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A pilot study on the relation between irisin single-nucleotide polymorphism and risk of myocardial infarction

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ABSTRACT

Background: Myocardial infarction (MI) is the major cause of death and disability worldwide. Many recent studies revealed the relationship between circulating irisin levels, endothelial dysfunctions and subclinical atherosclerosis in adult patients.

Objectives: The aim of this study was to investigate the distribution of Irisin gene single nucleotide polymorphism in patients with MI and its association with other clinical and laboratory variables in these patients.

Patients and methods: This study was carried out in 100 patients with MI, and 100 healthy subjects served as controls. All studied subjects underwent laboratory investigations, including measurement of total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-c) high-density lipoprotein cholesterol (HDL-c), creatinine kinase-MB (CK-MB), troponin I (TnI) and genotyping of rs 3480 and rs726344 of Irisin genes using the TaqMan Allelic Discrimination assay technique.

Results: There was a significant difference of Irisin genotypes in patients when compared to controls. By estimating odd ratio (OR) an association was found between G allele of rs 3480 and A allele of rs726344with increase the risk of developing myocardial infarction by 4.03 and 3.47 fold respectively. GG of rs 3480 carriers had significantly increased Troponin I and triglyceride levels, while GA carriers of rs726344 had significantly increased CKMB, Total cholesterol, LDLc, HDLc, troponin I and triglyceride levels compared with other genotypes.

Conclusion: G allele of rs 3480 and A allele of rs726344can considered as genetic risk factors for MI; these findings could have an impact on preventive strategy for myocardial infarction.

1. Introduction

Acute myocardial infarction (AMI) is a severe consequence of the progression of coronary atherosclerotic heart disease (CAD) and probably the most critical form of CAD [1].

MI is a complex disease characterized by the inheritance of multiple genetic variants acting in concert with environmental factors to promote the disease state [2]. It causes energy depletion through imbalance between coronary blood supply and myocardial demand [3].

Myokines are substances that are produced by skeletal muscles, especially induced by exercise, and modulate different metabolic processes locally or in other target tissues [4]. Irisin is a newly discovered Myokine that is secreted by the heart, skeletal muscle, liver and kidneys and plays an important role in the homeostasis and metabolism of energy balance. It was reported that cardiac muscle produces more irisin than skeletal muscle [5].

Irisin is a 112-amino acid glycosylated protein-hormone has been shown to be secreted from fibronectin type III domain containing 5 (FNDC5), a trans-membrane protein of skeletal muscle by an unknown protease [6]. After its secretion by muscle, it circulates in the fat tissue and regulates energy metabolism. It is known as the cold induced endocrine regulator of brown fat function and its secretion is also

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promoted by the cold exposure. In humans, mRNA expression of FNDC5 is approximately 100 times lower in the adipose tissue than in the skeletal muscle [7]. The irisin precursor) FNDC5) gene is a candidate to influence the risk of cardiometabolic diseases as well as the aging process. It has been reported that irisin had the potential to become a therapeutic target for endothelial dysfunction and metabolic disorders [8].

Irisin levels can predict telomere length in healthy adults, serum irisin levels were in fact higher in healthy centenarians compared to young healthy controls and, especially, to young adults with precocious myocardial infarction [9].

Different studies have indicated association between serum irisin and many major chronic diseases including cardiovascular diseases [10]. However, the role of serum irisin as a predictor for mortality risk in acute heart failure patients is not clear [11].

The aim of this study was to detect any association between single nucleotide polymorphism (SNP) of irisin gene and Myocardial Infarction and its risk factors.

2. Subject and methods

This study was carried out by cooperation between cardiology, Medical Biochemistry & Molecular Biology, Microbiology & Immunology Departments, Faculty of Medicine, Menoufia University in the period from august 2018 to February 2019. It was conducted on 200 individuals classified into group I: included 100 patients with MI and group II: 100 healthy subjects served as controls, age, and gender matched apparently healthy control subjects were volunteers from the hospitals staff, medical and nursing students and members of the local community.

Inclusion criteria: The diagnosis of MI was based on typical electrocardiographic changes and on raises in the serum cardiac markers, such as creatinine kinase and troponin I. The diagnosis was verified by the recognition of the responsible stenosis in any of the major coronary arteries or in the left main trunk by coronary angiography.

Prior to collection of blood samples, written informed consent (approved from Committee of Ethicsand Human Rights in Research at Faculty of Medicine, Menoufia University) was obtained from all subjects enrolled in this study. They were subjected to the following: ***Thorough medical history taking, Complete physical examination and Routine investigations*** *including* the following: CBC, Serum Lipid profile: Total cholesterol, Triglycerides, HDL-cholesterol and LDL-cholesterol, liver and kidney functions, fasting and 2 h postprandial blood glucose and HbA1C.

All male or female between the age of 21 and 65, has experienced a first myocardial infarction one to 10 days prior to randomization, has a patent infarct-related artery demonstrated by coronary arteriogram performed for clinical reasons, has an elevation of > 2 times upper limit of normal of CK-MB or troponin during initial hospitalization for the index MI were included in the study. While, patients who: underwent revascularization via a surgical coronary artery bypass procedure, has decompensated heart failure (NYHA Class IV), Subject is currently using mechanical ventilation or has required mechanical ventilation at any time after the index event, has a prior clinical history of myocardial infarction, cardiomyopathy, previous admissions for congestive heart failure, or depressed left ventricular function before the index event were excluded from the study.

2.1. Sample collection and assay

Seven ml of venous blood were collected from all subjects included in this study after overnight fasting by venipuncture from the cubital vein, and were divided as follow: 2 ml of blood were put into EDTA containing tubes, for DNA extraction. The remaining 5 ml were divided to 2 ml put into a citrate containing tube from which plasma was separated for measurement of serum fasting glucose level by glucose oxidase method using (Spinreact diagnostics kit, Spain), while 3 ml put into a plain vacutainer tube, which was left 15 min for coagulation, then centrifuged at 3000 rpm for 10 min, the serum was separated into several aliquots for further analysis of the following parameters.

Serum colorimetric measurement of, total creatine kinase (CK) and CK-MB level using a commercial kit was supplied by Bio System Spain [12].

Measurement of lipid profile [10]: high density lipoproteins cholesterol (HDLc), total cholesterol (TC) and triacylglycerol (TG) using standard enzymatic colorimetric kits (Spinreact diagnostics kit, Spain), Low-density lipoprotein cholesterol (LDL-c) was calculated according to the Friedewald equation [13]. Enzyme-linked immunosorbent assay (ELISA) was done for the measurement of serum TnI [14].

DNA extraction and genotyping was performed by using Real-Time PCR technique at the central laboratory of Menoufia Faculty of Medicine.

2.2. Genotyping of the rs 3480 and rs726344SNP of irisin gene

DNA was extracted from whole blood using GeneJET Whole Blood Genomic DNA Purification Mini Kit (Thermo FisherScientific, Waltham, MA, USA). Rs3480 and rs726344 SNP of irisin gene were genotyped using the TaqMan allelicDiscrimination method, which determines variants of single nucleic acid sequence. Using two primer/probe pairs in each reaction allows genotyping of the two possible variants atthe single nucleotide polymorphism in a target template sequence. Using the maxima probe qPCR Master Mix (2X), primers and probes were applied from Thermo FisherScientific; SNPrs726344probeSequence [VIC/FAM]AGCCCCAAGAAGCTGAACCTCTTCT [G/A]AGGGAGGGCG AAGGCAAGTACTCAT, SNPrs3480probeSequence [VIC/FAM]AGACCG GAAGGAAGGGGCGGTCATT [A/G]GGTGATGGCTTCTGGCTCTCTG GCT.

The genotyping reaction was done by adding 10 μL of master mix, 1.25 μL of the genotyping ready-made assay mix (probes and primers) and 3.75 μL of DNAase-free water, for every unknown reaction, 5 μL of genomic DNA template and5μL of DNAase-free water were added for samples and the negative control real time PCR tube respectively. The cycling parameters were as follows: first, denaturation was done at 95 °C for 10 min, followed by 40 cycles of denaturation at 94 °C for 15 s, annealing at 50°Cfor 60 s and then extension at 72 °C for 2 min andthe last extension at 72 °C for 1 min. Data analysis was performed using 7500 Real-Time PCR System, software version 2.0.1.

3. Statistical analysis

Results were collected, tabulated and statistically analyzed by IBM personal computer and statistical package SPSS version 20(IBM Corporation, Armonk, NY, USA). Chi-square test (χ2was used to study the association between two qualitative variables. Odds ratio (OR) describes the probability that people who are exposed to a certain factor will have a disease compared to people who are not exposed to the factor.

Student's t-test was used for comparison between two groups having quantitative variables. Analysis of variance (ANOVA) (F) test was used for comparison between three or more groups having quantitative variables. Multiple regression analysis was performed to calculate the effects of risk factors as independent ORs with the effects of other confounders removed. P-value < 0.05 was statistically significant.

4. Results

The present study included 200 individuals (124 male and 76 female), there was a non significant statistical differences between patients and controls regarding age (p = 0.30) and gender (p = 0.41) indicating group matching. Also a non significant statistical difference was detected between both groups as regards smoking (P = 0.12).

Table 1
Statistical comparison between the studied groups regarding socio-demographic data.

Parameters	Group I patients (No. = 100)		Group II Controls (No. = 100)		Test of significance	P value
Age (years)	Mean ± SD		Mean ± SD		t = 1.03	0.30
	57.02 ± 8.39		55.26 ± 8.63			
Heart rate (beats/min)	74.5 ± 14.53		77.14 ± 7.89		t = 11.72	< 0.01*
SBP(mmHg)	126.8 ± 18.89		112.8 ± 7.57		t = 31.27	< 0.001*
DBP(mmHg)	77.0 ± 9.31		74.2 ± 9.49		t = 0.07	0.79
Gender	No.	%	No.	%	χ^2 = 0.68	0.41
Male	58	58.0	66	66.0		
Female	42	42.0	34	34.0		
Smoking						
Yes	64	64.0	78	78.0	χ^2 = 2.38	0.12
No	32	32.0	22	22.0		
Hypertension						
Yes	54	54.0	0	0.0	χ2 = 36.98	< 0.001
No	46	46.0	100	100.0		
Diabetes						
Yes	40	40.0	0	0.0	χ2 = 25.00	< 0.001
No	60	60.0	100	100.0		
Hyperlipidaemia						
Yes	38	38	0	0.0	χ2 = 23.49	< 0.001
No	62	62	100	100.0		

* significant difference.

There was a statistically significant difference between the two studied groups regarding heart rate, systolic blood pressure (P < 0.01), the presence of hypertension, diabetes and hyperlipidemia (P < 0.001). While there was a non-significant difference as regards diastolic blood pressure (p = 0.79).(Table 1).

Furthermore, there was a statistically significant difference between the two studied groups regarding total cholesterol (TC), triglyceride (TG), LDL-c, HDL-c, CK-MB, TnI)P < 0.001), (Table 2).

The population of the studied sample was find to be in equilibrium with Hardy-Weinberg equation (not shown).

There was a statistically significant difference regarding rs3480 and rs726344 of irisin genotypes and alleles distribution between patients and control, there was increase in number and percentage of GG genotype and G allele of rs3480 in patients when compared to controls. By estimating odd ratio (OR) an association was found between G allele and increase the risk of developing myocardial infarction by4.03 fold. Also, there was increase in number and percentage of GA genotype and A allele of rs726344 in patients when compared to controls. By estimating odd ratio (OR) an association was found between A allele genotype and increase the risk of developing myocardial infarction by3.47 fold (Table 3 and Fig. 1).

Comparison between different rs3480 genotypes in the studied groups regarding different parameters revealed that there was no statistical significant difference between the different parameters as regards the age, sex, Smoking, Heart rate, Hypertension, CKMB, Total cholesterol, LDL, HDL. While there was significant difference between them as regards SBP, DBP level, presence of Diabetes, Hyperlipidemia, Troponin I and triglyceride levels (P < 0.05) (Table 4 and Fig. 2).

On the other hand comparisons between different rs726344 genotypes in the two studied subjects regarding different parameters gave different results as there was significant statistical difference between them as regards presence of hypertension, diabetes, hyperlipidemia, levels of CKMB, Total cholesterol, LDLc, HDLc, troponin I and triglyceride (P < 0.05) while there was no significant difference as regards age, gender, smoking, Heart rate, SBP and DBP only (Table 5 and Fig. 3).

Interestingly, combined genotype distribution in rs3480 and rs726344 SNP of irisin gene between the two studied groups showed a significant difference, with combined AG/GA as the most frequent (34%) followed by GG/GA (26%)in the patient group. Combined AA/GG as the most frequent (42%) followed by AG/GG (22%) inthe control group (p < 0.001) (Table 6 and Fig. 4).

5. Discussion

Myocardial infarction (MI) is the death of the myocardial tissue that

Table 2
Statistical comparison between the studied groups regarding laboratory investigation.

Parameters	Group I patients (No. = 100)	Group II Controls (No. = 100)	*t*-Test	P value
	Mean ± SD	Mean ± SD		
Troponin I (pg/ml)	354.86 ± 494.96	48.96 ± 3.26	#8.015	< 0.001*
CKMB(ng/ml)	23.83 ± 51.39	6.06 ± 0.21	#3.029	0.002*
Total cholesterol (mg/dl)	200.4 ± 39.59	154.70 ± 10.44	7.89	< 0.001
LDL (mg/dl)	118.44 ± 35.07	84.66 ± 10.89	6.50	< 0.001
HDL (mg/dl)	48.84 ± 3.26	52.5 ± 6.79	3.43	< 0.01
Triglyceride (mg/dl)	145.26 ± 34.52	106.10 ± 11.29	7.62	< 0.001

Mann-Whitney *U* test.

Table 3
Statistical comparison between the studied groups regarding rs3480 and rs726344 genotypes and allele frequencies.

Parameters	Group I patients (No. = 50)		Group II Controls (No. = 50)		Test of significance	P value	Odds ratio (CI)
rs 3480	22	22.0	58	58.0	χ^2 = 18.30	< 0.001	Reference
A/A	44	44.0	36	36.0			0.31 (0.12–0.79)
A/G	34	34.0	06	6.0			0.07 (0.02–0.27)
G/G							
Allele	44	44.0	76	76.0	21.33	< 0.001	Reference
A	56	56.0	24	24.0			4.03 (2.20–7.38)
G							
rs726344	76	76.0	30	30.0	χ^2 = 21.236	< 0.001	0.14 (0.06–0.33)
G/A	24	24.0	70	70.0			Reference
G/G							
Allele	38	38.0	15	15.0	13.58	< 0.001	3.47 (1.76–6.87)
A	62	62.0	85	85.0			Reference
G							

*significant difference.

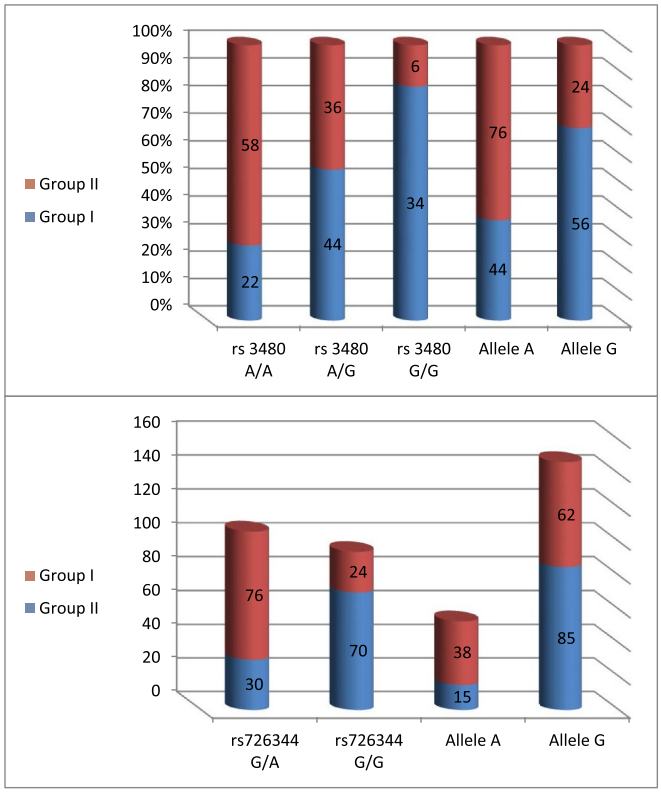

Fig. 1. Statistical comparison between the studied groups regarding rs3480 and rs726344 genotypes and allele frequencies.

occurs as a result of inadequate coronary blood supply compared to myocardial demand. According to the third monitoring report of the World Health Organization (WHO), 17.3 million people die annually of MI throughout the world [3]. AMI is caused by the combined action of multiple environmental and genetic factors [15].

Troponin T (cTnT), troponin I (cTnI), and creatinine kinase-MB (CK-MB) are the common markers for the diagnosis of myocardial injury and stratification of the risk in acute coronary syndrome. European Society of Cardiology (ESC (and the American College of Cardiology (ACC) guidelines have recommended cardiac troponins as markers for the acute myocardial infarction. These sensitive markers (cTnTandcTnI) begin to rise in the first 4–8 h following injury and peak at 12–24 h. These two detect myocardial injury below the detection limit of CK-MB. Some of the clinicians measured CKMB to rule out myocardial infarction and to monitor for additional cardiac muscle injury overtime [16]. So, in our study, there was a statistically significant difference between the two studied groups regarding total cholesterol (TC), triglyceride (TG), LDL-c, HDL-c, CK-MB, TnI)P < 0.001).

It has been observed that the browning of white adipose tissue can help protect against metabolic disorders caused by diet, obesity and metabolic diseases such as type II diabetes, Because such disorders are closely related to cardiovascular diseases including coronary diseases [17], it is plausible that stimulating particular brown adipose sources or facilitating the alteration of white to brown adipose can be a promising strategy in treating metabolic disorders and cardiovascular diseases [18].

Irisin acts in the white adipose tissue, promoting the acquisition of a brown adipocyte phenotype prone to energy expenditure [8]. Accordingly, irisin might play an important role in reducing the risk of obesity, insulin resistance diabetes or several related diseases. It can also help to preserve vascular function and skeletal muscle mass [19].

Previous studies revealed the relationship between circulating irisin levels, endothelial dysfunctions and subclinical atherosclerosis in non-diabetic adult patients. In another recent study, it was demonstrated that serum irisin level was significantly correlated with carotid atherosclerosis in patients receiving dialysis [20].

Irisin level is believed to be susceptibility factor of AMI, but the correlation between SNPinirisin gene and AMI has been rarely investigated. According to the present study, the risk of developing AMI was increased in **GG genotype and** G allele of rs3480 by 4.03 fold and **GA genotype and**Aallele of rs 726,344 by 3.47 fold compared to the controls.

The G allele of rs3480 associated with greater FNDC5 mRNA degradation compared to A allele, the study of ***Letícia et al., 2015*** [21] found that G allele of rs3480 with higher HbA1c and of the T allele of rs1746661 with higher systolic BP and dyslipidemia in women with T2DM.

Intronic genomic variants (e.g., rs726344) can influence gene expression and thus phenotype, by altering mRNA stability, alternative mRNA splicing, or the binding of transcription factors [22]***(Sasabe et al.*** 2007***).***

The minor A-allele of rs726344 is characterized by higher luciferase activity compared with the wild-type G-allele and has been recently associated with decreased insulin sensitivity in vivo [23] ***(Staiger et al.*** 2013).

Similar to our results, ***Icli et al(2016)*** [19]who found a strong association between low irisin levels and accelerated atherosclerosis. Also, ***Kulogluaet* al(2014)** [3] had showed that there was a gradual decrease in serum irisin levels and this could be used as a diagnostic marker for AMI. Unlike our study, some studies, interestingly, showed cardioprotective effects of low serum irisin levels. Some studies have

Table 4
Statistical comparisons between different rs 3480 genotypes in the studied groups regarding different parameters.

Parameters	Rs 3480 of studied subjects (n = 200)			F Test	P value	Post hoc test
	AA (No. = 80)	AG (No. = 80)	GG (No. = 40)			
	Mean ± SD	Mean ± SD	Mean ± SD			
Age (years)	54.45 ± 8.49	57.50 ± 8.71	56.80 ± 7.99	1.367	0.26	= = = = =
Gender	44 (55.0)	50 (62.5)	30 (75.0)	2.271	0.321	= = = = = =
Male	36 (45.0)	30 (37.5)	10 (25.0)			
Female						
Smoking	8 (10.0)	14 (17.5)	14 (35.0)	5.657	0.059	
Yes	72 (90.0)	66 (82.5)	26 (65.0)			
No						
Heart rate (beats/min)	76.65 ± 10.12	77.92 ± 11.16	69.95 ± 14.17	3.42	0.37	
SBP(mmHg)	118.0 ± 13.99	116.25 ± 13.90	130.5 ± 19.32	6.37	0.003	P1 = 0.607 P2 = 0.003 P3 = 0.001
DBP(mmHg)	76.25 ± 9.25	73.00 ± 9.92	79.5 ± 7.59	3.27#	0.04	P1 = 0.119 P2 = 0.202 P3 = 0.012
Hypertension	16 (20.0)	24 (30.0)	14 (35.0)	1.826	0.401	
Yes	64 (80.0)	56 (70.0)	26 (65.0)			
No						
Diabetes	12 (15.0)	12 (15.0)	16 (40.0)	6.250	0.044	
Yes	68 (85.0)	68 (85.0)	24 (60.0)			
No						
Hyperlipidaemia	8 (10.0)	14 (17.5)	16 (40.0)	7.895	0.019	
Yes	72 (90.0)	66 (82.5)	24 (60.0)			
No						
Troponin I (pg/ml)	85.87 ± 85.61	306.65 ± 562.08	224.50 ± 197.79	3.46	0.035	P1 = 0.009 P2 = 0.176 P3 = 0.421
CKMB(ng/ml)	15.13 ± 45.68	15.42 ± 36.47	13.62 ± 14.48	0.796	0.672	
Total cholesterol (mg/dl)	169.65 ± 31.28	177.66 ± 41.20	193.12 ± 34.52	2.803	0.066	
LDL (mg/dl)	96.71 ± 27.61	100.93 ± 34.88	112.47 ± 27.25	1.77	0.175	
HDL (mg/dl)	49.92 ± 4.75	51.0 ± 6.62	51.5 ± 5.07	0.635	0.532	
Triglyceride (mg/dl)	113.85 ± 20.41	129.6 ± 36.62	141.5 ± 34.94	5.928	0.004	P1 = 0.024 P2 = 0.001 P3 = 0.161

P1 = AA versus AG P2 = AA versus GG P3 = AG versus GG.

reported that a low serum irisin level plays a protective role in acute coronary events such as myocardial infarction by decelerating energy metabolism of myocardial tissue, and decreasing tissue oxygenation and ATP expenditure**,** It was reported that high irisinlevels cause ATP loss during uncoupled biochemical reactions [3]***(Kulogulo et al., 2014).*** In another study done by Ref. [24]***Aydin et al., 2014*** it was reported that the level of irisin was lower during the first 2 days of myocardial infarction and it increased after the 72 nd h of infarction. ***Sarioğlu et al., 2016*** [25] demonstrated an increase in irisin levels in the cardiac tissue of rats with experimentally induced MI which may has a relation to increase delays myocardial necrosis due to ischemia or to facilitate the repair process. Irisin could protect against ischemia/reperfusion injury in vitro through its antioxidant and anti-inflammatory properties, by limiting the infarction area**.** While, the study of ***Shen et al., 2017*** [26] found that acute heart failure patients with higher serum irisin had significantly higher mortality.

Comparison of general physiological and biochemical indicators between the two groups suggested that AMI was usually accompanied by hypertension, hyperlipidemia and diabetes, as there was a statistically significant difference between the two studied groups regarding heart rate, systolic blood pressure ($P < 0.01$), the presence of hypertension, diabetes and hyperlipidemia ($P < 0.001$), indicating that these are risk factors for AMI, as has been confirmed by a large number of studies so far [27]***(Anand et al., 2008)***. Smoking is another risk factor for AMI, but we did not observe significant differences between smokers and non-smokers. This is probably due to the small sample size and the lack of further discrimination of the smoking status instead of simply dividing the cases into smokers and non-smokers.

In this study, there was significant difference between rs 3480 genotypes as regards SBP, DBP level, and presence of Diabetes, Hyperlipidaemia and triglyceride levels. On the other hand, there were significant difference betweenrs726344 genotypes as regards presence of hypertension, diabetes, hyperlipidaemia, Total cholesterol, LDLc, HDLc and triglyceride. The study of Zhang et al., 2015 [28] found that administration of recombinant human irisin into the 3rd brain ventricle of rats activated neurons in the Para ventricular nuclei of the hypothalamus with a subsequent increases in blood pressure (BP) and cardiac contractibility, while peripheral administration of this myokine reduced BP in both control and spontaneously hypertensive rats.

Also, the study of ***Park et al.2013*** [29] demonstrated a positive correlation between irisin concentration and both systolic and diastolic blood pressure in healthy middle-age individuals.

Many studies have shown either positive or negative associations of irisin with total cholesterol, high (HDL) and low density lipoproteins (LDL), and triglycerides). In obese individuals with other cardiovascular risk factors, increased circulating irisin levels were found to be correlated with unfavorable lower HDL [30–32].

Plasma irisin level in diabetes varies depending on the type of disease. Previous studies demonstrating that irisin level increase in type 1 diabetes and newly diagnosed T2DM [33, 34]. Also, The study of ***Sanchis-Gomar et al., 2014,*** stated that rs726344 SNP is a candidate to influence exceptional longevity by influence the risk of many diseases, as it had functional significance differences in luciferase activity between the constructs of this SNP (all $P \leq 0.05$), with the variant A-allele having higher luciferase activity compared with the G-allele [35].While, The study of ***Hagit et al, 2018***, found that maternal and

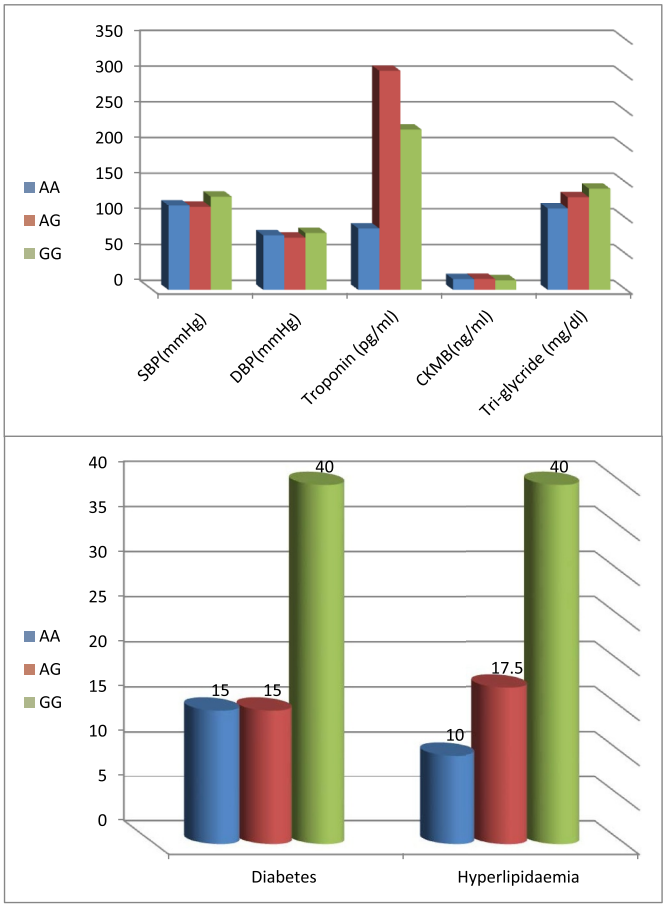

Fig. 2. Statistical comparisons between different rs3480 genotypes in the studied groups regarding different parameters.

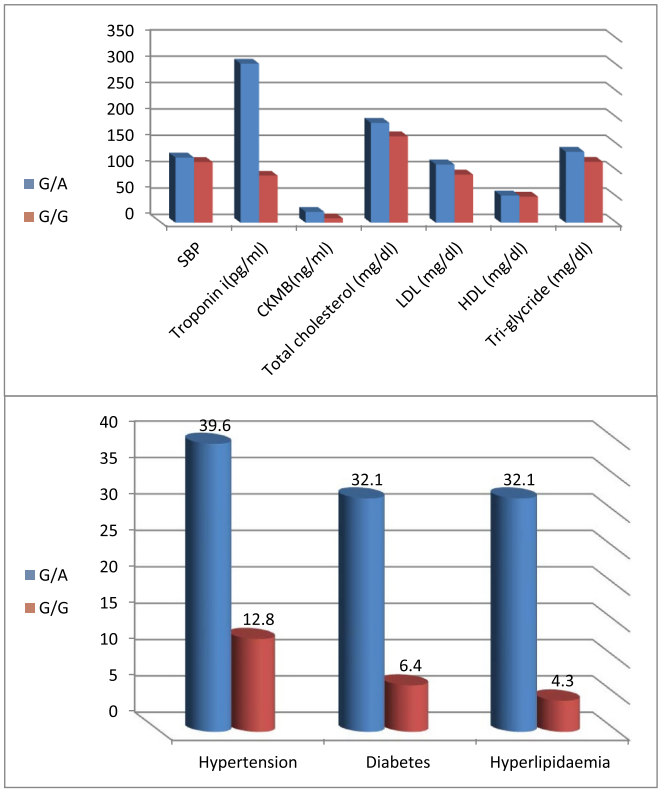

Fig. 3. Statistical comparisons between different rs726344 genotypes in the two studied groups regarding different parameters.

Table 5
Statistical comparisons between different rs726344genotypes in the two studied subjects regarding different parameters.

Parameters	rs726344 of studied subjects (n = 200)		F Test	P value
	G/A (No. = 106)	G/G (No. = 94)		
	Mean ± SD	Mean ± SD		
Age (years)	56.30 ± 8.35	55.96 ± **8.78**	0.201	0.841
Gender				
Male	60 (56.6)	64 (68.1)	1.394	0.238
Female	46 (43.4)	30 (31.9)		
Smoking				
Yes	24 (22.6)	12 (12.8)	1.646	0.20
No	82 (77.4)	82 (87.2)		
Heart rate (beats/min)	75.19 ± **13.40**	76.53 ± **9.52**	0.58	0.569
SBP(mmHg)	123.77 ± **17.89**	115.32 ± **12.13**	2.73	0.008
DBP(mmHg)	76.60 ± **9.18**	74.47 ± **9.74**	1.13	0.262
Hypertension				
Yes	42 (39.6)	12 (12.8)	9.116	0.003
No	64 (60.4)	82 (87.2)		
Diabetes				
Yes	34 (32.1)	6 (6.4)	10.277	0.001
No	72 (67.9)	88 (93.6)		
Hyperlipidaemia				
Yes	34 (32.1)	4 (4.3)	12.527	< 0.001
No	72 (67.9)	90 (95.7)		
Troponin I (pg/ml)	301.84 ± 492.77	89.21 ± 112.79	4.03	< 0.001
CKMB(ng/ml)	20.65 ± 49.88	8.51 ± 9.61	2.26	0.024
Total cholesterol (mg/dl)	189.59 ± 42.51	163.97 ± 22.86	3.68	< 0.001
LDLc (mg/dl)	110.60 ± ± 36.26	91.35 ± 19.23	3.25	0.002
HDLc (mg/dl)	51.69 ± 6.45	49.51 ± 4.26	1.97	0.051
Triglyceride (mg/dl)	134.64 ± 36.58	115.57 ± 23.00	3.07	0.003

Table 6
Statistical comparison between studied groups regarding combined genes.

	Group I (No. = 100)		Group II (No. = 100)		χ^2 test	P value
	No.	%	No.	%		
AA/GA	18	18.0	16	16.0	35.314	< 0.001
AA/GG	4	4.0	42	42.0		
AG/GA	34	34.0	14	14.0		
AG/GG	10	10.0	22	22.0		
GG/GA	26	26.0	0	0.0		
GG/GG	8	8.0	6	6.0		

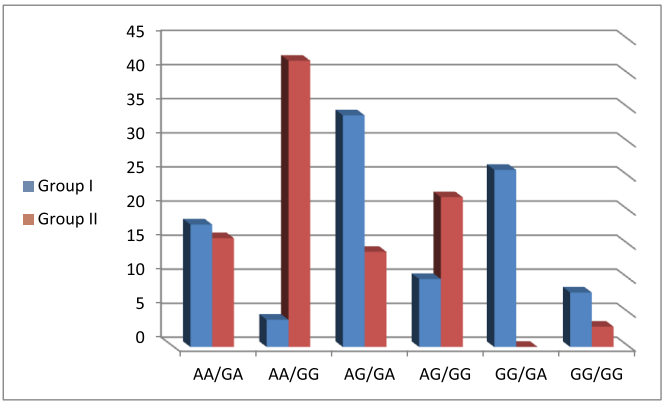

Fig. 4. Statistical comparison between studied groups regarding combined genes.

neonatal FNDC5 rs726344 polymorphism is significantly associated with increased risk for preterm baby [36].

6. Conclusion

Irisin (FNDC5) gene SNP GG genotype and G allele of rs3480 and GA genotype and A allele of rs 726,344 may confer susceptibility to MI. Patients carrying GG genotype of rs3480 and GA genotype and A allele of rs 726,344 are associated with criteria of bad prognosis as presence of hypertension, diabetes, hyperlipidaemia. Further studies, including Irisin gene expression are necessary to explain its role in pathology of MI and to evaluate the role in management.

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Ethical approval

Research Involving Human Participants. The study was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent, and the Ethics Committee of Faculty of Medicine, MenoufiaUniversity approved the study protocol.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.bbrep.2020.100742.

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