HORMONES 2013, 12(3):379-385

Research paper

A 50-year follow-up of the Seven Countries Study: Prevalence of cardiovascular risk factors, food and nutrient intakes among Cretans

Christos M. Hatzis,[1] Christopher Papandreou,[1,2] Evridiki Patelarou,[1,3] Constantine I. Vardavas,[1] Eleni Kimioni,[4] Dimitra Sifaki-Pistolla,[1] Anna Vergetaki,[1] Anthony G. Kafatos[1]

[1]Department of Social Medicine, Preventive Medicine and Nutrition Clinic, Medical School, University of Crete, Heraklion, [2]Department of Nutrition & Dietetics, Harokopio University of Athens, Athens, Greece, [3]Florence Nightingale School of Nursing and Midwifery, Department of Postgraduate Research, King's College London, London, UK, [4]Health Center of Kastelli, Heraklion, Greece

ABSTRACT

OBJECTIVE To identify the cardiovascular disease (CVD) risk-factor status and dietary habits of the surviving elderly participants of the initial Seven Countries Study (SCS) cohort and newly recruited middle-aged men from the same villages. DESIGN Our total cohort of remaining survivors of the SCS consisted of 27 men aged 90 years old and over, while a younger cross-sectional study of 85 men between 53 and 73 years of age of the same catchment area were also examined. Biochemical, anthropometric, dietetic and lifestyle CVD risk factors information was obtained. RESULTS It was found that being overweight and having systolic blood pressure higher than the recommended were highly prevalent (>75%) among both age groups as well as abdominal obesity (about 50%). Hypercholesterolemia was highly prevalent in the younger population (68.8%), while smoking rates were relatively low among elderly. The daily meat consumption of SCS participants had doubled, from 35g in the 1960s to 76g among the SCS survivors in 2010 ($p=0.002$), while daily fruit and vegetable consumption had dropped from 656g to 266g ($p<0.001$). The younger participants also had increased dietary meat (130g/day) ($p<0.001$) and decreased fruits-vegetables intake (412g/day) ($p<0.001$) compared to 50 years ago. However, the younger population and elderly subjects showed higher fish intake (91g/day and 38g/day respectively, $p<0.001$) compared to 1960 and favorable olive oil consumption. In regard to nutrient intake, the majority of the subjects did not meet the recommendations for CVD prevention. CONCLUSIONS The study population is at increased risk for the development of CVD, while current dietary habits of the SCS survivors partially differed from those of 50 years ago.

Key words: Cardiovascular disease, Dietary habits, Hypercholesterolemia, Hypertension, Nutrients, Obesity, Seven Countries Study

Address for correspondence:
Christopher Papandreou, Department of Social Medicine, University of Crete, Medical School, P.O.B. 2208 GR-71003, Heraklion, Crete, Greece, e-mail: papchris10@gmail.com

Received 13-12-2012, Accepted 16-05-2013

INTRODUCTION

During the past few decades, cardiovascular disease (CVD) has emerged as a frequent cause of death at the age of 70, 80 or 90 years.[1] Several factors have been established as risk markers for the development of CVD, such as smoking, obesity and elevated cholesterol and blood pressure.[2] Diet may thus play a dominant role in promoting or preventing CVD. There is evidence that a healthy diet such as the 'Mediterranean diet' could have a favorable effect on the prevention of CVD.[3] The term 'Mediterranean diet' was first described during an epidemiological study called the Seven Countries Study initiated in 1960 and is based on the food patterns typical of Crete.[4] The Seven Countries Study (SCS) determined that Cretan men had low death rates from CVD compared to the other 15 populations from seven countries,[5] which was attributed to their lifestyle and especially to their dietary habits. However, between 1970 and 1992, the increment of CVD risk factors that resulted in increasing mortality from CVD was documented in the Greek population.[6] A recent study examining CVD mortality during the 40-year follow-up of the Seven Countries cohorts identified a slight decline in the US, Finnish, Dutch and Japanese cohorts, a moderate increase in Italy and an exponential increase in CVD mortality in cohorts of Serbia and Greece.[7] Previous studies that examined CVD risk factors and dietary changes of surviving elderly subjects in Crete who took part in the SCS over a 31-year period revealed an increase in CVD incidence and in the intake of saturated fat, but decreases in monounsaturated fat.[8,9] The Cretans' diet in the 1960s consisted mostly of olive oil, bread, abundant fruits and vegetables, a moderate consumption of fish, dairy products and wine and rare consumption of red meat. The inverse association between this diet and CVD could be attributed to the protective effect of its components containing an ample source of molecules with antioxidant and anti-inflammatory actions, among which omega-3 fatty acids, oleic acid, vitamins B6, B12, C, E, folic acid and phenolic compounds,[10] fibers.[11] Abandoning this dietary pattern could have adverse effects on cardiovascular risk factors. Therefore, we aimed to describe the CVD risk factors and compare the dietary habits between the survivors of the Cretan cohort of the SCS 2010 and participants of the SCS 1960, while we also assessed the nutrient intake among a cross-sectional sample of middle-aged men from the same region.

MATERIALS AND METHODS

Subjects

The Cretan cohort of the SCS was first examined in 1960 among 97.6% of all men aged between 40 and 59 years in 11 villages in the central region of Crete, Greece. There were 686 participants in total. Follow-up examinations of the Cretan men took place 5 and 10 years after the baseline examinations, using identical protocols. Subsequently, re-examinations were undertaken after 31 years (in 1991), 37 years (in 1997/1998), 40 years (in 2000) and 50 years (in 2010). Our total cohort in 2010 consisted of 27 men aged 90 years old and over. Two nonagenarians were not examined due to their changing their place of residence to outside Crete. Our second study sample consisted of all middle-aged men with permanent residency and employment in the same villages as the participants in the 1960s between 53 and 73 years of age, recruited in 1997 and assessed in 2000 and 2010 (85 subjects). No loss of follow-up among these 85 men from 1997 and 2010 was noted. Informed consent was obtained from all participants. The ethical committee at the University of Crete had previously approved the protocol of the study.

Cardiovascular risk factors assessment

Factors taken into account within this study as those that influence CVD development were current smoking status, systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), waist circumference, total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), triacylglycerols (TAG), blood glucose and dietary habits. Cigarette smoking status was elicited by a standard questionnaire. A subject was classified as a current smoker if he/she reported smoking at least one cigarette a day. Height, weight, waist circumference and blood pressure were measured following the original protocol.[5] While a concerted effort was made to take all measurements following identical protocols to those used at baselines, several adjustments had to be made, particularly when working with the nonagenarians, as many were unable to stand for measurements over

long periods of time. Heights for nonagenarians and middle-aged men were taken from the measurements conducted in 1991 and 2000, respectively. For several patients weight could not easily be recorded. Regardless, height was recorded without shoes, with the subject standing with heels flat against the scale, to the nearest 0.1 cm; weight was taken using a digital scale with an accuracy of 100g and once again with no shoes and empty pockets. BMI was calculated as weight divided by height squared (kg/m^2). Waist circumference was determined by locating the upper hip bone and placing a measuring tape around the abdomen (ensuring that the tape measure was horizontal). The waist-to-height ratio was calculated. Blood pressure was taken using an automatic monitor. Subjects rested >10 min before blood pressure measurements. The measurement was taken three times with a 2 min interval between each reading. Participants were classified as having elevated blood pressure if they had a SBP >130 mmHg or DBP > 90 mmHg. Blood was drawn from each patient after a 12-h overnight fast. Levels of TC, HDL-C, TAG and blood glucose were estimated. Hyperglycemia was defined as blood glucose >126 mg/dl.[12] Total cholesterol levels less than 200 mg/dl and/or TAG levels less than 150 mg/dl and/or HDL-C levels equal or above 40 mg/dl and/or LDL-C levels below 130 mg/dl are associated with low risk for CVD.[13]

Dietary evaluation

Among the middle-aged men recruited in 2010 and the survivors of the SCS, estimates of dietary habits were obtained by a single 24 h dietary recall questionnaire applied on weekdays. A dietitian was responsible for the face to face interviews. Food models and household measuring instruments were used to increase the accuracy of portion sizes. Information about dietary supplements intake was also obtained as well as about adherence to the Orthodox Christian dietary guidelines. When an elderly person had difficulty providing information, another family member or housekeeper helped (this was performed among eight elderly participants). Nutrient contents were analyzed according to the food database developed at the Department of Social Medicine of the University of Crete in 1990 and updated in 2000.[14] Then, nutrient intakes were compared to the recommended intakes for >65 years old as proposed by the German Nutrition Society (DGE), Austrian Nutrition Society (ÖGE), Swiss Society for Nutrition Research (SGE), Swiss Nutrition Association (SVE).[15]

Statistical analysis

The descriptive data are presented as mean ± standard deviation for continuous variables and in percentages (n) for categorical. A normality test was applied on all variables, some of which were found to follow a normal distribution (accepting the null hypothesis, $p>0.05$), whereas others did not follow a normal distribution (rejecting the null hypothesis, $p<0.05$). For the parametric test, Student's t test was used for detecting differences between study groups in regard to their dietary intake of food groups. Additionally, for non-parametric tests, one sample Kolmogorov-Smirnov test was performed for scale variables and a non-parametric chi-square test for nominal variables. The SPSS software (SPSS for Windows, Chicago, IL, release 18.0, 2009) was used to analyze all data.

RESULTS

The selected risk factors for CVD such as smoking habits, blood pressure, anthropometric and biochemical indices of the study population are indicated in Table 1. Specifically, SBP was higher than recommended in 77.8% of elderly and 88.0% of younger men and the DBP was higher than recommended in 7.4% and 40%, respectively. Hyperglycemia was found among 11.5% of elderly and 32.5% of younger men. Hypercholesterolemia was noted among 38.5% of elderly and 68.8% of younger participants, elevated LDL in 38.5% of elderly and 62.3% of younger subjects and lower HDL in 23.1% and 15.6%, respectively. Hypertriglyceridemia was prevalent in 34.6% of elderly and 31.2% of younger men and overweight in 76.2% of elderly (WC >102cm in 50%) and 90.7% of middle-aged men (WC >102cm in 59.5%).

Table 2 depicts the daily intake of food groups of the current study population in comparison to the initial intake recorded in 1960. The daily intake of bread had dropped from 380g in the 1960s to 46g among the surviving elderly ($p<0.001$). The daily meat intake was 35g in the 1960s and 76g (77.6% red meat) among elderly and 130 (59% red meat) among younger males in 2010 ($p=0.002$ and $p=0.001$, respectively). Legumes daily consumption was 30g/day in the 1960s and 35g/day among elderly and 83g/

Table 1. Age, smoking habit, blood pressure, body measurements and biochemical indices of elderly and younger people of the study (2010)

	Elderly	Younger
	Mean±SD (N)	
Age (years)	93.2±2.8 (27)	66.2±5.1 (85)
Smokers (%)	3.7	32.4
SBP (mm Hg)	149±24 (27)	153±20 (74)
DBP (mm Hg)	67±12 (27)	82±11 (74)
Weight (kg)	67.3±10.0 (22)	81.1±11.5 (74)
BMI (kg/m^2)	26.4±3.7 (21)	28.6±3.6 (74)
WC (cm)	99.2±12.3 (20)	103.9±9.6 (73)
Glucose (mg/dl)	106±21 (26)	128±44 (76)
TC (mg/dl)	193±38 (26)	227±45 (76)
HDL-C (*mg/dl)*	50±11 (26)	57±17 (76)
TAG (*mg/dl)*	127±77 (26)	131±70 (76)
LDL-C (*mg/dl)*	118±30 (26)	144±45 (76)
SBP >130	77.8% (21)	88% (66)
DBP >85	7.4% (2)	40% (30)
Glucose >126	11.5% (3)	32.5% (25)
TC >200	38.5% (10)	68.8% (53)
HDL <40	23.1% (6)	15.6% (12)
LDL >130	38.5% (10)	62.3% (48)
TAG >150	34.6% (9)	31.2% (24)
BMI ≥25	76.2% (16)	90.7% (68)
WC >102	50% (10)	59.5% (44)

SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; WC, waist circumference; TC, total cholesterol; HDL, high density lipoprotein; LDL, low density lipoprotein; TAG, triacylglycerols.

day among younger males in 2010 ($p<0.001$ in both cases). Fruit alone and combined fruit and vegetable daily consumption within the SCS was 464g and 656g in the 1960s and 171g ($p=0.03$), 266g ($p<0.001$) among the SCS elderly and 191g, 412g among younger people ($p<0.001$). As concerns fish consumption, there was an increase from 18g/day in the 1960s to 38g/day among the surviving elderly ($p<0.001$) and to 91g/day among younger males ($p<0.001$). Regarding olive oil, its consumption in 1960 was 100 g/day, among the SCS survivors was 51g/day ($p=0.01$) while among middle-aged men in 2010 was 65g/day ($p=0.01$).

Table 3 illustrates the macro- (expressed as percentage of daily energy intakes) and micronutrient intake of all participants in comparison to the recommended intakes for CVD prevention. More than half of elderly and younger men were found to exceed the recommended intake for total and saturated fat, n-6 polyunsaturated fatty acid (PUFAs) and were below the recommendations for PUFAs, n-3 PUFAs, dietary fiber, vitamins E, C, B6, B12, folic acid and potassium. Nearly one-tenth of survivors and middle-aged men showed excess cholesterol and sodium intake, whereas 26.9% of elderly and 14.3% of younger people had a daily intake below the recommendations for monounsaturated fatty acids.

DISCUSSION

The present study showed that most of the participants had an unfavorable CVD risk profile. The survivors of the SCS appear to be delaying or even escaping various age-related diseases such CVD that typically develop at younger ages.[16] These individuals may possess genetic and physiological traits that contribute to their exceptional longevity and this needs further investigation. A previous study that assessed lifestyle factors including physical activity, smoking, alcohol consumption and dietary habits in men and women 95-109 years old suggested that exceptional longevity is based more on genetic factors than lifestyle choices.[17]

A high percentage of middle-aged men and elderly were overweight (BMI>25kg/m^2) and nearly half of them had abdominal obesity (high WC) predisposing mainly the youngest group to CVD.[18] Based on the authors' knowledge, in the middle-aged group, this could be attributed to reduced manual work due to the mechanization of traditional farming and the shift from walking to driving with regard to transportation from the houses to the farming areas. In the elderly group a plausible reason for the decrease in physical activity would be aging.[19] Most of the youngest population had hypercholesterolemia and hypertension burdening their health.[20,21] This is in line with the general phenomenon observed in Greece during the last decade, that is the high prevalence of major risk factors in the general population.[22] On the other hand, smoking rates were found relatively low, especially among elderly, compared to the percentage of those smoking in the 1960s (57.5%) and this is encouraging due to the fact that research has revealed a positive

Table 2. Differences in food intake between elderly and younger people of the study (2010) and of middle-aged males in 1960

	Elderly, 2010, n=26	1960, males, n=31, (40-59 years old)		Younger,	
g/day	Mean ± SD	Mean	*p* value	2010, n=76	*p* value
Bread	46±47	380	<0.001	84±90	<0.001
Cereals*	138±182	30	<0.001	62±111	<0.001
Potatoes*	95±134	190	<0.001	71±94	<0.001
Legumes*	35±109	30	<0.001	83±139	<0.001
Vegetables*	95±132	191	0.001	221±187	0.001
Fruits [a]	171±156	464	0.03	191±188	<0.001
Vegetables, fruits*	266±206	656	0.02	412±279	<0.001
Meat*	76±81	35	<0.001	130±198	<0.001
Eggs	11±32	25	0.005	6±24	0.003
Cheese	22±39	13	0.007	33±38	0.003
Fish [a]	38±63	18	<0.001	91±119	<0.001
Olive oil*	51±51	100	0.01	65±48	0.01
Energy intake in kcal/d	1782±419	2820	<0.001	2358±1030	<0.001

One sample Student's *t*-test (standard deviations were not available for the SCS data).
[a]One sample Kolmogorov-Smirnov test, *Non-parametric chi-square test

Table 3. Selected nutrients related to CVD by elderly and younger people of the study compared with recommended intakes[15]

	Elderly		Younger		
Nutrient (unit)	Mean ±SD	% (n) < or > and/or = Recommended intakes	Mean ±SD	% (n) < or > and/or = Recommended intakes	Recommended intakes (>65 years old)
Total fat (% en.)	42.9±10.1	76.9 (20) >35	42.1±11.4	70.1 (54) >35	25-35
SFA (% en.)	12.7±4.1	88.5 (23) >8	10.5±3.6	67.5 (52) >8	8
MUFA (% en.)	21.1±7.4	26.9 (7) <15	21.6±7.5	14.3 (11) <15	>15
PUFA (% en.)	4.8±2.2	92.3 (24) <8	4.8±1.8	90.9 (70) <8	8
Dietary fiber (g)	16.0±8.5	84.6 (22) <25	21.8±9.4	59.7 (46) <25	25-35
Vitamin E (mg)	8.1±4.0	76.9 (20) <11	12.2±6.6	50.6 (39) <11	11-15
Vitamin C (mg)	102.6±99.6	69.2 (18) <100	111.6±102.2	61.0 (47) <100	100
Vitamin B6 (mg)	1.4±0.9	69.2 (18) <1.6	1.8±0.8	50.6 (39) <1.6	1.6
Vitamin B12 (μg)	2.3±1.9	69.2 (18) <3	4.9±8.3	64.9 (50) <3	3
Folic acid (μg)	239±235	84.6 (22) <400	266±184	83.1 (64) <400	400
n-3 PUFAs (g)	0.50±0.20	96.2 (26) <1	1.15±2.20	84.4 (77) <1	1-2
n-6 PUFAs (g)	6.78±2.83	57.7 (15) >6	9.17±5.18	66.2 (51) >6	1-6
Cholesterol (mg)	169±147	19.2 (5) ≥300	213±226	22.1 (17) ≥300	<300
Potassium (mg)	2654±1347	69.2 (18) <2000	3224±1444	87.0 (67) <2000	>2000
Sodium (mg)	1576±598	11.5 (3) >2400	1905±917	18.2 (14) >2400	<2400

SFA: saturated fat; MUFA: monounsaturated fat; PUFA: polyunsaturated fat;

association between smoking and CVD.[23] It is possible that the majority of smokers from the elderly population have died, leaving a small percentage of them under study.[24] Another possible reason for the above observation is that elderly persons may have quit smoking due to health reasons.

The above findings are of historic interest since this population consisted of the survivors of the SCS and middle-aged men from the same rural areas. Fifty years ago, Crete became known for its low cardiovascular mortality among adult men.[5] This was mainly attributed to their dietary patterns and particularly to their low saturated fat and high monounsaturated fat intakes. In the meantime, many socioeconomic changes have occurred in Crete[25] affecting their lifestyle and dietary habits. Namely, the traditional Mediterranean diet has been gradually abandoned and current Cretans consume higher amounts of meat and cheese, and lower amounts of bread, fruits, vegetables.[8,9,14] Moreover, the Greek Orthodox Christian diet, a periodic vegetarianism, was followed for 180-200 days each year by 60% of Cretan men from the Seven Countries Study in the 1960s and research has shown its favorable effects on health indices.[26] Our data confirm the partial abandoning of the traditional Mediterranean diet and the adoption of a more westernized dietary pattern. On the other hand, the consumption of higher amounts of fish and legumes in 2010 compared to that in the 1960s would be protective against CVD and this is explained by the increased access to these foods over the past decade, particularly fish.[27] Regarding olive oil consumption, it was found to be a significant energy source among the study participants (25.7% of total daily energy in the SCS survivors and 24.8% in the middle-aged group in 2010 compared to 31.9% of total daily energy in 1960). The wide range of benefits associated with olive oil consumption could contribute to explaining the low rate of cardiovascular mortality found in Crete, in comparison with other countries from the SCS, despite a high prevalence of coronary heart disease risk factors.[7] This could also explain the higher percentage of survivors in Crete in 2010 compared to the other six countries from the SCS according to unpublished data. The present study revealed that a substantial percentage of elderly and middle-aged people do not meet the recommended intakes for nutrients related to CVD. The available evidence suggests that people falling into dietary pattern clusters that are high in total and saturated fat and low in fiber and antioxidant vitamins are positively associated with the progression of atherosclerosis.[28-30] The beneficial effects of replacing saturated fat with polyunsaturated fatty acids (PUFAs) and particularly n-3 PUFAs on CVD risk have also been revealed.[30] Vitamins B6, B12 and folic acid were among those nutrients not consumed in adequate amounts by most of the participants and this could increase homocysteine concentrations, a significant factor for atherosclerosis.[31] Low potassium intake was also prevalent in most of the study subjects, putting them at increased risk for hypertension independent of cardiovascular risk factors.[32]

Time trends in CVD risk factors status and dietary patterns in the surviving men of the SCS over a 30-year period has shown an increase in arterial blood pressure, serum cholesterol, abdominal obesity and deterioration of dietary habits,[25] observed in 2010, these same factors and patterns also creating a great threat for younger generations. The last could be confirmed by the fact that the middle-aged men recruited from the same area as the nonagenarians shared similar or worse CVD risk factor profiles and dietary habits. In the middle-age group, a multifactorial treatment including healthy lifestyle advice, administration of new drugs or titration of already prescribed drugs would benefit them as regards improvement of multiple CVD risk factors.[33]

A limitation of the study was the small size of the sample studied. Moreover, the use of the 24-h dietary recall is not very reliable for dietary data collection because individuals may not report their food consumption accurately for various reasons related to knowledge, memory and the interview situation. To increase its reliability, a detailed protocol was followed for administration, training and retraining sessions for the interviewer. The use of this tool was indispensable in nonagenarians since other dietary methods need more memory and writing skills. Moreover, although repeated 24hour recalls are required for evaluating an individual's dietary adequacy or prevalence of low/high intakes, a single recall is considered appropriate for estimating group mean nutrient intake in a population, when conducted in a random sample and carefully taken and analyzed.

In conclusion, there was a high prevalence of CVD risk factors among the survivors of the SCS re-examined in 2010 and middle-aged men from the same rural areas. The return to the traditional diet, consumed 50 years ago, appears to be a necessity for people living in rural as well as urban areas. Nutritional tradition, culture and paradigms not only connect us with the past but show us a "path" contemplate in the current period of economic, social and psychological crisis.

REFERENCES

1. Galioto A, Dominguez LJ, Pineo A, et al, 2008 Cardiovascular risk factors in centenarians. Exp Gerontol 43: 106-113.
2. Emberson JR, Whincup PH, Morris RW, et al, 2003 Re-assessing the contribution of serum total cholesterol, blood pressure and cigarette smoking to the aetiology of coronary heart disease: impact of regression dilution bias. Eur Heart J 24: 1719-1726.
3. de Lorgeril M, Salen P, 2006 The Mediterranean-style diet for the prevention of cardiovascular diseases. Public Health Nutr 9: 118-123.
4. Willett WC, Sacks F, Trichopoulou A, et al, 1995 "Mediterranean diet pyramid: a cultural model for healthy eating". Am J Clin Nutr 61: S1402-S1406.
5. Keys A, 1970 Coronary heart disease in seven countries. Circulation 41: S1380-S1367.
6. Sans S, Kesteloot H, Kromhout D, 1997 The burden of cardiovascular diseases mortality in Europe. Task Force of the European Society of Cardiology on Cardiovascular Mortality and Morbidity Statistics in Europe. Eur Heart J 18: 1231-1248.
7. Menotti A, Lanti M, Kromhout D, et al, 2007 Forty-year coronary mortality trends and changes in major risk factors in the first 10 years of follow-up in the seven countries study. Eur J Epidemiol 22: 747-754.
8. Kafatos A, Diacatou A, Voukiklaris G, et al, 1997 Heart disease risk-factor status and dietary changes in the Cretan population over the past 30 y: the Seven Countries Study. Am J Clin Nutr 65: 1882-1886.
9. Voukiklaris GE, Kafatos AG, Dontas AS, 1996 Changing prevalence of coronary heart disease risk factors and cardiovascular diseases in men of a rural area of Crete from 1960 to 1991. Angiology 47: 43-49.
10. Pauwels EK, 2011 The protective effect of the Mediterranean diet: focus on cancer and cardiovascular risk. Med Princ Pract 20: 103-111.
11. Park Y, Subar AF, Hollenbeck A, et al, 2011 Dietary fiber intake and mortality in the NIH-AARP diet and health study. Arch Intern Med 171: 1061-1068.
12. Total Health Life 2005 "High Blood Sugar". Total Health Institute. Retrieved November 13, 2011.
13. American Heart Association. Understand Your Risk of Heart Attack. www.heart.org/HEARTORG/Conditions/HeartAttack/UnderstandYourRiskofHeartAttack/Understand-Your-Risk-of-Heart Attack_UCM_002040_Article.jsp#.TtzbH7KG_nY. Accessed 11 November 2011.
14. Kafatos A, Verhagen H, Moschandreas J, et al, 2000 Mediterranean diet of Crete: foods and nutrient content. J Am Diet Assoc 100: 1487-1493.
15. German Nutrition Society (DGE), Austrian Nutrition Society (ÖGE), Swiss Society for Nutrition Research (SGE), Swish Nutrition Association (SVE). Reference values for nutrients intake. 1st ed. in English: 2002.
16. Perls T, Terry DF, Silver M, et al, 2000 Centenarians and the genetics of longevity. Results Probl Cell Differ 29: 1-20.
17. Rajpathak SN, Liu Y, Ben-David O, et al, 2011 Lifestyle factors of people with exceptional longevity. J Am Geriatr Soc 59: 1509-1512.
18. Ardern CI, Janssen I, Ross R, et al, 2004 Development of health-related waist circumference thresholds within BMI categories. Obes Res 12: 1094-1103.
19. Westerterp KR, Meijer EP, 2001 Physical activity and parameters of aging: a physiological perspective. J Gerontol A Biol Sci Med Sci 56: 7-12.
20. Anderson KM, Odell PM, Wilson PW, et al, 1991 Cardiovascular disease risk profiles. Am Heart J 121: 293-298.
21. Vasan RS, Larson MG, Leip EP, et al, 2001 Impact of high-normal blood pressure on the risk of cardiovascular disease. N Engl J Med 345: 1291-1297.
22. Pitsavos C, Panagiotakos DB, Chrysohoou C, et al, 2003 Epidemiology of cardiovascular risk factors in Greece: aims, design and baseline characteristics of the ATTICA study. BMC Public Health 20: 32.
23. Burns DM, 2003 Epidemiology of smoking-induced cardiovascular disease. Prog Cardiovasc Dis 46: 11-29.
24. Moschandreas J, Kafatos A, Aravanis C, et al, 2005 Long-term predictors of survival for the Seven Countries Study cohort from Crete: from 1960 to 2000. Int J Cardiol 100: 85-91.
25. Kafatos A, Mamalakis G, 1993 Policies and programs in nutrition and physical fitness in Greece. World Rev Nutr Diet 72: 206-217.
26. Sarri KO, Tzanakis NE, Linardakis MK, et al, 2003 Effects of Greek Orthodox Christian Church fasting on serum lipids and obesity. BMC Public Health 16: 16.
27. Panagiotakos DB, Polystipioti A, Papairakleous N, et al, 2007 Long-term adoption of a Mediterranean diet is associated with a better health status in elderly people; a cross-sectional survey in Cyprus. Asia Pac J Clin Nutr 16: 331-337.
28. Wang L, Folsom AR, Eckfeldt JH, 2003 Plasma fatty acid composition and incidence of coronary heart disease in middle aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. Nutr Metab Cardiovasc Dis 13: 256-266.
29. Wu H, Dwyer KM, Fan Z, et al, 2003 Dietary fiber and progression of atherosclerosis: the Los Angeles Atherosclerosis Study. Am J Clin Nutr 78: 1085-1091.
30. Bhupathiraju SN, Tucker KL, 2011 Coronary heart disease prevention: nutrients, foods, and dietary patterns. Clin Chim Acta 412: 1493-1514.
31. Debreceni B, Debreceni L, 2012 Why do homocysteine-lowering B vitamin and antioxidant E vitamin supplementations appear to be ineffective in the prevention of cardiovascular diseases? Cardiovasc Ther 30: 227-233.
32. Hedayati SS, Minhajuddin AT, Ijaz A, et al, 2012 Association of urinary sodium/potassium ratio with blood pressure: Sex and racial differences. Clin J Am Soc Nephrol 7: 315-322.
33. Athyros VG, Hatzitolios AI, Karagiannis A, et al, 2011 Improving the implementation of current guidelines for the management of major coronary heart disease risk factors by multifactorial intervention. The imperative renal analysis. Arch Med Sci 7: 984-992.