Med. J. Cairo Univ., Vol. 87, No. 6, September: 3961-3968, 2019
www.medicaljournalofcairouniversity.net

Cytochrome 2J2 (CYP2J2) Gene Polymorphism in Coronary Artery Disease

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Abstract

Background: Coronary artery disease is a multifactorial disease where genetic risk factors are targeted by the environmental risk factors leads to disease pathogenesis. CYP2J2 is a monooxygenase which metabolize arachidonic acid into cardioprotective compounds. Genetic polymorphisms in CYP2J2 are common especially CYP2J2*7 (rs890293) which reduce CYP2J2 gene expression and subsequently its cardioprotective effects.

Aim of Study: The aim of the present case control study to investigate the relation between CYP2J2*7 (G-50T) (rs890293) gene polymorphism and coronary artery disease (CAD) susceptibility and severity in a cohort of Egyptian individuals.

Patients and Methods: The study was conducted on 50 CAD patients and 50 age and sex-matched apparently healthy individuals. Assay of CYP2J2*7 gene SNP (rs890293) was performed by PCR amplification and Restriction Fragment Length Polymorphism (PCR-RFLP) technique.

Results: Our results revealed that the genotypic and allelic frequencies of G-50T didn't show any statistically significant association neither with the susceptibility of coronary artery disease or with the number of significantly diseased coronaries. Also no statistically significant difference between GG genotypes patients and GT genotypes patients as regard risk factors for CAD.

Conclusions: There was no significant association between CYP2J2*7 gene polymorphism (G-50T) (rs890293) and risk of coronary artery disease and also no association between this gene polymorphism and the severity of CAD in the sample of Egyptian population included in this study.

Key Words: *CAD – Cytochrome P450 – CYP2J2*7 – PCR-RFLP.*

Introduction

CORONARY Artery Disease (CAD) is a major cause of cardiovascular morbidity and mortality worldwide [1]. The mortality rate from cardiovascular diseases has been predicted to reach 36% by 2020 [2]. However, its fundamental mechanism is not totally understood till now. CAD is a multifaceted and polygenic illness resulting from interactions between various environmental influences and genetic factors [3,4]. CAD is the consequence of several risk factors, such as age, Body Mass Index (BMI), smoking, less exercise, gender, diabetes, hypercholesterolemia. In addition to these risks, it is undeniable that hereditary factors play a crucial role. Both Genome-Wide Association Studies (GWASs) and candidate gene studies have stated that there are numerous genetic variants associated with increased susceptibility to CAD [5,6].

Cytochrome P450 (CYP) enzyme 2J2 (CYP2J2) is one of the predominant CYP epoxygenase isoforms and is abundantly expressed in heart tissue [7]. In endothelial cells and cardiomyocytes, epoxyeicosatrienoic acids (EETs) are predominantly synthesized by CYP2J2 [8], which has been considered a vascular protective factor [9,10]. In CYP2J2, the G-50T (CYP2J2-76G >T; *7 allele) polymorphism in the proximal promoter disturbs a Sp 1 transcription factor binding site and brings about less CYP2J2 transcription [11]. Some previous studies have reported that the CYP2J2-50T variant allele was associated with CAD risk [11,12], but at the same time, there are many opposing published results [13-20]. Therefore, the aim of the present case control study was to evaluate the association between the G-50T (CYP2J2*7) (rs890293) gene polymorphism and CAD susceptibility and severity in a cohort of Egyptian individuals.

Subjects and Methods

Following approval by the "Ethical Committee" of Ain-Shams University and the patients' consents,

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this case control study was carried out in Ain shams University Hospitals in Egypt, during the period from August 2016 to March 2018. The study included a convenient sample of 100 subjects divided into two groups. They were 50 cases (CAD group) and 50 controls (control group). All subjects were from Egypt with both Egyptian parents.

The CAD group included 50 patients with atherosclerotic coronary artery disease confirmed by coronary angiography who were recruited from the Cardiology Department at Ain Shams University Hospitals.

They were further divided into three subgroups based on the number of affected coronary arteries with a significant luminal narrowing of 50% or more. They were divided into single vessel disease, two vessels disease and multivessel disease.

Exclusion criteria:

Patients with previous myocardial infarction or previous revascularization.

Patients with end stage renal disease or advanced liver cirrhosis.

The control group was age and sex matched healthy subjects with no clinical evidence of CAD, arterial Hypertension (HTN) or Diabetes Mellitus (DM) or any structural heart disease. They were recruited from other departments. Eligibility criteria for controls: Fully conscious, co-operative, and well-oriented with time, place, and person, who voluntary agree to participate in the study.

2- *Methodology:* All individuals in this study were subjected to full history taking, thorough clinical examination with special emphasis on cardiac examination and laboratory investigations including: Lipid profile {Total Cholesterol (TC), Triglycerides (TG), High Density Lipoprotein Cholesterol (HDL-C) and Low Density Lipoprotein Cholesterol (LDL-C)}, serum urea nitrogen (BUN), serum creatinine and finally G-50T (CYP2J2*7) (rs890293) gene polymorphism genotyping in peripheral blood using Polymerase Chain Reaction and Restriction Fragment Length Polymorphism (PCR-RFLP) technique.

3- *Study tools:*

A- Lipid profile (Total cholesterol, TG, HDL-C and LDL-C), BUN and creatinine were performed on Beckman Coulter Au 680 autoanalyzer (Beckman Instruments Inc., Scientific Instruments Division, Inc. 250 S. Kraemer Blvd. Brea, CA92634-3100, USA).

B- Genotyping of CYP2J2*7 (G-50T) (rs-890293) gene polymorphism was done in peripheral blood using Polymerase Chain Reaction and Restriction Fragment Length Polymorphism (PCR-RFLP) technique. Genomic DNA was extracted from EDTA-anticoagulated peripheral whole blood by a GeneJET DNA purification kit supplied by Thermo Scientific (168 Third Avenue, Waltham, MA, USA). Amplification of extracted DNA was done using master mix supplied by Thermo Scientific (168 Third Avenue, Waltham, MA, USA), which contains chemically modified Maxima hot start Taq DNA polymerase, optimized hot start PCR buffer, Mg^{+2}, and dNTPs (deoxynucleotide triphosphates), and the primers supplied by (Applied Biosystems, USA, Inc 850 Lincoln Centre Drive Foster City, CA 94404. USA) with the following sequence: Forward 5"- TTTTCTGAGAC-CGGTGCGTG-"3 & reverse 5"- TAGGAGAGTC-CGAGGATGGA-"3. PCR amplification started with initial activation of hot start Taq DNA polymerase for 4 minutes at 95ºC, followed by 35 cycles (95ºC for 30 seconds for DNA denaturation, 58ºC for 30 seconds for annealing and extension at 72ºC for 60 seconds) and finished by a final extension step at 72ºC for 10 minutes. The PCR reaction mixture (total volume 50 µL) contained 20 µL of DNA template, 2 µL of each primer and 25 µL of master mix, then molecular-grade H_2O was added at the end to adjust the total volume of the PCR reaction mixture to 50 µL. PCR products were then digested with the restriction enzyme AluI (Fast Digest, Thermo Scientific, 168 Third Avenue, Waltham, MA, USA) at 37ºC for 15 minutes.

Finally, the reaction mixture and the DNA ladder (50 base pair (bp)) were loaded on 2% agarose gel and the DNA fragments were separated by electrophoresis (100 volts for 30 minutes). The subject was considered homozygous mutation if two bands developed at 143-bp and 99-bp, heterozygous mutation if the three bands develop at 242-bp, 143-bp and 99-bp and wild type if only one band develops at 242 bp as shown in Fig. (1).

Statistical analysis:

Data analysis was done using IBM SPSS statistics (V. 22.0, IBM Corp., USA, 2013). Data were expressed descriptively as mean (X) ± Standard Deviation (SD) for quantitative parametric data, median and Interquartile Range (IQR) for quantitative non parametric values and as percent for qualitative data. Comparison between two groups in case of parametric data was done using Student's *t*-test while One way ANOVA (analysis of variance)

was applied for the comparison between more than two groups in case of parametric data. Mann-Whitney U-test (Wilcoxon Rank-Sum test) was used for statistical comparison between two independent sets of data if one or both of them have a skewed distribution. Kruskal-Wallis test (H-test) was applied for statistical comparison between two or more sets of data if one or more of them have a skewed distribution. As regards the categorized data Chi square test was used for comparison between the independent groups while Fisher's exact test was used instead when the expected frequency was less than 5. p-values >0.05 indicate a non-significant difference, p<0.05 indicates a significant difference, and p<0.01 indicates a highly significant difference.

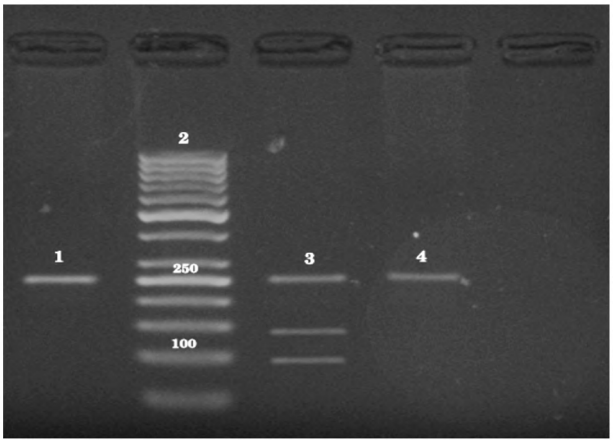

Fig. (1): Gel electrophoresis shows lane 1 and 4 are wild type with a non-digested band at 242bp, lane 2 is a ladder (50bp) and lane 3 with heterozygous mutation of CYP2J2*7 (G50T) with a digested bands at 99bp, 143bp and non-digested band at 242bp.

Results

Baseline characteristics of study population:

Table (1) showed that both CAD patients and control groups were matched regarding age and gender.

Table (1): Age and gender distribution among study groups.

Characteristic	CAD group	Control group	p-value
Age (years)	50.78± 12.04	54.24±9.46	0.113
Gender:			
Male	43 (68%)	41 (82%)	0.106
Female	16 (32%)	9 (18%)	

Clinical characteristics of the study populations:

Baseline characteristics of CAD patients are summarized in (Table 2).

Table (2): Clinical and laboratory characteristics of study population.

	CAD group (n=50)	Control group (n=50)	p-value
Family history of CAD:			
Yes	41 (82%)	0	0.002
No	9 (18%)	50 (100%)	
Smoking:			
Smoker	26 (52%)	0	0.001
Non smoker	24 (48%)	50 (100%)	
HTN:			
Yes	23 (46%)	0	0.001
No	27 (54%)	50 (100%)	
DM:			
Yes	28 (56%)	0	0.001
No	22 (44%)	50 (100%)	
Lipid profile:			
Total cholesterol (mg/dl)	190.8± 16.6	180.6±30.5	0.040
Mean ± SD	2 (4%)	41 (82%)	
<200	48 (96%)	9 (18%)	
≥200			
TG (mg/dl):			
Mean ± SD	139±28.9	124.8±40.4	0.046
<150	39 (78%)	38 (76%)	
≥150	11 (22%)	12 (24%)	
LDL (mg/dl):			
Mean ± SD	131.9± 14.8	108.3 ±23.5	0.045
<130	7 (14%)	42 (84%)	
≥130	43 (86%)	8 (16%)	
HDL (mg/dl):			
Mean ± SD	47.1 ±5.4	48.9± 15.9	0.442
>45	3 (6%)	50 (100%)	
≤45	47 (94%)	0	
Serum creatinine (mg/dl):			
Mean ± SD	0.87±0.2	1.01± 1.6	0.549
BUN (mg/dl):			
Mean ± SD	15.7±3.2	15.9±3.6	0.689
LV EF%:			
Mean ± SD	55.6± 11.2	58.7±3.2	0.075
>50%	37 (74%)	50 (100%)	
≤50%	13 (26%)	0 (0%)	
Coronary angiography:			
Single vessel disease	26 (52%)		
Two vessel disease	15 (30%)		
Multivessel disease	9 (18%)		
Arterial luminal stenosis >50%:			
LAD	38 (76%)		
RCA	22 (44%)		
LCX	17 (34%)		
LM	6 (12%)		
Gensini score:			
Range	4-20		

CAD : Coronary Artery Disease. HTN : Arterial Hypertension.
LDL : Low Density Lipoprotein. DM : Diabetes Mellitus.
HDL : High Density Lipoprotein. TG : Triglycerides.
LV EF : Left Ventricular Ejection Fraction.
LAD : Left Anterior Descending artery.
RCA : Right Coronary Artery. mg/dl : Milligrams per deciliter.
LCX : Left Circumflex artery. BUN : Blood Urea Nitrogen.
LM : Left Main coronary artery.

Laboratory investigations among study population are also summarized in (Table 2). There was a highly significant level of total cholesterol, LDL, triglyceride (p-value <0.05) in patient of CAD group compared to the control group.

Genotype distribution among the studied population:

In the CAD group: 96% of the patients (n=48) were GG genotype, 4% of the patients (n=2) were GT genotype and no patients were TT genotype. While in the control group, all subjects were GG genotype (100%). But there was no significant statistical difference in the genotype distribution of GG genotype, GT genotype and TT genotype between the two groups (p-value=0.115).

As regard Allele frequencies of the CYP 2J2*7 gene SNP (G50T), G allele was found in 98 (98%) patients in the CAD group while T allele was found in only two patients (2%). In the control group, G allele was found in all subjects (100%). But, there was no significant statistical difference in the G and T allele frequency between CAD group and control group (p-value=0.153) as shown in (Table 3).

Table (3): Distribution of CYP 2J2*7 gene SNP (G50T) alleles and genotypes in CHD patients and healthy controls.

G-50T (CYP2J2*7) (rs890293) gene polymorphism	CAD group (n=50)	Control group (n=50)	p-value
Alleles (n=100):			
G	98 (98%)	100 (100%)	0.153
T	2 (2%)	0 (0%)	
Genotypes:			
GG	48 (96%)	50 (100%)	0.115
GT	2 (4%)	0 (0%)	
TT	0 (0%)	0 (0%)	

In the CAD group, 95.1% (n=39) of males were GG genotype and 4.8% (n=2) were GT genotype. On the other hand 100% (n=9) of females were GG genotype. But there was no significant statistical difference in the genotype frequency in males and females (p-value=0.49) (Table 4).

We found that 27 out of 28 diabetic patients were GG genotype while only one patient was GT genotype. 22 out of 23 hypertensive patients were GG genotype while only one patient was GT genotype. All smokers and all patients with family history of CAD were GG genotype (Table 4).

Regarding lipid profile, there was no statistically difference between GG genotype patients and GT genotype patients (p-value >0.05) as shown in (Table 4).

Table (4): Relation between G-50T (CYP2J2*7) (rs890293) genotype polymorphism and clinical characteristics of CAD patients.

CAD group (n=50)	GG (n=48)	GT (n=2)	p-value
Age	53.92±9.34	62.00±12.73	0.241
Gender:			
Males	39 (95.1%)	2 (4.8%)	0.49
Females	9 (100%)	0 (0%)	
Family history of CAD1:			
Yes	9 (18.8%)	0 (0%)	0.49
No	39 (81.2%)	2 (100%)	
Smoking:			
Smoker	26 (54.2%)	2 (100%)	0.13
Non smoker	22 (45.8%)	0 (0%)	
HTN:			
Yes	22 (45.8%)	1 (50%)	0.908
No	26 (54.2%)	1 (50%)	
DM:			
Yes	27 (56.2%)	1 (50%)	0.861
No	21 (43.8%)	1 (50%)	
Lipid profile:			
• *Total cholesterol (mg/dl):*			
Mean ± SD	191.02±16.53	185.50±23.33	0.649
<200	41 (85.4%)	1 (50%)	0.237
≥200	7 (14.5%)	1 (50%)	
• *TG (mg/dl):*			
Mean ± SD	138.65±29.41	147.50±16.26	0.676
<150	37 (77.1%)	2 (100%)	0.745
≥150	11 (22.9%)	0 (0%)	
• *LDL (mg/dl):*			
Mean ± SD	130.19±14.65	125.50±23.33	0.478
<130	7 (14.5%)	0 (0%)	0.560
≥130	41 (85.4%)	2 (100%)	
• *HDL (mg/dl):*			
Mean ± SD	47.08±5.50	47.50±3.54	0.916
>45	45 (93.7%)	2 (100%)	0.715
≤45	3 (6.3%)	0 (0%)	
Serum creatinine (mg/dl):			
Mean ± SD	0.86±0.19	0.95±0.21	0.530
BUN (mg/dl):			
Mean ± SD	15.71±3.25	14.50±3.54	0.610
LV EF%:			
Mean ± SD	56.02±11.17	45.50±7.78	0.196
>50%	36 (75%)	1 (50%)	0.430
≤50%	12 (25%)	1 (50%)	
Coronary angiography:			
Single vessel disease	26 (54.2%)	0 (0%)	0.280
Two vessel disease	14 (29.2%)	1 (50%)	
Multivessel disease	8 (16.7%)	1 (50%)	
Arterial luminal stenosis >50%:			
LAD	36 (75%)	2 (100%)	0.417
RCA	20 (41.7%)	2 (100%)	0.103
LCX	17 (35.4%)	1 (50%)	0.626
LM	5 (10.4%)	0 (0%)	0.630
Gensini score:			
Range/median	2-20/12	8-40/24	0.441

CAD : Coronary Artery Disease. HTN: Arterial Hypertension.
DM : Diabetes Mellitus. TG : Triglycerides.
LDL : Low Density Lipoprotein. HDL : High Density Lipoprotein.
mg/dl : Milligrams per deciliter. BUN: Blood Urea Nitrogen.
LV EF : Left Ventricular Ejection Fraction.
LAD : Left Anterior Descending artery.
RCA : Right Coronary Artery.
LCX : Left Circumflex artery. LM : Left Main coronary artery.

Table (5): Clinical and laboratory characteristics of subgroups of the patient group.

	Single vessel disease (n=26)	Two vessel disease (n=15)	Multi-vessel disease (n=9)	*p*-value
Age (years)	52.5±10.1	55.5±7.8	57.3±10.3	0.352
Gender:				
Males	21 (80.8%)	12 (80%)	8 (89%)	0.837
Females	5 (19.2%)	3 (20%)	1 (11%)	
Family history of CAD:				
Yes	4 (15.4%)	3 (20%)	2 (22.2%)	0.874
No	22 (84.6%)	12 (80%)	7 (77.8%)	
Smoking:				
Smoker	15 (57.7%)	4 (26.7%)	7 (77.8%)	0.037
Non smoker	11 (42.3%)	11 (73.3%)	2 (22.2%)	
HTN:				
Yes	12 (46.2%)	7 (46.7%)	4 (44.4%)	0.994
No	14 (53.8%)	8 (53.3%)	5 (55.6%)	
DM:				
Yes	12 (46.2%)	12 (80%)	4 (44.4%)	0.081
No	14 (53.8%)	3 (20%)	5 (55.6%)	
Lipid profile:				
• *Total cholesterol (mg/dl):*				
Mean ± SD	188.4±12.1	197.7±20.5	186.1±18.7	0.145
<200	24 (92.3%)	11 (73.3%)	7 (77.8%)	0.176
≥200	2 (7.7%)	4 (26.7%)	2 (22.2%)	
• *TG (mg/dl):*				
Mean ± SD	133.3±20.5	152.3±40.4	133.4±22.1	0.104
<150	22 (84.6%)	11 (73.3%)	6 (66.7%)	0.167
≥150	4 (15.4%)	4 (26.7%)	3 (33.3%)	
• *LDL (mg/dl):*				
Mean ± SD	130.7±11.2	136.4±15.9	133.4±21.2	0.494
<130	3 (11.5%)	2 (13.3%)	2 (22.2%)	0.726
≥130	23 (88.5%)	13 (86.7%)	7 (77.8%)	
• *HDL (mg/dl):*				
Mean ± SD	48±4.34	47.9±5.1	43.2±7.43	0.057
>45	26 (100%)	14 (93.3%)	7 (77.8%)	0.053
≤45	0 (0%)	1 (6.7%)	2 (22.2%)	
Serum creatinine (mg/dl):				
Mean ± SD	0.87±0.19	0.83±0.17	0.94±0.19	0.343
BUN (mg/dl):				
Mean ± SD	16.19±3.20	14.73±3.26	15.67±3.32	0.388
LV EF%:				
Mean ± SD	57.92±9.84	53.13±12.05	53.00±13.17	0.317
>50%	22 (84.6%)	9 (60%)	6 (66.7%)	0.192
≤50%	4 (15.4%)	6 (40%)	3 (33.3%)	
Arterial luminal stenosis >50% by coronary angiography:				
LAD	17 (65.4%)	12 (80%)	9 (100%)	0.101
RCA	8 (30.8%)	8 (53.3%)	6 (66.7%)	0.119
LCX	1 (3.8%)	8 (53.3%)	9 (100%)	0.000
LM	0 (0%)	2 (13.3%)	3 (33.3%)	0.014
Gensini score:				
Range/median	3-6/5	12-20/14	28-120/39	0.000

CAD : Coronary Artery Disease. HTN : Arterial Hypertension.
DM : Diabetes Mellitus. TG : Triglycerides.
LDL : Low Density Lipoprotein. HDL : High Density Lipoprotein.
mg/dl : Milligrams per deciliter. BUN : Blood Urea Nitrogen.
LV EF: Left Ventricular Ejection Fraction.
LAD : Left Anterior Descending artery.
RCA : Right Coronary Artery.
LCX : Left Circumflex artery. LM : Left Main coronary artery.

Subgroup analysis in CAD group:

Risk factors for CAD and laboratory details for subgroups are depicted in (Table 5).

100% of patients with single vessel disease (n= 26) were GG genotype. 93.3% of patients with two vessel disease (n=14) were GG genotype and 6.7% (n=1) were GT genotype. While 88.9% of patients with multivessel disease (n=8) were GG genotype and 11.1% (n=1) were GT genotype. There was no significant statistical difference in the genotype distribution of patients with single vessel disease when compared to patients with two vessel and multi vessel coronary artery disease (*p*-value=0.28) as shown in (Table 6).

As regard Allele Frequencies, G allele was found in all patients (100%) with single vessel disease. While G allele was found in 96.7% of patients with two vessel disease (n=29) and T allele was found in only one patient (3.3%). In patients with multivessel disease, G allele was found in 94.4% of patients (n=17) and T allele was found in only one patient (5.6%). But, there was no significant statistical difference in the G and T allele frequency among the three subgroups (*p*-value=0.28) (Table 6).

Table (6): Distribution of CYP 2J2*7 gene SNP (G50T) alleles and genotypes in subgroups of CAD patients.

G-50T (CYP2J2*7) (rs890293) gene polymorphism	Single vessel disease (n=26)	Two vessel disease (n=15)	*p*-value
Alleles:			
G	52 (100%)	29 (96.7%)	0.280
T	0 (0%)	1 (3.3%)	
Genotypes:			
GG	26 (100%)	14 (93.3%)	0.287
GT	0 (0%)	1 (6.7%)	
kTT	0 (0%)	0 (0%)	

Discussion

CYP2J2 gene, is a unique member of the 2J subfamily of cytochrome P450-containing epoxygenases **[21]**. Cytochrome P450 (CYP) enzyme 2J2 (CYP2J2) is one of the predominant CYP epoxygenase isoforms and is abundantly expressed in heart tissue, endothelial cells and cardiomyocytes. EETs, synthesized by CYP2J2, have many important physiological actions including maintaining cardiomyocyte viability suffering from damaging stimuli and enhance the recovery of cells from oxygen deprivation **[22]**.

In CYP2J2, the G-50T SNP (rs890293) in the proximal promoter disturbs a Sp1 transcription factor binding site with a considerable decrease in

activity of the promoter in the CYP2J2 gene, followed by a decrease in CYP2J2 protein and EETs generation [23].

In view of the above data, the study aimed to investigate the clinical utility of the CYP2J2*7 gene polymorphism (G-50T) (rs890293) in a cohort of Egyptian individuals in order to explore their association with CAD susceptibility or its severity. The study was conducted on 100 subjects included 50 CAD patients and 50 age and sex matched apparently healthy control subjects at Ain Shams University Hospitals.

The current study revealed that the genotypic and allelic frequencies of G-50T were not statistically significant different between CAD patients' group and the control group (p=0.115 and 0.153, respectively). These results are in agreement with those of Zhu et al., [13] and Chen et al., [24] done on Chinese population.

Zhu et al., [13] reported that CYP2J2*7 (G-50T) polymorphism did not reveal a significant role in the development of coronary artery disease and myocardial infarction by being present in 8.9% (51/521) of CAD patients versus 9.7% (44/411) in the control group.

On the contrary to our study, Spiecker et al., [11] who studied the association between CYP2J2*7 (G-50T) polymorphism and coronary artery disease in German population and reported a significant association between CYP2J2*7 polymorphism (G-50T) and coronary artery disease being present in 17.3% (50/289) of CAD patients versus 10.6% (27/255) in the control group. Also, a study on Taiwanese population performed by Yen et al., [25] showed a significant association between CYP-2J2*7 (G-50T) polymorphism and premature MI being present in 32% (64/200) of MI patients versus 22% (44/200) in control group. Moreover, they reported that in vascular endothelial cells, the (G-50T) polymorphism was associated with a 50% reduction in CYP2J2 promoter activity compared with that of the wild type promoter. As a consequence, individuals with the CYP2J2*7 (G-50T) polymorphism had significantly lower plasma (EETs), compared to wild type individuals [11,25].

Lee et al., [17] investigated the association between CYP2J2 (G-50T) polymorphism and CAD and reported that the CYP2J2 G-50T polymorphism was associated with significantly lower risk of coronary artery disease in African-Americans however, no significant association was observed in Caucasians.

The discrepancies of results between our study and those of the mentioned researchers may be attributed not only to different study designs and sample sizes but also to the ethnic variation. Moreover, it became evident that single-locus effects cannot explain multifactorial chronic diseases. Thus, when the single polymorphism effect is not present alone or is not strong enough, it is important to characterize the other gene polymorphisms related to susceptibility. Another explanation for that discrepancy was given by Sato et al., [26] who reported that reduced P450-mediated EETs biosynthesis could have protective effects against the development of CAD clinical events. They also stated that despite the well-characterized vasodilator and anti-inflammatory effects of EETs, evidence has demonstrated that increased EETs generation also significantly increases Matrix Metalloproteinases (MMPs) enzyme activity in endothelial cells. The matrix metalloproteinase are potent stimulators of vascular remodeling and atherosclerotic plaque destabilization, and are integrally involved in the precipitation of plaque rupture and acute cardiovascular events [26].

Furthermore, the current study did not find any significant association of G50T genotypes and alleles with smoking, hypertension, diabetes mellitus as well as, hyperlipidemia and positive family history of CAD in the study population. In that respect, these results are in accordance with those previously obtained by Zhu et al., [13].

One of the main aims of the current study was to clarify if there is an association between CYP2J2*7 (G-50T) SNP and CAD disease severity. The current study revealed a non-significant association of the G-50T genotypes and alleles with CAD severity neither with the number of atherosclerotic coronaries nor with Gensini score. In accordance with our findings, Lung et al., [16] had reported that there was no consistent relationship between the G50T genotypes and alleles and the number of significantly diseased coronaries. Addition of Gensini score may add better assessment for severity of CAD in each patient in the current study than numbering only significant diseased coronaries.

Conclusion:

Our study had demonstrated that there was no significant association between CYP2J2*7 gene polymorphism (G-50T) (rs890293) and risk of coronary artery disease and also no association between this gene polymorphism and the severity of CAD in the sample of Egyptian population included in this study.

Declaration of conflicting interests:

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

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تقييم إرتباط تعدد آشكال جين G-50T (CYP2J2) بمرض الشريان التاجى

خلفية: يمثل تصلب الشرايين وما يترتب عليه من تكون الجلطة الشريانية على اللويحة العصيدية المتمزقة الآلية الرئيسية المسؤولة عن حدوث آمراض الشرايين التاجية وقد إكتسبت الحاجة إلى تحديد عوامل الخطر بآمراض القلب والآوعية الدموية قدراً كبيراً من الإهتمام فى السنوات الآخيرة. إن السيتوكروم هو إنزيم موجود بشكل رئيسى فى الآنسجة خارج الكبد، موجود بوفرة فى القلب والآوعية الدموية. ويتم التمثيل الغذائى لحمض الآراكيدونيك عن طريق السيتوكروم إبوكسيجيناز إلى التى لها تآثيرات بيولوجية مختلفة، خاصة فى القلب والآوعية علاوة على ذلك، إنه موجود بدرجة كبيرة فى الخلايا الدموية.

\الهدف: هدفت الدراسة الحالية إلى تقييم إرتباط تعدد آشكال جين G-50T (CYP2J2) بمرض الشريان التاجى.

\المواد وطرق \البحث: تم تجميع العينات من ٥٠ من المرضى فى قسم آمراض القلب فى مستشفيات جامعة عين شمس و٥٠ فرداً من الآصحاء المتكافئين مع المرضى فى السن والجنس. تم تشخيص مرضى الشريان التاجى وفقاً للفحص السريرى وقسطرة تصوير الآوعية التاجية وتم تصنيف مرضى الشريان التاجى وفقاً لقسطرة تصوير الآوعية التاجية طبقاً لعدد الشرايين المصابة إلى ٣ مجموعات فرعية، مرضى يعانون من المرض فى وعاء دموى واحد، وعائين دمويين ومرضى يعانون بثلاثة آوعية ودراسة تعدد آشكال الجين تمت بإستخدام تفاعل البلمرة المتسلسل وتقنية تعدد آطوال قطع التقييد فى الدم.

\النتائج: وكشفت نتائجنا آن الشكل الجينى T والنسخة الجينية G-50T (CYP2J2) لم يظهروا إرتباط ذو دلالة إحصائية بمرض الشريان التاجى.

\الخلاصة: فى الختام، آظهرت دراستنا عدم وجود إرتباط ذو دلالة إحصائية بين تعدد الآشكال الجينية ووجود وشدة مرض الشريان التاجى فى عينة المصريين المدرجة فى دراستنا.