The long term effect of dietary habits and physical activity on type 2 diabetes incidence: 10-year follow up of the ATTICA study (2002-2012)

Diet, physical activity and diabetes

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Abstract

Aim: to record the 10-year diabetes incidence and investigate the effect of dietary habits and physical activity on its development.

Material and methods: from May 2001 to December 2002, 1514 men and 1528 women (>18 years) without any clinical evidence of CVD or any other chronic disease, at baseline, living in greater Athens area, were enrolled in ATTICA study. Socio-demographic, clinical, lifestyle and biochemical characteristics were evaluated. Dietary habits were assessed through a validated semi-quantitative, food frequency questionnaire and physical activity through a translated, validated, version of International Physical Activity Questionnaire (IPAQ). Diabetes diagnosis was defined as glucose>125mg/dL or use of antidiabetic medication. In 2011-2012, the 10-year follow-up was performed.

SUBMISSION: 26/12/2017 | ACCEPTANCE: 27/02/2018

Citation

Koloverou E, Panagiotakos DB, Pitsavos C, Chrysohoou C, Georgousopoulou EN, Tousoulis D, Stefanadis C and the ATTICA Study group. The long term effect of dietary habits and physical activity on type 2 diabetes incidence: 10-year follow up of the ATTICA study (2002-2012). Diet, physical activity and diabetes. *Hell J Atheroscler* 2018; 9: 5-16

*Corresponding author: Prof Demosthenes B. Panagiotakos, 46 Paleon Polemiston St. Glyfada, Attica, 166 74, Greece Tel. +30210-9603116 - +30210-9600719 (Fax), E-mail d.b.panagiotakos@usa.net Results: 191 incident cases of diabetes were documented, yielding an incidence of 12.9%. Medium and high adherence to the Mediterranean diet decreased 10-year diabetes risk by 49% (OR=0.51; 95%CI: 0.30, 0.88) and 62% (OR=0.38; 95%CI: 0.16, 0.88) respectively. Moderate coffee consumption (≥250mL/day, adjusted for 28% caffeine containment) and low alcohol consumption (<1 glass/day) also decreased risk by 54% (OR=0.46; 95%CI: 0.24, 0.90) and 53% (OR=0.47; 95%CI: 0.26, 0.83), compared to abstention. Finally, moderate level of physical (331-1484 vs. <150 MET minutes/ week) led to a risk reduction of 44% (OR=0.56, 95% CI: 0.34, 0.92).

Conclusions: The present work reported the importance of non-pharmacological interventions in the primary prevention of diabetes. Mediterranean diet, moderate coffee consumption, low alcohol consumption, and moderate level of physical activity exert a beneficial effect against diabetes onset.

Key words: diabetes incidence; Mediterranean diet; alcohol; coffee; physical activity

Introduction

Type 2 diabetes remains a global emergency, being responsible for approximately 16 million new cases annually, yielding a prevalence of 9%; while one in two people with diabetes still remain unaware of the disease. In 2015, diabetes cost the lives of 5 million people worldwide, imposing at the same time a significant economic cost on both the families of people with diabetes and countries with a high prevalence of the disease, accounting at the same time for 5-20% of the total cost of health care. These costs mainly result from the care or treatment of conditions related to diabetes; especially micro-and macrovascular complications (retinopathy, nephropathy, heart disease) and neuropathy [1].

While genetic predisposition is constantly gaining ground, with more than 60 polymorphisms being linked to diabetes development, as a whole they can explain only 10% of the disease's inheritance [2], shifting the burden to environmental risk factors. Obesity, physical inactivity and poor nutrition are considered among the most important risk factors [1]; thus lifestyle changes constitute the cornerstone of the global response to the disease, with weight loss, medical nutrition therapy, regular exercise and smoking cessation being of the utmost importance for individuals with diabetes [3-7]. However, in terms of primary prevention, the long term

effect of various dietary and biochemical parameters is not fully established. Specifically, the dietary pattern and exercise module that offer the greatest protection against diabetes onset, as well as the link of alcohol and coffee with the disease, particularly the quantity at which they could act beneficially, remain to be elucidated.

Thus, and under the context of the ATTICA study, the purpose of the present work was to investigate the long term effect of several dietary habits (adherence to the Mediterranean diet, coffee and alcohol consumption) and physical activity on 10-year diabetes incidence, in a Greek sample of cardiovascular free adults.

Methods

Baseline sampling procedure (2001-2002)

The ATTICA study is a large-scale, health and nutrition, prospective survey, which was carried out during 2001-2002, in the province of Attica, where Athens is a major metropolis. People with history of CVD or other atherosclerotic disease, or having chronic viral infections or living in institutions were excluded from participation. Of the initially invited 4056 individuals and after excluding those with CVD (i.e., n=117) or those having chronic viral infections (n=107), 3042 finally agreed to participate

(75% participation rate); 1514 of the participants were men (aged 46±13 years; range 18-87 years) and 1528 were women (aged 45±13 years; range: 18-89 years). Standardized procedures by trained personnel (i.e., cardiologists, general practitioners, dietitians and nurses) were followed for interviews of participants. More details about the aims, design and methods used in the ATTICA Study may be found elsewhere in the literature [8].

Baseline measurements

Baseline assessment included information about socio-demographic characteristics (age, sex, years of school), history of hypertension, hypercholesterolemia and diabetes, family history of CVD, dietary habits, smoking status and physical activity. Smokers were defined as those who smoked at least one cigarette per day or had quitted within the previous year; the rest were defined as non-smokers.

Weight (in Kg), height (in m), waist (in cm) and hip (in cm) circumferences, as well as clinical characteristics, were measured using standardized procedures. Arterial blood pressure was measured 3 times by using the right arm. All measurements were made at the end of the physical examination while subjects were in a sitting position for at least 30 min. Patients whose average blood pressure was ≥140/90 mmHg or those under antihypertensive medication were classified as hypertensive.

The evaluation of the nutritional habits was based on a validated semi-quantitative food-frequency questionnaire, the EPIC-Greek questionnaire that was kindly provided by the Unit of Nutrition of Athens Medical School; participants were asked to report the average intake of several food items and liquids consumed during the previous year [9]. Adherence to the Mediterranean diet was evaluated using *MedDietScore* (range 0-55, higher values indicating greater adherence) [10]. The tertiles of the score were calculated, yielding three categories, i.e., low, medium and high level of adherence.

Regarding coffee consumption, participants were asked about average coffee drinking habits during the preceding year. All reported types of coffee (that is, instant coffee, brewed coffee, Greek-type coffee,

cappuccino or filtered coffee) were recorded in ml, and then recalculated in ml, after adjustment for 28% caffeine containment for analytical reasons. After this re-calculation, one 'adjusted' cup of coffee (that is, 150 ml) could be equivalent to 450 ml brewed coffee or 300 ml instant coffee. According to the observed distribution of coffee drinking pattern, four coffee categories were created: abstention, low (<250 ml/day), moderate (250-400 ml/ day) and high (≥400 ml/day). However, because of the very small number of participants in the highest category (that is, n=64), the two higher groups were combined into one (≥250 ml/day). Coffee drinking of <250 ml/day was defined here as 'casual' and ≥250 ml/day as 'habitual'. Information of decaffeinated coffee drinking was also recorded but not used in the analyses because of the very small number of participants reported drinking this type of coffee (n=47).

As for alcohol intake, alcoholic beverages usually consumed in Greece such as wine, beer, whisky, traditional alcoholic drinks (i.e., retsina, tsipouro, ouzo) and other spirits i.e., liqueur were recorded using a seven-day food record. For the present analyses, alcohol intake was categorized into five groups: abstention; low intake (>0 but <1 glass/day); moderate intake (1–2 glasses/day); high (>2 but <4 glasses/day); very high (> 4 glasses/day). One standard glass was the equivalent of 12g of alcohol. Due to the very small number of participants in the highest category (*n* = 28), again the two highest classes were combined into one (>2 glasses/day). Daily alcohol intake (in g) was calculated using food composition tables [11].

Physical activity was assessed through a translated version of the validated "International Physical Activity Questionnaire" (IPAQ), suitable for assessing population levels of self-reported physical activities [12]. The short version of IPAQ (7 items) that we used provided information on weekly time spent walking, in vigorous intensity, moderate intensity and sedentary activity. Participants were instructed to refer to all domains of physical activity and report only episodes of activities of at least 10 minutes, since this is the minimum required to

achieve health benefit. After, the sum of MET (Metabolic Equivalent of Task) minutes/week was calculated for each participant, and the quartiles of MET minutes/week were constructed, yielding four categories, i.e. very low, low, moderate and high physical activity level. This type of analysis was preferred in order to quantify total physical activity across all domains and thus provide an overall picture of physical activity's effect on diabetes development.

Biochemical measurements were carried out in the same laboratory that followed the criteria of the World Health Organization Lipid Reference Laboratories. Blood samples were collected from the antecubital vein between 8 to 10 a.m., in a sitting position after 12 hours of fasting and avoiding of alcohol. Serum total cholesterol, HDL-cholesterol, triglycerides and glucose concentrations were measured using chromatographic enzymic method in a Technicon automatic analyser RA-1000. LDL cholesterol calculated using the Friedewald formulae. Hypercholesterolemia was defined as total serum cholesterol concentrations >200 mg/dL or the use of lipid-lowering agents. Diagnosis of diabetes mellitus (type 2) was based on the criteria of the American Diabetes Association [13], i.e., fasting blood glucose >125 mg/dL or the use of antidiabetic medication. Serum insulin concentrations were assayed by means of radioimmunoassay. Inflammatory markers were assayed using the following techniques: C-reactive protein (CRP) and Serum Amyloid-A (SAA) by particle-enhanced immunonephelometry, interleukin 6 (IL-6) by a high-sensitivity enzyme-linked immunoassay, human tumor necrosis factor -a (TNF-a) by the enzyme-linked immunosorbent assay method for the quantitative determination, homocysteine levels by an automatic analyzer based on the technology of fluorescence polarization immunoassay and fibrinogen by automatic nephelometry.

10-year follow-up (2011-2012)

During 2011-2012, the 10-year follow-up was performed. Of the n=3042 participants, n=2583 completed the follow-up (85% participation rate). Diagnosis of diabetes was based on ADA criteria, as

performed in the baseline examination. Participants who did not provide biological samples-those who were reached only by telephone-were asked whether they had been diagnosed by a physician. Participants with diabetes at baseline (n=210) or with no information about diabetes status at the 10-year follow up (n=1347) were excluded for these analyses, yielding to a final sample of n=1485 subjects. Statistically, but not clinically significant, differences between our working sample (n=1485 individuals) and participants who were not included in these analyses (n=1347 participants), existed for age (43±13 vs. 45±13 years, p<0.001), hypertension status (30% vs. 26%, p=0.036), smoking status (58% vs. 54%, p=0.028), fasting glucose (88±12 vs. 80±13, p=0.005) and fasting insulin (12±3.0, 13±3.4 μ U / ml, p=0.014). No statistical significant differences existed for sex, years of education, hypercholesterolemia, family history of diabetes and BMI (ps>0.05). Further details about the baseline procedures and the 10-year follow-up of the study have been presented elsewhere [8, 14].

Statistical analysis

Incidence of diabetes was calculated as the ratio of new cases (n=191) to the total number (n=1485) of participants in the follow-up. Continuous variables are presented as mean values ± standard deviation and categorical variables as frequencies. Associations between categorical variables were tested using chi-squared test. Comparisons of mean values of normally distributed variables between those who developed diabetes and the rest of the participants were performed using Student's t-test, after ensuring equality of variances using Levene's test. For non-normally distributed variables, the Kruskall-Wallis test was applied, and next the Mann-Whitney test was performed between every two groups, so as to detect significant mean differences. Continuous variables were tested for normality through histograms. Multivariate logistic regression analysis was performed to evaluate independent associations. This type of analysis was preferred (instead of survival) because there were no accurate data about diabetes

Table 1. Demographic, lifestyle, clinical and biochemical factors among ATTICA participants, by T2DM status, at the 10-year follow up (*n*=1485).

	Did not develop T2DM $(n = 1294)$	Developed T2DM (n = 191)	p
Age, years	44±13	53±11	<0.001
Male gender, n (%)	629 (49)	97 (51)	0.57
Education, years	13±3.4	11±3.9	<0.001
Smokers now, n (%)	702 (54)	100 (52)	0.62
Fasting glucose, mg/dL	88±12	95±14	<0.001
Fasting insulin, μU/mL	13±3.4	14±3.4	<0.001
Family history of T2DM, n (%)	230 (20)	61 (36)	<0.001
Hypertensive, nv (%)	333 (27)	82 (46)	<0.001
Hypercholesterolemic, n (%)	475 (37)	106 (56)	<0.001
Energy intake, kcal/day	2335±917	2616±1095	0.10
Lifestyle behaviors			
MedDietScore (range 0-55)	26±6.8	24±6.4	<0.001
Physically active, n (%)	552 (43)	73 (38)	0.25
Coffee drinking (ml/day)	117±123	103±123	0.004
Alcohol intake (g/day)	14±16	21±16	<0.001
Anthropometric indices			
BMI, kg/m²	26±4.0	29±5.0	<0.001
Waist circumference (cm)	88±14	98±16	<0.001
Visceral obesity, as WC≥102/88cm for men and women	303 (27)	92 (57)	<0.001
Visceral obesity, as WC ≥94/80cm for men and women	598 (54)	129 (80)	<0.001
Inflammatory markers			
CRP, mg/L	1.7±2.3	2.7±2.8	<0.001
IL-6, pg/mL	1.4±0.49	1.6±0.42	<0.001
TNF-a, pg/mL	6.1±4.4	6.8±3.6	<0.001
Fibrinogen, mg/dL	302±66	336±77	<0.001
SAA, mg/dL	4.4±4.6	4.6±3.8	0.05
Homocysteine, µmol/L	12±6.6	12±5.5	0.15

Data are presented as mean values and standard deviations for continuous variables; and absolute and relative frequencies for categorical variables. P-values derived from Student's t-test for the normally distributed variables and Mann-Whitney test for the non-normally distributed variables (i.e., years of school, MedDietScore, fasting insulin, inflammatory markers), or chi-square test for the categorical variables.

onset, but only diagnosis. As previously demonstrated, the estimation of the odds ratio approximated the relative risk given an infrequent disease occurrence [15]. All known confounders were included in the models after testing for collinearity. Finally, interactions with the parameter of interest were checked in all steps, and when significant sub-group analyses were performed. The SPSS version 18 (Statistical Package for Social Sciences, IBM Hellas SA, Greece) software was used for all statistical calculations.

Results

10-year diabetes incidence

During the 10-year follow-up period, 191 diabetes cases were documented; yielding a crude incidence of 129 per 1000 participants (or 12.9%); of them, 97 (13.4%) were men and 94 (12.4%) were women (p=0.79 for gender difference).

The distribution of baseline demographic, lifestyle, clinical and biochemical parameters of ATTI-CA study participants, based on their diabetes status at the 10-year follow up is presented in Table 1. Unadjusted analysis revealed that people who developed diabetes were approximately 10 years older, less educated, had higher mean fasting glucose and insulin values; they were more likely to have family history of diabetes, hypertension and hypercholesterolemia. Also, they exhibited lower adherence to the Mediterranean diet and coffee consumption but higher alcohol consumption. No clinically or statistically significant differences existed for smoking status, energy intake or physical activity between the two groups. Individuals who developed diabetes had additionally higher mean BMI and waist circumference and they were more likely to have visceral obesity, defined as WC \geq 94/80cm or \geq 102/88cm. Finally, the group that developed diabetes had higher baseline mean CRP, IL-6, fibrinogen and TNF-a values, whereas SAA or homocysteine did not differ significantly.

In order to evaluate the association of lifestyle factors with 10-year diabetes risk, nested logistic regression models were constructed for each variable of interest. In **Table 2**, the results of fully adjusted models are presented for each variable:

- Adherence to the Mediterranean diet: individuals with medium adherence to the Mediterranean diet experienced 49% lower risk of developing diabetes, within the next 10 years (RR=0.51; 95%CI: 0.30, 0.88), whereas for individuals with high adherence, the risk was found decreased by 62% (RR=0.38; 95% CI: 0.16, 0.88), compared to participants with low level of adherence to the pattern. The interaction between MedDietScore and WC category was found significant (p = 0.045) and was kept in the final model. Also, the analysis was repeated after stratification by WC, i.e., n=727 participants with increased WC (WC>94cm for men and >80cm for women) versus n=549 participants with normal WC. In the fully adjusted model, the protective effect remained only among participants with increased abdominal fat (RR=0.44, 95%CI: 0.25, 0.77 for medium adherence to the Mediterranean diet, and RR=0.26, 95% CI: 0.10, 0.70 for high adherence). For individuals with normal WC, results were not significant (RR=0.97, 95%CI: 0.29, 3.25 and RR=0.89, 95%CI: 0.16, 4.90 for medium and high adherence respectively).
- Coffee consumption: individuals who drank ≥250ml coffee daily experienced 54% lower risk of developing diabetes within 10 years, as compared to coffee abstainers (OR=0.46; 95%CI: 0.24, 0.90). When caffeinated drinks consumption (i.e., tea, cola) was taken into account, the protective association of coffee drinking was not altered; however significance was marginally reached (OR for ≥250ml coffee daily vs. abstainers =0.23; 95%CI: 0.04, 1.04). For casual coffee drinking results were not significant.
- Alcohol consumption: individuals who consumed <1 glass alcohol daily experienced 53% lower risk of developing T2DM within 10 years as compared with abstainers (OR=0.47; 95%CI: 0.26, 0.83). However, moderate and high alcohol intake were not significantly associated with diabetes development (OR=1.05; 95%CI: 0.57, 1.93 and OR=1.25; 95%CI: 0.65, 2.37, respectively).
- **Physical activity:** participants with moderate physical activity level (MET minutes/week 331-

Lifestyle behaviors					
Adherence to the Mediterranean diet	Tertile 1 (Low) (<i>n</i> = 490)	Tertile 2 (Medium)(<i>n</i> =518)	Tertile 3 (High) (n=477)		
Cases; incidence	105; 21%	62; 12%	24; 5%		p<0.001
Fully adjusted model ^a	Reference	0.51; 0.30, 0.88	0.38; 0.16, 0.88		
Coffee consumption	0 ml/day (Abstention) (n=239)	<250 mL/day (Casual) (n=816)	≥250 ml/day (Habitual) (<i>n</i> =385)		
Cases; incidence	23; 9.6%	57; 7%	20; 5.2%		p<0.001
Fully adjusted model ^b	Αναφ.	0.66; 0.39, 1.11	0.46; 0.24, 0.90		
Alcohol consumption	0 glass/day (Abstention) (n=592)	0 to < 1 glass/day (Low) (n=366)	1–2 glasses/day (Moderate) (n=208)	>2 glasses/day (High) (n=137)	
Cases; incidence	100; 17%	21; 5.7%	29; 14%	23; 17%	p<0.001
Fully adjusted model ^c	Reference	0.47; 0.26, 0.83	1.05; 0.57, 1.93	1.25; 0.65, 2.37	
Physical activity (MET-min/ wk)	Very low (<150) (<i>n</i> =509)	Low (150 - 330) (<i>n</i> =334)	Moderate (331 - 1484) (n=271)	High (>1484) (<i>n</i> =371)	
Cases; incidence	68; 13%	48; 14%	25; 9%	50; 14%	p<0.001
Fully adjusted model ^d	Reference	0.77; 0.41, 1.49	0.47; 0.24, 0.93	1.04; 0.59, 1.82	
Inflammation status					
CRP (mg/dL)	Tertile 1 (0.01 – 0.58)	Tertile 2 (0.59 – 1.60)	Tertile 3 (1.61 – 15.9)		
Cases; incidence	35; 8.5%	44; 10.9%	80; 19.5%		P=0.078
Fully adjusted model ^e	Reference	0.87; 0.51, 1.50	1.46; 0.89, 2.40		
IL-6 (pg/mL)	Tertile 1 (0.3 – 1.25)	Tertile 2 (1.26 – 1.46)	Tertile 3 (1.47 - 7.1)		p<0.001
Cases; incidence	21; 4.9%	39; 9.8%	100; 23.4%		
Fully adjusted model ^f	1 (referent)	1.07; 0.55, 2.08	2.20; 1.13, 4.28		•

^aadjusted for age, sex, family history of diabetes, hypertension, hypercholesterolemia, smoking status), education, physical activity and abnormal WC (i.e. WC>94 cm for men or>80 cm for women)

^{b,c}adjusted for age, sex, family history of diabetes, hypertension, hypercholesterolemia, smoking status, education, physical activity, WC and adherence to the Mediterranean diet

^dadjusted for confounders of models b,c plus fasting glucose and triglycerides

^{e,f}adjusted for age, sex, family history of diabetes, hypertension, hypercholesterolemia, smoking status, physical activity and adherence to the Mediterranean diet

1484, e.g. half an hour of walking 4 days/week - 1 hour of walking everyday) had 44% lower 10-year diabetes risk, compared to participants with very low physical activity level (MET minutes/week <150) (OR=0.56, 95% CI: 0.34, 0.92). For participants in low and high physical activity groups an inverse trend were observed, though not statistical significant.

• Inflammation status: the role of chronic subclinical inflammation was also investigated. Elevated IL-6 levels increased by 2.2 times the 10-year diabetes risk (OR3rd vs. 1st tertile=2.2, 95%CI: 1.13, 4.28), whereas for CRP results were not significant in the fully-adjusted model. Interestingly, when IL-6 model was further adjusted for BMI, statistical significance was lost, indicating the potential mediating effect of obesity in inflammation-diabetes link (OR=1.30; 95%CI: 0.65, 2.60). For all other inflammatory markers results were not significant even in age-sex adjusted models (results not shown).

Discussion

Diabetes is a chronic complex disease with a significant lifestyle basis. In the present work the 10-year diabetes incidence was studied in relation to various lifestyle factors. Medium and high adherence to the Mediterranean diet, were found protective. Firstly, even moderate adherence to the Mediterranean diet was found to significantly decrease diabetes risk by approximately 50%, which is very important from a public health point of view, since even small dietary changes are enough to achieve moderate adherence to the pattern. In addition to this, the benefit was maximized for individuals with visceral obesity, a finding which was further confirmed by the mediating effect of obesity in inflammation-diabetes relationship. With regards to the rest lifestyle parameters, habitual coffee consumption (≥250ml/ day, i.e. 3 cups of brewed or 2 cups of instant coffee), low alcohol consumption (<1 glass/day, i.e., <120ml wine, 330ml beer or 45 ml of whisky, vodka, gin etc) and moderate physical activity levels (331-1484 MET-minutes; corresponding, for example, to almost 30-60 minutes of walking 4-7 times/ week or 30-50 minutes of moderate intensity physical activity 3-7 times/week or 20-40 minutes of vigorous physical acivity 2-5 times/week) were also found to confer significant antidiabetic protection. Despite the limitations of the present observational study, the large, representative sample, the prospective design and follow-up of 10 years, as well as the detailed assessment of lifestyle information, and, therefore, the ability to adjust for several known confounders, may guarantee that the reported findings are of considerable public health importance, as they shed light into the extent at which several modifiable risk factors can decrease diabetes risk, as well as the importance of obesity in the initiation and/ or aggravation of inflammatory diathesis.

The aforementioned risk factors have been previously linked to a lower diabetes incidence. The beneficial effect of the Mediterranean diet, also reported in a meta-analysis of 10 prospective studies [16], may be ascribed among others to the pattern's increased content in dietary fiber, which lower glucose absorption, mitigating insulin secretion need [17], magnesium, an inadequacy of which increases insulin resistance [18], as well as antioxidants, which inhibit oxidative damage in sensitive b-cells [19]. De Koning et al, have also observed that Mediterranean diet yields its benefit among individuals with high BMI [20], which is in line with our findings. Indeed, under obesity state fat tissue becomes the major producer of inflammatory molecules [21], which chronically get implicated in the sustainment or aggravation of insulin resistance [22]. Of the proposed inflammatory markers in this work, IL-6 and CRP have been well documented to independently increase diabetes risk, which was confirmed by a recent meta-analysis [23]. In relation to the composite effects CRP-IL-6 combined effect was expected, due to the single aggravating effect of both markers, however, this is the first study to document the potential combined action of two acute phase proteins, CRP and fibrinogen on diabetes incidence. In relation to coffee consumption, consistency exists regarding its effect on diabetes development [24, 25]. Coffee, a mixture of caffeine, chlorogenic acid, micronutrients, helps maintain normal glucose tolerance, improves insulin sensitivity, stimulates pancreatic insulin secretion and inhibits of glucose-6-phosphatase, which releases glucose to circulation [26]. Despite its observed beneficial effect, coffee should always be consumed in moderation, depending on individuals need, and not overconsumption is suggested. Alcohol's protective effect at low doses has also been shown in previous studies [6, 27], which is mostly ethanol-related, since no significant differences have been proposed between types of drinks [28]. Alcohol increases anti-inflammatory adiponectin [29] and decreases plasma glucose and insulin [30] and fetuin-A, a glucoprotein implicated in disturbance of insulin signaling [31]. Last but not least, exercise normalizes liver and skeletal muscle insulin resistance, not only by itself but also through weight loss process [32]. Similarly to our findings, a very recent meta-analysis of 55 studies, concluded that the greatest antidiabetic benefit is attained in medium levels of physical activity [33].

Limitations

Regardless of the aforementioned findings, we cannot rule out the limitations of an observational study. Firstly, the baseline evaluation was performed once, and may be prone to measurement error. Also, for some individuals diabetes diagnosis was based upon self-report and/or physician-diagnosis, but this is common for prospective studies. Moreover, the accurate date of diabetes development was not accessible (only the date of

diagnosis was identified); as a result hazard ratios were estimated through ORs that may have overestimated the true effect; however, it has been reported that, for low frequency diseases, OR is an accurate estimate (converges) of the relative risk. Another concern in prospective studies is that many lifestyle factors (i.e., physical activity, energy intake) may have changed during the 10-year time period without timely information updates.

Conclusions

In conclusion, the current study has provided additional evidence in the literature concerning the effect of lifestyle parameters on 10-year incidence of type 2 diabetes mellitus. The presented results carry a hopeful public health message suggesting that even medium adherence to different health behaviors can lead to a clinically significant reduction in diabetes risk. Targeting individuals who are very far from the Mediterranean diet or very sedentary might be particularly important from a public health perspective. It is consequently imperative to promote strategies to achieve small dietary changes and increase physical activity levels especially among obese and/or inactive individuals, while it is also important to recognize facilitators and barriers that patients with established prediabetes deal with, in terms of diet and physical activity compliance.

Conflict of Interest

All authors declare no conflict of interest.

Περίληψη

Η μακροχρόνια επίδραση της διατροφής και άσκησης στην ανάπτυξη σακχαρώδη διαβήτη τύπου 2: 10ετής επανέλεγχος της μελέτης ΑΤΤΙΚΗ (2002-2012)

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Σκοπός: να καταγραφεί η 10-ετής επίπτωση σακχαρώδη διαβήτη τύπου 2 και να διερευνηθεί η επίδραση των διατροφικών συνηθειών και της σωματικής δραστηριότητας στην ανάπτυξή του.

Υλικό και Μέθοδος: από τον Μάιο 2001 έως το Δεκέμβριο 2002, εντάχθηκαν στη μελέτη ΑΤΤΙΚΗ 1514 άνδρες και 1528 γυναίκες (> 18 ετών) χωρίς κλινική ένδειξη καρδιαγγειακής νόσου ή άλλης χρόνιας νόσου, που ζούσαν στην ευρύτερη περιοχή της Αθήνας. Αξιολογήθηκαν κοινωνικο-δημογραφικά, κλινικά, βιοχημικά χαρακτηριστικά και στοιχεία του τρόπου ζωής. Οι διατροφικές συνήθειες αξιολογήθηκαν μέσω έγκυρου ημι-ποσοτικού ερωτηματολογίου συχνότητας κατανάλωσης τροφίμων και η φυσικής δραστηριότητα με το έγκυρο Διεθνές Ερωτηματολόγιο Σωματικής Δραστηριότητας (IPAQ). Η διάγνωση του σακχαρώδη διαβήτη ορίστηκε ως γλυκόζη> 125mg/dL ή/και χρήση αντιδιαβητικής αγωγής. Μεταξύ 2011-2012 πραγματοποιήθηκε ο 10ετης επανέλεγχος.

Αποτελέσματα: 191 περιπτώσεις σακχαρώδη διαβήτη καταγράφηκαν, διαμορφώνοντας την επίπτωση στο 12.9%. Η μέση και υψηλή προσκόλληση στη Μεσογειακή Δίαιτα μείωσε τον 10ετή κίνδυνο ανάπτυξης σακχαρώδη διαβήτη κατά 49% ($\Sigma\Lambda$ =0.51, 95% ΔΕ: 0.30, 0.88) και 62% ($\Sigma\Lambda$ =0,38, 95% ΔΕ: 0.16, 0.88) αντίστοιχα. Η μέτρια κατανάλωση καφέ (\geq 250mL/ημέρα, προσαρμοσμένο για 28% περιεκτικότητα σε καφεΐνη) και η χαμηλή κατανάλωση αλκοόλ (<1 ποτήρι/ημέρα) μείωσαν επίσης τον κίνδυνο κατά 54% ($\Sigma\Lambda$ =0.46, 95% ΔΕ: 0.24, 0.47) και 3% ($\Sigma\Lambda$ =0.47, 95% CI: 0.26, 0.83), σε σύγκριση με την αποχή. Τέλος, το μέτριο επίπεδο φυσικής δραστηριότητας (331-1484 έναντι <150 ΜΕΤ / εβδομάδα) οδήγησε σε μείωση κινδύνου 44% ($\Sigma\Lambda$ =0.56, 95% ΔΕ: 0.34, 0.92).

Συμπεράσματα: η παρούσα εργασία τόνισε τη σημασία μη φαρμακολογικών παρεμβάσεων στην πρωτογενή πρόληψη του σακχαρώδη διαβήτη. Η μεσογειακή δίαιτα, η μέτρια κατανάλωση καφέ, η χαμηλή κατανάλωση αλκοόλ και το μέτριο επίπεδο φυσικής δραστηριότητας ασκούν ευεργετική δράση ενάντια στην ανάπτυξη της νόσου.

Λέξεις ευρετηρίου: συχνότητα εμφάνισης σακχαρώδη διαβήτη, μεσογειακή δίαιτα, αλκοόλ, καφές, σωματική δραστηριότητα

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References

- International Diabetes Federation, IDF Atlas 7th edition. 2015
- 2. Billings LK and Florez JC. The genetics of type 2 diabetes: what have we learned from GWAS? *Ann N Y Acad Sci* 2010; 1212: 59-77
- 3. Khazrai YM, Defeudis G, Pozzilli P. Effect of diet on type 2 diabetes mellitus: a review. *Diabetes Metab Res Rev* 2014; 30: Suppl 1,24-33
- 4. Mayor S. International Diabetes Federation consensus on prevention of type 2 diabetes. *Int J Clin Pract* 2007; 61: 1773-1775
- Beziaud F, Halimi JM, Lecomte P et al. Cigarette smoking and diabetes mellitus. *Diabetes Metab* 2004; 30: 161-166
- 6. Baliunas DO, Taylor BJ, Irving H et al. Alcohol as a risk factor for type 2 diabetes: A systematic review and meta-analysis. *Diabetes Care* 2009; 32: 2123-2132
- Colberg SR, Sigal RJ, Fernhall B et al. Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement. *Diabetes Care* 2010; 33: e147-167
- 8. Pitsavos C, Panagiotakos DB, Chrysohoou C et al. Epidemiology of cardiovascular risk factors in Greece: aims, design and baseline characteristics of the ATTI-CA study. *BMC Public Health* 2003; 3: 3-32
- Katsouyanni K, rimm EB, Gnardellis C et al. Reproducibility and relative validity of an extensive semi-quantitative food frequency questionnaire using dietary records and biochemical markers among Greek schoolteachers. *Int J Epidemiol* 1997; 26: Suppl 1, S118-127
- 10. Panagiotakos DB, Pitsavos C, Stefanadis C. Dietary patterns: a Mediterranean diet score and its relation to clinical and biological markers of cardiovascular disease risk. *Nutr Metab Cardiovasc Dis* 2006; 16: 559-568
- USDA, National Nutrient Database for Standard Reference. Composition of Foods Raw, Processed, Prepared. Release 26, Available at: http://ndb.nal.usda.gov/.2013
- 12. Papathanasiou G, Georgoudis G, Papandreou M et al. Reliability measures of the short Internation-

- al Physical Activity Questionnaire (IPAQ) in Greek young adults. *Hellenic J Cardiol* 2009; 50: 283-294
- American Diabetes Association, Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 1997; 20: 1183-1197
- Koloverou E, Panagiotakos DB, Pitsavos C et al. 10year Incidence of Diabetes and Associated Risk Factors in Greece: the ATTICA study (2002-2012). Rev Diabet Stud 2014; 11: 181-189
- Cornfield J. A method of estimating comparative rates from clinical data; applications to cancer of the lung, breast, and cervix. *J Natl Cancer Inst* 1951; 11: 1269-1275
- Koloverou E, Panagiotakos DB, Pitsavos C et al. Adherence to Mediterranean diet and 10-year incidence (2002-2012) of diabetes: correlations with inflammatory and oxidative stress biomarkers in the ATTICA cohort study. *Diabetes Metab Res Rev* 2016; 32: 73-81
- 17. Liese AD, Schulz M, Fang F et al. Dietary glycemic index and glycemic load, carbohydrate and fiber intake, and measures of insulin sensitivity, secretion, and adiposity in the Insulin Resistance Atherosclerosis Study. *Diabetes Care* 2005; 28: 2832-2838
- Barbagallo M, Dominguez LJ, Galioto A et al. Role of magnesium in insulin action, diabetes and cardio-metabolic syndrome X. Mol Aspects Med 2003; 24: 39-52
- Evans JL, Goldfine ID, Maddux BA et al. Are oxidative stress-activated signaling pathways mediators of insulin resistance and beta-cell dysfunction? *Diabetes* 2003; 52: 1-8
- 20. de Koning L, Chiuve SE, Fung TT, et al. Diet-quality scores and the risk of type 2 diabetes in men. *Diabetes Care* 2011; 34: 1150-1156
- 21. Calder PC, Ahluwalia N, Brouns F et al. Dietary factors and low-grade inflammation in relation to overweight and obesity. *Br J Nutr* 2011; 106 Suppl 3: S5-78.
- 22. Shoelson SE, Lee J and Goldfine AB, Inflammation and insulin resistance. *J Clin Invest* 2006; 116: 1793-1801
- 23. Wang X, Bao W, Liu J et al. Inflammatory markers and risk of type 2 diabetes: a systematic review and me-

- ta-analysis. Diabetes Care 2013; 36: 166-175
- 24. van Dam RM Hu FB, Coffee consumption and risk of type 2 diabetes: a systematic review. *JAMA* 2005; 294: 97-104
- 25. Jiang X and Zhang D Jiang W. Coffee and caffeine intake and incidence of type 2 diabetes mellitus: a meta-analysis of prospective studies. *Eur J Nutr* 2013; 53: 25-38
- 26. Akash MS, Rehman K, Chen S. Effects of coffee on type 2 diabetes mellitus. *Nutrition* 2014; 30: 755-763
- Rasouli B, Ahlbom A, Andersson T et al. Alcohol consumption is associated with reduced risk of Type 2 diabetes and autoimmune diabetes in adults: results from the Nord-Trondelag health study. *Diabet Med* 2013; 30: 56-64
- Clerc O, Nanchen D, Cornuz J et al. Alcohol drinking, the metabolic syndrome and diabetes in a population with high mean alcohol consumption. *Diabet Med* 2010; 27: 1241-1249
- 29. Beulens JW, Rimm EB, Hu FB et al. Alcohol consumption, mediating biomarkers, and risk of type 2

- diabetes among middle-aged women. *Diabetes Care* 2008; 31: 2050-2055
- 30. Bonnet F, Disse E, Laville M et al. Moderate alcohol consumption is associated with improved insulin sensitivity, reduced basal insulin secretion rate and lower fasting glucagon concentration in healthy women. *Diabetologia* 2012; 55: 3228-3237
- 31. Ley SH, Sun Q, Jimenez MC et al. Association between alcohol consumption and plasma fetuin-A and its contribution to incident type 2 diabetes in women. *Diabetologia* 2014; 57: 93-101
- 32. Yeo S and Coker RH. Aerobic exercise training versus the aetiology of insulin resistance. *Eur J Sport Sci* 2008; 8: 3-14
- 33. Kyu HH, Bachman VF, Alexander JE et al. Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose-response meta-analysis for the Global Burden of Disease *Study* 2013, *BMJ* 2016; 354: i3857