Mediterr J Nutr Metab (2013) 6:127–133
DOI 10.1007/s12349-013-0122-6

ORIGINAL ARTICLE

Alcohol and stimulants dietary pattern is associated with haptoglobin blood levels, among apparently healthy individuals

Konstantinos M. Lampropoulos · Maria Bonou · Vassiliki Bountziouka · Angelos Evangelopoulos · Amalia Giotopoulou · Natalia Vallianou · Peter Avgerinos · Demosthenes Panagiotakos · John Barbetseas

Received: 14 August 2012 / Accepted: 20 February 2013 / Published online: 14 March 2013

Abstract Studying dietary patterns and its relation to the development of various chronic diseases have received much interest during the past years, since they capture a holistic approach of true diet. Haptoglobin (Hp) has been associated with cardiovascular heart disease risk especially with acute myocardial infarction, coronary and peripheral artery disease, stroke, and heart failure. This study aimed to evaluate the relationship between dietary patterns and Hp blood levels among apparently healthy adults. During 2009, 490 volunteers (46 ± 16 years, 40 % male) were consecutively enrolled to the study (participation rate 85 %). Biochemical analyses were performed through established procedures, after 12 h fasting. Anthropometric, lifestyle and dietary characteristics were also recorded to account for potential confounders. Principal components analysis (PCA) was the data-driven technique to extract the dietary patterns. Pattern analysis revealed eight dietary patterns through the application of PCA; however, four of them were considered nutritionally important as they explained 35 % of total variance in food consumption ("Western diet", "Mediterranean diet", "Meat and bakery products" and "Alcohol and stimulants pattern"). The fourth pattern (alcohol and stimulants intake) has been characterised by intake of alcoholic drinks (wine, beer, and spirits) and stimulants (coffee and tea). Adherence to the latter pattern was associated with reduced Hp levels ($b \pm$ SE -5.9 ± 2.7, $p = 0.03$), adjusted for age, sex, body mass index, physical activity, and smoking habits. However, multi-adjusted analysis revealed that the individual effect of alcohol or stimulants on lowering Hp levels was not significant ($p = 0.27$ and $p = 0.05$, respectively). Moderate drinking of alcoholic drinks and stimulants seems to be associated with lower haptoglobin levels, suggesting another potential mechanism for the health benefits achieved through alcohol and stimulants drinking.

Keywords Haptoglobin · Alcohol · Dietary pattern · Healthy individuals

Abbreviations

BMI	Body mass index
CV	Coefficients of variation
FFQ	Food frequency questionnaire
Hp	Haptoglobin
PCA	Principal components analysis

Introduction

The role of overall dietary patterns in predicting outcomes for cardiovascular diseases has been previously demonstrated [1]. The Mediterranean diet, one of the most known patterns for its cardioprotective actions was first considered in the 1960s in Crete, Greece [2]. This pattern was characterized by high consumption of monounsaturated fatty

K. M. Lampropoulos (✉) · M. Bonou · P. Avgerinos · J. Barbetseas
"Polyclinic" General Hospital, 3 Pireos Ave., Omonia Sq., 10552 Athens, Greece
e-mail: konlampropoulos@yahoo.gr

V. Bountziouka · A. Giotopoulou · D. Panagiotakos
Department of Nutrition and Dietetics, Harokopio University of Athens, Athens, Greece

A. Evangelopoulos
Roche Diagnostics (Hellas) SA, Athens, Greece

N. Vallianou
"Evangelismos", General Hospital Athens, Athens, Greece

acids, primarily from olive oil, daily consumption of vegetables, fruits, whole grain cereals and low-fat dairy products, weekly consumption of poultry, fish, legumes, and tree nuts, monthly consumption of red meat, as well as a moderate daily consumption of alcohol, normally with meals. The Mediterranean dietary pattern has long been associated with low cardiovascular disease risk in adult population [3]. In addition, it is possible to reduce the incidence of coronary heart disease with this diet [4, 5].

Among various inflammation markers, haptoglobin (Hp) has been known as an indicator of haemolytic diseases associated with the development of inflammation and infection. Hp is a haemoglobin circulation binding protein released from erythrocytes with high affinity and thereby inhibits its oxidative activity. Hp is a protein that in humans is encoded by the HP gene and it was found to be related with the increased cardiovascular disease risk [6, 7].

To date, the protective role of healthy dietary habits to the development of cardiovascular disease has been established. However, diet's protective mechanism is not been fully understand. In particular, the relationship of alcohol consumption with Hp regarding the development of cardiovascular outcomes or coronary heart disease remains unclear. Thus, the aim of this study was to investigate the relationship between dietary patterns and Hp blood levels among apparently healthy adults.

Materials and methods

Participants

Between April 2009 and January 2010, a total of 490 consecutive adults (46 ± 16 years, 40 % men) who had visited the "Polyclinic" General Hospital for an annual health check, agreed to participate in the study (85 % participation rate). Individuals with history of cancer or recent infection were not included in the study. The retrieved data were confidential, and the study followed the ethical considerations provided by the World Medical Association (52nd WMA General Assembly, Edinburgh, Scotland, October 2000). Moreover, the Institutional Review Board approved the design, procedures, and aims of the study (GA 23/14.05.2009). All participants were informed about the procedures of the study and agreed to participate providing written informed consent.

Lifestyle and anthropometric characteristics

All the participants were Caucasians. Information regarding age (years), sex (males vs. females), level of education (years of school) and family status [singles (i.e., single, divorced, widowed) vs. married] were recorded in a self-administrated questionnaire.

With respect to lifestyle characteristics, participants were asked to fill in a 10-grade scale range regarding their physical activity status (grade of scale used: 1–10, where one denotes sedentary lifestyle and 10 daily hard activity of at least 30 min). Participants with score ≤7 were classified as with low/moderate activity, while those with score >7 were considered as highly active. Current smoking was defined as those who smoke at least one cigarette/day for the past year. The number of cigarettes per day and the total years of smoking were also recorded. Finally, a 76-item valid semi-quantitative food frequency questionnaire (FFQ) was used to record participants' dietary habits [8].

Waist circumference and height (without shoes) were measured to the nearest 0.5 cm, and weight was measured with a lever balance, to the nearest 100 g, without shoes, in light undergarments. Body mass index (BMI) was then calculated as weight in kilograms divided by the square of standing height in meters (kg/m^2). Participants were then classified in those with normal values of BMI (i.e., <25 kg/m^2) and to overweight/obese (BMI ≥25 kg/m^2).

Biochemical and clinical characteristics

Systolic and diastolic blood pressure was measured in all participants by the same physician using a standard mercury sphygmomanometer on the right arm of the seated subject. Venipuncture was performed for each participant, early in the morning (between 07:00 and 11:00 a.m.), after a 12-h fasting period by applying a natural latex rubber strap and using a 20-mL syringe. Blood was immediately transferred to two tubes without anticoagulant (Greiner Vacuette, Cat. no. 455071). Samples were left undisturbed for 20 min to clot and then centrifuged at 1,500 rpm.

Glucose and total cholesterol were determined by enzymatic colorimetric tests (GOD-PAP, CHOD-PAP Abell-Kendal, GPO-PAP and BCG, respectively). Haptoglobin was determined via an immunoturbidimetric assay. Reproducibility in the lab has been determined using human samples and controls in an internal protocol. Within run and between day coefficients of variation (CV) were less than 7 %. All measurements were performed on a Roche/Modular Analytics analyzer. Reagents, calibrators, controls, and consumables were purchased from the same supplier (Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim, Germany).

Hypertension was defined as a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg or the use of anti-hypertensive drugs. Coronary heart disease, heart failure, cerebrovascular disease, and peripheral arterial disease were assessed by self-report and medication use. Diabetes was assessed by self-report, medication use or a positive diagnosis by fasting blood glucose level (≥7.0 mmol/L) [9]. Hyper-cholesterolemia was defined as a serum cholesterol ≥200 mg/dL or by the use of cholesterol-lowering drugs.

Statistical analysis

Results are presented as mean values ± SD for the normally distributed continuous variables (i.e., age, years of school, physical activity scale, waist circumference, BMI, systolic and diastolic blood pressure, total cholesterol, haptoglobin), as median (1st, 3rd quartile) for the skewed ones (i.e., glucose) and as frequencies [*N* (%)] for the categorical variables (i.e., sex, family status, high physically active, smoking, obesity status). Normality was tested using graphical methods (i.e., p–p plots and histograms). Differences between males and females regarding participants' sociodemographic, anthropometric, lifestyle and biomarkers' characteristics were evaluated using the Student's *t* test for the normally distributed variables, the Mann–Whitney *U* test for the skewed ones and the Chi-square test for the categorical ones.

Principal components analysis was applied in order to a posteriori extract dietary patterns using 24 food groups of the FFQ (refer "Appendix1"). The varimax orthogonal rotation type was furthermore applied in order to derive more interpretable dietary patterns. The Kaiser criterion (i.e., components with eigenvalues of ≥1.0) was used to retain meaningful patterns. The percentage of variance explained was used to finally consider the number of the components to be included in the analysis. Each rotated component was interpreted ("named") based on the foods that had loadings ≥|0.3|, which were considered as significantly contributing to the specific diet component (pattern). The extracted patterns were afterwards included in linear regression models to evaluate the association with the levels of Hp, adjusted for age, sex, physical activity status, BMI and smoking. Results are presented as *b*-coefficients ± standard error, along with their 95 % confidence intervals (95 % CI).

Significance level for all tested hypothesis was set at 0.05 %. All statistical analyses were performed using SPSS v18.0 (SPSS Inc., Chicago, IL, USA).

Results

Participants' sociodemographic, lifestyle and clinical characteristics are presented in Table 1. Males were found to have higher values of waist circumference, BMI, systolic

Table 1 Participants sociodemographic, lifestyle and clinical characteristics. Results presented as mean ± SD, P50 (P25-P75), or frequencies

	Males	Females	$p^{‡}$
N (%)	194 (40)	296 (60)	
Age (years)	47 ± 16	46 ± 16	0.34
Married versus singles[a], *N* (%)	113 (58)	168 (57)	0.74
Years of school (years)	14 ± 4.7	13 ± 4.8	0.003
Physical activity (1–10)	5.5 ± 2.1	6 ± 2.3	0.64
High physically active (vs. sedentary), *N* (%)	35 (18)	68 (23)	0.42
Smoking (vs. no), *N* (%)	70 (36)	92 (31)	0.25
Waist circumference (cm)	99 ± 12	87 ± 13	<0.0001
Body mass index (kg/m^2)	28 ± 4.0	26 ± 5.3	<0.0001
Overweight/obesity (vs. no), *N* (%)	149 (77)	132 (45)	<0.0001
Systolic blood pressure (mmHg)	123 ± 17	116 ± 19	<0.0001
Diastolic blood pressure (mmHg)	77 ± 11	72 ± 11	<0.0001
Glucose (mg/dL)	97 (91, 106)	92 (85, 100)	<0.0001
Total cholesterol (mg/dL)	199 ± 43	201 ± 38	0.61
Haptoglobin (mg/dL)	126 ± 54	128 ± 57	0.74

‡ *p*-values derived through the Student's *t* test for the normally distributed continuous variables (i.e., age, years of school, physical activity scale, waist circumference, body mass index, systolic and diastolic blood pressure, total cholesterol, haptoglobin), the Mann–Whitney *U* test for the skewed ones (i.e., glucose) and the Chi-square test for the categorical (i.e., family status, high physically active, smoking, prevalence of overweight/obesity)

[a] Widowers and divorced are included under the "singles" family status category

and diastolic blood pressure and glucose blood levels. Additionally, the prevalence of overweight/obese was higher among males (Table 1).

Dietary pattern analysis revealed eight dietary patterns through the application of PCA; however, four of them were considered nutritionally important as they explained 35 % of total variance in food consumption. In particular, the first component was characterized by high intakes of full fat dairy products, white starchy products, eggs, potatoes, red meat, full fat delicatessens, sweets, sodas, and fats and oils (olive oil excluded) and lower intake of low fat dairy products (i.e., Western diet). The second component reflected the "Mediterranean diet", as it was mainly characterized by high intakes of low fat dairy products, whole meal starchy products, poultry, fish, legumes, vegetables, fruit, stimulants (i.e., coffee and tea) and olive oil. The third component was high loaded by whole meal starchy products, red meat, full and low fat delicatessens, bakery products and light sodas, describing a "Meat and bakery" pattern. Finally, the fourth component was

Table 2 Components' score coefficients[a], for four major dietary patterns, derived from the application of Principal Components Analysis (orthogonal rotation) in 24 food groups, from a 76-item semi-quantitative FFQ ($n = 490$)

Food group (g mL/day)	Principal components[b]			
	1st	2nd	3rd	4th
Full fat dairy	**0.52**	0.03	−0.12	−0.20
Low fat dairy	**−0.47**	**0.32**	0.21	−0.05
White starchy	**0.42**	0.08	−0.05	**0.40**
Wholemeal starchy	−0.27	**0.45**	**0.37**	−0.16
Egg	**0.35**	0.22	0.08	−0.01
Potato	**0.56**	0.24	0.09	0.09
Red meat	**0.54**	0.19	**0.33**	0.15
Poultry	0.20	**0.31**	0.21	0.09
Full fat delicatessens	**0.50**	0.00	**0.40**	−0.01
Low fat delicatessens	−0.16	−0.09	**0.73**	0.06
Fish	0.05	**0.42**	−0.08	0.06
Legumes	0.15	**0.51**	−0.02	0.01
Vegetables	0.01	**0.72**	0.15	0.05
Fruit	−0.06	**0.56**	0.05	−0.23
Bakery	0.27	−0.05	**0.68**	0.00
Sweets	**0.43**	0.05	0.11	0.01
Wine	−0.10	0.10	0.03	**0.66**
Beer	0.05	−0.04	0.23	**0.62**
Spirits	0.04	−0.04	0.01	**0.67**
Stimulants	0.00	0.32	−0.01	0.31
Sodas	**0.56**	−0.09	−0.02	0.06
Light sodas	0.03	0.06	**0.43**	0.10
Olive oil	−0.01	**0.51**	−0.20	0.22
Other oils and fats	**0.46**	−0.07	−0.04	−0.03
% of variance explained by each component	11	9.3	7.6	7.3

Bold fonts indicate values ≥|0.3|, which was considered as the critical value for the interpretation of the components

[a] Score coefficients are similar to the correlation coefficients. Higher absolute values indicate that the food variable is correlated with the respective component

[b] Patterns derived from the administration of the 76-item FFQ were: first "Western diet", second "Mediterranean diet", third "Meat and bakery products", fourth "Alcohol and stimulants pattern"

interpreted as "Alcohol and stimulants" pattern, as it was characterized by high intakes of wine, beer, spirits, stimulants, and white starchy products. Component's scores coefficients are presented in Table 2.

Results of the regression models adjusted for age, sex, body mass index, physical activity, and smoking habits revealed that from the aforementioned patterns, adherence to the latter pattern (i.e., "alcohol and stimulants") was associated with reduced Hp levels ($b \pm$ SE: -5.9 ± 2.7, $p = 0.03$) (Table 3). However, when the analysis was performed separately for alcohol and stimulants, their relationship with Hp blood levels was not significant ($p = 0.27$, $p = 0.05$; data not shown here). Moreover, gender was related to Hp levels in all four models tested. Therefore, sensitivity analyses by gender were also performed. Results shown that the "alcohol and stimulants" pattern was related with ~ 9 mg/dL lower levels of Hp among females ($b \pm$ SE -8.6 ± 4.1, $p = 0.04$), while no association was found for males ($b \pm$ SE -4.0 ± 3.7, $p = 0.28$).

Table 3 Results from linear regression analysis that evaluated the association between dietary patterns and the haptoglobin blood levels

	$b \pm$ SE	(95 % CI)	p
Pattern 1: western diet	−2.4 ± 3.1	(−8.6, 3.8)	0.45
Pattern 2: mediterranean diet	−2.8 ± 3.5	(−9.6, 3.9)	0.41
Pattern 3: meat and bakery products	3.9 ± 3.4	(−2.7, 11)	0.24
Pattern 4: alcohol and stimulants	−5.9 ± 2.7	(−11, −0.63)	0.03

All models were additionally adjusted for: age, sex (males vs. females), physical activity status (1–10), body mass index (kg/m^2) and smoking (yes vs. no)

Discussion

The present work is one of the first in the literature to examine the role of the relationship between dietary patterns and Hp blood levels among apparently healthy adults. Data revealed that moderate drinking of alcoholic drinks and stimulants seems to be associated with lower haptoglobin levels, suggesting another potential mechanism for the health benefits achieved through alcohol and stimulants drinking.

The findings of this study, regarding the influence of alcohol, did not differ from previous reports [10–14] in the literature indicating that moderate drinking of alcoholic drinks decreased the cardiovascular diseases. In addition, this study depicted a correlation with alcohol and stimulants pattern and Hp, which may possibly lead to a suspension of inflammatory diseases appearance, according to the drinking alcohol guidelines.

In a previous study, it was found that the association between light-to-moderate alcohol intake and the risk of developing hypertension differed in women and men while confirming that heavy alcohol intake increases hypertension risk [15]. However, clinical guidelines on the primary prevention of hypertension recommend limiting alcohol intake to <2 drinks per day in men and to <1 drink per day in women [16, 17].

Alcohol has been part of the diet for many people and a very important component of the dietary patterns. When enjoyed in small amounts and together with meals, alcohol may have positive effects on health, especially on the prevention of coronary heart disease. Research suggests that moderate alcohol intake is associated with some health benefits, among them a decreased risk of cardiovascular disease [18, 19]. Several studies observed an independent effect of alcohol on survival [20–22]. A specific study demonstrated that when alcohol was included in the Mediterranean diet, a 14 % lower risk of mortality was found [1]. Numerous studies indicate that a moderate intake of alcohol is associated with a reduced risk of morbidity and mortality and secondary to cardiovascular diseases [23, 24]. In larger amounts, alcohol is a toxic and dependence-inducing substance, with many short- and long-term detrimental effects [25]. Excessive alcohol intake has been associated with an elevated risk of liver disease, heart failure, some cancers, and accidental injury, and is a leading cause of death in industrialized countries [26].

Findings of a recent study [27] showed that the cardioprotective effect of the Mediterranean diet expands its protective actions regarding stroke development, even in participants with hypercholesterolemia. Rissanen et al. [28] in a prospective, cohort study indicate that a higher intake of fruits, berries, and vegetables is associated with a reduced risk of cardiovascular disease-related, non-cardiovascular disease related and overall mortality in middle-aged men in eastern Finland. Several dietary patterns may help prevent cardiovascular outcomes, especially diets with low fat products as well as the Mediterranean are still considered to be a healthy choice for prevention of cardiovascular events [29].

The relation between dietary patterns and inflammation markers has been recently evaluated in several studies [30]. Results of these studies revealed a negative association between the Mediterranean dietary pattern and the inflammation markers. However, the association with Hp has not been previously detected. With respect to our data, analysis revealed a significant negative association between the "Alcohol and stimulants" pattern and Hp blood levels, while no association of the rest dietary patterns (i.e., "Western", "Mediterranean", "Meat and bakery") with Hp blood levels was observed. The analyses were performed taking into account age, gender, physical activity status, body mass index and smoking. All of them are well-known factors that are related with cardiovascular disease. Thus, adjusted for the above factors the potential relationship of "Western", "Mediterranean" or "Meat and bakery" dietary pattern with Hp blood levels is negligible. It is well known that moderate alcohol consumption has been associated with reduction of inflammation markers. Hp is a haemolysis index, has antioxidant properties and has been associated with inflammation, infection, and increased cardiovascular disease risk. Thus, probably the association of Hp blood levels with alcohol may provide an indication of the mechanism through ethanol or flavonoids of alcohol and inflammation.

Hp genotype is an independent risk factor for cardiovascular disease and this relationship is specific for diabetes [31]. Furthermore, a previous study demonstrated that Hp phenotype may contribute to the algorithm used in cardiovascular disease risk stratification, and in the evaluation of new therapies to prevent cardiovascular events in diabetic patients [32]. In one recent study with male diabetic patients, increased plasma levels of homocysteine and the Hp 2-2 genotype had higher carotid plaque iron deposition. The increased intraplaque iron deposition may be associated with increased oxidative stress, affecting the stability of the carotid plaque [33]. Hp is a genetically determined acute phase protein, the synthesis of which is increased during inflammation. Inflammation is associated with the disruption of the aortic media and appears to play a significant role not only in cardiovascular events but also in the progression and development of abdominal aortic aneurysm. Pan et al. [34], demonstrated that plasma Hp concentrations are elevated in patients with abdominal aortic aneurysm, particularly those with the Hp 2-2 phenotype. In addition HP and especially HP 2-2 type is associated with prevalence of coronary artery disease, shorter graft survival time in coronary artery bypass surgery, arterial hypertension, extension of coronary lesions and myocardial infarct size. Thus, our results suggest that moderate drinking of alcoholic drinks and stimulants may be related to lowering the cardiovascular risk by reducing the haptoglobin levels.

Conclusion

The consumption pattern of "alcohol and stimulants intake" was found to be related with decreased levels of haptoglobin, inhibiting the appearance of inflammatory disease, but always within a balanced consumption of beverages in accordance with the common recommendations. The adoption of proper eating behavior and daily habits can ensure long term quality of life by preventing the development of chronic diseases. However, further studies are required to better understand the underlying mechanism of light-to-moderate alcohol intake impact on Hp in healthy adults.

Conflict of interest The authors declare that they have no competing interests.

Appendix

See Table 4

Table 4 Food groups used in PCA to extract dietary patterns

Food groups	Food items
Full fat dairy products	Full fat milk/yogurt, yellow cheese, white cheese
Low fat dairy products	Low fat milk/yogurt, low fat cheese (i.e., light/cottage cheese)
Refined grains	White bread/toast, burger bread, white rice, pasta, pearl barley
Whole-wheat grains	Whole-wheat bread/toast, crisp breads, cereals, brown rice, whole-wheat pasta
Eggs	Eggs
Potato	Potato baked/mashed/fried
Red meat	Pork, beef, lamp, minced meat
Poultry	Chicken, turkey
Full fat delicatessens	Cold, sliced meat, sausages, bacon, processed meat products
Low fat delicatessens	Light/no fat cold sliced meat, processed meat products
Fish and seafood	Fish (small, large), seafood
Legumes	Lentils, beans, fava beans
Vegetables	Tomato, cucumber, carrots, fresh green vegetables, cabbage, broccoli
Fruit	Fresh fruit (orange, apple, pear, banana, cherries, strawberries etc.), fresh fruit juice
Bakery	Pies (spinach pie, cheese pie, meat pie etc.), sandwiches
Sweets	Jelly, sugar, marmalade, croissant, cake, gofer, biscuits, chocolate, tartes, ice-cream
Wine	Red wine, white wine
Beer	Beer
Spirits	Whiskey, vodka, gin, liqueurs
Stimulants	Coffee, tea
Soft drinks	Cola type sodas
Light soft drinks	Light cola type sodas
Olive oil	Olive oil
Other oils and fats	Seed oil, butter, margarine

References

1. Knoops KT, de Groot LC, Kromhout D, Perrin AE, Moreiras-Varela O, Menotti A, van Staveren WA (2004) Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. JAMA 292:1433–1439
2. Keys A, Menotti A, Karvonen MJ, Aravanis C, Blackburn H, Buzina R, Djordjevic BS, Dontas AS, Fidanza F, Keys MH et al (1986) The diet and 15-year death rate in the seven countries study. Am J Epidemiol 124:903–915
3. Mitrou PN, Kipnis V, Thiébaut AC, Reedy J, Subar AF, Wirfält E, Flood A, Mouw T, Hollenbeck AR, Leitzmann MF, Schatzkin A (2007) Mediterranean dietary pattern and prediction of all-cause mortality in a US population: results from the NIH-AARP Diet and Health Study. Arch Intern Med 167:2461–2468
4. Giugliano D, Ceriello A, Esposito K (2006) The effects of diet on inflammation: emphasis on the metabolic syndrome. J Am Coll Cardiol 48:677–685
5. Dontas AS, Zerefos NS, Panagiotakos DB, Vlachou C, Valis DA (2007) Mediterranean diet and prevention of coronary heart disease in the elderly. Clin Interv Aging 2:109–115
6. Sadrzadeh SM, Bozorgmehr J (2004) Haptoglobin phenotypes in health and disorders. Am J Clin Pathol 121(Suppl):S97–S104
7. Wassell J (2000) Haptoglobin: function and polymorphism. Clin Lab 46:547–552
8. Bountziouka V, Bathrellou E, Giotopoulou A, Katsagoni C, Bonou M, Vallianou N, Barbetseas J, Avgerinos PC, Panagiotakos DB (2011) Development, repeatability and validity regarding energy and macronutrient intake of a semi-quantitative food frequency questionnaire: methodological considerations. Nutr Metabol Cardiovasc Dis. doi:10.1016/j.numecd.2010.10.015
9. American Diabetes Association (2010) Diagnosis and classification of diabetes mellitus. Diabetes Care 33:S62–S69
10. Anderson P, Cremona A, Paton A, Turner C, Wallace P (1993) The risk of alcohol. Addiction 88:1493–1508
11. Marmot M, Brunner E (1991) Alcohol and cardiovascular disease: the status of the U shaped curve. BMJ 303:565–568
12. Maclure M (1993) Demonstration of deductive meta-analysis: ethanol intake and risk of myocardial infarction. Epidemiol Rev 15:328–351
13. Klatsky AL (1994) Epidemiology of coronary heart disease—influence of alcohol. Alcohol Clin Exp Res 18:88–96
14. Chick J (1998) Alcohol, health, and the heart: implications for clinicians. Alcohol Alcohol 33:576–591
15. Beilin LJ, Puddey IB (2006) Alcohol and hypertension: an update. Hypertension 47:1035–1038
16. Whelton PK, He J, Appel LJ, Cutler JA, Havas S, Kotchen TA, Roccella EJ, Stout R, Vallbona C, Winston MC, Karimbakas J (2002) Primary prevention of hypertension: clinical and public health advisory from the National High Blood Pressure Education Program. JAMA 288:1882–1888
17. Appel LJ, Brands MW, Daniels SR, Karanja N, Elmer PJ, Sacks FM (2006) Dietary approaches to prevent and treat hypertension: a scientific statement from the American Heart Association. Hypertension 47:296–308
18. O'Keefe JH, Bybee KA, Lavie CJ (2007) Alcohol and cardiovascular health: the razor-sharp double-edged sword. J Am Coll Cardiol 50:1009–1014
19. Corrao G, Rubbiaty L, Bagnardi V, Zambon A, Poikolainen K (2000) Alcohol and coronary heart disease: a meta-analysis. Addiction 95:1505–1523
20. Mukamal KJ, Conigrave KM, Mittleman MA, Camargo CA Jr, Stampfer MJ, Willett WC, Rimm EB (2003) Roles of drinking pattern and type of alcohol consumed in coronary heart disease in men. N Engl J Med 348:109–118
21. White IR, Altmann DR, Nanchahal K (2002) Alcohol consumption and mortality: modelling risks for men and women at different ages. BMJ 325:191–198
22. Liao Y, McGee DL, Cao G, Cooper RS (2000) Alcohol intake and mortality: findings from the National Health Interview Surveys (1988 and 1990). Am J Epidemiol 151:651–659
23. Lippi G, Franchini M, Favaloro EJ, Targher G (2010) Moderate red wine consumption and cardiovascular disease risk: beyond the "French paradox". Semin Thromb Hemost 36:59–70
24. Rimm EB, Giovannucci EL, Willett WC, Colditz GA, Ascherio A, Rosner B, Stampfer MJ (1991) Prospective study of alcohol consumption and risk of coronary disease in men. Lancet 338:464–468

25. Movva R, Figueredo VM (2012) Alcohol and the heart: to abstain or not to abstain? Int J Cardiol.http://dx.doi.org/10.1016/j.ijcard.2012.01.030
26. Centers for Disease Control and Prevention (CDC) (2004) Alcohol-attributable deaths and years of potential life lost—United States, 2001. MMWR Morb Mortal Wkly Rep. 53:866–870
27. Kastorini CM, Milionis HJ, Esposito K, Giugliano D, Goudevenos JA, Panagiotakos DB (2011) The effect of Mediterranean diet on metabolic syndrome and its components a meta-analysis of 50 studies and 534, 906 individuals. J Am Coll Cardiol 57:1299–1313
28. Rissanen TH, Voutilainen S, Virtanen JK, Venho B, Vanharanta M, Mursu J, Salonen JT (2003) Low intake of fruits, berries, and vegetables is associated with excess mortality in men: the Kuopio Ischaemic Heart Disease Risk Factor (KIHD) Study. J Nutr 133:199–204
29. Parikh P, McDaniel MC, Ashen MD, Miller JI, Sorrentino M, Chan V, Blumenthal RS, Sperling LS (2005) Diets and cardiovascular disease: an evidence-based assessment. J Am Coll Cardiol 45:1379–1387
30. Nettleton JA, Steffen LM, Mayer-Davis EJ, Jenny NS, Jiang R, Herrington DM, Jacobs DR Jr (2006) Dietary patterns are associated with biochemical markers of inflammation and endothelial activation in the Multi-ethnic Study of Atherosclerosis (MESA). Am J Clin Nutr 83:1369–1379
31. Levy AP (2004) Haptoglobin: a major susceptibility gene for diabetic cardiovascular disease. Isr Med Assoc J 6:308–310
32. Levy AP, Hochberg I, Jablonski K, Resnick HE, Lee ET, Best L, Howard BV (2002) Strong Heart Study. Haptoglobin phenotype is an independent risk factor for cardiovascular disease in individuals with diabetes: the Strong Heart Study. J Am Coll Cardiol 40:1984–1990
33. Lioupis C, Barbatis C, Drougou A, Koliaraki V, Mamalaki A, Klonaris C, Georgopoulos S, Andrikopoulos V, Bastounis E (2011) Association of haptoglobin genotype and common cardiovascular risk factors with the amount of iron in atherosclerotic carotid plaques. Atherosclerosis 216:131–138
34. Pan JP, Cheng TM, Shih CC, Chiang SC, Chou SC, Mao SJ, Lai ST (2011) Haptoglobin phenotypes and plasma haptoglobin levels in patients with abdominal aortic aneurysm. J Vasc Surg 53:1189–1194