trans-fatty acids significantly increase LDL-C. Lichtenstein et al[13] monitored serum lipid levels in 36 healthy young subjects who were required to randomly consume each of 6 different diets for 35-day periods. Each diet consisted of oils with increasing amounts of saturated and trans-fat, in addition to decreased quantities of polyunsaturated fat. These oils ranged from soya bean-based oils to margarine, shortening, and butter. LDL-C was reduced by approximately 11% when soybean oil foods were compared with butter-containing foods. Lower-fat oils were also associated with smaller reductions in HDL-C: 3% with soybean, up to 6% with stick margarine. Therefore, this study demonstrated that low saturated and trans-fat diets significantly improve serum lipids, which may possibly reduce future CV events.

Diet and CRP

CRP is an acute-phase reactant that has been linked to the development of CAD and had underlined a pathophysiological role for inflammation in the development of atherosclerosis. Numerous population studies have found an association between CRP levels and CV risk.[14,15] More recently, the Justification for the Use of statins in primary Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) study[16] demonstrated that reducing levels of CRP with statin therapy was associated with reduced CV events and mortality.

One retrospective study,[17] using the National Health And Nutritional Examination Survey (NHANES) database on patients with diabetes, hypertension, and obesity, found an inverse relationship between dietary fibre intake and CRP levels. Patients who were in the 2 lowest quartiles for fibre intake were more likely to have elevated CRP levels. Another study using the NHANES database also found an inversely proportional relationship between flavanoid intake and CRP levels.[18]

In a prospective study of 12 elderly patients, Tsitouras et al[19] found diminished CRP levels with a high intake of omega (Ω)-3 fatty acids. In addition, a randomized controlled trial[20] of 40 post-MI patients found that supplementation with Ω-3 fatty acids in combination with folic acid, and vitamins A, B_6, D, and E was associated with improved lipid profiles, and decreased CRP levels. Cardiac outcomes based on diet-reduced CRP levels were not assessed in the above trials. However, considering that CRP levels were not accounted for in the INTERHEART and the Nurses' Health studies, lower CRP levels may account for the cardioprotective effect of the prudent diet, or a lower DRS, and explain the possible relationship between diet and CV disease independent of other known risk factors.

Diet and obesity

A poor diet in addition to diminished physical activity can result in significant weight gain and obesity. Wilson et al[21] examined 4780 adults from the Framingham Offspring Study to determine the risk factors for first-time presentation of CAD (angina pectoris, acute coronary event, and cardiac death), cerebrovascular disease (transient ischemic attack, stroke, and stroke-related death), and combined endpoints. After 24 years of follow-up, using multivariate

analysis, an elevated BMI significantly predicted the occurrence of coronary events (HR 1.28; 95% CI, 1.17-1.39) when adjusted for age, sex, and current smoking. When adjusting for all risk factors, including diabetes mellitus, hypertension, and total cholesterol (TC):HDL-C ratios, the risk was reduced, but remained significant (HR 1.10; 95% CI, 1.00-1.21). Obesity had a stronger prediction for first cerebrovascular event when adjusted for all other risk factors (HR of 1.21; 95% CI, 1.01-1.44).[21] Diabetes, hypertension, dyslipidemia, age, and smoking were also found to be independently associated with an increased risk for a first coronary event. Therefore, this study suggests that a poor diet and an unhealthy lifestyle leading to obesity may, by itself, increase the risk of future coronary events, regardless of other coronary risk factors.

Ω-3 polyunsaturated fatty acids

Ω-3 fatty acids deserve special mention because of their potential cardioprotective effects. These polyunsaturated fatty acids (PUFAs) are essential in daily diets because humans are unable to synthesize them. Ω-3 fatty acids can be found naturally in fatty cold-water fish, such as salmon, mackerel, cod, herring, and sardines. Multiple studies on the effects of PUFAs have revealed inconsistent results. These essential fatty acids may exert their effect by their influence on serum lipids, blood pressure,[22,23] heart rate,[24] improved arterial compliance and ventricular diastolic filling,[25,26] antiarrhythmic properties,[27] improved insulin sensitivity,[28] and other potential mechanisms not entirely understood. A more detailed review of Ω-3 fatty acids can be found in the most recent issue of *Cardiology Rounds*.

The efficacy of Ω-3 fatty acids was assessed in a randomized controlled trial on 18 645 Japanese patients with elevated cholesterol.[29] Both arms received statin therapy and the treatment arm received 1800 mg of eicosapentaenoic acid. After 4-6 years, there was a statistically significant 19% RR reduction in the primary endpoint, involving: fatal and non-fatal MI, angioplasty, CABG, and cardiac and noncardiac death. There was a significant reduction in unstable angina and nonfatal cardiac events; however, no significant difference was found between the 2 groups in cardiac mortality and sudden cardiac death. There was no significant difference in LDL-C levels, therefore the beneficial effects of eicosapentaenoic acid was independent of lipid lowering.[29]

Diet and guidelines

The 2007 American Heart Association/American College of Cardiology (AHA/ACC) guidelines[30] recommend all cardiac patients to implement a heart-healthy diet for secondary prevention. Saturated fats and trans-fatty acid intake should be <7% of total caloric intake per day. Cholesterol consumption should be <200 mg/day. Increased Ω-3 fatty acid intake (≥1 g/day) is encouraged either through consumption of fatty fish or as supplements. Increased plant sterol intake and fibre are also strongly recommended.[30] Similar recommendations are stated in the AHA guidelines for prevention of CVD in women.[31] The European Society of Cardiology (ESC) guidelines[32] have similar dietary recommendations for CV risk reduction. They suggest that total fat intake should be <25%-35% of total caloric intake. As with the AHA/ACC guidelines, saturated fat intake should be <7% of total caloric intake. In addition, CV patients are encouraged to consume fresh fruits and vegetables, whole-grain cereals, fatty fish, lean meat, and dairy products. Salt intake should also be reduced by avoiding high-salt food, such as processed meats, and restricting the addition of salt.

Conclusion

The evidence is clear that diet has a significant impact on CV disease; epidemiological population-based studies have demonstrated that a poor diet can increase the risk of MI. Some data, such as results from the INTERHEART study,[2] suggest that this relationship may be independent of other coronary risk factors. On the other hand, it is also demonstrably clear that there is a complex influence of diet on underlying cardiac risk factors. As a result, the question is whether the relationship between diet and CVD is determined by the impact on underlying coronary risk factors, or is it through, or in addition to, other mechanisms?

The cumulative risk of CVD based on dietary intake is complex and is likely due to a balance of the harmful and protective foods one consumes, analogous to the DRS. Ultimately, a patient with a healthier lifestyle would be more likely to avoid harmful foods such as salty foods and saturated fats, and consume higher amounts of cardioprotective foods such as polyunsaturated fatty acids, fruits, and vegetables. Likewise, a patient with an unhealthy lifestyle would be more likely to consume higher amounts of harmful foods than cardioprotective ones.

Whether diet has an impact on the risk of CVD through mechanisms that are independent of traditional coronary risk factors has yet to be determined. However, considering that epidemiological data reveal a possible relationship (independent of other known risk factors) between diet and CV health suggests that heart-healthy eating should be encouraged for all CV patients, irrespective of adequate control of underlying coronary risk factors with medications.

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Abstract of Interest

Comparison of 3 ad libitum diets for weight-loss maintenance, risk of cardiovascular disease, and diabetes: a 6-month randomized, controlled trial

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BACKGROUND: The optimal dietary content and type of fat and carbohydrate for weight management has been debated for decades.

OBJECTIVE: The objective was to compare the effects of 3 ad libitum diets on the maintenance of an initial weight loss of ≥8% and risk factors for CVD and diabetes during a 6-mo controlled dietary intervention.

DESIGN: Nondiabetic overweight or obese [mean ± SD body mass index (kg/m^2): 31.5 ± 2.6] men (n = 55) and women (n = 76) aged 28.2 ± 4.8 y were randomly assigned to a diet providing a moderate amount of fat (35-45% of energy) and >20% of fat as monounsaturated fatty acids (MUFA diet; n = 54), to a low-fat (20-30% of energy) diet (LF diet; n = 51), or to a control diet (35% of energy as fat; n = 26). Protein constituted 10-20% of energy in all 3 diets. All foods were provided free of charge from a purpose-built supermarket.

RESULTS: More subjects dropped out of the MUFA (28%) group than out of the LF group (16%) and control group (8%) (MUFA compared with control: $P < 0.05$). All groups regained weight (MUFA: 2.5 ± 0.7 kg; LF: 2.2 ± 0.7 kg; and control: 3.8 ± 0.8 kg; NS). Body fat regain was lower in the LF (0.6 ± 0.6%) and MUFA (1.6 ± 0.6%) groups than in the control group (2.6 ± 0.5%) ($P < 0.05$). In the MUFA group, fasting insulin decreased by 2.6 ± 3.5 pmol/L, the homeostasis model assessment of insulin resistance by 0.17 ± 0.13, and the ratio of LDL to HDL by 0.33 ± 0.13; in the LF group, these variables increased by 4.3 ± 3.0 pmol/L ($P < 0.08$) and 0.17 ± 0.10 ($P < 0.05$) and decreased by 0.02 ± 0.09 ($P = 0.005$), respectively; and in the control group, increased by 14.0 ± 4.3 pmol/L ($P < 0.001$), 0.57 ± 0.17 ($P < 0.001$), and 0.05 ± 0.14 ($P = 0.036$), respectively. Dietary adherence was high on the basis of fatty acid changes in adipose tissue.

CONCLUSIONS: Diet composition had no major effect on preventing weight regain. However, both the LF and MUFA diets produced less body fat regain than did the control diet, and the dropout rate was lowest in the LF diet group, whereas fasting insulin decreased and the homeostasis model assessment of insulin resistance and ratio of LDL to HDL improved with the MUFA diet. This trial was registered at clinicaltrials.gov as NCT00274729.

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