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RESEARCH ARTICLE

Adherence to a Mediterranean diet is associated with reduced risk of heart failure in men

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Aims We examined the hypothesis that high adherence to a Mediterranean diet reduces the risk of developing heart failure (HF) as well as the risk of death from HF.

Methods and results The study population comprised 37 308 men from the Cohort of Swedish Men who were free from cardiovascular disease at baseline. The modified Mediterranean diet (mMED) score was created from a self-administered food frequency questionnaire, based on consumption of presumed beneficial/detrimental foods, on a 0–8 scale. Incident HF events were ascertained by linkage to the Swedish National Patient and the Cause of Death Registers. Relative risks (RR) with 95% confidence intervals (CI), adjusted for potential confounders, were estimated by Cox proportional hazards regression models. We identified 146 deaths from HF and 1269 incident HF events over a median follow-up of 10.9 years (1998–2008). The mMED score was inversely associated with risk of HF (multivariable RR for the highest vs. lowest quartile 0.69, 95% CI 0.57, 0.83); the corresponding RR of HF mortality was 0.55 (95% CI 0.31, 0.98). The multivariable RR for every two-point increment in the mMED score was 0.85 (95% CI 0.78, 0.91) for incidence of HF and 0.78 (95% CI 0.62, 0.98) for mortality from HF, respectively.

Conclusions High adherence to a Mediterranean diet was associated with a lower risk of HF and mortality from HF in men. Further studies are needed to replicate these findings in other populations.

Keywords Mediterranean diet • Heart failure • Prospective studies • Primary prevention • Men

Introduction

Heart failure (HF) is the greatest cause of hospitalization in older adults[1] and is associated with substantial health-care cost.[2] The overall lifetime risk of developing HF among individuals over 40 years of age is 20% and half of the HF patients die within 5 years after diagnosis.[3] Lifetime risk of HF is substantially higher for those with parental history of HF and for those with myocardial infarction (MI), atrial fibrillation (AF), hypertension, and diabetes mellitus.[3] Moreover, in the presence of HF there is an increased risk of cardiovascular disease (CVD), in particular AF.[3]

The role of nutrition in prevention and improvement of prognosis of HF is recognized, but still under investigation.[4] There are no specific dietary recommendations explicitly for primary prevention of HF and dietary guidance aims mainly to keep risk factors, in particular hypertension and hyperlipidaemia, in optimal status.[4,5] In this respect, sodium restriction as a part of a healthy lifestyle has been the main focus regarding primary prevention of HF.[5] Nevertheless, modifying overall diet might be of greater relevance and effectiveness. Recently, studies have reported favourable results for specific clinical biomarkers of HF or HF-related disorders in relation to healthy dietary patterns.[6–8] Moreover a sodium-restricted

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'Dietary Approaches to Stop Hypertension' (DASH) diet has been modestly inversely associated with the incidence of HF[9,10] and mortality.[11] A typical Mediterranean diet is fundamentally similar to the DASH diet but without sodium restriction. Hence, it is easily achievable and is likely to be equally beneficial against HF and its comorbidities, but available data is mainly in women[11] and for people at high risk of HF or with established HF.[11,12] Our aim was to determine the association between the adherence to a Mediterranean diet, as indicated by a modified Mediterranean diet (mMED) score, and incidence of HF as well as death from HF in a large Swedish general male population.

Methods

Study population

For this study, we used data from the population-based Cohort of Swedish Men (COSM), which is representative of age distribution, education level, and prevalence of overweight of Swedish men aged 45–79 years.[13] During the autumn of 1997, 48 850 men (49% of the source population), who were aged 45–79 years and were residents of the Örebro and Västmanland counties of central Sweden, completed a ≈350-item questionnaire on diet and lifestyle factors. We omitted men with a missing or an erroneous National Registration Number. We also excluded men with history of cancer ($n = 2592$) or CVD (HF, ischaemic heart disease and stroke, $n = 5761$) at baseline, after linkage to the national registries, because of possible modifications in diet. Finally, we excluded those with implausible energy intakes (i.e. three standard deviations from the $\log_e$-transformed mean total energy intake; $n = 441$) and missing values of the components of the mMED score ($n = 2396$), resulting in a final study population of 37 308 men at the start of follow-up. The investigation conforms to the principles outlined in the Declaration of Helsinki; the research protocol was approved by the Regional Ethical Review Board at Karolinska Institutet in Stockholm, Sweden. A completed questionnaire was obtained and considered as informed consent.

Baseline data collection

We obtained information on education, body weight and height, tobacco-smoking status, aspirin use, physical activity, prevalence of hypertension and hypercholesterolemia, family history of MI before 60 years of age, alcohol consumption, and diet through a self-administered questionnaire. A validated questionnaire assessed activity level at work, home and during leisure time, for the year before participation in the study, including questions on time spent walking or bicycling (six predefined duration categories) and leisure-time exercise (five predefined duration categories). We defined history of diabetes as a diagnosis of diabetes in the National Diabetes Register or the Swedish National Inpatient Register at the National Board of Health and Welfare, after a computerized linkage to our cohort and complemented with self-reported diabetes from the questionnaire (sensitivity of self-reported diabetes was 84.6%). We calculated body mass index (BMI) by dividing the weight in kilograms by the square of height in metres.

Baseline dietary assessment

We used a 96-item semi-quantitative food frequency questionnaire (FFQ) to assess the average habitual dietary intake of the previous year, including foods/food items and beverages. Men responded to open-ended questions with predefined serving sizes (one glass, one cup, teaspoon, tablespoon, and slice) for commonly consumed foods (e.g. dairy products including whole, semi-skimmed, and skimmed milk, sour milk and yogurt, cheese, including full-fat, reduced fat and low-fat, bread, including crisp, white and whole-grain, butter and margarine, and beverages including coffee, tea and sodas). For other food items, including vegetables, fruits, legumes, nuts, grains, fish, red and processed meat, and alcoholic beverages, they responded to questions with eight predefined categories of food frequency, ranging from 'never/seldom' to 'three or more times per day'. For alcohol consumption, we multiplied reported frequencies of specific alcoholic beverages (wine, beer, and liquor) with the reported amount, consumed at a single occasion, resulting in an average total alcohol consumption per day.[14] We calculated total energy intake by multiplying the frequency of consumption of each food item by the energy of age-specific portion sizes, respectively, using composition values from the Swedish Food Administration Database.[15] The FFQ has been validated for nutrients by comparison with 14 24-h dietary recall interviews completed by 248 Swedish men and the mean Spearman correlation coefficient were 0.65 for macronutrients and 0.62 for micronutrients, including supplements.[16]

The mMED score

We used the mMED score, which is a revised version of the one created by Trichopoulou *et al.*[17,18] to assess relative adherence to the traditional Mediterranean diet. The mMED score included: (i) vegetables and fruits (excluding fruit juices and potatoes), (ii) legumes and nuts, (iii) non-refined/high fibre grains (whole-meal bread, crisp bread, oatmeal, and wheat bran), (iv) fermented dairy products (cultured milk, yogurt, and cheese), (v) fish, (vi) red and processed meat, (vii) use of olive oil and/or rapeseed oil and (vii) alcohol. Participants with a consumption at or above the median consumption received one point for the presumed beneficial components (vegetables and fruits, legumes and nuts, non-refined/high fibre grains, fermented dairy products, and fish) and for consumption below the median consumption they received zero points. For red and processed meat, the reverse was applied. For alcohol, one point was assigned to men who consumed on average between 10 and 30 g of ethanol per day, otherwise zero points. For olive and rapeseed oil, men reported whether they used it on bread and when cooking and one point was assigned to men who used olive oil and/or rapeseed oil as a main source of fat for cooking or as dressing, otherwise zero points. We included rapeseed oil, in addition to olive oil, as a presumed beneficial source of fat because of its high monounsaturated fatty acid content (it has the lowest omega-6 to omega-3 ratio of the commonly used vegetable oils),[19,20] hence it can be considered a representative indicator of fat quality in Swedish population. In Sweden, the yearly per capita use of olive oil is quite low (0.8 vs. 2.6 kg in Europe), while the use of rapeseed oil is high (7.0 vs. 2.3 kg in Europe).[19] The total mMED score ranged from 0 (low adherence) to 8 (high adherence to Mediterranean diet).

Ascertainment of heart failure events and follow-up

Incident events of HF during follow-up were ascertained by record linkage of the study cohort to the Swedish National Patient (NPR) and the Swedish Cause of Death (CDR) Registers. In the main analysis, we used the International Statistical Classification of Disease, 10th revision, codes I11 and I50 to classify all HF events, listed as primary

diagnosis and defined as HF hospitalization, non-hospitalized specialist care or deaths from HF, from 1 January 1998 to 31 December 2008. In secondary analysis, we included these codes to identify incident HF events in any diagnosis position. In a validation study using the criteria of the European Society of Cardiology, the positive predictive value of HF in the NPR was 95% for HF as primary diagnosis and 82% for HF in any diagnosis position.[21] Dates of death were ascertained by record linkage to the Swedish Death Register.

Statistical analysis

We followed participants up to the date of diagnosis of HF, death, or end of follow-up, whichever occurred first. Men were assigned into quartiles of the mMED score (slightly larger 1st quartile). The mMED score was also used as a continuous variable per two-point increment. We estimated age-standardized rates per 100 000 person-years by quartiles of the mMED score. We used Cox proportional hazards regression models with attained age as the underlying time-scale to estimate relative risks (RR) with corresponding 95% confidence intervals (CIs). All models were adjusted for education level (≤12 years, >12 years) and proposed/established risk factors for CVD, including family history of MI before 60 years of age (yes or no), cigarette smoking (current, former, never), physical activity (>40 minutes walking and/or cycling per day, >1 h of exercise per week), BMI (<20, 20–24.9, 25–29.9, ≥30 kg/m^2), history of hypertension (yes or no), history of hypercholesterolaemia (yes or no), history of diabetes (yes or no), aspirin use (never, 1–6 tablets/week, ≥7 tablets/week) and total energy intake (continuous, kcal/day). We treated missing values (<2%, with the exception of physical activity <10%) as a separate category.

To examine a potential modification of our results through reverse causation, we excluded all incident HF events during the first 2 years of follow-up from the analysis, because early-stage HF symptoms could have affected reporting/adherence to the Mediterranean diet. In addition, as people who have suffered a previous MI or AF have a substantially higher risk of developing HF,[3] we conducted a separate analysis after censoring HF events occurring after an MI or AF. We conducted analyses for the following covariates: diabetes, hypertension, hypercholesterolaemia and smoking status, as these are major risk factors of CVD[3] and could potentially modify the association between the mMED score and HF risk. Finally, to determine whether associations could be described solely by single components, we tested each single component of the mMED score separately as a dichotomous variable (above/below the median), after mutual adjustment for all other components and risk factors.

Tests for trend across quartiles of the mMED score were conducted by assigning the median value for each quartile, modelled as a continuous variable. We tested whether the proportional hazard assumption was reasonable, based on scaled Schoenfeld residuals and graphical methods (Kaplan–Meier curves); there was no evidence of violation of the assumption. All the statistical analyses were performed using Stata software, version 12.1 (StataCorp, LP, College Station, TX, USA). All *P*-values were two-sided and the level of statistical significance was set to 5%.

Results

Over a median follow-up of 10.9 years of 37 308 men, we identified 146 deaths from HF, 1269 incident HF events listed as primary diagnosis and a total of 2210 HF events in any diagnosis position. *Table 1* shows daily consumption of each component of the mMED score. Compared with men in the lowest quartile of the mMED score, those in the highest quartile had higher education, were more physically active, had a higher energy intake, and were less likely to be current smokers and overweight or obese (*Table 2*).

Table 1 Baseline consumption of each food component of the modified Mediterranean diet (mMED) score in the Cohort of Swedish Men (*n* = 37 308)

mMED score component[b] (servings/day)	Median value[a] 4.0	Range 0–8
Vegetables and fruits	3.3	0–27.2
Legumes and nuts	0.2	0–6.0
Non-refined/high fibre grains	3.5	0–24.2
Fermented dairy	3.5	0–25.7
Fish	0.2	0–6.0
Red and processed meat	1.1	0–12.2
	%	
Use of olive oil and/or rapeseed oil	34.1	
Moderate alcohol consumption, 10–30 g/day	37.9	

[a]The 50th percentile (median value) for each component was used as cut-off point to create the mMED score, unless otherwise stated.
[b]For vegetables and fruits, legume and nuts, non-refined/high-fibre grains, fermented dairy and fish: 1 point if at or above the median, 0 points if below the median. For red and processed meat: 1 point if at or below the median, 0 points if above the median. For olive oil and/or rapeseed oil: 1 point if use of olive oil or rapeseed oil, (spread or/and cooking), 0 points if no use. For alcohol consumption: 1 point if alcohol consumption is 10–30 g/day, 0 points if alcohol consumption <10 or >30 g/day.

Men in the highest quartile of the mMED score (6–8, i.e. those with a high adherence to the Mediterranean diet) had a statistically significant 31% (95% CI 17%, 43%) lower risk of HF (as primary diagnosis) in the multivariable model compared with those in the lowest quartile of the mMED score (0–3) (*Table 3*). Every two-point increment in the mMED score was associated with a 15% reduction in risk of HF (*Table 3*). Including all incident HF events in any diagnosis position attenuated the inverse association between the mMED score and risk of HF (RR 0.77, 95% CI 0.68, 0.88 for the highest vs. lowest quartile of the mMED score). The results did not change when we excluded all incident HF events that occurred during the first 2 years of follow-up. Excluding all incident HF events that occurred after an incident MI (*n* = 252) or AF (*n* = 318) resulted in RRs of 0.72 (95% CI 0.59, 0.87) and 0.61 (95% CI 0.49, 0.75), respectively, when comparing the highest with the lowest quartile of the mMED score.

The association between the mMED score and HF risk was not modified by history of diabetes, hypertension, or hypercholesterolaemia, or by smoking status (*Table 4*). In addition, analyses of the association of single mMED score components with HF risk showed inverse but non-significant associations for consumption above the median for all presumed beneficial food groups and below the median for red and processed meat as well for moderate alcohol consumption, and inverse significant

Table 2 Age-standardized[a] baseline characteristics by quartiles of the modified Mediterranean diet (mMED) score in the study population of the Cohort of Swedish Men, 1997 ($n = 37\,308$)

	Quartiles of mMED score			
	Quartile 1 ($n = 14\,003$)	Quartile 2 ($n = 8569$)	Quartile 3 ($n = 7805$)	Quartile 4 ($n = 6931$)
Median mMED score (0–8)	**3.0**	**4.0**	**5.0**	**6.0**
Characteristics[b]				
Age, years	59.6	59.0	58.9	58.3
Education >12 years, yes (%)	13	17	21	26
Current smoker, yes (%)	28	24	22	20
Body mass index[c], kg/m^2	25.8	25.6	25.6	25.3
Overweight and obese, >25 kg/m^2 (%)	58	55	54	51
Physical activity				
Walking or/and cycling, >40 min/day (%)	26	31	32	35
Exercise, >1 h/week (%)	64	71	74	78
Aspirin use, >=7 tablets per week (%)	46	42	44	47
Family history of myocardial infarction (%)	11	11	12	11
Prevalence of hypertension (%)	21	20	20	18
Prevalence of hypercholesterolaemia (%)	11	11	12	11
Prevalence of diabetes (%)	6	6	6	5
Energy intake, kcal/day	2400	2700	2900	3100
Alcohol consumption, g/day	13.5	14.1	14.3	15.3
Never and former drinkers (%)	10	8	7	4
Components of mMED score (servings/day or %)				
mMED score (0–8)	2.3	4.0	5.0	6.3
Vegetables and fruits	2.5	3.7	4.4	5.1
Legumes and nuts	0.2	0.3	0.3	0.4
Non-refined/high-fibre grains	2.9	3.8	4.4	5.2
Fermented dairy	3.1	3.9	4.4	5.2
Fish	0.2	0.3	0.3	0.3
Red and processed meat	1.3	1.3	1.3	1.1
Olive oil and/or rapeseed oil use, yes (%)	13	29	44	71
Moderate alcohol consumption, 10–30 g/day (%)	21	37	46	65

[a]Mean values of age and mMED score are not age-standardized.
[b]Continuous variables are presented as means and categorical as proportions.
[c]Calculated by dividing weight in kilograms by the square of height in metres.

associations for olive oil/rapeseed oil use (see the Supplementary material online, *Appendix S1*).

A high adherence to the Mediterranean diet, as indicated by a high mMED score, was also inversely associated with mortality owing to HF (*Table 3*). Every two-point increment in the mMED score was associated with a 22% (95% CI 2%, 38%) lower HF mortality in the multivariable model. Finally, none of the single mMED score components was significantly associated with HF mortality (*Appendix S1*).

Discussion

In this prospective study of men, high adherence to a Mediterranean diet, as indicated by a high mMED score, was associated with a 31% reduction in risk of developing HF. These findings suggest that a healthy dietary pattern—the Mediterranean diet—may play a role in reducing the incidence of HF.

To our knowledge, there are no data on Mediterranean diet and risk of HF and there is only one single study on HF and total CVD mortality, in which Levitan *et al.*[11] observed a non-significant inverse association between high Mediterranean diet score and mortality caused by HF (15% reduction) among 3215 postmenopausal US women (1385 HF deaths) with established HF. Similarly, a primary prevention randomized trial (PREDIMED) of a Mediterranean diet supplemented with extra virgin olive oil and nuts vs. a low-fat diet, showed a 29% lower risk of any CVD event (including death from HF) in a Spanish population with high CVD risk.[22] In agreement with this, we observed a significant 45% lower mortality from HF among men in the highest quartile of the mMED score compared with those in the low quartile; however, these results need to be interpreted with caution, as the number of deaths caused by HF was limited.

Healthy dietary patterns in general, including components of the Mediterranean diet, have been inversely associated with incidence

Table 3 Relative risk of heart failure by quartiles of the modified Mediterranean diet (mMED) score in the Cohort of Swedish Men 1998–2008 ($n = 37\,308$)

	Quartiles of mMED[a] score (0–8)					
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*P*-trend	Two-point increment in mMED score
Median mMED score (range)	3 (0–3)	4 (4)	5 (5)	6 (6–8)		4 (0–8)
Heart failure[b]						
Events ($n = 1269$)	594	273	233	169		1269
Person-years	142 788	88 502	81 101	72 665		385 056
Age-standardized rates[c]	424 (390, 458)	341 (301, 382)	324 (282, 366)	277 (235, 320)		
Age-adjusted RR (95% CI)	Reference	0.80 (0.69–0.93)	0.76 (0.65–0.88)	0.65 (0.55–0.77)	<0.001	0.82 (0.77–0.88)
Multivariable adjusted RR[a] (95% CI)	Reference	0.82 (0.71–0.96)	0.78 (0.67–0.92)	0.69 (0.57–0.83)	<0.001	0.85 (0.78–0.91)
Heart failure mortality[d]						
Events ($n = 146$)	74	38	18	16		146
Person-years	144 288	89 182	81 749	73 168		388 387
Age-standardized rates[e]	52 (40, 64)	48 (33, 64)	27 (14, 39)	28 (14, 42)		
Age-adjusted RR (95% CI)	Reference	0.94 (0.64–1.40)	0.49 (0.29–0.83)	0.53 (0.31–0.92)	0.002	0.76 (0.62–0.93)
Multivariable adjusted RR[a] (95% CI)	Reference	0.97 (0.64–1.44)	0.50 (0.29–0.86)	0.55 (0.31–0.98)	0.007	0.78 (0.62–0.98)

CI, confidence interval; mMED, modified Mediterranean; RR, relative risk.
[a]Includes eight components: vegetables and fruits, legumes and nuts, non-refined/high-fibre grains, fermented dairy products, fish, red and processed meat (negative), olive or rapeseed oil and moderate alcohol consumption.
[b]Relative risk for an incident heart failure event listed as primary diagnosis. Models were adjusted for education level (up to 12 years, >12 years), family history of myocardial infarction (yes or no), cigarette smoking (current, former, never), >40 minutes of walking or/and cycling per day, >1 h of exercise per week, body mass index (BMI) (<20, 20–24.9, 25–29.9, ≥30 kg/m^2), history of hypertension (yes or no), history of hypercholesterolaemia (yes or no), history of diabetes (yes or no), aspirin use (never, 1–6 tablets/week, ≥7 tablets/week), and total energy intake (continuous, kcal/day).
[c]Age-standardized incidence rates of heart failure per 100 000 person-years with 95% CI.
[d]Relative risk for heart failure mortality. Models were adjusted as above.
[e]Age-standardized mortality rates of heart failure per 100 000 person-years with 95% CI.

of HF.[9,10,23] In the Women's Health Initiative (WHI), of about 83 100 older women and 1836 HF events, a 30% lower risk of HF was found among those in the highest quintile of the Alternate Healthy Eating Index (AHEI) vs. the lowest, which is in line with our findings for the Mediterranean diet.[23] Both the mMED score we generated and the AHEI include the consumption of vegetables and fruits, nuts, fish, red meat, fibre, and grains as well as alcohol consumption in moderation. The DASH diet, which is also similar to a Mediterranean diet, has been inversely associated with incidence of HF in both men and women from two Swedish cohorts.[9,10] Levitan *et al.* observed a 22% and 37% lower risk of HF in women and men, respectively, in the highest quartiles of the DASH index compared with the lowest quartiles. These results corroborate our findings, deriving from the same cohort (COSM). The DASH and the Mediterranean diet share main components, with the exception that the traditional DASH diet does not specifically promote the consumption of monounsaturated and omega-3 polyunsaturated fatty acids, or of moderate alcohol and is sodium-restricted. In contrast to earlier findings, in the Cardiovascular Health Study of about 4500 older men and women, neither the DASH nor the AHEI diet was associated with risk of HF.[24]

Oxidative stress, high blood pressure, endothelial dysfunction and increased inflammation are known to be the main mechanistic pathways leading to the development and progression of HF.[25] Recently, total antioxidant capacity of the diet was reported to be inversely associated with risk of HF in the Swedish Mammography Cohort.[26] A Mediterranean diet is mainly characterized by a high anti-oxidant index from fresh vegetables and fruits, nuts, olive oil, and moderate alcohol consumption (mainly red wine) as well as anti-inflammatory properties from olive oil/rapeseed oil (oleic acid and low saturated fat content), moderate alcohol consumption, oily fish (rich in omega-3 and complex long-chain polyunsaturated fats), and likely from fermented dairy products. Consistent evidence confirms that a Mediterranean diet improves systolic and diastolic blood pressure,[27] endothelial and left ventricular function,[7,28] and lipid profile;[27] it also reduces oxidative stress, coronary atherosclerosis/thrombosis and inflammatory markers.[6,12,28]

To our knowledge, this is the first prospective study to examine the association between the Mediterranean diet and incidence of HF. Strengths of this study include the large sample size, the large number of HF events, the prospective assessment of diet, and the objective data on HF events. The mMED score was a modified version of the original score by Trichopoulou *et al.*,[17,18] based on literature to match the cultural food differences in the study population. To date, several indexes that measure adherence to the Mediterranean diet have been created and used to examine associations with health conditions.[29] Unlike dietary scores used in other studies, we included fermented dairy because recent evidence suggests an inverse association between fermented dairy consumption and mortality caused by CVD.[30] Furthermore, we included only whole grains or grains high in fibre rather than total cereals as was done in previous studies. The Mediterranean

Table 4 Analysis for covariates of heart failure, according to adherence to the modified Mediterranean diet (mMED) score in the Cohort of Swedish Men, 1998–2008

			mMED[c] score 6–8 vs. score 0–3		
Covariates[a]	No. of events[b]	No. of participants[b]	RR	95% CI	*P*-interaction
Diabetes					0.7
No	1088	35 079	0.67	0.55–0.82	
Yes	181	2229	0.91	0.55–1.48	
Hypertension					0.95
No	795	29 897	0.67	0.54–0.84	
Yes	474	7411	0.72	0.53–0.98	
Hypercholesterolaemia					0.46
No	1 142	33 095	0.71	0.58–0.85	
Yes	127	4213	0.50	0.27–0.94	
Smoking status					0.38
No	926	27 915	0.65	0.53–0.81	
Yes	319	8926	0.83	0.57–1.20	

CI, confidence interval; mMED, modified Mediterranean diet; RR, relative risk.
[a]Relative risk for an incident heart failure event listed as primary diagnosis. In all analyses, the lowest quartile of the mMED score was used as a reference group. Models were adjusted for education level (up to 12 years, >12 years), family history of myocardial infarction (yes or no), cigarette smoking (current, former, never), >40 min of walking or/and cycling per day, >1 h of exercise per week, body mass index (BMI) (<20, 20–24.9, 25–29.9, ≥30 kg/m^2), history of hypertension (yes or no), history of hypercholesterolaemia (yes or no), history of diabetes (yes or no), aspirin use (never, 1–6 tablets/week, ≥7 tablets/week) and total energy intake (continuous, kcal/day).
[b]The number of events and participants may not sum up to the total number because of missing data on the covariates.
[c]Includes eight components: vegetables and fruits, legumes and nuts, non-refined/high-fibre grains, fermented dairy products, fish, red and processed meat (negative), olive or rapeseed oil and moderate alcohol consumption.

diet is a difficult pattern to define and quantify precisely as it mainly depends on the cultural differences between regions.[29] Nevertheless, regardless of the design of the Mediterranean-like diet score, most studies have reported an inverse association between a Mediterranean-like diet and all-cause mortality[17,18] as well as cardiovascular risk factors and inflammatory markers.[27]

This study also has limitations. Heart failure is a chronic progressive disease with heterogeneous pathogenesis and different stages of severity. Dietary approaches and their effect differ among healthy people, those at high risk and those at stage C or D of the disease.[4] In this study, we were unable to differentiate HF in terms of pathogenesis or severity of the disease. As both AF and MI are major risk factors of HF[3] and <45% of HF events had previous AF or MI during the follow-up, a potential mediation of the association between the Mediterranean diet and HF by these previous events cannot be excluded. Owing to lack of repeated measurements of the adherence to the mMED score, we were unable to formally test this, but excluding all HF events occurring after AF or MI did not alter the results. Dietary intake was measured through an FFQ and at baseline only. Moreover, we were unable to quantitatively measure consumption of olive oil/rapeseed oil, which is one of the major components of the Mediterranean diet, as the FFQ did not include quantities for fat. The mMED score we used has not been validated to ensure that it accurately captures adherence to a Mediterranean diet and has the general limitations of cut-off specific scores;[29] however, it is a modified version of the original score by Trichopoulou *et al.*[17,18] and follows a common design with most indexes and scores which measure adherence to a Mediterranean diet.[29] Finally, although we adjusted for major CVD risk factors, unmeasured or residual confounding is a potential problem in observational studies.

In conclusion, high adherence to a Mediterranean diet, as indicated by the mMED score, was associated with a lower risk of developing HF and with a lower mortality from HF in men. This research provides a framework for the exploration of a universal, easily manageable and palatable dietary concept, the Mediterranean diet, as an effective diet in the primary prevention of HF. As this is the first study on the association between a Mediterranean diet and risk of HF, the present findings need to be replicated in women and in other populations.

Supplementary Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Relative risk of heart failure incidence and mortality by consumption of single food components of the modified Mediterranean diet (mMED) score above or below the median in the Cohort of Swedish Men, 1998–2008 ($n = 37\,308$).

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