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Research paper

Association of dietary intake of fruit and green vegetables with PTEN and P53 mRNA gene expression in visceral and subcutaneous adipose tissues of obese and non-obese adults

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ABSTRACT

Objective: The present study investigates the association of dietary intake of fruit and green Vegetables with PTEN and P53 mRNA gene expression in visceral (VAT) and subcutaneous adipose tissues (SAT) of obese and non-obese adults.

Methods: VAT and SAT were obtained from 151 individuals, aged ~40 years, who had undergone elective abdominal surgery. The participants were grouped according to their body mass index (BMI), as obese (BMI > 30 kg/m^2) and non-obese (BMI = 18.5–30 kg/m^2). Dietary intakes were obtained using a valid and reliable food-frequency questionnaire (FFQ). Real-time PCR was carried out for *PTEN* and *P53* mRNA expressions. Associations between expression levels and dietary parameters were analyzed.

Results: P53 mRNA expression of obese participants was significantly higher than the non-obese, only in VAT ($p < 0.001$). After adjusting for total energy intake, age and BMI, fruit intake was inversely associated with *P53* gene expression in both VAT ($\beta = -0.38$, $P = 0.01$) and SAT ($\beta = -0.35$, $P = 0.03$) among non-obese participants. Furthermore, fruit consumption was inversely associated with *P53* gene expression in obese individuals, only in VAT ($\beta = -0.21$, $P = 0.05$). More so, intake of green vegetables in obese subjects was negatively associated with *P53* gene expression in VAT ($\beta = -0.27$, $P = 0.01$) and SAT ($\beta = -0.28$, $P < 0.001$). On the other hand, after adjustment for total energy intake, age and BMI, a positive association was observed between fruit intake and *PTEN* in VAT ($\beta = 0.27$, $P = 0.01$) and SAT ($\beta = 0.34$, $P < 0.001$) among obese participants. In addition, dietary consumption of fruits in non-obese individuals was negatively associated with*PTEN* expression in SAT ($\beta = -0.48$, $P < 0.001$).

Conclusion: Dietary intake of fruit and green vegetables was associated with *P53* gene expression in VAT and SAT of obese participants, suggesting their protective role in regulating *P53* mRNA expression in adipose tissue. Furthermore, higher fruit intake was inversely associated with *PTEN* mRNA levels in non-obese participants, implying the anti-adipogenic role of *PTEN* gene expression.

Abbreviations: VAT, Visceral adipose tissue; SAT, Subcutaneous adipose tissues; qPCR, Real-time PCR; BMI, Body mass index; FFQ, Food-frequency questionnaire; WAT, White adipose tissue; ROSs, Reactive oxygen species; FFAs, Free fatty acids; FBS, Fasting blood sugar; CVs, Coefficients of variation; TG, Triglyceride levels; TC, Total cholesterol; MET, Metabolic equivalents; IPAQ, International Physical Activity Questionnaire; FCT, Food composition table; USDA, United States Department of Agriculture; NCBI, National Center for Biotechnology Information; NTC, Non-template control; Ct, Threshold cycle; SPSS, Social Sciences program

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1. Introduction

Obesity is a complex multifactorial disorder with an important genetic component and etiologic heterogeneity, including behavioral and environmental factors (Walley et al., 2006). Obesity occurs mainly due to an imbalance between calorie intake and daily requirement of nutrients, resulting in excessive fat accumulation in white adipose tissue (WAT) and, in turn, chronic low-grade inflammation or systemic oxidative stress (Gonzalez-Muniesa et al., 2017). Although, along with the role of environmental factors such as diet, susceptible genes should not be neglected.

Recent molecular biology studies have revealed more about the genes effective in obesity, including the *P53* gene (Molchadsky et al., 2013). *P53* may also play a role in epigenetic processes through negative regulation of the adipogenic program, which can result in a protective effect on diet-induced obesity (Zhu, 2016). *P53*, as a stress response protein, is chronically increased in response to environmental stresses such as excess calorie intake, reactive oxygen species (ROSs), or free fatty acids (FFAs); and can consequently lead to WAT senescence and inflammation, especially in visceral adipose tissue (VAT) (Shimizu et al., 2012; Krstic et al., 2018). So, *P53* has an ability to regulate energetic homeostasis; however, it is at the expense of increasing inflammation. On the other hand, *PTEN* protein is a target gene for *P53* which is known as a cell proliferation and cell death regulator (Yamada and Araki, 2001; Bargonetti and Manfredi, 2002). *PTEN* has a physical association with *P53*, and plays a fundamental role in regulating the transcription of *P53* and its protein levels (Mayo and Donner, 2002). Therefore, *PTEN* is an important factor in controlling *P53* function (Freeman et al., 2003); while, *P53* can also promote the expression of *PTEN* in some cell types (Bouali et al., 2009), and its inhibition can cause a reduction in *PTEN* levels (Homayounfar et al., 2015). Thus, *PTEN-P53* may play a cooperative role in the regulation of normal cellular functions (Freeman et al., 2003). These findings rise questions regarding the role of anti-oxidant diets on *P53* or *PTEN* mRNA levels, and whether obesity, as a low-grade inflammation situation, effects these levels.

Based on previous studies, dietary intake of foods rich in a variety of antioxidants, such as fruits, vegetables, nuts and whole grain, has a protective role against oxidative stress related diseases or chronic inflammation states (Åsgård et al., 2007; Yu et al., 2016). Fruit and vegetables as a source of essential nutrients such as plant proteins, potassium, magnesium, vitamin C, folate and other bioactive components possess notable antioxidant (Alonso et al., 2004; Rodríguez et al., 2005) and anti-inflammatory capacities (Porrini et al., 2002; Esmaillzadeh et al., 2006), which can have a modulatory role in low-grade inflammation or processes mediated by oxidative stress (Hermsdorff et al., 2010). Furthermore, regular consumption of whole grains is inversely associated with diseases of an inflammatory origin, through providing phytochemicals and several unique bioactive compounds that may have a synergetic effect in combination with fruit and vegetables (Fardet, 2010; Jideani et al., 2014). More so, nuts are considered as a source of healthful antioxidants, magnesium, fiber, α-linolenic acid and l-arginine which have an anti-inflammatory effects (Blomhoff et al., 2006; Yu et al., 2016). So, obesity as a low-grade inflammatory state may benefit from increased consumption of these aforementioned foods in the diet. Although, the role of fruit, vegetables, nuts or whole grains in the diet for better management of body weight needs further assessment (Alinia et al., 2009). Few studies also consider how dietary intake can be associated with inflammation-related expression of genes and a predisposition to obesity. Hermsdorff et al. recently demonstrated that intake of fruit and vegetables was inversely associated with some pro-inflammatory mRNA expression markers in the peripheral blood mononuclear cells (PBMC) of healthy young adults (Hermsdorff et al., 2010).

To the best of our knowledge, the association between foods with anti-oxidant capacity and *P53* or *PTEN* gene expression has not been investigated before. Therefore, we used SAT and VAT tissues of obese and non-obese individuals (as they have different metabolic properties (Ibrahim, 2010)) to evaluate whether a diet with anti-oxidant capacity or obesity indices have an association with *P53* or *PTEN* mRNA levels.

2. Materials and methods

2.1. Participants

In the current cross-sectional study, we selected 151 participants aged ≥20 years. Subjects were classified according to their body mass index (BMI) as 97 obese subjects (obese and morbid obese) with BMI ≥ 30 kg/m^2 and 54 non-obese samples (normal and overweight) with BMI < 30 kg/m^2 (Rostami et al., 2017; Yuzbashian et al., 2019a), who underwent elective abdominal surgery, which was scheduled in advance and it did not involve a medical emergency such as: hernia repair apendicita, with minimal impact on dietary intakes at the Mostafa Khomeini and Khatam Al-Anbia hospitals, Tehran, Iran (Yuzbashian et al., 2019b). The eligibility criteria were subjects who were not pregnant or lactating, did not have diagnosed diabetes mellitus or cancer, were hospitalized less than 3 days, were not on any special diet, and not using any lipid-lowering or anti-obesity medications.

Ethics approval was collected from the ethics committee of the Research Institute for Endocrine Sciences (RIES) of the Shahid Beheshti University of Medical Sciences (IR.SBMU.ENDOCRINE.REC.1395.283), and the study was conducted according to the Declaration of Helsinki and RIES institutional guidelines. A written informed consent was obtained from all participants.

2.2. Anthropometric measurements

Weight was measured in light clothing with 0.1 kg precision on a SECA digital weighing scale (Seca 707; Seca Corporation, Hanover, Maryland; range 0.1–200 kg); and height was measured barefoot to the nearest 0.1 cm. BMI was calculated as weight (kg) divided by square of height (m^2).

2.3. Laboratory assays

Before surgery, blood samples were collected from all participants after 10–12 h of overnight fasting. Fasting blood sugar (FBS) was measured using an enzymatic colorimetric method with glucose oxidase. Inter- and intra-assay coefficients of variation (CVs) were both 1.0% for FBS. Triglyceride (TG) levels were determined using the enzymatic colorimetric method with glycerol phosphate oxidase. Inter- and intra-assay CVs for TG were 0.4 and 2.1%, respectively. Measurements of FBS and TG were performed using commercial kits (Pars Azmoon Inc., Tehran, Iran). Total cholesterol (TC) was assayed by the cholesterol esterase and cholesterol oxidizes method; inter- and intra-assay CVs were 0.5 and 1.7, respectively. Insulin was measured using the enzyme-linked immunosorbent assay (ELISA) with Mercodia kits (Uppsala, Sweden). Inter- and intra-assay CVs of insulin were 1.7 and 2.3%, respectively.

2.4. Physical activity measurements

Physical activity was assessed during interviews, using the long forms of the reliable and validated Persian version of the International Physical Activity Questionnaire (IPAQ) (Vasheghani-Farahani et al., 2011). In order to measure energy expenditure, the concept of metabolic equivalents (MET) was used. Physical activity levels were classified as low (MET < 600 min per week), moderate (MET = 600–3000 min per week), and vigorous activity (MET ≥ 3000 min per week).

2.5. Dietary measurements

Regular dietary intake of each participant was determined by an expert interviewer using a valid and reliable semi-quantitative food frequency questionnaire (FFQ) (Mirmiran et al., 2010; Asghari et al., 2012). Because the Iranian food composition table (FCT) is incomplete, we used the United States Department of Agriculture (USDA) FCT to analyze food and beverages. However, the Iranian FCT was used for some traditional food and beverages, not listed in the USDA FCT.

2.6. RNA samples and quantitative real-time polymerase chain reaction (qRT-PCR)

Total RNA was extracted from fresh snap-frozen VAT and SAT tissues (obtained during surgery) using TRIzol reagent (Invitrogen U.S. Cat. No. 15596-026) according to the manufacturer's protocol. RNA quantity and purity was assessed by NanoDrop spectrophotometer (Thermo Fisher Scientific, Waltham, USA) and the absorption ratio (260/280 nm) of all preparations was in an acceptable range. Total RNA was treated with DNase I in order to remove traces of genomic DNA before complementary DNA (cDNA) synthesis. The cDNA synthesis kit (Thermo Scientific, USA) was used according to the manufacturer's recommendations. The product was stored at −20 °C for further investigations. Primers based on the sequences of the National Center for Biotechnology Information (NCBI) GenBank database were checked by the Genrunner Software (version 3.05). Primer sequences were provided in Table 1.

The qRT-PCR was performed using the Rotor-Gene 6000 (Corbett Research, Sydney, Australia), in 20 μL volumes containing 10 μL 2X SYBR Green Master mix (BioFact, South Korea), 1 μL forward primer, 1 μL reverse primer, 7 μL RNase-free water, and 1 μL of the cDNA. The thermal program included initial denaturation (10 min at 95 °C) followed by 40 cycles of 15 s at 95 °C, 45 sec at 60 °C, and 40 s at 72 °C. Real-time quantification was monitored by measuring the fluorescence activity. For each gene, samples were run in duplicate for inter assay control along with *GAPDH* as reference gene and the non-template control (NTC). The relative expression of *P53* and *PTEN* in each sample was calculated based on its threshold cycle (Ct), normalized to the Ct of the reference gene. All qPCR laboratory procedures were performed according to the MIQE guidelines (Bustin et al., 2009).

2.7. Statistical analysis

Normality of the distribution of variables was assessed by histogram and the Kolmogorov–Smirnov test. Continuous variables were described as mean ± standard deviation. Because plasma TGs and insulin were skewed, we reported them as median and inter-quartile range. The *t*-test and chi-square test were used to compare demographic data, anthropometrics, dietary intake, and serum biochemical parameters between obese and non-obese participants. Spearman correlation was done between SAT and VAT in the studied population. Linear regression was performed to determine the association of fruit, vegetables, nuts and whole grains with *P53* and *PTEN* mRNA expression in SAT and VAT; and standardized β was reported after adjusting for total energy intake, age, and BMI. All data were analyzed using the Statistical Package for Social Sciences program (SPSS) (version 15.0; SPSS Inc, Chicago IL) and *P*-values < 0.05 were considered statistically significant.

Table 1
Sequences and information of primers.

Genes	NCBI Ref.		Primers' sequences 5′–3′	Tm	Product length (bp)
PTEN	NM_000314.7	F	AAGCTGGAAAGGGACGAACT	59	145
		R	CGCCTCTGACTGGGAATAGT		
P53	NM_001126118.1	F	CCAGCCAAAGAAGAAACCAC	58	92
		R	CCTCATTCAGCTCTCGGAAC		
GAPDH	NM_002046.7	F	CTGCTCCTCCTGTTCGACAGT	60	100
		R	CCGTTGACTCCGACCTTCAC		

F: forward, R: reverse

Table 2
General characteristics of study participants based on being non-obese and obese.

	Non-obese (n = 54)	Obese (n = 97)	P value
Age (years)	47.7(14.8)	36.9(10.8)	< 0.001
Body mass index (kg/m^2)	24.6(2.9)	43.5(6.0)	< 0.001
Cholesterol (mg/dl)	171.2 (46.7)	193.7(39.9)	0.018
Triglycerides (mg/dl)	67.0(60.5–77.5)	71.0(62.7–94.0)	0.120
Fasting blood sugar (mg/dl)	87.9(11.5)	86.6(11.5)	0.624
Insulin (μU/mL)	4.3(2.7–8.3)	8.1(5.2–12.5)	0.003
Insulin resistant (%)	11.1	20.0	0.212

Data are represented as mean (SD) or median (IQ 25–75).

3. Results

All 151 participants were categorized into non-obese (n = 54) and obese (n = 97) groups. General characteristics of subjects including age, sex, BMI, and levels of TC, TG, FBS and insulin are shown in Table 2. The mean age of the obese and non-obese participants were 47.7 ± 14.8 and 36.9 ± 10.8 (P < 0.001), respectively. Dietary intakes of subjects including total energy intake, carbohydrate, protein, fat, fruits, yellow and red vegetables, green vegetables, starchy vegetables, other vegetables, whole grains and nuts are presented in Table 3.

The expression of *P53* mRNA in obese participants was significantly higher than the non-obese, only in VAT (*P* = 0.008) (Fig. 1A). There was no significant difference between obese and non-obese individuals in *PTEN* gene expression in SAT and VAT (Fig. 1B).

The Spearman correlation showed that *P53* expression was positively correlated with SAT and VAT of non-obese and obese subjects, respectively (r = 0.631, P < 0.001 and r = 0.695, P < 0.001). Besides, *PTEN* expression was also positively correlated with SAT and VAT of obese subjects (r = 0.584, P < 0.001) (data not shown).

Linear association of dietary intake of fruits, vegetables, nuts, and whole grains with *P53* expression in VAT and SAT are presented in Table 4. Among non-obese individuals, after adjustment for total energy intake, age and BMI, dietary intake of fruit was significantly and inversely associated with *P53* gene expression in both VAT (β = −0.381, P = 0.012) and SAT (β = −0.352, P = 0.0293). Furthermore, dietary consumption of fruit in obese participants was significantly and inversely associated with *P53* expression, only in VAT (β = −0.219, P = 0.050). In addition, dietary intake of green vegetables in obese

Table 3
Dietary intakes of study subjects according to non-obese and obese participants.

	Non-obese (n = 54)	Obese (n = 97)	P value
Total energy intake (kcal)	2429 (659)	3188 (1018)	< 0.001
Carbohydrate (% energy)	57.9 (6.8)	55.6 (6.57)	0.046
Protein (% energy)	14.0 (2.1)	14.2 (2.6)	0.610
Fat (% energy)	30.4 (5.8)	32.5 (5.5)	0.031
Fruits (serv/d)	2.2 (2.0)	3.2 (4.3)	0.115
Yellow and red vegetables (serv/d)	0.66 (0.44)	0.89 (0.70)	0.031
Green vegetables (serv/d)	0.39 (0.48)	0.48 (0.40)	0.205
Starchy vegetables (serv/d)	0.19 (0.13)	0.21 (0.30)	0.557
Other vegetables (serv/d)	1.2 (1.0)	1.8 (1.3)	0.228
Nuts (serv/d)	0.42 (0.68)	0.80 (1.58)	0.980
Whole grains (serv/d)	4.11 (3.90)	5.42 (3.89)	0.050

Data are represented as mean (SD).

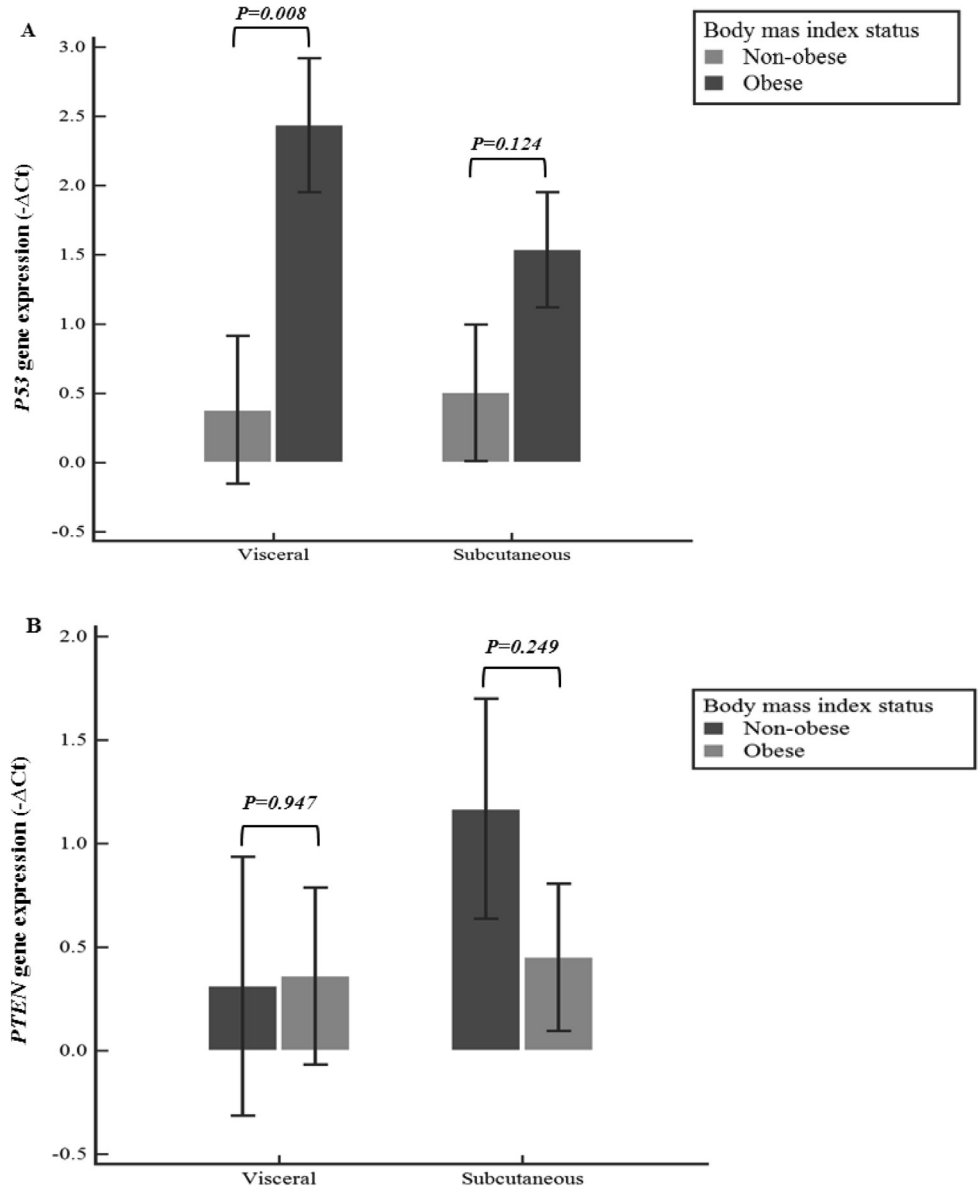

Fig. 1. The expression of (A) *P53* and (B) *PTEN* in visceral and subcutaneous adipose tissues in non-obese and morbidly obese participants; Results are expressed as mean ± SEM.

subjects was significantly and negatively associated with *P53* expression in VAT (β = −0.279, P = 0.013) and SAT (β = −0.286, P = 0.001).

After adjustment for total energy intake, age and BMI, a significant positive association was observed between fruit intake and *PTEN* expression in VAT (β = 0.277, P = 0.016) and SAT (β = 0.347, P = 0.002) among participants with obesity. Besides, dietary consumption of fruits in non-obese individuals was negatively associated with *PTEN* expression in SAT (β = −0.487, P = 0.002) (Table 5).

4. Discussion

In the current study, we analyzed *P53* and *PTEN* mRNA expression levels in VAT and SAT of Iranian obese and non-obese participants. This study deals with transcriptional control of different adipose tissues by dietary intake in obese and non-obese individuals. We found that the obese participants had higher expression of *P53* in VAT compared to the non-obese. Moreover, *P53* expression in VAT was higher in the obese individuals compared to the non-obese. The same tendency was observed in SAT, where *P53* levels were higher in obese participants compared to the non-obese; however, it was not significant. These results somehow agree with the cohort of 230 human subjects that showed a positive correlation between *P53* expression and BMI in VAT (and not in the SAT) (Ortega et al., 2014). Furthermore, *P53* level was significantly higher in VAT compared to SAT in obese individuals. While, there is also a significant positive correlation between *P53* expression with SAT and VAT in both groups, somehow, implying the similar *P53* expression pattern between SAT and VAT in obese or non-obese individual. Human VAT and SAT display discrepancies in metabolic and biochemical properties as well as different gene expression profiles (Barth et al., 2010). SAT is the principle site for TG removal from the circulation, so its fat expansion could have a protective effect on obesity-related complications by preventing the accumulation of ectopic fat in internal organs or VAT (Ravussin and Smith, 2002; Tan and Vidal-Puig, 2008). On the other hand, studies demonstrated that despite the protective nature of SAT, it has been reported to play a role in obesity-related disorders too, such as insulin resistance (Goodpaster et al., 1997; Ferreira et al., 2005). It has been documented that VAT is

Table 4
Standardized coefficients of fruits, nuts, and vegetable intakes with *P53* gene expression in non-obese and obese participants.

	Non-obese (n = 54)		Obese (n = 97)	
	Standardized β	*P* value	Standardized β	*P* value
Fruits				
Visceral	−0.381	0.012	−0.219	0.050
Subcutaneous	−0.352	0.029	−0.034	0.754
Yellow and red vegetable				
Visceral	−0.133	0.355	0.057	0.610
Subcutaneous	−0.057	0.708	−0.093	0.390
Green vegetable				
Visceral	0.035	0.806	−0.279	0.013
Subcutaneous	0.166	0.272	−0.286	0.008
Starchy vegetable				
Visceral	0.149	0.272	0.006	0.959
Subcutaneous	−0.012	0.934	−0.015	0.889
Other vegetable				
Visceral	−0.146	0.370	0.085	0.643
Subcutaneous	−0.145	0.400	0.004	0.975
Nuts				
Visceral	0.031	0.828	−0.077	0.468
Subcutaneous	0.166	0.271	−0.001	0.990
Whole Grains				
Visceral	0.073	0.598	−0.172	0.127
Subcutaneous	−0.057	0.695	−0.103	0.346

β coefficients adjusted for total energy intake, age, and BMI.

Table 5
Standardized coefficients of fruits, nuts, and vegetable intakes with *PTEN* gene expression in non-obese and obese participants.

	Non-obese (n = 54)		Obese (n = 97)	
	Standardized β	*P* value	Standardized β	*P* value
Fruits				
Visceral	−0.241	0.160	0.277	0.016
Subcutaneous	−0.487	0.002	0.347	0.002
Yellow and red vegetable				
Visceral	−0.094	0.550	−0.156	0.165
Subcutaneous	−0.262	0.083	−0.014	0.901
Green vegetable				
Visceral	0.175	0.260	−0.082	0.479
Subcutaneous	0.015	0.924	0.052	0.656
Starchy vegetable				
Visceral	−0.021	0.891	0.076	0.489
Subcutaneous	0.097	0.506	0.161	0.142
Other vegetable				
Visceral	−0.180	0.305	−0.026	0.821
Subcutaneous	−0.269	0.114	0.003	0.977
Nuts				
Visceral	0.127	0.416	−0.032	0.767
Subcutaneous	0.120	0.432	−0.107	0.325
Whole Grains				
Visceral	0.023	0.880	0.049	0.432
Subcutaneous	0.248	0.088	0.158	0.166

β coefficients adjusted for total energy intake, age, and BMI.

associated with a higher risk of metabolic disease (Klein et al., 2007; Demerath et al., 2008). Therefore, it seems that VAT and SAT probably have differences in the regulation of adipose tissue performance. In obese individuals, VAT dysfunction has a crucial role in systemic inflammation and the following metabolic disturbances such as insulin resistance (Wellen and Hotamisligil, 2003).

On the other hand, inflammation triggering factors like weight gain, calorie overload, or high-fat diet can lead to induction of *P53* expression (Shimizu et al., 2012; Krstic et al., 2018). *P53* induction can cause senescence in VAT and onset of inflammation (probably via the NF-kB signaling pathway) which in turn leads to stress response in adipose tissue through the negative feedback loop of *P53* (Krstic et al., 2018). Thus, it seems that *P53* itself has a regulatory role in metabolic homeostasis and adipose tissue metabolism, especially when diet is considered as an important environmental stressor (Krstic et al., 2018). More so, it is reasonable that diet may also have a protective role on *P53* mRNA levels, especially diets with anti-inflammatory properties. In this study, higher intake of calorie was positively associated with *P53* expression in VAT and SAT, only in obese participants, which is in line with previous documents (Goldstein and Hager, 2015; Vergoni et al., 2016). Furthermore, fruits and green vegetables also showed a protective role in increasing *P53* mRNA levels in VAT of obese participants, even after calorie intake adjustment. Moreover, in non-obese individuals, lower intake of fruit had a stressor effect on the rise of *P53* levels in VAT and SAT. It is worth noting that measuring the chronic elevation of *P53* levels is impossible, so our results can only determine the cross-sectional association (Krstic et al., 2018).

The beneficial effect of a diet rich in fruits and vegetables on metabolic health in overweight or obese individuals has been widely reported (Williams et al., 2017; Kopf et al., 2018). Williams et al observed that consumption of fruit and vegetables could have positive effects on inflammation markers in overweight or obese participants. Still, the exact anti-inflammatory mechanism of fruit and vegetable intake remains unknown, but can be attributed to the antioxidant capacity of the components of fruit and vegetables such as potassium, magnesium, fiber, folate, vitamin C and so on (Rodríguez et al., 2005; Esmaillzadeh et al., 2006). Therefore, antioxidant properties of fruit and vegetables constituents (specially flavonoids and carotenoids) can play an effective role in reducing oxidative stress and low-grade inflammation (Porrini et al., 2002; Holt et al., 2009). In the current study, consumption of fruit and vegetables was inversely associated with *P53* expression in VAT of obese individuals, suggesting a beneficial role of high fruit and vegetables consumption on management of *P53* metabolic stressors such as ROS, and then improving the chronic inflammatory status such as obesity (Krstic et al., 2018). Moreover, considering the interesting results in non-obese participants of the current study, the protective role of fruit in rising *P53* expression has been emphasized. The abovementioned arguments motivated the hypothesis that dietary intakes, especially fruit and vegetables, may have a profound effect on *P53* expression. *P53,* as a crucial factor in adipose tissue metabolism and energy homeostasis, may have an impact on the development of obesity.

PTEN expression in SAT was significantly higher in non-obese individuals compared to the obese participants. However, *PTEN* in VAT was higher in obese individuals compared to the non-obese but it was not significant. Furthermore, *PTEN* expression was significantly correlated with SAT and VAT only in obese participants, suggesting a lack of alignment between SAT and VAT in terms of *PTEN* expression pattern in non-obese individuals. A decade of work has documented that *PTEN* could have a regulatory role in energy expenditure and adipose tissue function, especially brown adipose tissue (Chalhoub and Baker, 2009; Li et al., 2017). Recently, it was also reported that higher *PTEN* expression might reduce the accumulation of adipose tissue through enhancement of calorie expenditure (Molfino et al., 2018). So, previous studies seem to consider *PTEN* as a positive regulator of energy expenditure (Garcia-Cao et al., 2012; Ortega-Molina et al., 2012). Molfino et al. showed that lower *PTEN* expression of patients receiving artificial nutrition was associated with calorie intake reduction (Molfino et al., 2018). We did not find any significant association between energy or macronutrient intake and *PTEN*. However, higher fruit consumption was positively associated with *PTEN* levels in SAT and VAT of obese individuals. More so, higher fruit consumption had a protective role in rising *PTEN* expression of SAT in non-obese individuals. Hypothetically, higher fruits intake in our study may have a protective effect on *P53*

induction in obese individuals. On the other hand, high level of *PTEN* in obese participants may related to its anti-adipogenic effect, which is not required in non-obese participants (Palian et al., 2014).

Despite the promising results, which highlight the role of energy, fruit and vegetable intakes on *P53* or *PTEN* mRNA levels in obese individuals, there are also some limitations, which need to be underlined. One limitation is related to the cross-sectional nature of the study design, hence causal inferences cannot be concluded; as it is less likely that dietary intake has an influence on *PTEN* and *P53* expression, we consider our inference that fruit and vegetables may have primary effects on *PTEN* and *P53* mRNA levels plausible. Secondly, only *P53* and *PTEN* expression was evaluated, further studies are recommended to assess the protein translation, as well. Thirdly, as there is no complete Iranian FCT available, we had to use the USDA FCT. Fourth, since all the subjects were Tehranian, the present findings may not directly apply to other races. Finally, difference in biochemical variables could justify with significant difference in the age of obese and non-obese participants. In spite of these limitations, to our knowledge, this was the first study to provide data on habitual dietary intake and its association with *P53* and *PTEN* levels. Besides, in the current study *P53* and *PTEN* mRNA level was directly measured in both VAT and SAT. Furthermore, all covariates were gathered during an interview instead of self-report, which increases the credibility of data.

5. Conclusion

The current study provides the first evidence that increased *P53* expression in VAT and SAT is inversely associated with intake of fruit and green vegetables in obese individuals, suggesting a protective role for this aforementioned diet in induction of *P53* levels. Furthermore, *PTEN* mRNA level was positively associated with fruit intake in VAT and SAT of obese individuals, higher fruit intake was inversely associated with *PTEN* expression in non-obese participants, implying the anti-adipogenic role of *PTEN* expression in obese participants. Thus, knowledge on the role of dietary intakes in VAT or SAT gene expression pattern may be important to implement therapeutic research in a specific manner.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors' contribution

Study concept and design: Saidpour; acquisition of data: Khalaj & Hajizadeh; analysis and interpretation of data: Zarkesh & Saidpour; drafting of the manuscript: Kadkhodaei & Saidpour & Zarkesh; critical revision of the manuscript for important intellectual content: Hedayati; statistical analysis: Saidpour & Zarkesh; study supervision: Saidpour

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