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A negative association of dietary advanced glycation end products with obesity and body composition in Iranian adults

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Abstract

Obesity caused by excessive deposited fat, is generally classified as body mass index (BMI) ≥30 kg/m^2. Research regarding the association between dietary advanced glycation end products (dAGEs) and obesity is limited. The aim of present study was to investigate the association between dAGEs and obesity and body composition in Iranian adults. This cross-sectional study included 265 adults aged 18-75 years from Tehran, Iran. Dietary AGEs was estimated using a validated semiquantitative food frequency questionnaire, according to the published food CML–AGE database for 549 routine consumed food items for the Northeastern American multiethnic urban population and was reported by dividing to total energy intake. Dietary intake, socio-demographic data and physical activity status were collected using validated questionnaires and anthropometric characteristics were measured. Body composition was assessed by bioelectrical impedance analysis (BIA) and obesity was defined based on world health organization (WHO) guidelines. The intake of fat and meat were significantly increased in higher tertiles, compared to the first tertile of dAGEs (P <0.001). No association between dAGEs and body composition measures and obesity was observed, however, there were a significant association between dAGEs and BMI (body mass index; P=0.01), WC (waist circumference; P=0.01), WHR (waist-to-hip ratio; P=0.03), FFM (fat free mass; P=0.02) and MMI (muscle mass index; P=0.01) in nonlinear models. In conclusion, higher consumption of dAGEs was associated with increased intake of fat and meat and was related to changes in body composition measurements. Therefore dAGEs may connect obesity to diet by energy imbalance.

Introduction

Obesity, defined as abundant and abnormal accumulation of fat in the body, has negative, long-term, effects on health [(1)]. This chronic disease is a serious concern in developed and developing

countries [1-3]. According to the SURFNCD-2007 , the prevalence of obesity and central obesity was 22.3% and 53.6% respectively in Iran[4] and WHO results showed that more than half of Iranian adults were overweight and obese in 2010[5].Obese people are exposed to various illnesses, such as cardiovascular disease (CVD), gastrointestinal disorders, type 2 diabetes (T2D), joint and muscular disorders, respiratory problems, and psychological issues, which have significant effects on quality of life ,and increases the risk of early mortality [6]. Obesity is regarded as a multifactorial disorder that involves genetics, hormonal, metabolic, and behavioral aspects [7]. Nutritional changes, particularly towards high energy and high fat diets and decreased physical activity, are some of the most important factors in increasing the prevalence of obesity [8-10]. Although Iranian dietary pattern is mainly contains carbohydrate (65%) specially bread and white rice[11], interest in processed foods high in fat and sugar as an indicator of a lifestyle characterized by urbanization and not to have enough time to prepare food, has been increased in recent years. More than 300,000 deaths, annually reported in the United States are attributed to poor nutritional behaviors, physical inactivity and obesity related issues[12], and thus, the importance of nutritional behaviors and consequential obesity is a serious concern [13].

Advanced glycation end products (AGEs) are compounds obtained from nonenzymatic reactions between reducing sugars and free amino groups in proteins, lipids, or nucleic acids [14]. AGEs can cause oxidative stress and chronic inflammation when they bind their receptors that are present in epithelial, immune, and endothelial cells [15]. In addition to AGE endogenous formation, the diet also affects the amount of bodily AGE, where it has been reported that 10% of a high AGE diet will be absorbed [16]. Foods with high amounts of fat and meat are considered high in AGE, especially if cooked with dry heat [17]. It has been shown that increasing the food AGEs leads to weight gain, and decreased insulin sensitivity and albumin excretion[18]. Moreover, studies have also shown the effect of receptor for advanced glycation end products (RAGE) on weight gain, abdominal obesity, adipocyte size, development of CVD and insulin resistance [14, 19, 20]. Carboxymethyl lysine (CML), which is the main type of AGEs in the diet, is typically used as a dietary AGE marker [21]. Controversial data exist regarding the effects of dietary AGEs on its circulating levels. Indeed, the results of some studies emphasize that intakes of CML can lead to excess serum AGE levels [22], whereas others show no effect of dietary AGEs on circulating levels of AGEs [23]. Few studies have reported on the relationship between intake of dietary AGEs and chronic disease, such as kidney disease, metabolic syndrome, and cardiovascular disease. Thus, in the present study, we sought to investigate the relationship between dietary AGEs and obesity and body composition in Iranian adults.

Methods

Study population

This cross sectional study was conducted on 265 subjects, aged 18-75 years, recruited by way of convenience sampling. Inclusion criteria was; aged 18-75 years old and to be willing to

participate in this study, whilst exclusion criteria included extreme values of dietary intake (less than 800 kcal/d or more than 4200 kcal/d, respectively), suffering from kidney, liver and lung diseases and other conditions affecting the cardiovascular or respiratory system health, or, infectious and active inflammatory diseases, pregnancy, lactation, routine supplement or drug use, such as weight loss, hormonal, sedative drugs, thermogenic supplements like caffeine and green tea, conjugated linoleic acid (CLA) etc. and the final analysis was conducted in 265 participants.

Dietary assessment

To record participant's consumption frequency for each food item, during the past year, on a daily, weekly, or monthly basis, was recorded by trained dietitians using a validated semi-quantitative food frequency questionnaire (FFQ), which contains 168 food items. The reliability and validity of the FFQ for food group intakes has been assessed and found to be acceptable [24]. The reported amounts were converted to grams per day by the manual for household measures book. Then, participant's nutrients consumption was analyzed by Nutritionist IV software. The most important type of dietary AGEs, Carboxymethyl lysine (CML), is usually used as a dietary AGE marker [21]. Because the Iranian Food Composition Table (FCT) does not detail AGEs content, we collected data from the published food CML–AGE database for 549 routine consumed food items for the Northeastern American multiethnic urban population, which was assessed by validated immunoassay method [17, 21]. We calculated CML–AGE values per day, according to kilo unit (kU) amounts in 100 g solid food or 100 ml liquid for 151 out of 168 food items in the validated FFQ list were determined by this database. The values for some Iranian specific food items, e.g. some kinds of bread and cookie like Sangak,Lavash,Pirashki that there are not in table, were estimated from similar food items and 17 items that had not similar food like some kinds of confectionaries for example: Gaz, Noghl, Sohan were considered as missing. Because AGEs amounts were not available for all fruits and vegetables, in this instance, we considered the mean values of comparable fruits and vegetables [25]. To make the AGEs intake assessment independent of energy, these amounts were divided by total energy intake and considered as dAGEs/EI that were categorized by tertile cutoffs (<2.96, 2.96 – 4.45 and 4.45<).

Data Collection

According to inclusion and exclusion criteria, subjects were chosen and interviewed to collect data on demographics, smoking status, physical activity, diet, and supplement use. Then, anthropometric assessment was conducted. We used short form of International Physical Activity Questionnaire (IPAQ) to assess the physical activity of the participants during the preceding week [26]. According to the IPAQ criteria, data were recorded regarding vigorous and moderate activity and walking, for at least 10 min/day during the previous 7 days. Duration and frequency

of activity days were multiplied by the metabolic equivalent task value of the activity to calculate the activity. The total physical activity per week was used to calculate the sum of the scores, and categorized into three groups: low, moderate, and high. Also, IPAQ was computed for a continuous score and reported as metabolic equivalent (MET)-minutes per week.

Subjects' weight was recorded while wearing light clothing and unshod, to the nearest 0.1 kg, using digital scales (Seca 808, Germany). Height was measured to the nearest 0.1 cm using a stadiometer (Seca 206, Germany), in standing position, unshod. BMI was calculated as weight (kg) divided by square of height (m^2). WC was measured between lower rib and iliac crest, at the widest portion, with light clothing, using a tape meter (Seca 201, Germany) without any pressure to the body[27] . WHR was calculated as waist circumference (cm) divided by hip circumference (cm). Blood pressure was measured twice, in a seated position following a 10-15 minute rest, using a digital sphygmomanometer (Beurer, BC 08, Germany), and the mean of the two measurements was considered as the participant's systolic and diastolic blood pressure.

We used BIA (InBody S10, JMW140, Korea) to assess visceral fat level (VFL), skeletal muscle mass (SMM), body fat percentage (PBF), body fat mass (BFM), fat free mass (FFM), and trunk fat (TF). For increased accuracy, participants were advised to refrain from moderate and intense exercises 1-2 hour before using BIA and to urinate before testing. Muscle mass index (MMI) was calculated as skeletal muscle mass (kg) divided by height square (m^2).

Obesity definition

General obesity was defined as BMI ≥30 kg/m^2, whilst WC≥102 cm for men and ≥88cm for women, and, WHR>0.9 for men and >0.85 for women were used as central obesity risk factors [28]. We then used median to categorize the VFL and BFM in two groups.

Statistical analysis

Analysis was conducted on 265 subjects. Participants were categorized based on the tertiles of the AGEs. For comparison of the participant characteristics among the AGEs tertiles, one-way analysis of variance (ANOVA) and chi-square tests were used for quantitative and qualitative variables, respectively. Analysis of variance (ANOVA) was performed to report dietary intakes of participants across the tertiles of the AGEs. We used ANOVA in crude models and ANCOVA in adjusted models for age, sex, physical activity, smoking status, education status, metabolic diseases and energy intake to investigate the association of dietary AGE intake and anthropometric measures and body composition.

According to WHO guidelines, BMI ≥ 30 kg/ m^2 was used to classify general obesity, and WC≥102 cm for men and ≥88cm for women and WHR>0.9 for men and >0.85 for women were considered as markers of central obesity [28]. Odds ratios and 95% confidence intervals were obtained using logistic regression to determine the relationship of the AGEs and risk of obesity. Logistic regression models included a dichotomous outcome (general obesity (yes or no) or central obesity (yes or no)) and AGEs as exposure. The risk was reported in crude and 3 adjusted

models for age, sex, physical activity, smoking status, education status, metabolic diseases and energy intake. In this analysis, the first tertile of exposure was considered as the reference category. Nonlinear regression was conducted to investigate nonlinear associations between AGEs and body composition measurements. We accepted statistical significance, *a* priori, at P< 0.05. We used SPSS version 22 (IBM) for all analyses.

Ethical approval

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the ethics committee of Tehran University of Medical Sciences (ethics Number: IR. TUMS.VCR.REC. 1398.503). Written informed consent was obtained from all subjects.

Results

The mean±SD of age and BMI of the participants (44.1% male) were 36.6±13.1 years and 25.6±4.69kg/m^2, respectively. The mean dAGEs/EI was 4.05 ± 1.83 kU/kcal (3.83 kU/kcal in men and 4.23 kU/kcal in women). The mean consumption of AGEs in each tertile was 2.37, 3.67 and 6.13 respectively. Also, the results of dAGEs did not dependent on energy intake. Demographic characteristics of all 265 participants across tertiles of AGEs are shown in **Table 1**.The distribution of the age and height in the tertiles of dAGEs was significant, so that participants in the higher tertile were younger (P=0.003) and taller (P=0.02). Subjects in the lowest compared with the highest tertile of AGEs had significantly more history of metabolic diseases (P=0.003). Other participants' characteristics were not related to intake of dAGEs. Dietary intakes of participants according to tertiles of dietary AGE intakes are presented in **Table 2**. The percentage of fat intake and meat consumption were significantly higher in participants with the highest, compared to the lowest consumption of AGEs (P <0.001). In addition, there was a significant decreasing trend in the percentage of carbohydrate intake across the increasing trend of AGE consumption (P <0.001) and the most intake of protein was related to second tertile of AGEs (P<0.001). However, there was no significant difference in energy intake and fiber consumption across tertiles of AGE consumption. We also re-analyzed data based on sex and found that results remained unchanged (**Supplementary Table 1).**

Table 3 shows the association between dietary AGEs intake and anthropometric measures and body composition. There were not significant associations between BMI (P=0.09), WC(P=0.10), WHR(P=0.20), VFL(P=0.35), SMM(P=0.23), PBF(P=0.89), BFM(P=0.22), FFM(P=0.14), MMI (P=0.13) and TF (P=0.23) and AGEs intake before and after adjustment for possible confounders such as age, sex, physical activity, smoking status, education status, metabolic diseases and energy intake. Analyses according to the sex showed that results remained unchanged (**Supplementary Table 2**).

The results of linear and nonlinear models association between AGEs intakes and body composition measures are presented in **Figure 1**. In linear models, with increases in AGEs intake, significant decrease in BMI ($P_{linearity}$=0.04), WC ($P_{linearity}$=0.03), FFM ($P_{linearity}$=0.02) and MMI ($P_{linearity}$=0.03) were observed. In nonlinear models, BMI ($P_{nonlinearity}$=0.01), WC ($P_{nonlinearity}$=0.01), WHR ($P_{nonlinearity}$=0.03), FFM ($P_{nonlinearity}$=0.02) and MMI ($P_{nonlinearity}$=0.01) were significantly decreased along with increased AGEs intake.

Odd ratios and 95% confidence interval for general and central obesity in each tertile category of AGEs intake are presented in **Table 4**. The association between AGE consumption and central obesity that measured by waist circumference (p=0.05), waist to hip ratio (p=0.83) and body fat mass (p=0.07), were not statistically significant after controlling for confounders. However, the odds of central obesity assessed by VFL had decreasing trends across increasing tertiles of AGEs intake in model 2 (P=0.03) and model 3 (P=0.03).Also, risk of general obesity was not significantly different across tertiles of AGEs intake.

Discussion

We found that there was no association between intake of AGEs, body composition and odds of central and general obesity. However, the relation between BMI, WC, WHR, FFM and MMI and intake of AGEs in the nonlinear model were significant. Moreover, higher intake of AGEs was associated with higher intake of fat and meat and lower intake of carbohydrate considering that mentioned findings were independent of total energy intake. Re-analyzing data based on sex also did not change our findings.

An important finding of the present study was that higher intake of AGEs was not related to general and central obesity. Our results confirmed the findings of a cross sectional study done by Mendoza-Herrera et al., who reported that higher intake of AGEs was not associated with higher risk of abdominal obesity [(29)]. Another study conducted by Angoorani et al., also showed that there were no significant relationships between AGEs intake and general obesity, and further reported significant association between AGEs intake and abdominal obesity that were related to dietary energy and macronutrient intakes and after adjustment of confounding factors, this relationship was lost [(30)]. Abdominal obesity is one of the risk factors for the metabolic syndrome, and it has been reported that patients with metabolic syndrome had a notably greater consumption of dietary AGEs [(31)]. In our study population, older people had lower intake of AGEs. Possibly, it is because of the history of metabolic diseases like hypertension, dyslipidemia, cardiovascular disease and following of the special diet like diet with low fat and free sugar, boiled and steamed food and related recommendations that limited their AGEs intake.

In the present study, we also found that body composition was not different across tertiles of AGEs. Poulsen et al., in a murine model, indicated no difference in body composition between high and low AGEs diet groups [(32)]. On the other hand, Mirmiran et al., showed there were significant associations between dietary AGEs intake and BMI, waist circumference, and body

adiposity index in crude models, and after adjustment for possible confounders, a relationship is independent of energy and macronutrient intake [33]. Increased visceral adiposity is the important indicator of accumulated adipose tissue, and is significantly related to oxidative stress biomarkers in systemic levels [34-36]. CML-AGE is harmful when it binds to RAGE, which causes a damaging cycle of chronic inflammation and production of reactive oxidative species [37].

Iranian culture includes diverse food and cooking methods. Although traditional foods do not include processed products and has a higher carbohydrate content especially white rice compared to fat and meat, the common cooking method is along with higher temperature and longer time and also, fried onion and green vegetables is the basic item in the preparing some of the Iranian food that all together can increase AGEs formation.

Another finding of the present study was significant decrease in BMI, WC, WHR and FFM and MMI across the AGEs categories. Assessment of associations in nonlinear models is an important aspect of nutritional epidemiology[38] ; indeed, according to our knowledge, this is the first study to use nonlinear models to show this kind of relationship and we have no similar data in other studies.

A further finding of this study was that higher intake of AGEs was associated with higher intake of fat and meat and lower intake of carbohydrate. These results were in agreement with the finding of Ejtahed et al., however, their results showed a decreasing intake of fiber in the highest quartile of AGEs intake [39]. It was reported that fiber contains more antioxidant content that prevents AGEs formation in body[40].Mean dietary intake of AGEs in our study (9401kU/day) was lower than cohort of healthy adults from the New York City (14700 kU/day) [41], which may be because of differences between Iranian and Western dietary patterns. In comparison to a Western diet, that includes more fat and meat foods, the Iranian population diet contains more complex carbohydrates and less fat and meat and lower contents of AGEs [42, 43]. It has been observed that fat and meat include relatively greater amounts of AGEs than carbohydrates, because the carbohydrate-based foods have higher water content, lower reducing sugar, and higher levels of antioxidants and vitamins, which may prevent AGE formation [17]. Additionally, the difference may also be related to the dietary intake assessment tools. Although we obtained dAGEs amounts by FFQ, 3-day dietary food records were used in a cohort study [41]. Contrary to our study, they included healthy people without any history of hypertension, CVD and other diseases associated with inflammation and oxidative stress. The dAGEs intake in present study was higher than that of reported by Mirmiran et al. in participants from Iran (7043 kU/day) which may be due to the larger sample size, to use FFQ with 147 food item (vs. 168 item FFQ) and characteristics of the participants such as age and living district [33]. To be noted that, comprehensive information about dAGEs intake in different population is not available.

It has been shown that 10% of a high AGE diet will be absorbed in the body [16]; however,

controversial data exist regarding the effects of dietary AGEs on its circulating levels. The results of some studies emphasize that intakes of CML can lead to excess serum AGE levels [22], whereas others show no effect of dietary AGEs on circulating levels of AGEs [23]. Furthermore, the method of cooking is very important in AGE generation; for instance, broiled chicken (5,828 kU/100 g) and broiled beef (5,963 kU/100 g) contain amounts of AGE, but can be considerably limited (1,124 kU/100 g and 2,230 kU/100 g, respectively) by either boiling or stewing. Also the use of acidic marinades, such as lemon juice and vinegar, before cooking, can decrease dAGEs formation [17, 44] that these methods are not widely used in assessed population who are from Iranian culture.

The modern western diet, which includes fast foods with high amount of energy, added sugar and fat, has also AGEs-rich component and not only directly contributes to increase risk of obesity with its high energy dense content, but also has adverse effects on weight management and health through cellular mechanisms[45]. Therefore, limiting dAGEs intake for obesity prevention should be advocated. Many studies have indicated the effect of AGEs intake on complications like increasing oxidative stress, diabetes, impaired kidney function, cardiovascular disease, are associated with abdominal obesity [46-48]. Mechanisms of how dietary AGEs consumption can increase obesity are not well understood yet, but one pathway is the effect of AGEs on insulin resistance, where circulating insulin increases and thus promotes the storage of fat, obesity, and diabetes. Dietary AGEs, such as CML, pyrraline, and pentosidine, are absorbed in intestine at different rates and their pathways are not clear [49]. Additionally, recent studies have shown that the dietary AGEs had no effect on circulating AGE [22, 50]. One prior study indicated that the serum levels of CML were not a useful biomarker for estimating the progression of chronic diseases, and serum levels of glyceraldehyde-derived AGEs (Glycer-AGEs) are more reliable than CML AGEs [51].

Although our study provides a much-needed insight into dAGEs and obesity, it has several limitations. In Iran, there are no published food AGE databases for Iranian food, thus, we used an American-based database, where only CML was measured as a marker of dietary AGEs, whilst the other dietary AGEs markers, such as Glycer-AGEs, that may be an important indicator, were not measured. Further, some special food items do not exist in the American-based table, and thus, missing items and other items were estimated using similar foods. Moreover, the use of BIA (InBody S10) for body composition evaluation, instead of more accurate methods like dual energy X-ray absorptiometry (DEXA) was other important limitation, because DEXA is known as a "gold standard" for this kind of measurement [52]. Cooking methods are an important factor for estimating the dietary AGEs, which has largely been ignored. Being cross-sectional in study design was a further limitation, because this kind of study prevents any indication of causality between AGEs intake and body composition and obesity. We used FFQ for the collection of data regarding participants' diet; however, recall bias is possible; whilst low sample size was another limitation that may result in a lack of association. In addition to all this, not measuring serum

AGEs level was a major limitation of present study, because it could help us to confirm if dietary AGEs intake affects serum AGEs level or not. To the best of our knowledge, this is the first study to have investigated association between dietary consumption of AGEs and body composition measurements and obesity. Controlling for confounders was further strength of this study; furthermore, we measured different components of body composition and nonlinear regression was conducted to investigate nonlinear associations between exposure and outcome. In summary, increasing intake of AGEs was associated with increasing intake of fat and meat. In linear models, AGEs intake had not significant relation with body composition measurements because of confounding variables, although nonlinear associations were found. We did not observe an association between AGEs intake and odds of obesity with attention to independence of dAGEs intake into energy intake in our study. However, further investigation, without all the limitations of this study, particularly considering cooking methods, is needed to confirm the veracity of our findings.

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Conflict of interest

None.

Authorship

PG and SSb contributed to conception/design of the research; PG, NB, SD and ME contributed to acquisition, analysis, or interpretation of the data; PG drafted the manuscript; KD, CC and SSb critically revised the manuscript; and SSb agree to be fully accountable for ensuring the integrity and accuracy of the work. All authors read and approved the final manuscript.

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Table 1. Characteristics of participants according to tertiles of AGE intakes

Table1	Tertile1 (n=88)			Tertile2 (n=89)			Tertile3 (n=88)			p-value *
	n		%	n		%	n		%	
Age(y)										0.003
Mean		40.4			35			34.4		
SD		14.1			12.2			12.3		
Weight(kg)										0.06
Mean		75.2			73.1			69.6		
SD		17.2			16.6			13.1		
Height(cm)										0.02
Mean		166			167			170		
SD		10.2			9.79			9.34		
BMI(kg/ m^2)										0.09
Mean		26.1			25.9			24.7		
SD		5.04			4.91			3.96		
WC(cm)										0.10
Mean		91.6			89.5			87.5		
SD		13.8			13.1			10.1		
WHR										0.20
Mean		0.91			0.90			0.89		
SD		0.07			0.06			0.05		
SBP(mm Hg)										0.34
Mean		113			110			109		
SD		23.9			10.2			20.6		
DBP(mm Hg)										0.22
Mean		72			69.3			70.3		
SD		13.5			7.78			9.52		
Sex (%)										0.55
Female	53		35.8	49		33.1	46		31.1	
Male	35		29.9	40		34.2	42		35.9	
Education (%)										0.42
Under diploma	11		52.4	5		23.8	5		23.8	
Diploma	16		32.7	16		32.7	17		34.7	
Educated	61		31.3	68		34.9	66		33.8	
Occupation (%)										0.56
Employee	50		35.5	46		32.6	45		31.9	
Housekeeper	18		40.9	11		25	15		34.1	
Retired	5		23.8	9		42.9	7		33.3	
Unemployed	15		25.4	23		39	21		35.6	
Marriage (%)										0.10
Single	28		24.6	45		39.5	41		36	
Married	57		40.1	40		28.2	45		31.7	
Divorced	1		16.7	3		50	2		33.3	
Dead spouse	2		66.7	1		33.3	0		0	
Life style (%)										0.59
Alone	8		33.3	10		41.7	6		25	
With someone	80		33.2	79		32.8	82		34	
Smoking (%)										0.46
Not smoking	77		33.6	78		34.1	74		32.3	
Quit smoking	6		42.9	2		14.3	6		42.9	
Smoker	5		22.7	9		40.9	8		36.4	
Activity score (%)										0.71
Low	33		32.7	34		33.7	34		33.7	

Moderate	41		37.3	35		31.8	34		30.9	
High	14		25.9	20		37	20		37	
Metabolic diseases ** **(%)**										0.03
Yes	21		50	12		28.6	9		21.4	
No	66		29.7	77		34.7	79		35.6	

AGE, advanced glycation end products; SD, standard deviation; BMI, body mass index; WC, waist circumference; WHR, waist to hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; Y, year; Cm, centimeter; kg/m^2, kilogram/meter^2; mm Hg, millimeters of mercury.

* Calculated by Chi-square and analysis of variance for qualitative and quantitative variables, respectively. p-value is considered significant at <0.05.

**hypertension, dyslipidemia, cardiovascular disease, stroke myocardial infarction, cancer, Respiratory disease, osteoporosis

Table 2. Dietary intakes of participants according to tertiles of dietary AGE intakes

Table 2	Tertile1 (n=88)	Tertile2 (n=89)	Tertile3 (n=88)	P-value*	p-trend**
AGE/Energy (kU/kcal)	<2.96	2.96 – 4.45	4.45<		
Mean	2.37	3.67	6.13		
SD	0.46	0.46	1.54		
Energy (kcal/d)				0.09	0.03
Mean	2179	2334	2407		
SD	663	747	724		
Carbohydrate (% of total energy)				<0.001	<0.001
Mean	63.4	56.4	51.7		
SD	5.75	6.75	6.06		
Fat (% of total energy)				<0.001	<0.001
Mean	23.6	29.4	36.4		
SD	4.96	4.77	6.13		
Protein (% of total energy)				<0.001	0.02
Mean	15.1	16.3	14		
SD	2.95	3.56	2.83		
Total fiber (g/d)				0.40	0.18
Mean	16.4	15.6	15.1		
SD	6.37	6.47	6.29		
Meats group(g/d)				<0.001	0.07
Mean	120	179	145		
SD	63.4	123	86.4		

dAGEs, dietary advanced glycation end products; EI, total energy intake; SD, standard deviation. *P value compared the dietary intakes of participants across tertiles of AGEs using one-way analysis of variance. **p-trend is considered significant at <0.05

Table 3. Association of dietary AGE intake and anthropometric measures and body composition.

Table 3	Tertile1 (n=88)	Tertile2 (n=89)	Tertile3 (n=88)	P-value*	p-trend	P-Ancova**
BMI(kg/ m^2)				0.09	0.04	0.24
Mean	26.1	25.9	24.7			
SD	5.04	4.91	3.96			
WC(cm)				0.10	0.03	0.25
Mean	91.6	89.5	87.5			
SD	13.8	13.1	10.1			
WHR				0.20	0.08	0.31
Mean	0.91	0.90	0.89			
SD	0.07	0.06	0.05			
VFL				0.35	0.18	0.22
Mean	10.1	10	9.27			
SD	4.88	4.70	4			
SMM(kg)				0.23	0.09	0.60
Mean	28.8	27.7	26.9			
SD	7.11	7.76	7.17			
PBF(%)				0.89	0.90	0.38
Mean	30.4	30.9	30.2			
SD	9.74	9.71	8.80			
BFM(kg)				0.22	0.10	0.15
Mean	23.4	22.8	21			
SD	10.6	9.88	7.53			
FFM(kg)				0.14	0.05	0.48
Mean	51.8	50.2	48.1			
SD	11.8	12.8	12.6			
MMI(kg/ m^2)				0.13	0.04	0.67
Mean	9.91	9.74	9.42			
SD	1.57	1.72	1.61			
TF(kg)				0.23	0.10	0.22
Mean	11.8	11.4	10.6			
SD	5.17	4.84	3.84			

AGE, advanced glycation end products; BMI, body mass index; SD, standard deviation; FM, fat mass; WC, waist circumference; WHR, waist to hip ratio; VFL, visceral fat level; SMM, skeletal muscle mass; PBF, percent body fat; BFM, body fat mass; FFM, fat free mass; MMI, muscle mass index; TF, trunk fat.

*Calculated by analysis of variance (ANOVA) in crude model and analysis of covariance (ANCOVA) in adjusted models and is considered significant at <0.05.

**Adjusted for age, sex, physical activity, smoking status, education status, metabolic diseases and energy intake

Table 4. Odds ratios (95% confidence interval) for general and central obesity according to categories of dAGEs

	Tertile1 (n=88)	P value*	Tertile2 (n=89)	P value	Tertile3 (n=88)	P value
General obesity						
BMI ≥ 30 kg/ m^2						
Crude	1 reference	0.12	1.34(0.62-2.89)	0.45	0.52(0.21-1.33)	0.17
Model 1	1 reference	0.22	1.30(0.57-2.94)	0.52	0.57(0.21-1.51)	0.26
Model 2	1 reference	0.12	1.31(0.57-3.03)	0.52	0.47(0.17-1.30)	0.14
Model 3	1 reference	0.12	1.32(0.56-3.09)	0.51	0.47(0.17-1.30)	0.15
Central obesity						
Men WC≥ 102cm Women WC≥ 88cm						
Crude	1 reference	0.27	0.80(0.43-1.49)	0.49	0.59(0.31-1.12)	0.11
Model 1	1 reference	0.21	0.75(0.39-1.43)	0.39	0.55(0.28-1.07)	0.07
Model 2	1 reference	0.15	0.76(0.39-1.47)	0.41	0.50(0.25-1.00)	0.05
Model 3	1 reference	0.14	0.77(0.39-1.51)	0.45	0.50(0.25-1.00)	0.05
Men WHR>0.9 Women WHR>0.85						
Crude	1 reference	0.66	1.25(0.66-2.36)	0.48	0.95(0.51-1.77)	0.87
Model 1	1 reference	0.73	1.26(0.64-2.47)	0.49	1.00(0.51-1.93)	0.99
Model 2	1 reference	0.72	1.22(0.61-2.42)	0.56	0.93(0.47-1.85)	0.85
Model 3	1 reference	0.68	1.25(0.62-2.50)	0.52	0.93(0.46-1.85)	0.83
VFL≥10						
Crude	1 reference	0.25	0.81(0.45-1.47)	0.49	0.60(0.33-1.09)	0.09
Model 1	1 reference	0.16	0.74(0.39-1.42)	0.37	0.53(0.27-1.02)	0.05
Model 2	1 reference	0.11	0.72(0.37-1.40)	0.34	0.48(0.24-0.95)	0.03
Model 3	1 reference	0.10	0.73(0.37-1.42)	0.35	0.47(0.24-0.94)	0.03
BFM(kg)≥21.9						
Crude	1 reference	0.31	0.85(0.47-1.53)	0.59	0.63(0.34-1.14)	0.13
Model 1	1 reference	0.26	0.79(0.42-1.50)	0.48	0.58(0.30-1.11)	0.10
Model 2	1 reference	0.21	0.79(0.41-1.53)	0.50	0.55(0.28-1.07)	0.08
Model 3	1 reference	0.20	0.80(0.41-1.56)	0.52	0.54(0.27-1.07)	0.07

AGE, advanced glycation end products; BMI, body mass index; WC, waist circumference; WHR, waist to hip ratio; VAT, visceral fat level; BFM, fat mass.

* P values are reported based on the logistic regression test and are considered significant at <0.05

Model 1: adjusted for age and sex

Model 2: model 1 + physical activity, smoking status, education status and metabolic diseases

Model 3: model 2 + energy intake

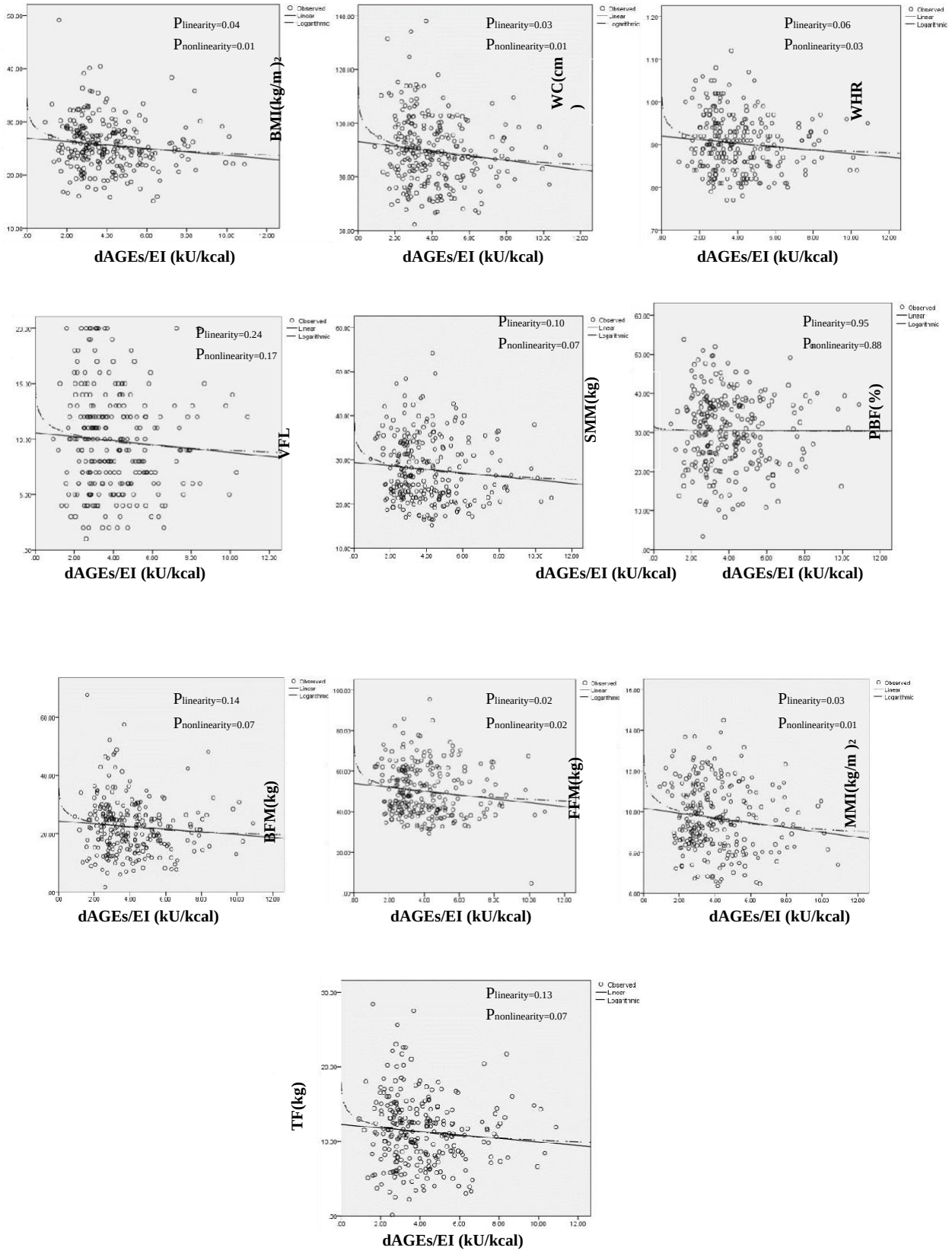

Fig 1. linear and nonlinear relations between AGEs intake and body composition measures dAGEs, dietary advanced glycation end products; EI, total energy intake; BMI, body mass index; WC, waist circumference; WHR, waist to hip ratio; VFL, visceral fat level; SMM, skeletal muscle mass; PBF, percent body fat; BFM, body fat mass; FFM, fat free mass; MMI, muscle mass index; TF, trunk fat.

Supplementary Table 1. Dietary intakes of participants according to tertiles of dietary AGE intakes

	Tertile1 (n=88)	Tertile2 (n=89)	Tertile3 (n=88)	P-value*	p-trend**
AGE/Energy (kU/kcal)	<2.96	2.96 – 4.45	4.45<		
Mean	2.37	3.67	6.13		
SD	0.46	0.46	1.54		
Energy (kcal/d)					
Male				0.06	0.03
Mean	2326	2651	2698		
SD	748	720	744		
Female				0.85	0.65
Mean	2082	2075	2140		
SD	588	670	598		
Carbohydrate (% of total energy)					
Male				<0.001	<0.001
Mean	64.6	56.4	52.3		
SD	6.12	7.58	5.49		
Female				<0.001	<0.001
Mean	62.6	56.5	51		
SD	5.41	6.07	6.54		
Fat (% of total energy)					
Male				<0.001	<0.001
Mean	21.9	28.5	34.2		
SD	4.52	4.71	5.20		
Female				<0.001	<0.001
Mean	24.7	30.2	38.3		
SD	4.96	4.71	6.31		
Protein (% of total energy)					
Male				0.04	0.93
Mean	15.3	17	15.2		
SD	3.01	4.06	3.22		
Female				<0.001	<0.001

Mean	15	15.7	13		
SD	2.93	3.03	1.93		
Total fiber (g/d)					
Male				0.92	0.77
Mean	16.3	16.9	16.8		
SD	5.77	6.81	7.09		
Female				0.06	0.02
Mean	16.4	14.5	13.5		
SD	6.79	6.02	5.06		
Meats group(g/d)					
Male				0.002	0.05
Mean	138	228	185		
SD	66.8	145	95.6		
Female				0.03	0.97
Mean	108	140	109		
SD	58.9	85	57.1		

dAGEs, dietary advanced glycation end products; SD, standard deviation. *P value compared the dietary intakes of participants across tertiles of AGEs using one-way analysis of variance. **p-trend is considered significant at <0.05

Supplementary Table 2. Association of dietary AGE intake and anthropometric measures and body composition.

	Tertile1 (n=88)	Tertile2 (n=89)	Tertile3 (n=88)	P-value*	p-trend	P-Ancova**
BMI(kg/ m^2)						
Male				0.47	0.24	0.28
Mean	26.7	26.4	25.5			
SD	4.78	4.15	2.86			
Female				0.30	0.19	0.46
Mean	25.5	25.5	24.2			
SD	5.28	5.49	4.42			
WC(cm)						
Male				0.35	0.16	0.17
Mean	95.8	92.9	92			
SD	14.2	12.7	8.42			
Female				0.54	0.28	0.67
Mean	87.5	86.7	85			
SD	12.3	12.9	10.2			
WHR						
Male				0.33	0.21	0.20
Mean	0.93	0.91	0.91			
SD	0.07	0.07	0.06			
Female				0.80	0.51	0.85
Mean	0.89	0.89	0.88			
SD	0.06	0.05	0.05			
VFL						
Male				0.23	0.09	0.15
Mean	9.30	8.56	7.62			
SD	4.70	4.30	3.30			
Female				0.41	0.34	0.58
Mean	11	11.3	10.2			
SD	4.96	4.69	4.08			
SMM(kg)						
Male						
Mean	34.5	34.3	34.9	0.90	0.77	0.95
SD	5.25	5.79	4.70			
Female				0.22	0.16	0.37
Mean	23.2	22.1	22.3			
SD	3.21	3.74	3.22			
PBF(%)						
Male				0.36	0.16	0.30
Mean	25.3	24.5	22.7			
SD	8.24	8.37	6.98			
Female				0.45	0.63	0.67
Mean	35.2	36.3	34.5			

SD	8.62	7.12	6.60			
BFM(kg)						
Male				0.22	0.08	0.10
Mean	22.1	20.5	18.4			
SD	10.3	9.69	6.49			
Female				0.39	0.27	0.51
Mean	24.6	24.8	22.5			
SD	10.7	9.70	7.70			
FFM(kg)						
Male				0.94	0.84	0.93
Mean	61.3	61	61.7			
SD	8.89	9.74	7.69			
Female				0.15	0.06	0.25
Mean	42.8	40.9	40.4			
SD	5.47	6.24	7.19			
MMI(kg/ m^2)						
Male				0.99	0.90	0.86
Mean	11	11	11.1			
SD	1.16	1.17	1.07			
Female				0.27	0.10	0.43
Mean	8.80	8.60	8.46			
SD	1	1.21	0.95			
TF(kg)						
Male				0.30	0.12	0.15
Mean	11.6	10.7	9.89			
SD	5.46	4.95	3.68			
Female				0.45	0.32	0.61
Mean	11.9	12	11			
SD	4.94	4.71	3.90			

AGE, advanced glycation end products; BMI, body mass index; SD, standard deviation; FM, fat mass; WC, waist circumference; WHR, waist to hip ratio; VFL, visceral fat level; SMM, skeletal muscle mass; PBF, percent body fat; BFM, body fat mass; FFM, fat free mass; MMI, muscle mass index; TF, trunk fat.

*Calculated by analysis of variance (ANOVA) in crude model and analysis of covariance (ANCOVA) in adjusted models and is considered significant at <0.05.

**Adjusted for age, sex, physical activity, smoking status, education status, metabolic diseases and energy intake