Healthy eating and lower mortality risk in a large cohort of cardiac patients who received state-of-the-art drug treatment[1–3]

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ABSTRACT

Background: Little is known about dietary scores and mortality risk in cardiac patients who are well treated with drugs with attendant relatively low risk of cardiovascular diseases (CVDs).

Objective: We assessed whether healthy eating lowers the risk of CVD and all-cause mortality in cardiac patients.

Design: We included 4307 patients from the Alpha Omega Trial aged 60–80 y with a clinically diagnosed myocardial infarction and monitored mortality for 10 y. Diet was assessed at baseline (2002–2006) with a validated 203-item food-frequency questionnaire. We created 2 dietary scores on the basis of nonoverlapping sets of foods: the Dutch Healthy Nutrient and Food Score (DHNaFS) and the Dutch Undesirable Nutrient and Food Score (DUNaFS). The associations of both dietary scores with CVD and all-cause mortality were assessed by using multivariable-adjusted Cox regression models.

Results: The median time after myocardial infarction at baseline was 3.7 y (IQR: 1.7–6.3 y). During a median of 6.5 y of follow-up (IQR: 5.3–7.6 y), 801 patients died; 342 of those died of CVD. One patient was lost to follow-up. A substantially higher average amount of DHNaFS foods (~1750 g/d) than DUNaFS foods (~650 g/d) was consumed. Almost all patients received drug treatment: 86% used statins, 90% used antihypertensive medication, and 98% used antithrombotic medication. Patients in the fifth quintile of the DHNaFS had a 30% (HR: 0.70; 95% CI: 0.55, 0.91) lower CVD risk and a 32% (HR: 0.68; 95% CI: 0.47, 0.99) lower all-cause mortality risk than did patients in the first quintile. The DUNaFS was unrelated to both CVD and all-cause mortality.

Conclusion: Beyond state-of-the-art drug treatment, healthy eating was associated with a lower risk of CVD and all-cause mortality in cardiac patients. This trial was registered at clinicaltrials.gov as NCT00127452. *Am J Clin Nutr* 2015;102:1527–33.

Keywords: food-based dietary scores, cardiac patients, cardiovascular disease, mortality, epidemiology

INTRODUCTION

Diet is an important modifiable risk factor for cardiovascular diseases (CVDs)[10] and all-cause mortality. Systematic reviews and a meta-analysis showed a lower risk of CVD and all-cause mortality for healthy dietary scores in general populations (1, 2). Secondary-prevention studies on diet quality in relation to CVD mortality were carried out mostly in study populations who were receiving limited state-of-the-art CVD drugs (3–7). One study showed that a higher-quality diet was associated with lower CVD mortality in patients taking secondary-preventive drugs but used a short and limited food-frequency questionnaire (FFQ) (8). Information is therefore needed about whether healthy eating can further lower the risk of CVD and all-cause mortality in patients, beyond state-of-the-art drug treatment.

Previous prospective cohort studies used dietary scores such as the Mediterranean Diet Score (MDS) (4, 5, 7) and the (modified) Alternative Healthy Eating Index (AHEI) (6, 8), which are based on nutrients as well as a limited number of broadly defined food groups. Consequently, these scores do not reflect the overall dietary pattern because they include mostly nutrient-dense foods but not snacks, ready-to-eat meals, and drinks such as tea and coffee. Dietary scores that are based solely on a broad set of more narrowly defined food groups have the advantage that they are easier to translate into dietary recommendations.

The objective of the present study was to assess the associations of 2 food-based dietary scores with CVD and all-cause mortality in

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[3] Supplemental Tables 1 and 2 and Supplemental Material are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

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[10] Abbreviations used: AHEI, Alternative Healthy Eating Index; CBS, Statistics Netherlands Centraal Bureau voor de Statistiek; CVD, cardiovascular disease; DHNaFS, Dutch Healthy Nutrient and Food Score; DUNaFS, Dutch Undesirable Nutrient and Food Score; FFQ, food-frequency questionnaire; MDS, Mediterranean Diet Score; MET, metabolic equivalents.

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cardiac patients who received state-of-the-art drug treatment. The classification of foods in each score was based on 5 nutrient criteria. We hypothesized that a dietary score higher in healthy nutrients and foods is associated with lower CVD and all-cause mortality risk and a dietary score higher in undesirable nutrients and foods is associated with a greater mortality risk in these patients.

METHODS

Patients and study design

The Alpha Omega Trial, a randomized, placebo-controlled, double-blind intervention study designed to investigate the effect of omega-3 fatty acids on CVD incidence, has been described in detail previously (9, 10). Patients were men and women aged 60–80 y with a verified clinically diagnosed myocardial infarction up to 10 y before being randomly assigned. Between 2002 and 2006, 4837 patients post–myocardial infarction were included in the trial. All patients provided written informed consent. The trial was approved by a central medical ethics committee (Haga Hospital, Leyenburg, The Hague, Netherlands) and by the ethics committee at each participating hospital.

Patients who had missing dietary ($n = 453$) data or implausibly high or low energy intakes (<800 or >8000 kcal/d for men, <600 or >6000 kcal/d for women; $n = 27$) were excluded. Physical activity was missing for 25 patients, smoking status for 1 patient, and educational level was missing for 24 patients. Accounting for analysis-specific exclusions due to missing data for covariates, we included 4307 patients in the fully adjusted Cox proportional hazards models.

Dietary data

Dietary data were collected at baseline and at the final examination (after, on average, 41 mo) by a 203-item FFQ developed for the Alpha Omega Trial. The FFQ was an extended and adapted version of a reproducible and biomarker-validated FFQ. The Pearson correlation coefficient of intake determined by the FFQ and dietary history was 0.83 for energy intake (11). The (8-wk) reproducibility was high for the food groups consumed daily, such as bread and butter/margarine, with Spearman correlation coefficients of up to 0.92 (12). Patients were asked to report their usual intake of foods consumed during the previous month; questions on the frequency, amount, and type of foods, as well as preparation methods were included. Trained dietitians checked the returned questionnaires and obtained additional information on unclear or missing items by phone. Quality-assurance procedures included double entry of the FFQ data. Food-consumption data were converted into energy and nutrient intake by using the 2006 Dutch food-composition database (13).

The 203 food items were collapsed into 24 food groups according to nutrient and energy criteria derived from the Netherlands food-based dietary guidelines (14). Classification criteria for each food were based on presumed positive, neutral, or negative effects on chronic diseases of 5 nutrients: 4 nutrients that likely increase (SFAs, mono-*trans* unsaturated fatty acids, sodium, and added sugar) and 1 nutrient that likely decreases (dietary fiber) the risk of chronic diseases and, for some food groups, energy. A few whole-food groups were classified regardless of nutrients and energy. Each food was classified on the most adverse interpretation of any of the criteria. Details about the classification of foods and food groups are reported in **Supplemental Table 1**. We made a distinction between food groups consisting of healthy nutrients and foods that contribute importantly to the nutrient supply and are typical of the Dutch diet and food groups that are high in undesirable nutrients and foods.

Dietary scores

To create 2 food-based dietary scores, food groups were categorized into quintiles of consumption. The Dutch Healthy Nutrient and Food Score (DHNaFS) included 11 nutrient-dense food groups: vegetables, fruit, whole grains, protein-rich plant foods (mostly legumes), potatoes, lean meat, fish, eggs, low-fat milk and yogurt, oils and soft margarines, and noncaloric drinks. The Dutch Undesirable Nutrient and Food Score (DUNaFS) included 13 food groups that were high in solid fats, sodium, and/or added sugar; processed fruit, high-fat meat, processed meat, full-fat milk, cheese; refined grains, butter and hard margarines, soups, spreads, ready-to-eat meals, savory snacks, sweet snacks, and sugar-sweetened beverages.

The scores were calculated by summing the category scores (0–4) of the food groups. Eggs had a large subset of nonconsumers; therefore, in this food group nonconsumers were coded "0" and consumers were split into quartiles with scores from 1 to 4 to ensure variability across 5 levels of consumption. The theoretical maximum for the DHNaFS was 44 and for the DUNaFS was 52. The correlation between the 2 scores was 0.25.

Baseline means ± SDs were 22.4 ± 6.1 for the DHNaFS and 25.8 ± 7.0 for the DUNaFS on the basis of 4357 FFQs; after 41 mo mean values were 22.3 ± 6.2 for the DHNaFS and 25.9 ± 7.1 for the DUNaFS on the basis of 2219 FFQs. Tracking correlations between baseline scores and the scores after 41 mo were 0.57 for the DHNaFS and 0.61 for the DUNaFS.

Ascertainment and classification of mortality

Vital status and causes of death were monitored through a computerized link with municipal registries. The median follow-up was 6.5 y (IQR: 5.3–7.6 y), and only one patient was lost to follow-up (censored after 2.9 y).

Information on the causes of death was obtained from the Dutch National Mortality Registry [Statistics Netherlands (CBS)] from May 2002 through January 2012. Causes of death were coded according to the *International Classification of Diseases, 10th Revision*. Cardiovascular mortality included ischemic heart diseases (codes: I20–I25), cardiac arrest (I46), sudden death undefined (R96), heart failure (I50), and stroke (I60–I69) as primary or secondary causes of death.

The classifications of the causes of death by the Endpoint Adjudication Committee of the Alpha Omega Trial and CBS were compared for the first 41 mo. On the basis of EAC classification there were 162 CVD events that occurred in the first 41 mo; post-trial there were 180 CVD events on the basis of less complete information of the CBS. Cardiovascular mortality data showed that there was 80% agreement between the 2 classifications when the primary and/or secondary cause of death was used. In total, we observed 801 deaths, of which 342 were CVD deaths. Of the CVD deaths, 265 (77%) had CVD coded as the primary cause of death.

Other measurements

Information on risk factor measurements has been described in detail in previous publications (9, 10). In summary, body weight

and height were measured and BMI was calculated as weight (kg) divided by height squared (m^2). Systolic and diastolic (first and fifth Korotkoff sound, respectively) blood pressures were measured twice with an automatic device, with the patient seated, after a 10-min rest. Blood lipids and glucose were analyzed by standard kits by using an autoanalyzer (Hitachi 912; Roche Diagnostics).

Information on chronic disease history, smoking habits (never, former, or current), and educational level (low, moderate, or high) was collected by a self-administered questionnaire. Alcohol intake was derived from the FFQ data and categorized as 0, >0 to ≤10, >10 to ≤20, or >20 g alcohol/d. Physical activity was assessed by the validated Physical Activity Scale for the Elderly (PASE) (15) and categorized as no activity or only light activity [≤3 metabolic equivalents (METs)], >0 to <5 d/wk of moderate or vigorous activity (>3 METs), or ≥5 d/wk of moderate or vigorous activity (>3 METs). Self-reported patient medications were coded according to the Anatomical Therapeutic Chemical Classification System. Anatomical Therapeutic Chemical Classification System codes were C02, C03, C07, C08, and C09 for blood pressure–lowering medication; C10AA for statins; and B01 for antithrombotic medication.

Statistical analysis

Although the Alpha Omega Trial has an experimental design, the current analyses were conducted as in observational prospective cohort studies (with adjustment for intervention groups). Unadjusted means of patient characteristics were calculated across quintiles of both dietary scores. To investigate the association of the baseline DHNaFS and DUNaFS with CVD and all-cause mortality we used Cox proportional hazard models including both scores simultaneously in the model. Proportional hazards assumptions were examined by a log-minus-log plot, and the assumptions were met. Survival time was defined as the period (in days) between assessment date at baseline and date of death (CVD or all-cause) or end of follow-up (for participants who survived). For the patient who was lost to follow-up, survival time was defined as the period in days between baseline and the last available update of CBS data for that patient. We studied different levels of adjustment. A minimal model (model 1) included sex and age (in years) and intervention groups [placebo, EPA+DHA and α-linolenic acid (18:3n−3; ALA), EPA+DHA, and ALA]. Model 2 was further adjusted for energy [energy (kcal)/SD], alcohol intake (0, >0 to ≤10, >10 to ≤20, or >20 g/d), level of education (low, moderate, or high), physical activity [no activity or only light activity (≤3 METs), >0 to <5 d/wk of moderate or vigorous activity (>3 METs), or ≥5 d/wk of moderate or vigorous activity (>3 METs)], and smoking status (never, former, or current). Model 3 was additionally adjusted for BMI (kg/m^2), systolic blood pressure (mm Hg), total cholesterol:HDL cholesterol (mmol/L), and prevalence of diabetes.

Sensitivity analysis included stratification models by sex (male vs. female), age (<65 vs. ≥65 y), BMI (<30 vs. ≥30), physical activity (no or only light activity vs. moderate to vigorous physical activity), alcohol [consumers (alcohol intake >0 g/d) vs. nonconsumers (alcohol intake = 0 g/d)], and smoking (ever vs. never). For these analyses, the DHNaFS was dichotomized at the median. Data were analyzed by using used the PC version 9.3 of the Statistical Analysis System (SAS Institute).

RESULTS

Dietary scores

The participants in this study consumed, on average, a substantially higher amount of the foods in the DHNaFS (~1750 g/d) than the foods in the DUNaFS (~650 g/d), resulting in an overall ratio of 2.9. The gram weight consumption of food groups generally increased across quintiles of both scores, with the exception of full-fat milk in the DHNaFS. The medians (quintile 3) of the food groups in the DHNaFS and DUNaFS were similar, but the range of intake (quintile 5 vs. quintile 1) of the DHNaFS food groups was at least 2 times greater across quintiles of the DHNaFS than across those of the DUNaFS (**Table 1**). Across quintiles of both scores, the absolute intake of energy and nutrients increased; however, the macronutrients expressed relative to energy as energy percentage decreased across quintiles of the DHNaFS and increased across quintiles of the DUNaFS (**Table 2**). There was a smaller range of intake (quintile 5–quintile 1) of saturated fat (5 vs. 14 g), sodium (762 vs. 1090 mg), and added sugar (31 vs. 67 g) and a larger range of intake of dietary fiber (12 vs. 7 g) across quintiles of the DHNaFS than across quintiles of the DUNaFS.

Baseline characteristics were generally similar across the quintiles of the 2 dietary scores (Table 2). Patients in the highest quintile of both scores were more likely to be male and have a lower prevalence of diabetes. Blood pressure and serum lipids did not differ across quintiles. Almost all of the patients received state-of-the-art antithrombotic, antihypertensive, and statin therapy. Patients in the highest quintile of both scores were more likely to be moderate to vigorously active, nonsmokers, more highly educated, and alcohol consumers. Differences for these lifestyle variables were generally smaller across quintiles of the DUNaFS.

Dietary scores, CVD, and all-cause mortality

Cox proportional HRs for CVD and all-cause mortality across quintiles of the DHNaFS and DUNaFS simultaneously modeled are presented in **Table 3**. A higher DHNaFS was significantly associated with a lower all-cause mortality risk (P-trend = 0.0006). In the fully adjusted model, patients in the highest quintile of the DHNaFS had a 30% lower all-cause mortality risk than patients in the lowest quintile. Higher DHNaFSs were also significantly associated with a lower CVD mortality risk. Patients in the highest quintile of the DHNaFS had a 32% lower CVD mortality risk than patients in the lowest quintile. The DUNaFS was not associated with all-cause or CVD mortality.

In sensitivity analysis we stratified patients for sex, age, prevalent diabetes, BMI, smoking, physical activity, and alcohol consumption and no major differences were observed between strata, except for alcohol, which showed only an inverse association in the consumers (**Supplemental Table 2**). In the adjusted model (model 3), the first alcohol category (>0–10 g alcohol/d) compared with no alcohol consumption (0 g alcohol/d) predicted lower all-cause mortality. Few individual food groups (adjusted for the dietary scores minus that specific food group) were associated with the outcomes. Whole-grain consumption modeled together with the DHNaFS (without whole grains) and the DUNaFS predicted mortality; however, the DHNaFS (without whole grains) remained significantly associated (data

TABLE 1
Intakes of food groups by 4357 cardiac patients in the Alpha Omega Trial across quintiles of the DHNaFS and the DUNaFS[1]

	DHNaFS,[2] g/d			DUNaFS,[3] g/d		
	Q1	Q3	Q5	Q1	Q3	Q5
DHNaFS food groups[4]						
Vegetables	48 (35–67)	77 (62–98)	105 (86–131)	69 (45–94)	77 (58–100)	85 (63–110)
Fruit	47 (14–114)	108 (43–217)	239 (111–310)	106 (35–254)	116 (46–264)	110 (69–255)
Whole grains	88 (66–130)	118 (88–158)	158 (111–181)	94 (88–158)	111 (88–158)	138 (88–167)
Potatoes	50 (47–99)	99 (50–99)	99 (99–140)	70 (50–99)	99 (50–99)	99 (70–132)
Protein-rich plant foods	6 (3–11)	12 (7–18)	18 (12–26)	9 (4–15)	12 (7–19)	14 (9–21)
Lean meat	15 (3–27)	27 (14–40)	36 (25–47)	19 (3–36)	25 (12–39)	30 (17–40)
Eggs	7 (3–18)	18 (7–18)	18 (7–18)	7 (3–18)	7 (7–18)	18 (7–18)
Fish	5 (0–14)	14 (4–17)	16 (13–38)	12 (2–18)	12 (4–17)	15 (8–22)
Low-fat milk and yogurt	106 (21–171)	160 (95–300)	300 (150–396)	150 (71–300)	166 (106–300)	167 (87–300)
Oils and soft margarines	0 (0–1)	2 (0–5)	4 (1–9)	1 (0–5)	1 (0–5)	2 (0–5)
Noncaloric drinks	750 (502–1006)	931 (676–1250)	1175 (892–1500)	900 (570–1275)	954 (712–1275)	949 (713–1250)
DUNaFS food groups						
Processed fruit	73 (20–156)	95 (29–176)	127 (42–212)	50 (0–127)	94 (21–168)	148 (73–237)
Refined grains	39 (17–80)	37 (20–67)	41 (23–68)	21 (10–41)	40 (23–66)	67 (42–97)
High-fat meat	17 (3–34)	24 (10–40)	31 (17–43)	12 (0–26)	23 (11–40)	35 (21–48)
Processed meat	12 (6–18)	16 (6–41)	18 (7–43)	7 (3–17)	13 (6–40)	18 (13–43)
Full-fat milk and yogurt	48 (11–128)	38 (6–106)	28 (2–82)	11 (0–45)	39 (11–103)	75 (36–153)
Cheese	14 (7–21)	19 (8–31)	20 (14–49)	10 (7–20)	19 (8–28)	21 (14–50)
Butter and hard margarines	9 (2–22)	10 (1–22)	9 (1–22)	2 (0–11)	10 (2–21)	18 (8–31)
Soups	31 (12–79)	35 (17–90)	35 (17–90)	17 (0–35)	35 (17–90)	67 (35–124)
Spreads	10 (2–17)	13 (4–20)	15 (6–30)	5 (2–15)	13 (5–20)	18 (11–36)
Ready-to-eat meals	35 (10–69)	45 (18–77)	59 (25–92)	22 (6–48)	49 (21–75)	80 (48–113)
Sweet snacks	44 (23–76)	51 (31–83)	57 (36–86)	27 (14–45)	51 (33–77)	84 (59–113)
Savory snacks	14 (7–24)	18 (9–29)	17 (10–29)	8 (4–14)	17 (9–26)	29 (19–39)
Sugar-sweetened beverages	21 (0–108)	28 (0–106)	25 (0–92)	0 (0–30)	21 (0–82)	75 (21–160)

[1]Values are medians; IQRs in parentheses. Tests for trend were based on general linear regression with dietary scores as a continuous independent variable. DHNaFS, Dutch Healthy Nutrient and Food Score; DUNaFS, Dutch Undesirable Nutrient and Food Score; Q, quintile.

[2]P-trend < 0.05 across quintiles of the DHNaFS for all food groups except for butter and hard margarines.

[3]P-trend < 0.05 across quintiles of the DUNaFS for all food groups except for fruit, low-fat milk and yogurt, oils, and soft margarines.

[4]Foods included in each food group can be found in Supplemental Table 1.

not shown). The consumption of sandwich spreads was also inversely associated with the outcomes but did not change associations with the dietary scores (data not shown).

DISCUSSION

Cardiac patients consumed 3 times more (by gram weight) of the foods in the DHNaFS than foods high in solid fats, sodium, and/or added sugar, which were included in the DUNaFS. The DHNaFS was associated with an ~30% lower risk of all-cause and CVD mortality when comparing the extreme score quintiles. The DUNaFS was not associated with all-cause and CVD mortality.

Dietary quality scores based solely on food groups have the advantage that they are easier to understand and implement compared with existing mixed-food group and nutrients scores such as the AHEI or MDS. In addition, our nutrient-based method of rating food groups mimics what a consumer would do if selecting foods to eat based primarily on 5 nutrient criteria and energy content. Furthermore, our DHNaFS and DUNaFS include all food groups that are part of the Dutch dietary pattern. In contrast, in the MDS, for example, only a few, broadly defined, nutrient-dense food groups are rated (e.g., total dairy and total meat), which are not easily translated into a healthy dietary pattern. The creation of 2 dietary scores, one with nutrient-rich foods and one with foods high in solid fats, sodium, and/or added sugar, allowed easy comparison of the value of higher intakes of foods considered by our criteria to be healthier vs. lower intakes of foods considered not to be healthy.

As in the present study, the Nurses' Health Study and the Health Professionals Follow-Up Study observed a lower risk of all-cause mortality in patients with previous CVD in the multivariable-adjusted pooled HRs in the highest quintile of the AHEI and MDS [HRs (95% CI): 0.76 (0.60, 0.96) and 0.81 (0.72, 0.91) respectively]. Neither of the scores reached significance for the association with CVD mortality in the pooled analysis [HRs (95% CI): 0.73 (0.51, 1.04) and 0.85 (0.67, 1.09), respectively]. Furthermore, after the exclusion of the alcohol component from the AHEI and MDS, the results were attenuated, suggesting that moderate alcohol intake was an important health contributor to both scores (6, 7). This was confirmed by both Trichoupoulou et al. (16) and Hoevenaar-Blom et al. (17), who showed that alcohol contributed most to the inverse association of the MDS with CVD and all-cause mortality. In our study, we excluded alcohol from our scores and nevertheless found associations of the DHNaFS with CVD and all-cause mortality.

The food groups scored in the DUNaFS were generally high in solid fats, sodium, and/or added sugar. Therefore, we hypothesized an unfavorable effect on health; however, this dietary score

TABLE 2
Baseline characteristics of 4357 cardiac patients in the Alpha Omega Trial across quintiles of the DHNaFS and the DUNaFS[1]

	DHNaFS[2]			DUNaFS[3]		
	Q1	Q3	Q5	Q1	Q3	Q5
Energy, kcal/d	1509 ± 4423[4]	1811 ± 446	2129 ± 470	1327 ± 323	1790 ± 334	2317 ± 416
Saturated fat, g	21.2 ± 9.9	23.8 ± 9.9	26.2 ± 9.7	15.3 ± 6.1	23.1 ± 7.7	32.3 ± 9.4
trans Fat, g	1.2 ± 0.6	1.4 ± 0.6	1.5 ± 0.6	0.9 ± 0.4	1.3 ± 0.4	1.9 ± 0.5
Sodium, mg	1829.9 ± 595.0	2174.9 ± 621.0	2591.6 ± 643.9	1670.0 ± 465.9	2121.9 ± 529.7	2760.4 ± 634.6
Fiber, g	15.7 ± 5.0	21.0 ± 5.1	27.6 ± 6.3	18.2 ± 6.3	21.2 ± 6.4	24.8 ± 7.2
Added sugar, g	87.0 ± 47.6	100.5 ± 46.3	118.0 ± 45.7	69.7 ± 34.2	100.0 ± 40.0	136.9 ± 47.7
Sex, *n* (%)						
Female	290 (30.7)	219 (20.2)	142 (15.4)	297 (36.2)	198 (20.7)	97 (10.5)
Male	656 (69.3)	864 (79.8)	783 (84.7)	523 (63.8)	759 (79.3)	831 (89.6)
Age, y	69.6 ± 5.5	68.9 ± 5.5	68.7 ± 5.5	69.5 ± 5.5	69.2 ± 5.5	68.6 ± 5.7
BMI, kg/m^2	27.8 ± 4.2	27.7 ± 3.8	27.5 ± 3.7	28.2 ± 4.1	27.7 ± 3.8	27.4 ± 3.6
BMI ≥30, *n* (%)	252 (26.6)	246 (22.7)	186 (20.1)	229 (27.9)	221 (23.1)	180 (19.4)
Time since myocardial infarction, y	4.3 ± 3	4.2 ± 3.1	4.2 ± 3.3	4.4 ± 3.5	4.4 ± 3.2	4.2 ± 3.2
Antithrombotic drugs,[5] *n* (%)	918 (97)	1056 (97.5)	910 (98.4)	790 (96.3)	933 (97.5)	911 (98.2)
Antihypertensive drugs,[6] *n* (%)	858 (90.7)	961 (88.7)	834 (90.2)	739 (90.1)	851 (88.9)	829 (89.3)
Statins, *n* (%)	785 (83.0)	924 (85.3)	810 (87.6)	724 (87.1)	827 (86.1)	766 (83.4)
Prevalent diabetes mellitus, *n* (%)	211 (22.3)	210 (19.4)	182 (19.7)	216 (26.3)	181 (18.9)	146 (15.7)
Systolic blood pressure, mm Hg	142.5 ± 22.6	141.2 ± 21.2	140.4 ± 21	142.7 ± 22.4	141.8 ± 20.8	139.8 ± 21.3
Diastolic blood pressure, mm Hg	79.8 ± 11.3	80.2 ± 10.8	79.8 ± 10.5	79.5 ± 11.4	80.4 ± 11.1	80 ± 11.3
Serum lipids,[7] mmol/L						
Total cholesterol	4.79 ± 1.00	4.69 ± 0.91	4.59 ± 0.87	4.81 ± 0.99	4.73 ± 0.94	4.64 ± 0.91
LDL cholesterol	2.62 ± 0.87	2.56 ± 0.78	2.51 ± 0.75	2.61 ± 0.87	2.58 ± 0.79	2.57 ± 0.81
HDL cholesterol	1.30 ± 0.36	1.28 ± 0.34	1.28 ± 0.32	1.33 ± 0.37	1.29 ± 0.34	1.25 ± 0.31
Triglycerides[8]	1.69 (1.28–2.33)	1.63 (1.19–2.31)	1.56 (1.15–2.18)	1.67 (1.20–2.35)	1.67 (1.25–2.31)	1.59 (1.16–2.29)
Physical activity, *n* (%)						
No activity or only light activity	502 (53.5)	450 (41.8)	284 (30.9)	367 (45.1)	381 (40)	354 (38.2)
0–5 d/wk of moderate or vigorous activity (>3 METs)	292 (31.1)	401 (37.3)	388 (42.2)	261 (32.1)	366 (38.4)	382 (41.3)
≥5 d/wk of moderate or vigorous activity (>3 METs)	144 (15.4)	225 (20.9)	248 (27)	185 (22.8)	206 (21.6)	190 (20.5)
Smoking, *n* (%)						
Never	158 (16.7)	162 (15)	174 (18.8)	155 (18.9)	154 (16.1)	154 (16.6)
Former	556 (58.8)	739 (68.2)	668 (72.2)	525 (64)	640 (66.9)	638 (68.8)
Current	232 (24.5)	182 (16.8)	83 (9)	140 (17.1)	163 (17)	136 (14.7)
Educational level, *n* (%)						
Low	610 (65)	615 (57.2)	444 (48.1)	497 (61.4)	537 (56.4)	482 (52.2)
Moderate	265 (28.2)	334 (31.1)	313 (33.9)	249 (30.7)	290 (30.4)	317 (34.3)
High	64 (6.8)	126 (11.7)	166 (18)	64 (7.9)	126 (13.2)	125 (13.5)
Alcohol consumption, *n* (%)						
0 g/d	286 (30.2)	187 (17.3)	127 (13.7)	247 (30.1)	176 (18.4)	119 (12.8)
>0–10 g/d	373 (39.4)	421 (38.9)	365 (39.5)	311 (37.9)	366 (38.2)	374 (40.3)
>10 to ≤20 g/d	112 (11.8)	207 (19.1)	204 (22.1)	105 (12.8)	185 (19.3)	205 (22.1)
>20 g/d	175 (18.5)	268 (24.8)	229 (24.8)	157 (19.2)	230 (24)	230 (24.8)

[1]Tests for trend of continuous variables were based on general linear regression with dietary scores as a continuous independent variable. Chi-square tests were used for categorical variables across all 5 levels of dietary scores. ATC, Anatomical Therapeutic Chemical Classification System; DHNaFS, Dutch Healthy Nutrient and Food Score; DUNaFS, Dutch Undesirable Nutrient and Food Score; METs, metabolic equivalents; Q, quintile.

[2]*P*-trend < 0.05 across quintiles of the DHNaFS for all characteristics except for time since myocardial infarction, prevalent diabetes mellitus, diastolic blood pressure, HDL cholesterol, antihypertensive drugs, and antithrombotic drugs.

[3]*P*-trend < 0.05 across quintiles of the DUNaFS for all characteristics except for time since myocardial infarction, diastolic blood pressure, triglycerides, LDL cholesterol, smoking, and antihypertensive drugs.

[4]Mean ± SD (all such values).

[5]ATC code B01.

[6]ATC codes C02, C03, C07, C08, and C09.

[7]To convert the values for serum cholesterol to milligrams per deciliter, divide by 0.02586. To convert the values for serum triglycerides to milligrams per deciliter, divide by 0.01129.

[8]Values are medians; IQRs in parentheses.

was not associated with mortality. Patients in the highest quintiles of the DUNaFS also consumed a substantial amount of DHNaFS foods; however, the ratio between DHNaFS and DUNaFS food groups was greater for the highest quintiles of the DHNaFS compared with the DUNaFS, which may partly explain the lack of association with mortality for the DUNaFS. Furthermore, some food

TABLE 3
Multivariable adjusted HRs for all-cause and CVD mortality across quintiles of the DHNaFS and the DUNaFS[1]

	Q1	Q2	Q3	Q4	Q5	*P*-trend
DHNaFS	14 (12, 16)[2]	20 (19, 21)	23 (22, 24)	27 (26, 28)	31 (30, 34)	
n	946	667	1083	736	925	
Person-years	5966.8	4204.3	6896.3	4475.0	4759.5	
Cases of all-cause mortality, *n*	228	137	193	120	123	
AR per 1000 person-years of all-cause mortality	38.2	32.6	28.0	26.8	25.8	
Cases of CVD mortality, *n*	102	58	73	48	61	
AR per 1000 person-years of CVD mortality	17.1	13.8	10.6	10.7	12.8	
DUNaFS	17 (14, 18)	22 (21, 23)	26 (25, 27)	29 (29, 30)	35 (33, 37)	
n	831	791	961	855	919	
Person-years	5363.2	4987.1	6074.8	5411.6	5865.4	
Cases of all-cause mortality, *n*	165	159	177	156	144	
AR per 1000 person-years of all-cause mortality	30.8	31.9	29.1	28.8	24.6	
Cases of CVD mortality, *n*	70	70	65	69	68	
AR per 1000 person-years of CVD mortality	13.1	14.0	10.7	12.8	11.6	
All-cause mortality						
DHNaFS						
Model 1	1	0.89 (0.72, 1.10)	0.74 (0.61, 0.90)	0.67 (0.54, 0.84)	0.57 (0.45, 0.71)	<0.0001
Model 2	1	0.97 (0.78, 1.20)	0.81 (0.66, 0.99)	0.78 (0.62, 0.99)	0.72 (0.56, 0.93)	0.0015
Model 3	1	0.95 (0.76, 1.18)	0.77 (0.63, 0.95)	0.76 (0.60, 0.97)	0.70 (0.55, 0.91)	0.0006
DUNaFS						
Model 1	1	1.12 (0.90, 1.39)	1.03 (0.83, 1.27)	1.09 (0.87, 1.36)	0.95 (0.75, 1.20)	0.552
Model 2	1	1.19 (0.94, 1.49)	1.10 (0.87, 1.39)	1.24 (0.95, 1.62)	1.08 (0.79, 1.48)	0.857
Model 3	1	1.22 (0.97, 1.54)	1.14 (0.89, 1.45)	1.28 (0.98, 1.68)	1.15 (0.84, 1.58)	0.702
Cardiovascular mortality						
DHNaFS						
Model 1	1	0.84 (0.60, 1.16)	0.62 (0.46, 0.84)	0.59 (0.41, 0.83)	0.61 (0.44, 0.85)	<0.0001
Model 2	1	0.88 (0.63, 1.23)	0.63 (0.46, 0.87)	0.65 (0.45, 0.94)	0.72 (0.50, 1.03)	0.008
Model 3	1	0.88 (0.63, 1.23)	0.59 (0.43, 0.82)	0.59 (0.41, 0.87)	0.68 (0.47, 0.99)	0.0002
DUNaFS						
Model 1	1	1.17 (0.83, 1.63)	0.90 (0.64, 1.26)	1.14 (0.81, 1.61)	1.05 (0.74, 1.48)	0.99
Model 2	1	1.19 (0.84, 1.68)	0.87 (0.60, 1.27)	1.17 (0.78, 1.76)	1.09 (0.68, 1.74)	0.651
Model 3	1	1.22 (0.86, 1.73)	0.92 (0.63, 1.34)	1.23 (0.82, 1.85)	1.15 (0.72, 1.84)	0.759

[1]HRs (95% CIs) were generated by Cox proportional hazards regression including both scores simultaneously in the model, with Q1 as the referent. Model 1 adjusted for age (in years) and sex (male or female) and intervention group (placebo, EPA-DHA and ALA, EPA-DHA, and ALA). Model 2 additionally adjusted for energy [energy (kcal)/SD], alcohol intake (0, >0–10, >10 to ≤20, or >20 g/d), level of education (low, moderate, or high), physical activity [no physical activity, 0–5 d/wk of moderate or vigorous activity (>3 metabolic equivalents), or ≥5 d/wk of moderate or vigorous activity (>3 metabolic equivalents)], and smoking status (never, former, or current). Model 3 additionally adjusted for BMI (kg/m^2), prevalent diabetes, systolic blood pressure, and total cholesterol:HDL cholesterol. ALA, α-linolenic acid; AR, absolute risk; CVD, cardiovascular disease; DHNaFS, Dutch Healthy Nutrient and Food Score; DUNaFS, Dutch Undesirable Nutrient and Food Score; Q, quintile.

[2]HR; 95% CI in parentheses (all such values).

groups may have been misclassified: for example, we found that sandwich fillings were inversely associated with the outcomes. This could relate to healthful effects of peanut butter (18) or chocolate (19), but we could not clearly isolate a reason for this finding.

Our study has limitations. The patients in the Alpha Omega Trial received additional amounts of ω-3 fatty acids (10). However, adjustment for intervention groups did not change our results. Patients may have received dietary advice to improve their diet after their first myocardial infarction and could have made changes in their diet during follow-up. The tracking correlation of the DHNaFS over 41 mo indicates that the score was tracked over time and was similar to the tracking correlations of the a priori diet quality score observed in the population-based Coronary Artery Risk Development in Young Adults study over 7 and 20 y (20). Because our study population included only patients, our results are not generalizable to the general "healthy" population. Although we accounted for many possible confounders, as in every observational analysis, we cannot rule out residual confounding.

Our study also has several strengths. We realized a complete mortality follow-up of the vital status and causes of death of the patients. We used an extensive and detailed FFQ, which enabled us to define food groups objectively and systematically using classification criteria for foods derived from the Netherlands' food-based dietary guidelines (14). Also, we assessed the association of diet quality in a cohort in which almost all of the patients received state-of-the-art antithrombotic, antihypertensive, and statin therapy. Previous studies assessed diet quality in populations who did not receive adequate statin treatment (3–5) or were heterogeneous for statin treatment (6, 7).

In conclusion, our results suggest that cardiac patients who consume a nutrient-rich diet have lower all-cause and CVD mortality risk. Despite the fact that our patients received state-of-the-art drug treatment, we observed an additional beneficial effect on mortality of a high-quality diet.

See the **Supplemental Material** for a list of committees and collaborators.

The authors' responsibilities were as follows—FPCS: conceptualization, statistical analysis, interpretation, and writing of the manuscript; SSS-M: conceptualization, interpretation, and writing and critical review of the manuscript; JdG, LMOG, JMG, and EJG: substantial contributions to conception and design, acquisition of data, and critical review of the manuscript; MJdB: acquisition of data and critical review; DRJ: conceptualization and critical review of the manuscript; and DK: conception and design of the study and conceptualization, interpretation, writing, and critical review of the manuscript. FPCS, LMOG, EJG, MJdB, and DK declared no conflicts of interest. SSS-M, JdG, and JMG received unrestricted research grants from the Dutch Dairy Association and Global Dairy Platform to carry out meta-analyses on the association between dairy products and cardiovascular diseases. DRJ is a consultant to the California Walnut Commission.

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