Association of β -1 and β -2 Adrenergic Receptor Gene Polymorphisms With Myocardial Infarction

Akin Yilmaz,¹ Mehmet G. Kaya,² Ulgen Merdanoglu,² Mehmet A. Ergun,³
Atiye Cengel,² and Sevda Menevse^{1*}

¹Department of Medical Biology and Genetics, Faculty of Medicine, Gazi University, Besevler, Ankara, Turkey

²Department of Cardiology, Faculty of Medicine, Gazi University, Besevler, Ankara, Turkey

³Department of Medical Genetics, Faculty of Medicine, Gazi University, Besevler, Ankara, Turkey

Both β_1 - and β_2 -adrenergic receptors (β_1 - and β_2 -AR) have important roles in heart function mainly in response to catecholamines. Some specific polymorphisms in the β_1 - and β_2 -AR genes, named ADRB1 and ADRB2, respectively, have been implicated in several cardiovascular and noncardiovascular phenotypes. In this study, we aimed to investigate the possible relationship between Ser49Gly and Arg389Gly polymorphisms of the ADRB1 and Arg16Gly and Gln27Glu polymorphisms of the ADRB2 gene with ST elevation myocardial infarction (MI) in a Turkish population. One hundred patients with ST elevation MI and 100 healthy control subjects were genotyped using the PCR-RFLP method. Although the Arg389 allele of the ADRB1 gene was associated with an elevated risk of MI, the

Glu27 allele of the ADRB2 gene was associated with a decreased risk of MI. Carriers of the ADRB1 Arg389 allele (heterozygotes+homozygotes) had an approximately 3.5-fold increased risk for MI than Gly389 homozygotes (OR = 3.59, 95% CI = 0.96–13.47, P = 0.045). For the ADRB2 Gln27Glu polymorphism, subjects having one or two copies of the Glu27 allele showed a decreased risk of MI compared with Gln27 homozygote subjects (OR = 0.48, 95% CI = 0.24–0.94, P = 0.03). Haplotype analysis of these polymorphisms showed no significant differences between groups. These results suggest that the Arg389Gly and Gln27Glu polymorphisms may be associated with an altered risk of MI in this Turkish population. *J. Clin. Lab. Anal.* 23:237–243, 2009. © 2009 Wiley-Liss, Inc.

Key words: ADRB1; ADRB2; myocardial infarction; polymorphism

INTRODUCTION

β -adrenergic receptors (β -ARs) can be divided into three subtypes, β_1 -, β_2 -, and β_3 -AR (1). Although β_3 -AR is expressed in the adipose tissue, both β_1 - and β_2 -ARs are present in the human heart where they play essential roles in heart function. In the atria and ventricles, the ratio of β_1/β_2 -AR is about 70%/30% and 80%/20%, respectively (2). The principal role of β ARs in the heart is to regulate heart rate and contractility in response to catecholamines such as epinephrine and norepinephrine (3).

Several polymorphisms have been identified in the β_1 - and β_2 -AR genes, named ADRB1 and ADRB2 respectively (4). Studies have focused on two polymorphisms of each gene: the Ser49Gly (c.145A > G, rs1801252) and Arg389Gly (c.1165C > G, rs1801253) polymorphisms of ADRB1 and the Gly16Arg (c.46A > G, rs1042713) and Gln27Glu (c.79C > G, rs1042714) polymorphisms of ADRB2. The Ser49Gly and Arg389Gly polymorphisms

of ADRB1 have been associated with a number of phenotypes, mostly related to the cardiovascular system, including heart rate (5,6), heart failure (7–10), dilated cardiomyopathy (11,12), myocardial infarction (MI) (13), and hypertension (14), but with conflicting results. In addition to ADRB1 polymorphisms, the ADRB2 polymorphisms, Gly16Arg and Gln27Glu, have been evaluated in relation to several cardiovascular diseases, including hypertension (15,16), MI (15,17–20), and heart failure (10,21). These polymorphisms have also

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*Correspondence to: Sevda Menevse, Department of Medical Biology and Genetics, Faculty of Medicine, Gazi University, Ankara, 06510, Turkey. E-mail: akinyilmaz2002@yahoo.com, akinyilmaz@gazi.edu.tr

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been studied in relation to idiopathic ventricular arrhythmias in a Turkish population (22).

Two of the ADRB1 gene polymorphisms, Ser49Gly and Arg389Gly, have been shown to be functionally important. With regards the Ser49Gly polymorphism that is localized in the extracellular terminus of the receptor (23), the Gly49 allele is associated with varied glycosylation (24) and more pronounced agonist-induced receptor downregulation compared with the Ser49 allele in a hamster fibroblast model (25). With regards the Arg389Gly polymorphism that is located in the intracellular cytoplasmic tail of the receptor, the Arg389 allele is associated with increased activation of the adenyl cyclase effector (26).

The Gly16Arg and Gln27Glu polymorphisms of ADRB2 are located in the intracellular cytoplasmic tail of the receptor (23). Although receptors carrying these polymorphisms have been shown to have normal agonist binding and functional coupling to G-proteins, these substitutions affected the degree of agonist-promoted downregulation of receptor expression (27).

Several risk factors for MI, including hypercholesterolemia, hypertension, and diabetes mellitus, have been determined in epidemiological studies. Each of the risk factors should have genetic components, whereas a positive family history of MI is an independent predictor, which indicates it has a genetic background of its own (28,29). In this regard, the aim of this study was to investigate whether ADRB1 and ADRB2 gene polymorphisms are associated with ST elevation MI in a Turkish population.

MATERIALS AND METHODS

Study Population

The study population was composed of 100 patients with ST elevation MI, recruited from the Gazi University Faculty of Medicine, Department of Cardiology, and 100 Turkish age-matched control subjects without documented coronary artery disease. The cardiovascular risk factors that were evaluated were age, sex, hypertension, diabetes mellitus, tobacco use, hyperlipidemia, and a family history of cardiovascular

disease (Table 1). The study protocol was approved by the Local Ethical Committee. Written informed consent was obtained from all subjects.

Genotyping

Genomic DNA was extracted from blood samples taken from the patients and controls using an extraction kit (EZ-DNA Genomic DNA Isolation Kit, Biological Industries, Israel) according to the manufacturer's instructions. Detection of polymorphisms in the ADRB1 and ADRB2 genes was carried out using the PCR-RFLP method. The results were evaluated with two blind observers after agarose gel electrophoresis. The ADRB1 gene Ser49Gly and Arg389Gly polymorphisms were screened using a previously described method (30). Briefly, for the ADRB1 gene Ser49Gly polymorphism, a PCR reaction was performed with the primers 5'-CCGGGCTTCTGGGGTGTTC-3' (forward) and 5'-GGCGAGGTGATGGCGAGGTAGC-3' (reverse). To amplify the DNA fragment containing the ADRB1 Arg389Gly polymorphism, primer pairs 5'-CGCTCTGCTGGCTGCCCTTCTTC-3' (forward) and 5'-TGGGCTTCGAGTTCACCTGCTATC-3' (reverse) were used. The PCR reaction was performed using the following steps for both of the ADRB1 gene polymorphisms: initial denaturation at 94°C for 5 min, then 30 cycles of denaturation at 94°C for 30 sec, annealing at 62°C for 30 sec and extension at 72°C for 1 min, and final extension at 72°C for 5 min.

After amplification of a 564 bp DNA fragment containing the Ser49Gly (c.145A>G, rs1801252) polymorphism, the PCR product was digested with 10 units of Eco109I restriction enzyme (Fermentas, St. Leon-Rot, Germany) at 37°C overnight and then electrophoresed in a 2% agarose gel. The PCR product containing the Ser49 allele was not digested with this restriction enzyme, whereas in the presence of the Gly49 allele, the 564 bp PCR product was digested into two fragments of 345 bp and 219 bp.

Screening of the ADRB1 Arg389Gly (c.1165C>G, rs1801253) polymorphism was performed by digesting the 530 bp PCR product with 10 units of BclI restriction enzyme (New England Biolabs, UK) at 37°C overnight.

TABLE 1. Characteristics of Patients and Control Subjects

	Patients (n = 100) (%)	Controls (n = 100) (%)	P-value
Age	54.2 ± 11.9	51.4 ± 11.6	0.101
Sex (Male/Female)	82/18 (82%/18%)	56/44 (56%/44%)	0.001
Hypertension	47 (47%)	20 (20%)	0.001
Diabetes	14 (14%)	15 (15%)	0.623
Smokers	73 (73%)	19 (19%)	0.001
Hyperlipidemia	23 (23%)	16 (16%)	0.32
Family history	24 (24%)	19 (19%)	0.56

After electrophoresis in a 2% agarose gel, alleles were identified as Gly389 when a 530 bp DNA fragment was present, and Arg389 when a 342 and 154 bp fragments were present.

For the Arg16Gly (c.46A>G, rs1042713) and Gln27Glu (c.79C>G, rs1042714) ADRB2 gene polymorphisms, a single PCR reaction was performed with the primers (8) 5'-CTTCTTGCTGGCACGCAAT-3' (forward) and 5'-CCAGTGAAGTGATGAAGTAG-TTGG-3' (reverse) using the following steps: initial denaturation at 94°C for 5 min, then 30 cycles of denaturation at 94°C for 30 sec, annealing at 54°C for 30 sec and extension at 72°C for 30 sec, and final extension at 72°C for 5 min. To screen for the Arg16Gly and Gln27Glu polymorphisms, the 200 bp PCR product was treated with 10 units of Bse3DI at 60°C (SibEnzyme, Russia) and 10 units of Fsp4HI (SibEnzyme, Russia) at 37°C overnight, respectively. Results were evaluated after electrophoresis in a 3.5% agarose gel. For the Arg16Gly polymorphism, the Arg16 allele was digested into two fragments (130 and 70 bp), whereas the Gly16 allele was digested into three fragments (108, 70, and 22 bp). After restriction enzyme digestion for the Gln27Glu polymorphism, the absence of restriction sites led to one 200 bp fragment that was identified as Glu27, and the presence of restriction sites led to two fragments, 150 and 50 bp, identified as Gln27. All restriction enzyme digestion results were evaluated by two blinded observers after electrophoresis.

Statistical Analysis

Differences between patients and control subjects were evaluated by the χ^2 test for dichotomous variables and analysis of variance for continuous variables. Differences in the allele frequency distribution and haplotypes between groups and the relationship between MI and the ADRB1 and ADRB2 gene polymorphisms was compared by the χ^2 test. Odds ratios (OR) are given with 95% confidence intervals (CI) and $P < 0.05$ was considered statistically significant. All statistical procedures were performed using SPSS 13.0 software (SPSS Inc., Chicago, IL). Online SNPStats software (<http://bioinfo.iconcologia.net/index.php?module=Snstats>) was used to construct the haplotypes of β_1 -adrenergic receptor polymorphisms (Ser49Gly and Arg389Gly) and β_2 -adrenergic receptor polymorphisms (Gly16Arg and Gln27Glu) (31).

RESULTS

The characteristics of the patients and control subjects are shown in Table 1. The mean age was 54.2 ± 11.9 years (range 35–87 years) in patients and 51.4 ± 11.6 (range 26–78 years) in control subjects. There were more

male subjects in patients than in control subjects ($P = 0.001$). The proportion of smokers and subjects with hypertension was higher in patients than in the control group ($P = 0.001$). On the other hand, there were no significant differences between groups for diabetes, hyperlipidemia, and the family history of cardiovascular disease ($P > 0.05$).

The genotypes and allele frequencies of the Ser49Gly and Arg389Gly polymorphisms of the ADRB1 gene and the Arg16Gly and Gln27Glu polymorphisms of the ADRB2 gene and their association with MI are shown in Tables 2 and 3, respectively.

With regards the ADRB1 Ser49Gly polymorphism, the Ser49 allele frequency was 91.5% in patients and 87.5% in the control group ($P = 0.192$). The ADRB1 Ser49Gly genotype distributions were not statistically significant between patients and control groups ($P = 0.429$). There were no significant differences between Ser49 homozygous vs. heterozygous and Gly49 homozygous subjects either ($P = 0.279$) (Table 2).

With regards the ADRB1 Arg389Gly polymorphism, although the Arg389 allele frequency was higher in patients than in control subjects, this difference was not statistically significant ($P = 0.317$). The distributions of the genotypes among patients was significantly different to those among control subjects ($P = 0.032$). Homozygote carriers of the Gly389 allele were significantly more frequent in controls than in patients with MI. Three out of the 100 patients had the Arg389 homozygous genotype but this genotype was not encountered in the control group. The OR of the homozygote Gly389 vs. the heterozygote genotype between patients and controls was 3.49 (95% CI = 0.93–13.06, $P = 0.051$) and there was a borderline significant association. Moreover, the OR of the homozygote Gly389 vs. heterozygote + homozygote Arg389 genotype between groups was 3.59 (95% CI = 0.96–13.47, $P = 0.045$) and this association was significant (Table 2).

The Gly16 allele frequency of the ADRB2 Arg16Gly polymorphism was 64 and 55.5% in patients and controls, respectively ($P = 0.083$). The genotype distribution of the Arg16Gly polymorphism among patients was not significantly different from that among control subjects ($P = 0.238$). There were no statistically significant differences between homozygote Gly16 subjects vs. heterozygote and Arg16 homozygote subjects ($P > 0.05$) (Table 3).

With regards the ADRB2 Gln27Glu polymorphism, the allele frequency distribution did not differ significantly between groups ($P = 0.687$). On the other hand the genotype distribution of this polymorphism was significantly different in patients and controls ($P = 0.004$). There were more heterozygote subjects in the control group than in patients (76 vs. 54%,

TABLE 2. Genotypes and Allele Frequencies of Ser49Gly and Arg389Gly Polymorphisms of the ADRB1 Gene and Their Association With AMI

Polymorphisms	Patients (<i>n</i> = 100) (%)	Controls (<i>n</i> = 100) (%)	<i>P</i> -value	ORs (95% CI)	<i>P</i> -value	
<i>Ser49Gly (rs1801252)</i>						
Ser/Ser	84 (84%)	78 (78%)	0.429	1.00 ^a	0.454	
Ser/Gly	15 (15%)	19 (19%)		0.73 (0.35–1.54)		
Gly/Gly	1 (1%)	3 (3%)		0.31 (0.03–3.04)		
Ser/Gly+ Gly/Gly ^b	16 (16%)	22 (22%)		0.67 (0.33–1.38)		
Alleles						
Ser	183 (91.5%)	175 (87.5%)	0.032	1.00 ^a	0.192	
Gly	17 (8.5%)	25 (12.5%)		0.65 (0.34–1.25)		
<i>Arg389Gly (rs1801253)</i>						
Gly/Gly	3 (3%)	10 (10%)		1.00 ^a	0.051	
Arg/Gly	94 (94%)	90 (90%)		3.49 (0.93–3.06)		
Arg/Arg	3 (3%)	—		NC		
Arg/Gly+ Arg/Arg ^c	97 (97%)	90 (90%)		3.59 (0.96–3.47)		
Alleles						
Gly	100 (50%)	110 (55%)	0.317	1.00 ^a	0.317	
Arg	100 (50%)	90 (45%)		1.22 (0.82–1.81)		

ORs, odds ratio; CI, confidence interval; NC, not calculated.

^aReference genotype/allele.

^bComparing of subjects with Ser/Ser genotype vs. Ser/Gly+Gly/Gly genotype.

^cComparing of subjects with Gly/Gly genotype vs. Arg/Gly+Arg/Arg genotype.

TABLE 3. Genotypes and Allele Frequencies of Arg16Gly and Gln27Glu Polymorphisms of the ADRB2 Gene and Their Association With AMI

Polymorphisms	Patients (<i>n</i> = 100) (%)	Controls (<i>n</i> = 100) (%)	<i>P</i> -value	ORs (95% CI)	<i>P</i> -value
<i>Arg16Gly (rs1042713)</i>					
Gly/Gly	42 (42%)	33 (33%)	0.238	1.00 ^a	0.402
Arg/Gly	44 (44%)	45 (45%)		0.77 (0.41–1.42)	
Arg/Arg	14 (14%)	22 (22%)		0.5 (0.22–1.12)	
Arg/Gly+Arg/Arg ^b	58 (58%)	67 (67%)		0.68 (0.38–1.21)	
Alleles					
Gly	128 (64%)	111 (55.5%)		1.00 ^a	0.083
Arg	72 (36%)	89 (44.5%)		0.70 (0.47–1.05)	
<i>Gln27Glu (rs1042714)</i>					
Gln/Gln	30 (30%)	17 (17%)	0.004	1.00 ^a	0.009
Gln/Glu	54 (54%)	76 (76%)		0.40 (0.20–0.80)	
Glu/Glu	16 (16%)	7 (7%)		1.30 (0.44–3.8)	
Gln/Glu+Glu/Glu ^c	70 (70%)	83 (83%)		0.48 (0.24–0.94)	
Alleles					
Gln	114 (57%)	110 (55%)		1.00 ^a	0.687
Glu	86 (43%)	90 (45%)		0.92 (0.62–1.37)	

ORs, odds ratio; CI, confidence interval.

^aReference genotype/allele.

^bComparing of subjects with Gly/Gly genotype vs. Arg/Gly+Arg/Arg genotype.

^cComparing of subjects with Gln/Gln genotype vs. Gln/Glu+Glu/Glu genotype.

respectively) compared with the Gln27 homozygous subjects ($P = 0.009$). Moreover, there were statistically significant differences between Gln27 homozygous vs. heterozygous+Glu27 homozygous ($P = 0.03$). On the one hand there were no differences between Gln27 homozygotes vs. Glu27 homozygotes in patients and

control subjects owing to excess heterozygosity ($P = 0.635$) (Table 3).

The results of the estimated haplotype frequency analyses for the ADRB1 and ADRB2 gene polymorphisms for the groups and their association with MI are shown in Table 4. As expected, there were

TABLE 4. ADRB1 and ADRB2 Haplotype Distributions and Their Association With MI

	Patients (2n = 200) (%)	Controls (2n = 200) (%)	ORs (95% CI)	P-value
<i>ADRB1 Haplotypes</i>				
Ser49Gly389	92 (0.4575)	103 (0.5139)	1.00 ^a	
Ser49Arg389	92 (0.4575)	72 (0.3611)	1.43 (0.94–2.17)	0.920
Gly49Arg389	8 (0.0425)	18 (0.0889)	0.50 (0.21–1.20)	0.114
Gly49Gly389	8 (0.0425)	7 (0.0361)	1.28 (0.45–3.67)	0.646
<i>ADRB2 Haplotypes</i>				
Gly16Glu27	67 (0.3359)	66 (0.3319)	1.00 ^a	
Arg16Gln27	53 (0.2659)	65 (0.3269)	0.80 (0.49–1.32)	0.387
Gly16Gln27	61 (0.3041)	45 (0.2231)	1.34 (0.80–2.23)	0.269
Arg16Glu27	19 (0.0941)	24 (0.1181)	0.78 (0.39–1.56)	0.480

ORs, odds ratio; CI, confidence interval.

^aReference haplotype.

four haplotypes for the two genes. The haplotype distributions did not differ significantly between groups for either gene ($P > 0.05$).

DISCUSSION

ADRB1 gene polymorphisms have been associated with several cardiovascular phenotypes, but with some conflicting results. Ranade et al. (6) found that the ADRB1 Ser49Gly polymorphism was associated with resting heart rate and that homozygote carriers of the Ser49 allele had a higher mean heart rate compared with Gly49 homozygotes. In contrast, Humma et al. (5) revealed an association between the ADRB1 Arg389Gly polymorphism and mean resting heart rate and diastolic blood pressure. Arg389 homozygotes had a higher resting heart rate and higher diastolic blood pressure than Gly389 carriers. Such a relationship was not found for the ADRB1 Ser49Gly polymorphism (5). Similar results were found in another study that used both a case-control and a sib pair analysis design (14). In another study carried out in Sweden, the ADRB1 Ser49Gly polymorphism was found to be associated with long-term survival in patients with congestive heart failure (8). In a study carried out in a Japanese population by Nonen et al. (9), no relationship was found between ADRB1 Ser49Gly and Arg389Gly polymorphisms and heart failure.

Regarding our findings for the ADRB1 Ser49Gly polymorphism, Ulucan et al. (22) found no association between idiopathic ventricular arrhythmias and controls, and also showed a higher frequency of the homozygote Arg389 genotype (22.4%) in patients with idiopathic ventricular arrhythmias when compared with controls (1.6%). In contrast, the Arg389 homozygote genotype was not found at a higher frequency in our MI population (Table 2). Such differences in the same population may result from the different

cardiovascular diseases studied, i.e., idiopathic ventricular arrhythmias vs. MI.

Although an association between the ADRB1 Arg389Gly polymorphism and idiopathic dilated cardiomyopathy has not been found (11,12), there is an association between the ADRB1 Ser49Gly variant and idiopathic dilated cardiomyopathy (12). White et al. (32) showed no association between the ADRB1 Arg389Gly polymorphism and coronary events.

A relationship between acute myocardial infarction (AMI) and the ADRB1 Arg389Gly polymorphism was reported in a Japanese population by Iwai et al. (13). The number of homozygote carriers of the Arg389 allele was significantly higher in patients with AMI than in control subjects. In concert with this finding we found that homozygote Gly389 carriers were more frequent in the control group compared with patients. Moreover heterozygotes+homozygote Arg389 carriers were more common in patients than in control subjects, at 97 vs. 90%, respectively. The Arg389 homozygote genotype was only encountered in patients with MI. In terms of the ADRB1 Ser49Gly polymorphism, no statistically significant differences were observed between groups (Table 2).

Another main finding of our study was the difference in genotype distribution of the ADRB2 Gln27Glu polymorphism between patients with MI and controls ($P = 0.004$). The Gln27 homozygote was more frequent in patients with MI than in control subjects (30 vs. 17%, $P = 0.009$). Carriers of one or two copies of the Glu 27 allele had a decreased risk of developing MI compared with homozygote Gln27 subjects (OR = 0.48, 95% CI = 0.24–0.94, $P = 0.03$) (Table 3). In agreement with our findings, the ADRB2 Glu27 allele was shown to have a protective effect against MI in young dyslipidemic males (17). Moreover, in a study investigating the possible relationships between Arg16Gly and Gln27Glu β_2 -AR polymorphisms and the risk of cardiovascular events in older patients, homozygote carriers of the

Gln27 allele were found to have a higher risk of coronary events than Glu27 allele carriers. A similar tendency was also observed for Gly16 allele carriers (18). On the other hand, there are also reports in which no association was observed between ADRB2 gene polymorphisms and MI. Hermann et al. (15) showed that four of the ADRB2 gene polymorphisms, named C19R, T220C, Arg16Gly, Gln27Glu, were not associated with MI and hypertension. Wallerstedt et al. (19) found that neither haplotypes nor genotypes of the Arg16Gly and Gln27Glu polymorphisms in the ADRB2 gene were associated with MI in Caucasian hypertensive subjects. In another study, although the genotype distribution of the ADRB2 Gly16Arg and Gln27Glu polymorphisms was not significantly different between MI patients and control subjects, the ADRB2 Thr164Ile polymorphism was found to be significant between MI patients and control subjects (20).

Contrasting effects of the ADRB2 Gln27Glu polymorphism have been shown in several cardiovascular diseases. Stanzione et al. (33), for instance, showed that Glu27 allele carriers had an increased risk of stroke. In other study, Liggett et al. (21) found no relationship between the Arg16Gly, Gln27Glu, and Thr164Ile polymorphisms of the ADRB2 gene and chronic heart failure (CHF). In addition, Covolo et al. (8) found that the distribution of the Arg16Gly and Gln27Glu polymorphisms did not differ between CHF patients and controls. In contrast, Forleo et al. (34) observed that patients with idiopathic dilated cardiomyopathy carrying the Cys-19, Arg16 and Gln27 alleles in the β_2 -AR gene had a lower risk of heart failure. Ulucan et al. (22) indicated an association between Gln27Glu and Arg16Gly polymorphisms and idiopathic ventricular arrhythmia.

Although our results showed no relationship between the ADRB1 and ADRB2 gene haplotypes for the studied polymorphisms and MI (Table 4), some studies have shown an association between ADRB1 and ADRB2 gene haplotypes and several cardiovascular phenotypes. In a study carried out in Italy, the Gly49-Arg389 haplotype of the ADRB1 gene was shown to be significantly more frequent in patients with idiopathic dilated cardiomyopathy than in the control group (35). The Gly49-Gly389 haplotype of the ADRB1 gene was not encountered in the Italian population, whereas this haplotype was present in our study population with a frequency of 4.25% in patients and 3.61% in controls (Table 4). In a prospective cohort study by Zee et al. (20), the possible relationship between MI and the Gly16Arg, Gln27Glu and Thr164Ile polymorphisms of the ADRB2 gene and their haplotype distributions was investigated. It was shown that Gly16-Gln27-Ile164 and a combination of Arg16-Gln27-Thr164 and

Gly16-Gln27-Thr164 haplotypes were significantly associated with an altered risk of MI. Recently Shin et al. (10) showed that the risk of adverse outcomes in patients with heart failure receiving contemporary heart failure pharmacotherapy was increased by the Arg16Gln27 haplotype of the ADRB2 gene. Ulucan et al. (22) revealed a significant relationship between the Gly49-Arg389 and Ser49-Arg389 haplotypes of the ADRB1 gene and the Gly16-Gln27-Thr164, Gly16-Glu27-Thr164, and Gly16-Glu27-Ile164 haplotypes of the ADRB2 gene and idiopathic ventricular arrhythmia.

Although the ADRB1 and ADRB2 polymorphisms have previously been studied in patients with idiopathic ventricular arrhythmia in a Turkish population (22), this is the first study showing the association between MI and ADRB1 and ADRB2 gene polymorphisms in this population. Our results also showed the distribution of genotype and allele frequencies of these polymorphisms in Turkish MI patients. A larger study population will be required to clarify the exact effect of these polymorphisms on developing MI.

In conclusion, the ADRB1 gene Arg389Gly and ADRB2 gene Gln27Glu polymorphisms were found to be associated with MI in a Turkish population. Identification of the molecular mechanisms underlying the relationship between β adrenergic receptor genes and MI may help to improve the prevention and treatment of this common disease.

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