Alu polymorphisms and Myocardial infarction in the Moroccan Population

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Abstract- Background: Myocardial infarction (MI) is one of the major causes of morbidity and mortality in developed countries. Currently, it becomes increasingly more common in developing countries as Morocco. The Alu family of short interspersed elements was widely used as a highly informative tool for studying genetic structure of human populations because of their unique mutational mechanism. In this study, we aim to investigate the association between four Alu polymorphisms located at the ACE, FXIII-B, PLAT TPA-25 and APOA1 genes and the risk of MI in Moroccan population.

Methods: A total sample of 413 unrelated subjects (210 patients with a history of MI and 203 healthy individuals) were enrolled in this study. Alu polymorphisms at the ACE, PLAT, FXIII-B and APOA1 genes were determined by simple assay based on polymerase chain reaction and direct electrophoresis of its products.

Results: Alu genotypes at ACE, PLAT and FXIII-B do not show any association with IM. The most interesting association was recorded with the APOA1 polymorphism, where the Ins/Ins genotype was significantly associated with a high risk of the MI.

Conclusion: Only the Alu/APOA1 insertion/deletion polymorphism between the four Alu polymorphisms studied shows a significant association with MI and can so constitute a good genetic marker of risk of developing MI in the Moroccan population.

Index Terms- MI, Alu, Polymophisms, ApoAI

I. INTRODUCTION

Myocardial infarction (MI) is a multifactorial Coronary Artery Disease (CAD) influenced by environmental and genetic factors. They constitute nowadays a major public health problem and remains the leading cause of death worldwide [1].

MI is a disease, prevalent predominantly in developed countries, and currently becomes increasingly more common in developing countries. Collecting extensive data about epidemiology and clinical findings becomes a necessity for a better comprehension and management of MI. In addition, studies on lifestyle and risk factors as smoking, alcohol consumption, hypertension, dyslipidemia and diabetes, must be controlled to prevent the MI disease in some developing countries [2].

Currently, one of the main researchers' objectives is to define new biomarkers for early diagnosis of MI for a better prevention of susceptible individuals and to provide validated clinical methods. Recently, several researches have been conducted to establish the association of functional variants on some candidate genes with the risk of developing MI.

The Alu family elements of short interspersed sequences are ~300 bp long and are commonly found in introns, 3′ untranslated regions of genes and intergenic genomic regions[3]. They represent a set of DNA markers that are unique for studying genetic structure of human populations, and becomes widely used as a highly informative tool in different domains. Their principal characteristics reside in their stability as polymorphisms identical by descent and that their ancestral state can be known, facilitating accurate rooting of population networks [4, 5;6]. In this study, their polymorphism is used to evaluate the genetic susceptibility to CAD and MI in the Moroccan population.

The markers were selected were for their involvement in one of the main roads leading to cardiovascular disease and particularly the MI and because of the presence of an Alu polymorphism within them or in their vicinity. The first one is the insertion/deletion (I/D) of a 288bp Alu repeat sequence within the intron 16 of the Angiotensin Converting Enzyme gene (ACE c.2306-117_404, rs4340). This polymorphism has been related to approximately 50% of the variability in the ACE levels in the bloodstream, with highest values within DD homozygotes [7], and this genotype was then widely considered as a CAD risk factor [8]. In contrast, the II genotype was indirectly associated with protection against myocardial infarction [9; 7].

The second polymorphism studied is the insertion/deletion (I/D) of a 310bp Alu repeat sequence within the intron 8 of the Tissular Plasminogen Activator gene (PLAT,OMIM 173370, 8p12). The ancestral state of this variation is an absence of the insertion, as reported on the evolutionary studies in Primates [4; 10]. Several studies have shown the importance of PLAT TPA-25 gene as a potential marker of susceptibility to the MI. However, the effect of this polymorphism is still uncertain.

Another important polymorphism Alu I/D studied in the genetic susceptibility to CAD and particularly to MI is located in intron 10 of FXIII-B gene, on chromosome 1 at position 1q31-q32.1. This gene encodes for the coagulation factor XIII B subunit and with subunit A it forms the Coagulation factor XIII that is the last zymogen to become activated in the blood coagulation cascade. Deficiency of this factor can result in a lifelong bleeding tendency, defective wound healing, and habitual abortion [11].

The fourth polymorphism is an insertion/deletion of an Alu sequence localized in the 5'UTR of *ApoA1* gene coding the

major protein component of high-density lipoprotein (HDL) in plasma [12].

The aim of the present study was to examine whether these four common Alu insertion/deletion are associated or not with the risk of myocardial infarction comparing results of a group of 210 MI patients with a control group of 203 apparently healthy individuals.

II. Subjects and methods

Subjects' recruitment

A total of 413 unrelated subjects were enrolled in this study, among them, 210 patients with a history of MI recruited at the Department of Cardiology of the University Hospital IbnRochd, Casablanca, Morocco, between January 2010 and June 2013. All patients were admitted with a coronary syndrome. Cardiologists established a MI diagnosis basically upon an abnormal ECG and elevated MI biomarkers. Patients' group included 129 men and 81 women, with an age ranging between 30 and 85 years old. Ethnicity, family history, cardiovascular risk factors (alcohol, tobacco, obesity) and other related data were obtained from each patient using a standard questionnaire. The study was approved by the Ethic's Committee of the University Hospital Center Ibn Rochd, and informed consent was obtained from all enrolled subjects. The medical case of each patient included anthropometric (Age, sex, BMI, Arterial Tension) and biochemical parameters (Diabetes mellitus, glycemic, cholesterol, TG, HDL, LDL).

The healthy control sample was constituted by two hundred and three healthy individuals (118 men and 85 women) with an age ranging between 28 and 80 years, matched for sex, age, and ethnic origin, were enrolled as a group of healthy controls.

Genotyping of ACE, PLAT, FXIII-B and APOA1 gene polymorphisms:

We carried out the analysis of the polymorphism of the four autosomal Alu insertions, mostly studied at four genes of susceptibility to MI (ACE, PLAT, FXIII-B and APOA1) on the total samples enrolled in the present study. DNA was extracted from peripheral venous blood sampled from MI patients and healthy controls. The extraction of genomic DNA from the leukocyte fraction of the blood samples was carried out using the Wizard Genomic DNA Purification kit according to the manufacturer's instructions (Promega Corporation, Madison, WI, USA). The extracted DNA was stored at -20°C. The four Alu insertions were typed by PCR amplification, using primers previously established as described below and using the Mytaq HS Mix, 2x for amplification, according to the manufacturer's instructions (Bioline Reagents Ltd). The separation was carried out by electrophoresis in 2% agarose gels and staining using ethidium bromide (0.5µl/ml).

The primers sequences used for the Alu_ACE polymorphism amplification are:
Forward (5'CTGGAGACCACTCCCATCCTTTCT3'),
Reverse (5'GATGTGGCCATCACATTCGTCAGAT3'),
PCR's mix composition and thermo-cycling conditions are that used by [7]. The PCR products were 490pb for the insertion (I) allele and 190 for the deletion (D) allele.

The TPA-25_Alu sequence of the PLAT gene was typed using the pair of primers :
Forward (5´ GTG AAA AGC AAG GTC TAC CAG 3'),
Reverse (5´ GAC ACC GAG TTC ATC TTG AC- 3'), using PCR conditions described by [10] . Allelic sizes were 570pb for the I allele and 260pb for the D one.

The Alu_FXIII-B sequence was amplified using the following primers:
Forward (5'TCAACTCCATGAGATTTTCAGAAGT3'),
Reverse (5'CTGGAAAAAATGTATTCAGGTGAGT3').
PCR reactions were performed using [5] conditions and the allelic sizes were 700pb for insertion allele and 410pb for deletion.

The amplification of ApoA1_Alu sequence was performed using the following primers :
Forward (5'-AAGTGCTGTAGGCCATTTAGATTAG-3'),
Reverse (5'AGTCTTCGATGACAGCGTATACAGA-3').
PCR reaction was performed using mix composition and cycling conditions used by [4], leading to PCR products of 510pb (I) and 210pb (D).

Statistical analysis

The four Alu polymorphisms were tested for Hardy-Weinberg equilibrium in the two main samples (patients MI and controls subjects) and the alleles frequencies were compared between them using comparisons $\chi 2$tests performed by Biosys-1 program.

Quantitative variables were expressed as mean ± standard deviation (SD), and qualitative variables were expressed as percentages. Multivariate association analyses with MI risk and genotype frequencies were assessed by comparison of variable means using $\chi 2$, odds ratios (ORs) and 95% confidence intervals (CIs) for the effect of polymorphisms on MI risk in association with age, sex, smoking, drinking, hypertension, diabetes and hyperlipidemia. These statistical analyses were performed using the SPSS software (version 21). A P value of less than 0.05 was used as the criterion of statistical significance.

III. Results

Samples characteristics of the study population

Anthropometric and laboratory analysis data of the studied population are shown in Table 1.

No statistically significant difference between cases and controls was observed in terms of age (p=0.054) and of sex ratio (p=0.547). There was a highly significant difference between MI patients and healthy controls with respect to BMI (p<0.001). When comparing lipid profiles, TG, total cholesterol and LDL were significantly higher in MI patients than in controls (P <0.001), whereas serum HDL levels were significantly higher among controls (P <0.001). In addition, the average of fasting plasma glucose (FPG) in MI cases was significantly higher than that of the controls (P < 0.001). The prevalence of smokers, and individuals with diabetes or hypertension was significantly higher among the MI patients. For alcohol intake data, 13,59% of MI cases present a history of alcohol intake. So far, these data demonstrated that smoking, alcohol intake, hypertension and diabetes were the important risk factors for CAD and MI development in Moroccan population.

Multivariate associations of studied Alu with the risk of MI

Alu Polymorphic insertions concerning four autosomal genes with a presumed role in the susceptibility of CAD and MI, were genotyped in 210 MI patients and 203 healthy controls. Genotypes and allele frequency distributions are presented in table 2. Except for FXIII-B Alu in MI patient's group, all the genotype and allele frequency distributions of the four polymorphisms followed Hardy-Weinberg equilibrium proportions (p>0.05).

The ACE_Alu deletion carrier ship was without effect on the risk of MI (Table 2), neither genotype nor allele distribution show significant differences between the two samples. In addition, no correlation between genotype distribution and independently associated variables has been encountered (Table 3-4). Similar results were obtained when comparing MI patients to healthy controls for the FXIII-B_Alu insertion carrier's. However, a trend without reaching significance was observed regarding the presence of FXIII-B Del/Del in the controls group compared to MI patients (64.5% vs 55.4%, p=0.0579).

Comparison of the allele distribution of PLAT TPA-25_Alu shows a trend of association of the deletion carrier's with the risk of MI without reaching significance (p=0.0755, OR=0.779, 95% CI [0.586-1.036]). Strikingly, we found that MI patients with high levels of cholesterol are frequently carriers of at least one deletion allele (genotype Ins/Del: p=0.010; Del/Del: p=0.039).

The most interesting results were recorded in association with the APOA1 polymorphism. Indeed, genotype distribution shows that there is a significant association of the Ins/Ins genotype with a high risk of MI (p<0.001; OR=2.524, 95% CI=[1.681-3.791]). The Del/Del genotype seems to be more protective (p=0.043; OR=0.369; 95% CI=[0.140-0.970]). Those results were confirmed when comparing allele distribution, showing that insertion is significantly associated to MI when comparing MI patients with healthy controls (84,3% vs 71,2% respectively; p<0.001; OR=2.171; 95% CI=[1.547-3.049]). Correlation with BMI data shows that patients with BMI >30 Kg/m^2 are more frequently carrying the insertion than subjects with BMI <25 Kg/m^2 (80,3% vs 61,2%, respectively; p=0,026, OR=2,5; 95%CI [1,116-5,598]) (cf. supplementary data). Regarding to hypertension profile, Ins/Ins genotype carriers are frequently hypertensive compared to Ins/Del+Del/Del genotypes carriers (80,3% vs 19,7%, respectively; p=0,035; OR=2,056; 95% CI=[1,053-4,014]). Ins/Ins genotype was also correlated with hyperglycemia (p=0,004, OR=3,370; 95% CI [1,466-7,727]), with hypertriglyceridemia (p=0,020, OR=2,140; 95% CI [1,125-4,073]), with cholesterol levels (p=0,003, OR=2,750; 95%CI [1,422-5,302]).

IV. Discussion

Factors involved in atherosclerosis, thrombosis and vasoconstriction pathogenesis can contribute independently or together - depending of the genetic pools - in the development of coronary heart disease leading mostly to myocardial infarction. In this study we aim to investigate the association between polymorphic Alu insertions on four genes presenting a suspected and sometimes demonstrated susceptibility with the risk of MI (ACE, FXIII-B, PLATTPA-25 and APOA1 genes). The association between ACE I/D polymorphism and risk of myocardial infarction (MI) has been extensively studied [(13)]. It was reported that ACE I/D polymorphism could influence on the right ventricular myocardial performance index in patients with a first acute anterior myocardial infarction [14]. Our results showed the absence of any association of this polymorphism with the risk of MI in the Moroccan samples. Previous reports showed that DD genotype is associated with higher levels of circulating ACE and with high risk of MI [9; 15].

The FXIII-B gene encodes the B subunit of the factor XIII, which is a zymogen for a fibrinoligase interfering in the stabilization of blood clots. Considering its role in the formation of fibrin structure and in the regulation of fibrinolysis, its involvement in coronary artery disease, atherothrombotic, ischemic stroke, and peripheral artery disease are not surprising, and constitute a topic of intensive study [16]. However, little is known about the effect of FXIII-B I/D on coronary artery health. In this study, a trend without reaching significance was observed regarding the presence of FXIII-B Del/Del in the controls group compared to MI patients.

The most interesting results of this work were recorded in association with the APOA1 polymorphism. We found a significant association of the Ins/Ins genotype with a high risk of MI, while the Del/Del genotype seems to be protector. Although the association of the Alu polymorphism in the APOA1 gene is associated with the risk of myocardial infarction (MI) remains unclear and related data are sparse [17; 18]. The apolipoprotein AI (*APOA1*) is known for its important role played in the metabolism of triglycerides (TG) and high-density lipoproteins cholesterol (HDL-C).

Correlations of APOA1 insertion with a high BMI, hypertension, hyperglycemia and cholesterol levels data suggest the important association of this polymorphism with the risk of MI.

V. Conclusion

In this study, we investigated the association between polymorphisms of four autosomal Alu insertions on ACE, PLAT TPA-25, FXIII-B and APOA1 genes and myocardial infarction. The association was searched in groups of MI patients, compared to a group of healthy controls. Our results suggest that subjects who carry the APOA1 Ins/Ins genotype and who have hypercholesterolemia, hyperglycemia and hypertriglyceridemia may be more predisposed to the development of MI. No association between the ACE, TPA-25 and FXIII-B Alu polymorphisms and MI has been found in the Moroccan patients.

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Legend to tables

Variables		Controls	Cases (n =210)	P value
Age (Mean±SD)		57,66±10,24	59,84±11,44	0.054 NS
Sex ratio (M/F)		1,39 (118/85)	1,59 (129/81)	0.547 NS
BMI (Kg/m^2)		24,34 ± 2,14	27,49±3,93	<0.001***
Riskfactors				
	Smoking (%)	35 (17%)	73 (34,76%)	<0.001***
	Drinking (%)	NA	29 (13,59%)	-
	Diabetes (%)	18 (9%)	89 (42,58%)	<0.001***
	Hypertension (%)	68 (33,6%)	76 (36,19%)	<0.001***
FPG (g/L)		1,12±0,9	1,52±0,72	<0.001***
Triglycerides (g/L)		1,67±0,79	1,88±0,87	<0.001***
Total cholesterol (g/L)		1,64±0,86	1,82±0,48	<0.001***
LDL cholesterol (g/L)		1,2±0,2	1,45±0,39	<0.001***
HDL cholesterol (g/L)		0,45±0,4	0,37±0,1	<0.001***

*(NS: not significant differences; ***: very highly significant differences)*

Table 1: Anthropometric and laboratory analysis data

Alu polymorphisms	MCV	Healthy controls		p-value	OR
ACE					
Ins	96 (23,3%)	106 (26,1%)	Ins Vs Del	0,352 NS	0,86 [0,617-1,197]
Del	316 (76,7%)	300 (73,9%)			
Ins/Ins	12 (5,9%)	11 (5,4%)	Ins/Ins Vs Ins/Del+Del/Del	0,858 NS	1,079 [0,425-2,772]
Ins/Del	72 (34,9%)	84 (41,4%)	Ins/Ins+Ins/Del Vs Del/Del	0,219 NS	0,783 [0,519-1,179]
Del/Del	122 (59,2%)	108 (53,2%)			
FXIII-B					
Ins	98 (23,8%)	82 (20,2%)	Ins Vs Del	0.215 NS	1.233 [0.873-1.744]
Del	314 (76,2%)	324 (79,8%)			
Ins/Ins	6 (2,9%)	10 (5%)	Ins/Ins Vs Ins/Del+Del/Del	0.294 NS	0.579 [0.169-1.800]
Ins/Del	86 (41,7%)	62 (30,5%)	Ins/Ins+Ins/Del Vs Del/Del	0.056 NS	1.468 [0.968-2.229]
Del/Del	114 (55,4%)	131 (64,5%)			
TPA25					
Ins	174 (41,6%)	194 (47,8%)	Ins Vs Del	0.075 NS	0.779 [0.586-1.036]
Del	244 (58,4%)	212 (52,2%)			
Ins/Ins	41 (19,6%)	50 (24,6%)	Ins/Ins Vs Ins/Del+Del/Del	0.220 NS	0.747 [0.455-1.224]
Ins/Del	92 (44%)	94 (46,3%)	Ins/Ins+Ins/Del Vs Del/Del	0.115 NS	1,395 [0.922-2.109]
Del/Del	76 (36,4%)	59 (29,1%)			
APOAI					
Ins	354 (84,3%)	289 (71,2%)	Ins Vs Del	**0.000 *** **	2.171 [1.647- 3.049]
Del	66 (15,7%)	117 (28,8%)			
Ins/Ins	150 (71,5%)	101 (49,8%)	Ins/Ins Vs Ins/Del+Del/Del	**0.000 *** **	2.524 [1.681-3.791]
Ins/Del	54 (28,7%)	87 (42,8%)	Del/Del vs Ins/Ins+Ins/Del	**0.043 ***	0.369 [0.140- 0.970]
Del/Del	6 (2,8%)	15 (7,4%)			

*(NS: not significant differences; *: significant differences; **: highly significant differences; ***: very highly significant differences)*

Table 2: Distribution of genotype and allele frequencies

	Sexe		OR IC p-value,	Age			OR IC p-value		
	H (%)	F (%)		(a):30-49 years (%)	(b):50-69 years (%)	(c):70-85 years (%)	(a) vs (b)	(a) vs (c)	(b) vs (c)
ACE									
II	8 (6,3)	4 (5,2)	1,233 [0,359;4,239] 0,739 NS	3 (7,8)	7 (6)	2 (4)	1,335 [0,327;5,440] 0,687 NS	2,143 [0,340;13,50] 0,417 NS	1,606 [0,322;8,006] 0,564 NS
ID	42 (32,8)	30 (38,4)	0,781 [0,435;1,405] 0,41 NS	14 (36,9)	42 (36,2)	16 (30,7)	1,028 [0,481;2,198] 0,944 NS	1,313 [0,542;3,177] 0,547 NS	1,277 [0,634;2,572] 0,494 NS
DD	78 (60,9)	44 (56,4)	1,205 [0,681;2,134] 0,521 NS	21 (55,3)	67 (57,8)	34 (65,3)	0,903 [0,432;1,890] 0,787 NS	0,654 [0,277;1,542] 0,332 NS	0,724 [0,367;1,429] 0,352 NS
FXIIIB									
II	4 (3,1)	2 (2,6)	1,226 [0,219;6,854} 0,817 NS	1 (2,7)	4 (3,4)	1 (2)	0,757 [0,082;6,986] 0,806 NS	1,378 [0,083;22,75] 0,823 NS	1,821 [0,199;16,70] 0,596 NS
ID	53 (41,4)	33 (42,3)	0,964 [0,545;1,705] 0,899 NS	13 (34,2)	56 (48,3)	17 (32,7)	0,557 [0,260;1,195] 0,133 NS	1,071 [0,441;2,596] 0,880 NS	1,922 [0,969;3,810] 0,061 NS
DD	71 (55,5)	43 (55,1)	1,014 [0,576;1,786] 0,962 NS	24 (63,1)	56 (48,3)	34 (65,3)	1,837 [0,865;3,900] 0,114 NS	0,908 [0,379;2,171] 0,827 NS	0,494 [0,251;0,973] **0,041***
TPA25									
II	22 (17,1)	19 (23,7)	0,66 [0,331;1,316] 0,238 NS	8 (21,1)	26 (22)	7 (13,2)	0,944 [0,386;2,305] 0,899 NS	1,752 [0,575;5,338] 0,324 NS	1,857 [0,750;4,598] 0,181 NS
ID	54 (41,9)	38 (47,5)	0,796 [0,454;1,395] 0,425 NS	18 (47,3)	50 (42,4)	24 (45,3)	1,224 [0,587;2,550] 0,589 NS	1,088 [0,472;2,508] ; 0,844 NS	0,888 [0,463;1,706] 0,722 NS
DD	53 (41,1)	23 (28,8)	1,728 [0,951;3,142] 0,073 NS	12 (31,6)	42 (35,6)	22 (41,5)	0,835 [0,382;1,824] 0,651 NS	0,650 [0,271;1,561] 0,335 NS	0,779 [0,401;1,512] 0,460 NS
APOAI									
II	96 (74,4)	54 (66,6)	1,455 [0,792;2,672] 0,227 NS	27 (71,1)	83 (69,7)	40 (75,5)	1,065 [0,477;2,376] 0,878 NS	0,798 [0,312;2,042] 0,637 NS	0,749 [0,358;1,567] 0,443 NS
ID	29 (22,5)	25 (31)	0,65 [0,347;1,216] 0,177 NS	8 (21,1)	33 (27,7)	13 (24,5)	0,695 [0,289;1,671] 0,416 NS	0,821 [0,302;2,230] 0,698 NS	1,181 [0,561;2,483] 0,661 NS
DD	4 (3,1)	2 (2,4)	1,264 [0,226;7,063] 0,790 NS	3 (7,8)	3 (2,6)	0 (0)	3,314 [0,640;17,16] 0,153 NS	not calculated	not calculated

*(NS: not significant differences; *: significant differences; **: highly significant differences; ***: very highly significant differences)*

Table 3: Correlation between genetic data and anthropometric parameters of MI patients

	Glycémie (g/l)		**OR ; IC ; p-value**	**Cholestérol** (g/l)		**OR IC p-value**	**Triglycérides (g/l)**		**OR IC p-value**
	(a) : > 1,10	(b) : < 1,10	(a) vs (b)	(c) : > 2	(d) : < 2	(c) vs (d)	(e) : > 2	(f) : < 2	(e) vs (f)
ACE									
II	5 (8,9%)	7 (5,5%)	1,695 [0,514;5,589] 0,389 NS	7 (7,2%)	5 (5,7%)	1,277 ; [0,390;4,179] 0,686 NS	7 (6,7%)	5 (6,1%)	1,111 [0,339;3,638] 0,862 NS
ID	23 (41,1%)	43 (33,6%)	1,378 [0,722;2,630] 0,331 NS	40 (40,8%)	26 (29,5%)	1,645 ; [0,894;3,026] 0,110 NS	34 (32,7%)	32 (39%)	0,759 [0,415;1,388] 0,371 NS
DD	28 (50%)	78 (60,9%)	0,641 [0,340;1,207] 0,168 NS	51 (52%)	57 (64,8%)	0,590 ; [0,327;1,065] 0,080 NS	63 (60,6%)	45 (54,9%)	1,263 [0,703;2,271] 0,435 NS
FXIIIB									
II	1 (1,9%)	4 (3,1%)	0,564 [0,062;5,160] 0,612 NS	3 (3,1%)	2 (2,3%)	1,358 ; [0,222;8,321] 0,741 NS	3 (2,9%)	2 (2,5%)	1,188 [0,194;7,282] 0,852 NS
ID	24 (44,4%)	56 (43,1%)	1,070 [0,569;2,015] 0,833 NS	41 (41,8%)	39 (44,3%)	0,904 ; [0,505;1,616] 0,733 NS	44 (42,3%)	36 (43,9%)	0,937 [0,522;1,681] 0,827 NS
DD	29 (53,7%)	70 (53,8%)	0,987 [0,526;1,852] 0,967 NS	54 (55,1%)	47 (53,4%)	1,071 ; [0,601;1,908] 0,817 NS	57 (54,8%)	44 (53,6%)	1,047 [0,586;1,872] 0,876 NS
TPA25									
II	10 (18,5%)	30 (23,1%)	0,834 [0,383;1,817] 0,649 NS	19 (19,4%)	21 (23, 9%)	0,767 ; [0,381;1,546] 0,459 NS	21 (20,1%)	19 (23,2%)	0,839 [0,416;1,692] 0,624 NS
ID	23 (42,6%)	57 (43,8%)	0,868 [0,459;1,640] 0,663 NS	52 (53,1%)	30 (34,1%)	2,186 ; [1,208;3,955] **0,010***	47 (45,2%)	35 (42,7%)	1,107 [0,618;1,985] 0,732 NS
DD	21 (38,9%)	43 (33,1%)	1,325 [0,691;2,540] 0,397 NS	27 (27,5%)	37 (42%)	0,524 ; [0,284;0,967] **0,039***	36 (34,7%)	28 (34,1%)	1,021 [0,555;1,878] 0,947 NS
APOAI									
II	46 (85,2%)	84 (64,6%)	3,366 [1,466;7,727] **0,004****	79 (80,9%)	53 (60,3%)	2,746 ; [1,422;5,302] **0,003****	81 (77,9%)	51 (62,2%)	2,141 [1,125;4,073] **0,020***
ID	7 (13%)	41 (31,5%)	0,303 [0,126;0,727] **0,007****	16 (16,7%)	31 (35,2%)	0,386 ; [0,195;0,763] **0,006****	23 (22,1%)	25 (30,5%)	0,647 [0,335;1,253] 0,197 NS
DD	1 (1,8%)	5 (3,9%)	0,447 [0,051;3,919] 0,467 NS	2 (2,4%)	4 (4,5%)	0,438 ; [0,078;2,449] 0,347 NS	0 (0%)	6 (7,3%)	Not calculated

Table 4: Correlation between genetic data and biological status of MI patients