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Metabolic Age: A New Predictor for Metabolic Syndrome

Metabolik Yaş: Metabolik Sendrom İçin Yeni Bir Öngördürücü

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Abstract

Objective: This study aimed to investigate the prevalence of metabolic syndrome (MetS) among the employees of the Tehran University of Medical Sciences, along with presenting a predictor for its identification. Material and Methods: 1583 employees from the Tehran University of Medical Sciences (TUMS) participated in our cross-sectional study, who were originally a part of the enrollment phase in the TUMS Employees' Cohort study (TEC). Their basic information, physical activity questionnaire, biochemical blood test, and body composition were obtained through the Bioelectrical Impedance Analysis (BIA), blood pressure, anthropometric measurements, and history of diseases and medication. The prevalence of MetS was determined according to the criteria of the International Diabetes Federation (IDF) and the National Cholesterol Education Program (NCEP) Adult Treatment Panel-III (ATP-III). Result: According to the criteria of the IDF, the prevalence of MetS among total participants was 22.2%, where 21.9% were men and 22.4% were women. According to the criteria of ATP-III, the prevalence of MetS was found to be 15%. The prevalence of obesity (BMI \geq 30) and hyperglycemia (FBS \geq 100 mg/dL) among the study participants was 23.4% and 9.7%, respectively. The prevalence of hypertension (SBP $\geq\!130,$ DBP $\geq\!85$ mmHg) and high triglyceride level (TG \geq 150 mg/dL) was found to be 14.6% and 19.6%, respectively, while the prevalence of reduced high-density lipoprotein in men and women was found to be 40.3% and 74.7%, respectively.Logistic regression analysis revealed that the predictors of metabolic syndrome were age, sex, physique rate (the evaluated levels of muscle and body fat), and metabolic age (where the BMR of a person was compared to the mean of the BMR of the same age group). Conclusion: This study introduces metabolic age as a new predictor of MetS. However, more studies are needed to confirm this association.

Keywords: Metabolic syndrome; body composition; body mass index; physical activity

Özet

Amac: Bu calışmada, Tahran Tıp Bilimleri Üniversitesi calışanları arasında metabolik sendrom (MetS) prevalansını araştırmak ve tanımlanması için bir öngördürücü sunmak amaçlanmıştır. Gerec ve Yöntemler: Bu kesitsel calışmaya, Tahran Tıp Bilimleri Üniversitesi [Tehran University of Medical Sciences (TUMS)]'nden 1583 çalışan katıldı, bu kişiler aslında TUMS Çalışanları Kohort çalışması [TUMS Employees' Cohort study (TEC)]nın kayıt asamasına dâhildi. Temel bilgileri, fiziksel aktivite anketi, biyokimyasal kan testi ve vücut kompozisyonu Biyoelektrik Empedans Analizi [Bioelectrical Impedance Analysis (BIA)], kan basıncı, antropometrik ölçümler ve hastalık ve ilaç öyküsü aracılığıyla elde edildi. MetS prevalansı, Uluslararası Divabet Federasyonu [International Diabetes Federation (IDF)] ve Ulusal Kolesterol Eğitim Programı Yetişkin Tedavi Paneli-III [National Cholesterol Education Program Adult Treatment Panel-III (NCEP ATP-III)] kriterlerine göre belirlendi. Bulgular: IDF kriterlerine göre toplam katılımcılar arasında MetS prevalansı %22,2 idi ve %21,9'u erkek, %22,4'ü kadındı. ATP-III kriterlerine göre MetS prevalansı %15 olarak bulundu. Çalışma katılımcıları arasında obezite (BKİ ≥30) ve hiperglisemi (AKS ≥100 mg/dL) prevalansı sırasıyla %23,4 ve %9,7 idi. Hipertansiyon (SKB ≥130 mmHg, DKB ≥85 mmHg) ve yüksek trigliserid düzeyi (TG ≥150 mg/dL) prevalansı sırasıyla %14,6 ve %19,6 olarak bulunurken, erkeklerde ve kadınlarda düşük yoğunluklu lipoprotein prevalansı sırasıyla %40,3 ve %74,7 bulundu. Lojistik regresyon analizi, Mets'in öngördürücülerinin yaş, cinsiyet, vücut oranı (değerlendirilen kas ve vücut yağı seviyeleri) ve metabolik yaş [kişinin bazal metabolizma hızının (BMR) aynı yaş grubundakilerin BMR ortalamasıyla karşılaştırılması] olduğunu ortaya koydu. Sonuc: Bu çalışma, metabolik yaşın MetS için yeni bir öngördürücü olduğunu ortaya koymaktadır. Ancak, bu ilişkiyi doğrulamak için daha fazla çalışmaya ihtiyaç vardır.

Anahtar kelimeler: Metabolik sendrom; vücut kompozisyonu; beden kitle indeksi; fiziksel aktivite

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Peer review under responsibility of Turkish Journal of Endocrinology and Metabolism.

Received: 26 Sep 2020 Received in revised form: 18 Nov 020 Accepted: 27 Nov 2020 Available online: 19 Jan 2021

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Introduction

Metabolic syndrome is a complex and multirisk factor in atherosclerotic cardiovascular disease (ASCVD) and type 2 diabetes (1). Metabolic syndrome consists of five risk factors, including atherogenic dyslipidemia, increased blood pressure, dysglycemia, a pro-thrombotic and pro-inflammatory state (2). Metabolic syndrome also multiplies the potential danger of ASCVD and type 2 diabetes by five times (3). About a quarter of the world's population i.e., more than one billion people, are estimated to have metabolic syndrome (4). According to various epidemiological studies, the incidence rate of metabolic syndrome is reported between 20% and 45% (5). Also, many other studies around the world have been reporting the incidence of metabolic syndrome. In 2017, a research work conducted in Iran revealed that the incidence of metabolic syndrome according to the IDF and ATP III criteria was 30% and 25%, respectively (4). In another meta-analysis study in Iran, the incidence of metabolic syndrome in 2017 was found to be 31% (6). A study among Brazilian healthcare providers in 2019 revealed a metabolic syndrome incidence of 24.4% (7), while in the same year, another study found that the incidence rate of metabolic syndrome among the Japanese white-collar workers was 23.1% (8).

Predisposing factors of metabolic syndrome can be categorized into two groups. The first group is based on the metabolic syndrome criteria presented by the IDF, ATP III, and WHO and consists of hypertension, high blood sugar, low HDL, high TG and waist circumference, along with obesity. The second group is reported in various studies and consists of the predictors of metabolic syndrome such as inactivity, age, sex, BMI, smoking, alcohol, TG/HDL ratio, WHR, body shape, and serum uric acid (7,9-17).

New predictors for metabolic syndrome are an important concern for the researchers in this field. And, body composition analysis has been introduced as a new predictor for metabolic syndrome. However, our knowledge in this field needs to improve further. The purpose of this study was to investigate the incidence of metabolic syndrome among the staff of the Tehran University of Medical Sciences and also to find if some components of the body composition analysis such as metabolic age and physique rating could act as the predictors of metabolic syndrome.

Material and Methods

Procedure

The data for this cross-sectional study was taken from the TEC study (Tehran university of medical sciences Employees' Cohort study) during its enrollment phase, which was collected between January 2017 and September 2018. The TEC study further intended to enroll 5500 people from their staff between January 2017 and March 2021 (18). It is designed as a longitudinal study to track the long-term health of their employees. Participants were recruited from different departments. They voluntarily enrolled for the research project upon completing the informed consent form. All the examinations were performed, and the information was collected from the participants in a single day. This study was carried out according to the Helsinki Declaration Principles.

Participants

A total of 1583 participants (1012 women and 571 men), all being TUMS employees from different divisions (clinical, research, service, technical, etc.), were enrolled in this study.

Data collection

The participants were asked about their sex, age, marital status, ethnicity, age of marriage, education level, occupational group, shift work, and tobacco usage. Also, to file a record of diseases in the participants, their current illnesses were examined through general medical examinations. The records included hypertension, type 2 diabetes, hyperlipidemia, thyroid diseases, and medications.

Blood pressure measurement

The blood pressure of the participants was measured thrice, and the average was reported with a precision of one mmHg. The participant was made to sit for a 15 min break, and then the measurements were taken. An interval of 30 minutes was provided between the first and second round of measurements, while a 2-hour interval was given between the second and third rounds. Blood pressure was measured using a standard and calibrated clinical mercury manometer.

Anthropometry

The weight and height of the participants were measured with a precision of 0.1 kg and 0.1 cm, respectively. They were wearing light clothes with no shoes while the measurements were being taken. The waist circumference was calculated with a precision of 0.1 cm at the anatomical landmarks such as the middle of the lower rib margin and the iliac crest, and the widest portion of the hip. The BMI was measured as the weight (kg) of the participant divided by the square of their height (m).

Blood samples

After 12-hours of fasting, blood samples were taken between 7 and 9 am. The measured parameters in the blood samples included Fasting Blood Sugar (FBS), Triglyceride (TG), total cholesterol (CHO), and high-density and low-density lipoprotein cholesterol (HDL, LDL).

Body composition

One of the most common methods to study and analyze the body shape is the body composition analysis method, which can be performed using different technologies such as using of a Caliper, anthropometry, tracer dilution, densitometry, air displacement plethysmography, dual-energy X-ray absorptiometry, bioelectrical impedance analyzer, computed tomography, magnetic resonance imaging, and 3D body scanning. In the BIA method, the impedance from different tissues of the body is analyzed to predict the composition of the body. A very weak electrical current of 800 microamperes with a frequency of 50 kHz is passed through the body, and the impedance from the tissues is measured against this current. Due to the presence of electrolytes, water demonstrates high conductivity. However, adipose tissues show low conductivity (19,20). The body composition provides quantitative and qualitative information on various tissues such as fat-free mass, fat mass, total water content, bone mineral density and its content, metabolic age, and the physique rate. At the time

of measurement, all the metal accessories such as watches, rings, and other jewelry were removed, and all the measurements were performed by the same trained personnel based on the same protocol. The body composition of participants was measured and reported using the bioelectrical impedance analysis (BIA) by the *Tanita*[®] *MC-780U Body Composition Analyzer.*

Metabolic age is determined by comparing a person's basal metabolic rate with the average basal metabolic rate that corresponds to a similar age group. It is now emerging as a marker for metabolic health. If the metabolic age is less than the actual age, it means that the body is healthy, but if it is higher than the actual age, it may indicate that the person is not in good health and needs to change their eating and exercising habits and also maybe their lifestyle.

The Physique rate evaluates the levels of muscle and body fat in an individual. It can assess which of the nine body types does one belongs to. The Body Composition Analyzer can be used to assess whether a person is healthy. It is used to measure the fat percentage of the body, muscle mass, and even water and bone content, along with the physique rating. The nine body types, according to the physique rating is as follows: **Hidden Obese:** high-fat percentage with a low level of muscle mass.

Obese: high level of fat percentage with a standard level of muscle mass.

Solidly-built: high body fat percentage with a high level of muscle mass.

Under exercised: an average body fat with a low level of muscle mass.

Standard: an average level of body fat with average muscle mass.

Standard Muscular: an average amount of fat percentage with a high level of muscle mass.

Thin: a low amount of body fat with a low level of muscle mass.

Thin and Muscular: a low amount of body fat with a standard level of muscle mass.

Very Muscular: a low amount of body fat with a high level of muscle mass.

International Physical Activity Questionnaire- short form (IPAQ-SF)

The physical activity was calculated using the short form of the IPAQ (International

Physical Activity Questionnaire) along with the MET (the tasks that are equivalent to metabolic activity) hours per week (METhours/week). The validity of IPAQ has already been reported (21). Considering the frequency of participation in the activities mentioned over the past week, the MET scores for intense, medium, and hiking activities (for at least 10 min) were multiplied by the time each participant spent on the activity. The scores for the various activities were then summarized as MET-mins/week. Finally, they were categorized into three groups: low, medium, and high activity.

A HIGH-level of activity was scored upon the participant's engagement in vigorously intense activity for at least three days to achieve a minimum total physical activity of at least 1500 MET minutes a week OR 7 or more days of any combination of walking with moderately intense or vigorously intense activities to achieve a minimum total physical activity of at least 3000 MET minutes a week.

A MODERATE level of physical activity was scored upon engagement in 3 or more days of vigorously intense activity and/or walking at least 30 min per day OR 5 or more days of moderately intense activity and/or walking at least 30 min per day OR 5 or more days of any combination of walking with moderately intense or vigorously intense activities to achieve a minimum total physical activity of at least 600 MET minutes a week. Scoring a LOW level of physical activity on the IPAQ indicated that the participant was not meeting any of the criteria for either MODERATE or HIGH levels of physical activity.

Metabolic syndrome and its components

In this study, the metabolic syndrome was diagnosed according to the criteria of the National Cholesterol Education Program (NCEP) Adult Treatment Panel-III (ATP- III) and the International Diabetes Federation (IDF).

The criteria to diagnose the metabolic syndrome based on ATP III had to fulfill three or more of the following:

1. Waist circumference >=102 cm for men and greater than 88 cm for women,

2. Blood triglycerides >=150 mg/dL or if a person is on high triglyceride medication,

3. HDL cholesterol level of <40 mg/dL for men and <50 mg/dL for women,

4. Fasting blood glucose >=100 mg/dL or if a person is on medication for high blood sugar,

5. Systolic blood pressure (SBP) >130 mmHg or diastolic blood pressure (DBP) >=85 mmHg or if an individual is on medication for hypertension.

The diagnostic criteria for the metabolic syndrome based on the IDF criteria are:

Obesity that is based on the abdominal circumference, which is >94 cm in men and >80 cm in women,

And any two of the following:

Blood triglyceride (TG) more than 150 mg/dL or if a person is on high blood triglyceride therapy,

HDL cholesterol levels of <40 mg/dL in males and < 50 mg/dL in females,

Fasting blood glucose greater than 100 mg/dL or if a person is on high blood sugar medication,

Systolic blood pressure >130 mmHg or diastolic blood pressure >85 mmHg or if a person is on medication for hypertension.

Metabolic syndrome was assessed based on the above-mentioned criteria.

Statistical analysis

For descriptive statistics, means and standard deviations were used as quantitative variables, and frequency and percentage were used as qualitative variables. For univariate analysis, the Chi-square test was utilized for qualitative variables, while for the quantitative variables, the t-test was used to compare between the two groups, with and without metabolic syndrome. The logistic regression analysis was used to realize which one of our variables were the predictors of metabolic syndrome. The statistical analyses were done using the IBM SPSS®, version 24. P-values of less than 0.05 were considered statistically significant.

Ethical issues

This research was approved by the Ethics Committee for Research at Tehran University of Medical Sciences using the code of ethics IR.TUMS.VCR.REC.1398.246 (10 Jun 2019). We explained the details of the study, including the processes and procedures, to all the participants just before their enrollment, and

they signed and approved the informed consent form. The information of the participants was coded anonymously and kept confidential.

Results

The incidence of metabolic syndrome based on the IDF criteria was equivalent to 22.2% whereas it was 15% based on the ATP-III criteria. We used the IDF criteria in this study since it was stricter (it identifies a higher percentage of individuals having metabolic syndrome). In our study, the incidence rate of metabolic syndrome according to the IDF definition was found to be 21.9% and 22.4% in males and females, respectively (Table 1).

Physical activity was also classified into three categories, namely high, medium, and low physical activity. According to this study, 70.7% of the overall total population had low physical activity, where 68.4% were women, and 74.8% were men. Table 2 shows the details of the physical activity performed by the participants based on their aender.

Table 3 presents the variables other than the IDF criteria, which includes age, sex, physical activity, metabolic age, and physique rating in both the groups, with and without metabolic syndrome.

In the next step, logistic regression was employed to find the predictors of the metabolic syndrome among the participants. In this model, Nagelkerke R Square was found to be 0.176. Table 4 here exhibits the results.

Discussion

This research study aimed to review the incidence rate of metabolic syndrome and its predictors among the employees of the Tehran University of Medical Sciences, resulting in an incidence rate of 22.2% and 15.0% based on the IDF and ATP-III criteria, respectively.

das Merces et al. in 2019 reported the incidence of metabolic syndrome in Brazilian healthcare providers as 24.4% based on the ATP-III criteria, which is about 10% more than our results (7). However, in another study, Brazilian healthcare providers showed a much lower incidence rate of 4.5% (22). This discrepancy may be due to different categorizations of the participants in both the studies based on the existence of metabolic syndrome. Moreover, the results of Mango et al. were closer to ours. In a 2019 study, the incidence of metabolic syndrome in the Japanese white-collar employees was found to be 19.5% (8). In the same year, the incidence rate of metabolic syndrome in Iranian petrochemical workers was revealed as 18.4% as per the ATP-III criteria (23), and in Korean staff, the incidence of metabolic syndrome was found to be 19.8% according to the criteria of ATP-III (9). In a study close to our research, the incidence of

Table 1. Basic information on the data and elements of metabolic syndrome and	their incidence.
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	Total n=1583 Mean (SD)	Male n=571 Mean (SD)	Female n=1012 Mean (SD)	p value	Incidence* n (%)	
Age (year)	43.0 (8.7)	44.0 (9.2)	42.4 (8.4)	0.002	-	
TG (mg/dL)	119.1 (58.7)	137.4 (73.0)	108.7 (45.8)	<0.001	311 (19.6)	
HDL (mg/dL)	43.3 (9.3)	42.2 (8.0)	43.9 (9.9)	0.007	986 (62.3)	
FBS (mg/dL)	86.0 (20.8)	89.7 (26.2)	84.1 (16.7)	<0.001	153 (9.7)	
BP systolic (mmHg)	115.7 (12.8)	120.7 (12.7)	112.9 (12.0)	<0.001	230 (14.5)	
BP diastolic (mmHg)	77.4 (8.2)	79.8 (8.6)	76.1 (7.8)	<0.001		
BMI (kg/m ²)	27.2 (4.5)	27.6 (4.3)	27.0 (4.7)	<0.001	371 (23.4)	
Waist circumference (cm)	88.7 (11.6)	96.1(9.6)	84.5 (10.4)	<0.001	985 (62.2)	
Metabolic Age (year)	41.1 (12.5)	42.9 (11.8)	40.0 (12.8)	<0.001	-	

*According to IDF criteria.

TG: Triglyceride; HDL: High-density lipoprotein; FBS: Fasting Blood Sugar; BP: Blood pressure; BMI: Body mass index.

Turk J Endocrinol Metab. 2021;25:78-86

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Table 2. Levels of physical activity among the participants based on their gender.					
Physical activity status	Total n (%)	Male n (%)	Female n (%)	p value	
Low	1119 (70.7)	427 (74.8)	692 (68.4)		
Moderate	366 (23.1)	114 (20)	252 (24.9)	0.027	
High	98 (6.2)	30 (5.3)	68 (6.7)		

Table 3. Descriptive statistics of the study variables in both the groups, with and without metabolic syndrome.

	With Metabolic Syndrome			Withou			
	Total	Male	Female	Total	Male	Female	
	n=352	n=125	n=227	n=1231	n=446	n=785	p value
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Age (year)	47.0 (7.9)	47.3 (8.8)	46.8 (7.3)	41.8 (8.6)	43.0 (9.1)	41.1 (8.2)	<0.001
Physical Activity met/min/week	481.1 (619.2)	401.5 (484.2)	524.9 (679.2)	544.4 (799.4)	533.7 (884.2)	550.3 (747.5)	<0.001
Metabolic Age (year)	48.6 (11.2)	50.0 (10.9)	47.8 (11.3)	38.9 (12.0)	40.9 (11.3)	37.8 (12.3)	<0.001
Physique Rating	29.3 (8.1)	26.1 (7.1)	31.1 (8.0)	34.8 (9.9)	31.1 (9.6)	36.1(9.7)	<0.001

SD: Standard deviation.

Table 4. Metabolic syndrome predicting the elements.							
				95% C. I for EXP(B)			
Variable	В	Odds Ratio	Sig	Lower	Upper		
Metabolic age	0.037	1.037	0.002	1.014	1.061		
Physique rating	0.028	0.972	0.039	0.946	0.999		
Age	0.050	1.051	<0.001	1.028	1.074		
Sex	0.299	1.349	0.034	1.023	1.780		
Constant	-4.648	0.010	<0.001				

metabolic syndrome in Iranian health workers was found to be 22.4% (24). Also, the incidence of metabolic syndrome among hospital health workers in Nigeria and Kenya were 24.2% and 34%, respectively (25, 26). The incidence was also 21.2% in developing countries such as Ghana, as per the IDF criteria, where the incidence was proven to be greater in females than in males (11). These results were similar to our study, as well. In 2016, the incidence of metabolic syndrome in Japanese healthcare workers was 8.7% (27), which was very different from our results and could be due to the differences in the lifestyle. A meta-analysis of the metabolic syndrome among the Chinese people was reported to be 24.5% (28),

while the incidence among employees who participated in the Aragon Workers' Health Study (AWHS) was reported as 27.1% (29). Many studies have compared the incidence of metabolic syndrome between the employees with sedentary jobs and the ones with active jobs. The difference can be seen in some studies; for example, a study reported an incidence of metabolic syndrome in office workers to be 33% but found only a 14% incidence rate in firefighters (30). Various studies have also reported the incidence of the metabolic syndrome within different societies, which ranges from 20% to 35%, especially in developing countries. This incidence accounts for at least one-fifth of the population and could be an alarming

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signal for ASCVD and type 2 diabetes (31). Abdominal obesity is the most common part of metabolic syndrome, and many studies have shown a direct relationship between abdominal obesity and the incidence of metabolic syndrome. These studies also validate our results (32-34).

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Some studies argue that metabolic syndrome occurs at an older age. For example, at the age of 29 years, the incidence of metabolic syndrome accounted for as much as one-third of the total population, while at the age of 50 years, half of the population was having metabolic syndrome.

In our study, the mean \pm SD of the age in the group with metabolic syndrome was found to be 47 \pm 7.9 years, whereas the mean \pm SD of the age in the non-metabolic syndrome group was shown as 41.8 \pm 8.6 years.

Many studies have explored the predictive components of metabolic syndrome, such as levels of HDL, TG, FBS, waist circumference, and elevated blood pressure (35).

In addition to the components of MetS described by the criteria of the IDF, NCEP ATP-III, and WHO, other predictors have also been introduced in various studies, such as inactivity, age, sex, BMI, smoking, alcohol usage, TG to HDL ratio, waist to hip ratio, serum uric acid, and leptin (7,9-16,36). However, in our study, age and sex were identified as predictors of metabolic syndrome based on the logistic regression analysis.

Metabolic age is a new term used to describe the overall fitness and the metabolic activity of an individual and is obtained by comparing the basal metabolism of a person with the mean basal metabolism of the same age group. If the metabolic age of a person was found higher than their chronological age, it indicated a level of basic metabolism with low physical activity. Metabolic age can be a useful tool for assessing the metabolic status of individuals. A study by the European Society of Cardiology (ESC) used metabolic age as one of the predictors for cardiovascular disorders in people having a higher metabolic age than their chronological age (37).

In addition to the known variables of metabolic syndrome, we also used results of body composition analysis as probable predictors of metabolic syndrome. However, our main target was to confirm if the body composition results could predict metabolic syndrome. The results indicated that metabolic age and physique rating could be considered as independent predictors of metabolic syndrome.

We also investigated if metabolic age could predict metabolic disorders in individuals.

Basal Metabolic Rate (BMR) changes with age (38). Metabolic age is the comparison of the BMR of a person with the mean BMR of the same age group (39). According to the logistic regression analysis, metabolic age can be a new predictor for metabolic syndrome. Also, physique rating, which indicates the body-type (40), can be a simple predictor of metabolic syndrome. In 2016, a study found that type 2 diabetic individuals were significantly different from the control in terms of physique rating (41).

Our results might open the door to the world of metabolic syndrome.

The R-square of the model of regression in our study reached 0.176, which is not good enough, and the odds ratios were also small. Hence, we recommend other researchers to consider studies with more variables that could affect the metabolic syndrome. This can help in creating a better picture of metabolic syndrome along with its anticipating factors.

Conclusion

This study introduces metabolic age as a new predictor of metabolic syndrome. However, more studies are needed to confirm this association.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and/or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Ramin Mehrdad, Mohadeseh Vesal; Design: Zahra Banafsheh Alemohammad; Control/Supervision: Mohadeseh Vesal; Data Collection and/or Processing: Gholamreza Pouryaghoub, Mohadeseh Vesal; Analysis and/or Interpretation: Ramin Mehrdad; Literature Review: Writing the Article: Hamidreza Pouragha, Mohadeseh Vesal; Critical Review: Ramin Mehrdad.

Acknowledgment

This cross-sectional study was performed with the support, collaboration, and financing of the TUMS employees' cohort (TEC) study (Grant no: 97-01-159-38078). The paper has been prepared based on the data from the enrolment phase of the cohort study

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