# Association of platelet endothelial cell adhesion molecule-1 gene polymorphism (Leu125Val) with coronary artery disease in type II diabetics and nondiabetics

Maha M.S. El-Kishki[a], Amal M. Abdelfattah Alramly[a], Mohamed O. Taha[b], Rana A. El Din Medhat[c]

***Background and objectives*** Platelet endothelial cell adhesion molecule-1 (PECAM-1) plays a key role in the transendothelial migration of circulating leukocytes (diapedesis) during vascular inflammation. Polymorphism (Leu125Val) of the *PECAM-1 gene* (373C/G) is functional. It was reported to be associated with high serum level of PECAM-1. We hypothesized that this genetic variation of the *PECAM-1 gene* could be associated with the development of atherosclerosis. Therefore we conducted a study to investigate the association between single-nucleotide polymorphism of the *PECAM-1 gene*, C+373G (Leu125Val) at exon 3, in Egyptian patients with coronary artery disease.

***Patients and methods*** Blood samples were withdrawn from 40 coronary artery disease patients and 20 age-matched and sex-matched controls. The single-nucleotide polymorphism of the *PECAM-1 gene* was analyzed by PCR-restriction fragment length polymorphism strategy.

***Results*** Genotype distributions between patient and control groups showed no significant statistical difference regarding the CC genotype, where 22.5% of patients and 35% of controls carried this genotype ($P$=0.470). As for the CG genotype, a statistically significant higher CG genotype distribution was found in patients, where 52.5% of patients and only 20% of controls carried this genotype ($P$=0.033). There was no statistically significant difference in GG distributions between patient and control groups, where 25% of patients and 45% of controls carried this genotype ($P$=0.202). No significant statistical difference was observed in allele frequency between the two groups, where 51.25% of patients and 55% of controls carry the G allele and 48.7% of patients and 45% of controls carry the C allele ($P$=0.846).

***Interpretation and conclusion*** We concluded that our study demonstrated a possible effect of PECAM-1 (Leu125Val) polymorphism on the development of atherosclerosis.

*Sci J Al-Azhar Med Fac, Girls* 2019 3:23–32



**The Scientific Journal of Al-Azhar Medical Faculty, Girls** 2019 3:23–32

**Keywords:** atherosclerosis, coronary artery disease, gene polymorphism, platelet endothelial cell adhesion molecule-1, type 2 diabetes mellitus

[a]Department of Clinical Pathology, Al-Azhar University, [b]Department of Cardiology, National Heart Institute, [c]Department of Clinical Pathology, National Institute of Diabetes and Endocrinology, Cairo, Egypt

Correspondence to Rana Alaa ElDin Medhat, MSc, Fifth Settlement, Working in National Institute of Diabetes and Endocrinology, Cairo, Egypt.
Tel: 01224247277;
e-mail: dr.rana_86@hotmail.com

**Received** 20 September 2018 **Accepted** 8 October 2018

## Introduction

Atherosclerosis represents the etiological factor of coronary artery disease (CAD), causing narrowing of the coronary arteries which results to myocardial ischemia. CAD is regarded as a complex, multifactorial disease where genetic as well as environmental factors strongly interplay in its pathogenesis [1]. It is undeniable that type 2 diabetes mellitus (DM), which has become a modern-day disease, significantly accelerates the progress of atherosclerosis and thus increases the risk of CAD [2].

Atherosclerosis is characterized by a chronic nonresolving low-grade sterile inflammation of the arterial wall where inflammatory macrophages are the most abundant immune cells within the atherosclerotic plaques, originating from circulating monocytes [3]. Leukocyte adhesion and their transendothelial migration is regulated by various types of adhesion molecules such as platelet endothelial cell adhesion molecule-1 (PECAM-1), intercellular adhesion molecule-1, and vascular cell adhesion molecule-1 [4]. PECAM-1, also called CD31, is a transmembrane glycoprotein (relative molecular weight 130 kDa) which belongs to the Ig superfamily. PECAM-1 is expressed on the surface of circulatory platelets, monocytes, neutrophilic granulocytes, and subgroup of T cells. *PECAM-1 gene* is located at the end of the long arm of chromosome 17 (17q23) [5].

PECAM-1 homophilic interactions, which are mediated by the first $NH_2$-terminal Ig homology domain, are primarily responsible for leukocyte transmigration. The first Ig domain of PECAM-1 is encoded by the third exon of the *PECAM-1 gene* [6]. A mutation in the *PECAM-1 gene* in exon 3 at position +373 involves a C>G substitution, causing a leucine to valine substitution at position 125 (rs668). This

polymorphism might affect the homophilic binding capability and influence individual susceptibility to the development of atherosclerosis. Using the mouse model, the effect of PECAM-1 deficiency (double knockout mice model without the presence of the *PECAM-1 gene*), reduced atherosclerotic lesions were reported [4]. The purpose of this study was to investigate an association between Leu125Val polymorphism of *PECAM-1 gene* and the occurrence of coronary atherosclerosis.

## Patients and methods

### Patients

The study included 40 selected patients (27 men and 13 women) with CAD in the age range of 35–73 years. These CAD patients attended the Outpatient Clinic and Emergency Department of National Heart Institute and were angiographically defined (having 1, 2, 3, or more major coronary arteries with ≥70% luminal stenosis). The patients were subgrouped according to the presence of DM into 20 diabetics and 20 nondiabetics and according to the presence of dyslipidemia (hypercholesterolemia) into 17 hypercholesterolemics and 23 normocholesterolemics.

As our study investigates the effect of PECAM-1 polymorphism in the presence and absence of type 2 DM on the development of atherosclerosis, other factors that could contribute to atherosclerosis should be excluded from the study such as hypertension and smoking. Given the frequency of hypertension and secondary diabetes seen with acromegalics, it is likely that these patients are at an increased risk for developing atherosclerosis and thus were excluded from the study. As for cocaine addicts, mismatch between myocardial oxygen supply and demand from cocaine-induced vasoconstriction, that is not due to coronary atherosclerosis, and increased myocardial workload are often invoked as the major postulated mechanism by which cocaine induces myocardial ischemia and were therefore excluded from the study.

The control group included 20 age-matched and sex-matched unrelated healthy volunteers including 11 men and nine women in the age range of 36–75 years, with no history of angina pectoris or MI having normal ECG, free from DM with normal lipid profile.

Our study was approved by the Institutional Review Board of Al-Azhar University and oral informed consent was obtained from all participants.

All participants in the study were subjected to full history taking as well as clinical examination, which included blood pressure measurement, pulse rate, breathing rate, chest examination, and cardiac auscultation. Patient groups were subjected to angiography to assess the number of stenosed coronary vessels, and ECG and echocardiography to mark ischemic changes. Control groups were subjected to ECG only. All participants performed routine laboratory investigations, such as lipid profile which includes total cholesterol (TC), triglycerides, high-density lipoprotein (HDL) and low-density lipoprotein, cardiac biomarkers such as creatine kinase MB and troponin I, random blood glucose, glycated hemoglobin (HbA1c) and microalbumin were also done.

### Screening for *PECAM-1 gene* polymorphism

Molecular detection of *PECAM-1 gene* polymorphism (Leu125Val) was done using the PCR-restriction fragment length polymorphism method. Genomic DNA was extracted from white blood cell pellets using QIAamp DNA Blood Mini Kit (QIAGEN, Hilden, Germany). Each extracted DNA sample was subjected to amplification by using Taq PCR Master Mix Kit (Cat. No. 102443; QIAGEN) and *PECAM-1 gene* polymorphism primers which included a pair of oligonucleotide primers, forward (5′-CTATCA GCCTGGCCCTGTAG-3′)/reverse (5′-TATTCA CGCCA- CTGTGTGCT-3′), with a product size of 504 nucleotides covering the single-nucleotide polymorphism (SNP) C+373G (Leu125Val) at exon 3. The conditions for PCR were initial denaturation at 95°C for 4 min followed by 40 cycles of amplification consisting of denaturation at 95°C for 30 s, annealing at 62°C for 45 s, extension at 72°C for 60 s, and a final extension at 72°C for 7 min. The amplified DNA was digested by using the PvuII restriction enzyme whose recognition sequence is 5′ . . . CAG CTG . . . 3′. Digested PCR products were subjected to agarose gel electrophoresis. An ultraviolet transilluminator was then used to view DNA that has been isolated by electrophoresis. Agarose gel contained a fluorescent colur (ethidium bromide), which binds to the nucleic acid. Exposure of the colored gel to UVB light causes DNA/color to fluoresce which was then measured by the detector and visualized as a band on screen. Genotyping of PECAM-1 C+373G (Leu125Val) polymorphism showing the possible genotypes when the PvuII enzyme was used were homozygous GG genotype if: two bands develop at 420 and 84 bp, heterozygous CG genotype if: the two bands develop at 504 and420 bp.

**Table 1 Statistical comparison between patient and control groups according to laboratory data**

| Laboratory data | Patients (*N*=40) | Control (*N*=20) | *t* test | *P* value |
|---|---|---|---|---|
| TC (mg/dl) | | | | |
| Mean±SD | 186.45±56.01 | 154.20±20.31 | 6.178 | 0.016 |
| Range | 113–339 | 110–192 | | |
| TG (mg/dl) | | | | |
| Mean±SD | 115.98±60.57 | 108.20±26.63 | 0.299 | 0.587 |
| Range | 48–364 | 55–148 | | |
| HDL (mg/dl) | | | | |
| Mean±SD | 46.10±7.65 | 52.50±9.00 | 8.291 | 0.006 |
| Range | 27–60 | 38–65 | | |
| LDL (mg/dl) | | | | |
| Mean±SD | 117.03±47.58 | 80.05±16.37 | 11.324 | <0.001 |
| Range | 47–226 | 52–100 | | |
| RBS (mg/dl) | | | | |
| Mean±SD | 145.63±63.92 | 105.60±21.70 | 7.362 | 0.009 |
| Range | 75–310 | 74–155 | | |
| HbA1c % | | | | |
| Mean±SD | 6.12±1.49 | 5.14±0.40 | 8.291 | 0.006 |
| Range | 4.3–9.1 | 4.5–6 | | |

HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RBS, random blood sugar; TC, total cholesterol; TG, triglycerides.

Homozygous CC genotype if: only the band develops at 504 bp.
The first band on the left (504 bp), homozygous CC.
The next band (420 bp), homozygous GG.
The last bands on the right (420 and 504 bp), heterozygous CG.
DNA ladder on the right.

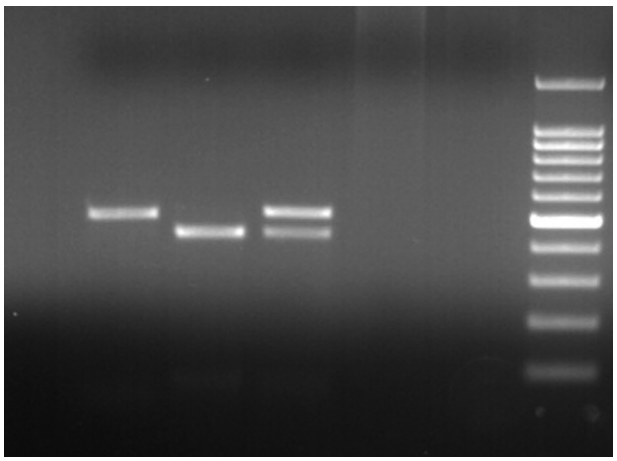
### Statistical analysis

Data were analyzed using the Statistical Program for the Social Sciences, version 20.0 (IBM Corp., New York, USA). Quantitative data were expressed as mean ±SD. Qualitative data were expressed as frequency and percentage. Independent samples *t* test of significance was used when comparing between two means. Paired sample *t* test of significance was used when comparing between related samples. Mann–Whitney *U* test: for two-group comparisons in nonparametric data. A one-way analysis of variance when comparing between more than two means. $\chi^2$ test of significance was used in order to compare proportions between two qualitative parameters. The confidence interval was set to 95% and the margin of error accepted was set to 5%, so a *P* value less than 0.05 was considered significant; *P* value less than or equal to 0.001 was considered as highly significant, and a *P* value more than 0.05 was considered insignificant.

## Results

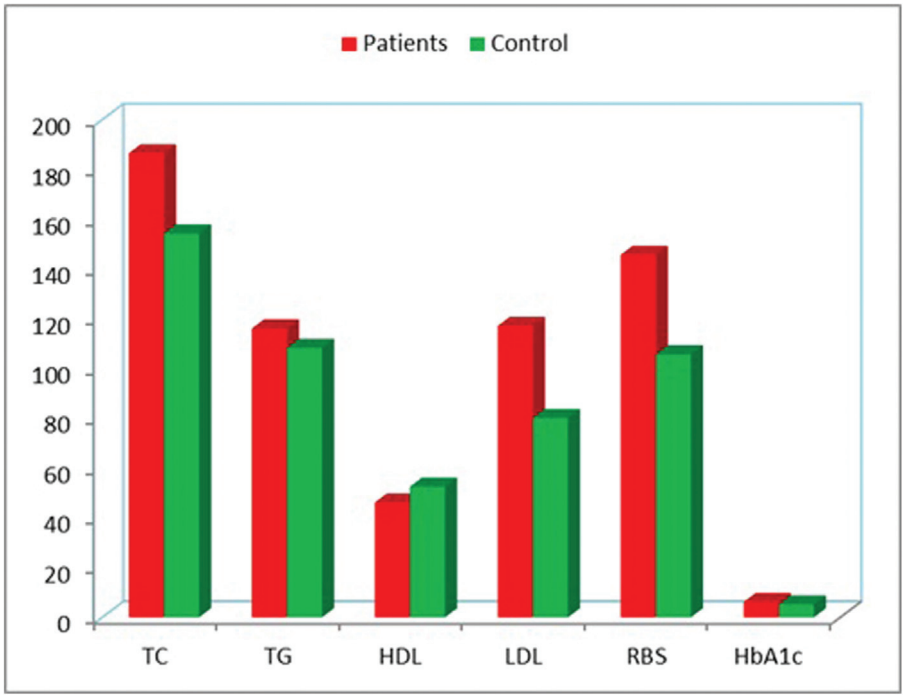
As shown in Table 1 and Figs 1 and 2, the mean±SD of TC and HDL concentrations were 186.45±56.01 and 46.10±7.65, respectively, in patients, which showed a significant difference with TC and HDL mean±SD of controls 154.20±20.31 and 52.50±9.00, respectively, where *P* value=0.016 for TC and 0.006 for HDL. Similarly, random blood sugar (RBS) and HbA1c mean±SD for patients 145.63±63.92 and 6.12±1.49, respectively, showed a significant statistical difference with RBS and HbA1c mean±SD of controls 105.60 ±21.70 and 5.14±0.40, respectively, where *P* value=0.009 for RBS and 0.006 for HbA1c. However, the mean±SD of low-density lipoprotein concentration, which was 117.03±47.58, in the patients' group showed a highly significant difference than that of the control group which was 80.05±16.37, with a *P* value of less than 0.001. In contrast, when

**Figure 1**



DNA bands in different genotypes.

**Figure 2**




Bar chart showing Laboratory data.

**Table 2 Statistical comparison between patient and control groups according to the genotype**

| Genotype | Patients (*N*=40) [*n* (%)] | Control (*N*=20) [*n* (%)] | $\chi^2$ | *P* value |
|---|---|---|---|---|
| CC | 9 (22.5) | 7 (35.0) | 0.522 | 0.470 |
| CG | 21 (52.5) | 4 (20.0) | 4.534 | 0.033 |
| GG | 10 (25) | 9 (45.0) | 1.627 | 0.202 |
| Allele frequency% | *N*=80 | *N*=40 | | |
| C | 39 (48.75) | 18 (45) | 0.038 | 0.846 |
| G | 41 (51.25) | 22 (55) | | |

comparing mean±SD of triglycerides concentration in patients 115.98±60.57 and controls 108.20±26.63, there was no statistically significant difference (*P*=0.587).

Table 2 and Fig. 3 show a statistical significance in heterozygous genotype distribution, where 52.5% of patients and only 20% of controls carry the CG genotype (*P*=0.033). However, there was no significant statistical difference in allele frequency between the two groups (*P*=0.846).

Table 3 shows nonsignificant deviations between observed genotype distributions in the patient group and expected distributions, which is calculated by the Hardy–Weinberg equilibrium.

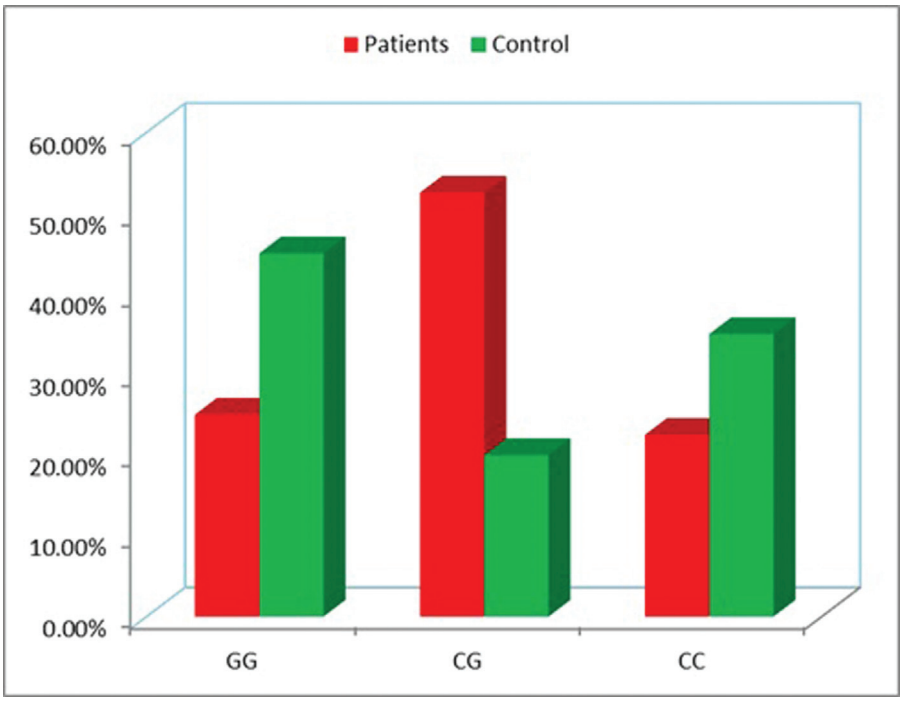
Table 4 shows the expected genotype distribution in the control group, which is calculated by the Hardy–Weinberg equilibrium, revealing significant deviations in the expected values of genotype CG and GG distributions, 48 and 16%, respectively, from the observed CG and GG distributions which are 20 and 45%, respectively. *P* value equals 0.006 for CG and 0.003 for GG. No significant difference in the CC genotype where the expected value is 36% and the observed value is 35% (*P*=0.917).

Table 5 shows a statistical comparison between the number of stenosed vessels by angiography and demographic data as well as laboratory data, revealing insignificant correlations, where the *P* value is always more than 0.05 in each compared item.

Table 6 and Fig. 4 show the relation between the number of stenosed vessels by angiography among CAD patients and genotypes. An insignificant association was found between the number of stenosed vessels and genotypes, where *P* value=0.610.

Table 7 shows statistical comparison between genotypes of patients and demographic data as well as laboratory data. No significant statistical difference

**Figure 3**




Bar chart between groups according to genotype.

**Table 3 Observed genotype distribution and expected distribution according to the Hardy–Weinberg equilibrium among the patient group**

| Genotype | Observed (%) | Expected (%) | $\chi^2$ | *P* value |
|---|---|---|---|---|
| CC | 22.5 | 24 | 0.004 | 0.953 |
| CG | 52.5 | 49 | 0.023 | 0.881 |
| GG | 25 | 27 | 0.004 | 0.998 |

**Table 4 Observed genotype distribution and expected distribution according to the Hardy–Weinberg equilibrium among the control group**

| Genotype | Observed (%) | Expected (%) | $\chi^2$ | *P* value |
|---|---|---|---|---|
| CC | 35 | 36 | 0.011 | 0.917 |
| CG | 20 | 48 | 7.531 | 0.006 |
| GG | 45 | 16 | 8.598 | 0.003 |

was observed between genotype groups and demographic data as well as laboratory data except for TC. There was significantly higher TC in the CC genotype group (213.00±54.89) as compared with mean±SD of CG and GG genotype groups, which are 179.00±58.74 and 178.20±48.38, respectively ($P$=0.027), as shown in Fig. 5. Table 7 also reveals that the % of hypercholesterolemics in the CC genotype group is 77.8% which shows a significant difference than the % of hypercholesterolemics present in CG and GG genotype groups, which are 33.3 and 30.0, respectively ($P$=0.047), also shown in Fig. 6. However, there is no significant statistical difference between genotypes in diabetic and nondiabetic groups, where the *P* value is more than 0.05, also shown in Fig. 7.

## Discussion

Cell adhesion molecules mediate inflammatory cell aggregation and adhesion to endothelial cells, which are important initial steps in the development of atherosclerosis. PECAM-1, as a CAM expressed on endothelial cells and circulating monocytes, plays an important role in the atherosclerotic inflammatory process, by mediating cell adhesion and transendothelial migration of monocytes to the intimal layer of coronary arteries [7].

Genetic variants of PECAM-1 such as single-nucleotide polymorphism (C373G) in exon 3 of the *PECAM-1 gene* at codon 125 which causes a mutation of leucine to valine (Leu125Val) might influence susceptibility to CAD. The first IgG domain of PECAM-1 is encoded by the third exon of the *PECAM-1 gene* that contains the Leu125Val polymorphism which may affect monocyte/endothelial homophilic binding capability of PECAM-1, with more monocyte adherence to endothelium and transendothelial migration to the intima [6].

Our study aims to evaluate the effect of Leu125Val polymorphism of the *PECAM-1 gene*, as a novel genetic biomarker, in the development of atherosclerosis in CAD patients, using the PCR-restriction fragment length polymorphism strategy.

**Table 5 Statistical relation between angiography according to demographic data and laboratory data in the patient group**

| | Angiography | | | $F/\chi^2$ | *P* value |
|---|---|---|---|---|---|
| | Vessel I (*N*=13) | Vessel II (*N*=16) | Vessel III (*N*=11) | | |
| Age (years) | | | | | |
| Mean±SD | 52.38±8.03 | 52.13±9.19 | 57.09±10.30 | 1.122 | 0.337 |
| Range | 39–63 | 35–66 | 41–73 | | |
| Sex [*n* (%)] | | | | | |
| Male | 7 (53.8) | 12 (75.0) | 8 (72.7) | 1.652 ($\chi^2$) | 0.438 |
| Female | 6 (46.2) | 4 (25.0) | 3 (27.3) | | |
| TC (mg/dl) | | | | | |
| Mean±SD | 171.08±40.69 | 175.31±55.35 | 220.82±62.04 | 3.201 | 0.052 |
| Range | 122–239 | 113–264 | 148–339 | | |
| TG (mg/dl) | | | | | |
| Mean±SD | 102.54±48.42 | 103.19±38.77 | 150.45±86.22 | 2.669 | 0.083 |
| Range | 48–232 | 54–165 | 72–364 | | |
| HDL (mg/dl) | | | | | |
| Mean±SD | 47.23±6.61 | 43.44±6.60 | 48.64±9.50 | 1.785 | 0.182 |
| Range | 37–58 | 27–56 | 30–60 | | |
| LDL (mg/dl) | | | | | |
| Mean±SD | 103.23±35.00 | 111.06±49.96 | 142.00±51.21 | 2.338 | 0.111 |
| Range | 61–160 | 47–198 | 88–226 | | |
| RBS (mg/dl) | | | | | |
| Mean±SD | 137.77±64.64 | 139.25±64.39 | 164.18±64.64 | 0.629 | 0.539 |
| Range | 75–273 | 75–310 | 99–277 | | |
| HbA1c % | | | | | |
| Mean±SD | 6.00±1.36 | 5.85±1.37 | 6.66±1.79 | 1.034 | 0.366 |
| Range | 4.3–8.2 | 4.5–9.1 | 4.4–9.1 | | |
| Microalbumin (mg/dl) in the diabetic group (20) [*n* (%)] | | | | | |
| >30 | 3 (42.9) | 2 (33.3) | 4 (57.1) | 0.76 ($\chi^2$) | 0.684 |
| <30 | 4 (57.1) | 4 (66.7) | 3 (42.9) | | |
| DM | | | | | |
| Diabetics | 7 (53.8) | 6 (37.5) | 7 (63.6) | | |
| Nondiabetics | 6 (46.2) | 10 (62.5) | 4 (36.4) | | |
| Hyperlipidemia | | | | | |
| Normocholesterolemia | 8 (61.5) | 10 (62.5) | 5 (45.5) | 0.904 ($\chi^2$) | 0.636 |
| Hypercholesterolemia | 5 (38.5) | 6 (37.5) | 6 (54.5) | | |

DM, diabetes mellitus; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RBS, random blood sugar; TC, total cholesterol; TG, triglycerides.

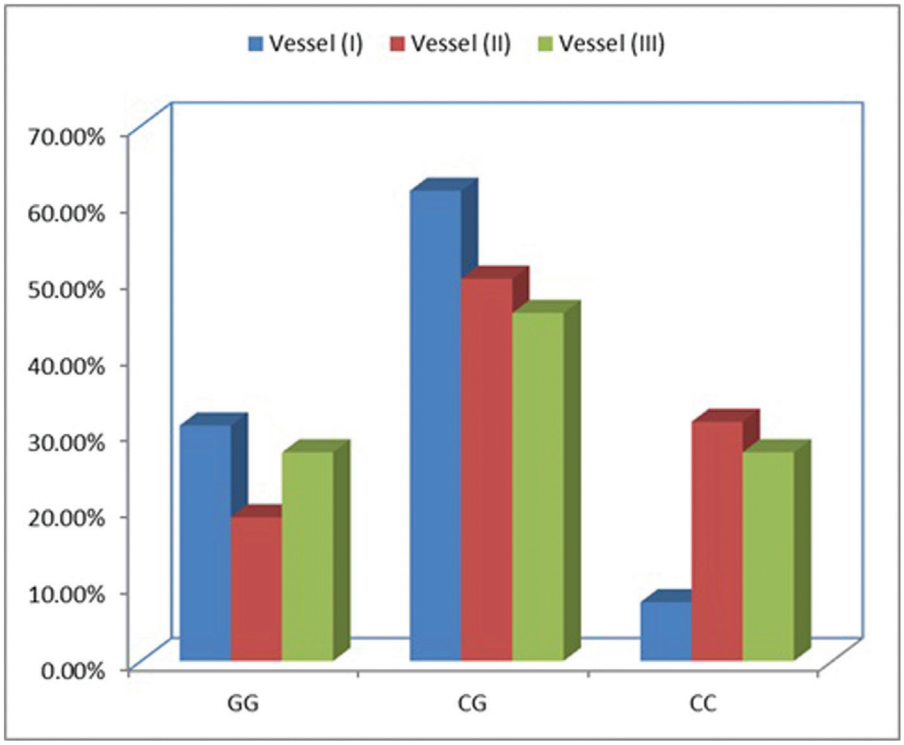
**Table 6 Statistical relation between angiography according to the genotype in the patient group**

| Genotype | Vessel I [*n* (%)] | Vessel II [*n* (%)] | Vessel III [*n* (%)] | $\chi^2$ | *P* value |
|---|---|---|---|---|---|
| CC | 1 (7.7) | 5 (31.3) | 3 (27.3) | | |
| CG | 8 (61.5) | 8 (50.0) | 5 (45.5) | 2.694 | 0.610 |
| GG | 4 (30.8) | 3 (18.8) | 3 (27.3) | | |

According to our present study, a probable association was found between Leu125Val polymorphism and the presence of CAD. A statistically significant higher heterozygous genotype distribution was found in patients, where 52.5% of patients and only 20% of controls carry the CG genotype (*P*=0.033), but no statistically significant difference in GG and CC genotype distributions between patient and control groups, where 25% of patients and 45% of controls had the GG genotype (*P*=0.202) and 22.5% of patients and 35% of controls had the CC genotype (*P*=0.470). No significant statistical difference was observed in allele frequency between the two groups, where 51.25% of patients and 55% of controls carry the G allele and 48.7% of patients and 45% of controls carry the C allele (*P*=0.846).

According to the Hardy–Weinberg equilibrium, there were no significant deviations between observed and expected genotype distributions in the patient group, where the CC genotype showed an observed value of 22.5% and an expected value of 24%, *P*=0.953. The CG genotype showed an observed value of 52.5% and an expected value of 49%, *P*=0.881 and the GG

**Figure 4**




Relation between angiography and genotypes in Patients.

genotype showed an observed value of 25% and an expected value of 27%, *P*=0.998. However, there were significant deviations from the Hardy–Weinberg equilibrium observed in the control group regarding PECAM-1 CG and GG genotypes, where the CG distribution was expected to be higher, the expected value of 48% in relation to the observed which was 20%, *P*=0.006 and the GG distribution was expected to be lower. The expected value of 16% in relation to the observed value was 45%, *P*=0.003 for GG, but there was no significant difference regarding the CC genotype, where the observed value was 35% and the expected value was 36%, *P*=0.917. This may be due to the small size of the control group.

According to a similar previously performed study by Hegazy *et al.* [8] on a total of 50 CAD Egyptian patients, referred to the coronary care center at Kasr El Aini Teaching Hospital and 40 healthy volunteers serving as the control group, the results demonstrated that PEACAM-1 Leu125Val (C+373G) gene polymorphism were significantly increased in CAD patients, compared with controls, where GG, CG, and CC genotype distribution among patients were 8, 36, and 56%, respectively, while GG, CG, and CC genotype distribution among controls were 0, 17.5, and 82.5%, respectively (*P*=0.007). Also the G allele frequency was significantly higher in CAD patients, where 26% of patients and only 7% of controls carried the G allele (*P*=0.005). Our results were consistent with what was obtained by Matej *et al.* [6] and Gang *et al.* [9] who reported an association between the polymorphism and CAD patients. On the contrary Tao *et al.* [10], found no association between Leu125Val polymorphism and CAD in the general population from Germany.

As regards the number of occluded vessels revealed by coronary angiography, no statistical significance was found between demographic as well as laboratory data in relation to the number of occluded vessels, where the *P* value was always more than 0.05 in each parameter. The results of the study also showed that there was no statistically significant difference in Leu125Val polymorphism and the number of affected vessels. The same conclusion was adopted by Hegazy *et al.* [8] who found no correlation between the number of occluded vessels and polymorphism.When the patients were divided into genotype groups, no statistical significance was found between the three groups in relation to demographic data, where the *P* value was 0.216 for age and 0.219 for sex. Also no statistical significance was observed between groups in terms of laboratory data, except for TC. There was a significantly higher TC mean concentration in the CC genotype group 213.00±54.89 as compared with that of CG and GG genotype groups which were 179.00±58.74 and 178.20±48.38, respectively

**Table 7 Statistical relation between different genotypes and demographic data as well as laboratory data in the patient group**

| Parameters | Genotype (GG) (*N*=10) | Genotype (CG) (*N*=21) | Genotype (CC) (*N*=9) | $F/\chi^2$ | *P* value |
|---|---|---|---|---|---|
| Age (years) | | | | | |
| Mean±SD | 56.90±9.12 | 51.19±9.26 | 55.44±8.40 | 1.597 | 0.216 |
| Range | 42–73 | 35–66 | 40–71 | | |
| Sex [*n* (%)] | | | | | |
| Male | 8 (80.0) | 15 (71.4) | 4 (44.4) | 3.041 ($\chi^2$) | 0.219 |
| Female | 2 (20.0) | 6 (28.6) | 5 (55.6) | | |
| TC (mg/dl) | | | | | |
| Mean±SD | 178.20±48.38 | 179.00±58.74 | 213.00±54.89 | 4.327 | **0.027** |
| Range | 118–264 | 121–339 | 113–270 | | |
| TG (mg/dl) | | | | | |
| Mean±SD | 105.00±46.27 | 124.05±72.51 | 109.33±44.27 | 0.392 | 0.678 |
| Range | 57–211 | 58–364 | 48–165 | | |
| HDL (mg/dl) | | | | | |
| Mean±SD | 46.00±8.59 | 46.71±6.45 | 44.78±9.76 | 0.195 | 0.824 |
| Range | 30–58 | 36–58 | 27–60 | | |
| LDL (mg/dl) | | | | | |
| Mean±SD | 111.10±41.87 | 107.29±48.60 | 146.33±43.56 | 2.383 | 0.106 |
| Range | 66–188 | 47–226 | 75–198 | | |
| RBS (mg/dl) | | | | | |
| Mean±SD | 114.90±32.80 | 150.57±62.70 | 168.22±84.02 | 1.859 | 0.170 |
| Range | 75–190 | 75–277 | 84–310 | | |
| HbA1c % | | | | | |
| Mean±SD | 5.52±1.12 | 6.24±1.52 | 6.52±1.73 | 1.212 | 0.309 |
| Range | 4.4–8.2 | 4.3–9.1 | 4.5–9.1 | | |
| Microalbumin (mg/dl) in diabetic group (20) [*n* (%)] | | | | | |
| >30 | 1 (33.3) | 4 (33.3) | 4 (80.0) | 3.300 ($\chi^2$) | 0.192 |
| <30 | 2 (66.7) | 8 (66.7) | 1 (20.0) | | |
| DM [*n* (%)] | | | | | |
| Diabetics | 3(30.0) | 12 (57.1) | 5 (55.6) | 2.140 ($\chi^2$) | 0.343 |
| Nondiabetics | 7 (70.0) | 9 (42.9) | 4 (44.4) | | |
| Hyperlipidemia [*n* (%)] | | | | | |
| Normocholesterolemia | 7 (70.0) | 14 (66.7) | 2 (22.2) | 5.945 ($\chi^2$) | 0.047 |
| Hypercholesterolemia | 3 (30.0) | 7 (33.3) | 7 (77.8) | | |

DM, diabetes mellitus; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RBS, random blood sugar; TC, total cholesterol; TG, triglycerides.

(*P*=0.027). There was a statistically higher % of hypercholesterolemics in the CC genotype group which were 77.8%, in relation to the % of hypercholesterolemics present in CG and GG genotype groups which were 33.3 and 30.0%, respectively (*P*=0.047).

In agreement with Fang *et al*. [11], the results of our study revealed no significant statistical difference between genotype groups in diabetic and nondiabetic patients, where the *P* value is more than 0.05.

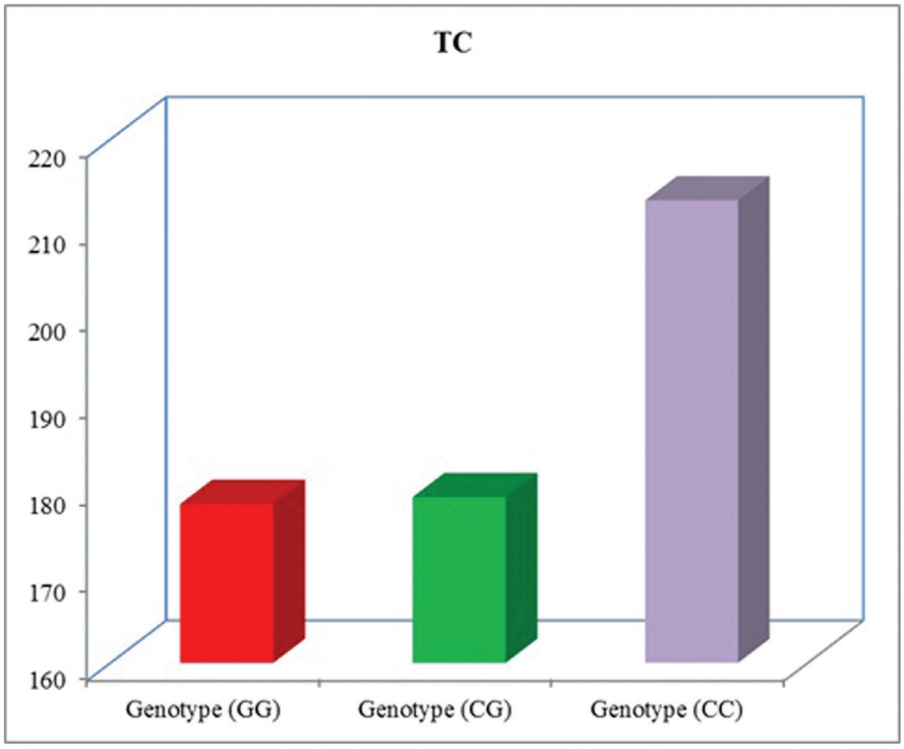
No significant statistical difference was observed between genotype groups among complicated diabetic cases, suffering diabetic nephropathy with microalbuminuria more than 30 mg and noncomplicated diabetic patients with microalbuminuria less than 30 mg, where the *P* value is more than 0.05. Our results agreed with Matej *et al*. [6] who stated that PECAM-1 expression is reduced in obliterated glomeruli with endothelial cell destruction, occurring in diabetic glomerulosclerosis.

## Conclusion

In conclusion, we investigated the polymorphism of the PECAM-1 molecule which may play a crucial role in the initial development of atherosclerosis. We found that the Leu125Val (C+373G) polymorphism could be associated with CAD in Egyptian patients, although there was an insignificant relation between the polymorphism and the number of vessels affected. Also there was no significant correlation between the presence of polymorphism in diabetic and nondiabetic CAD patients.

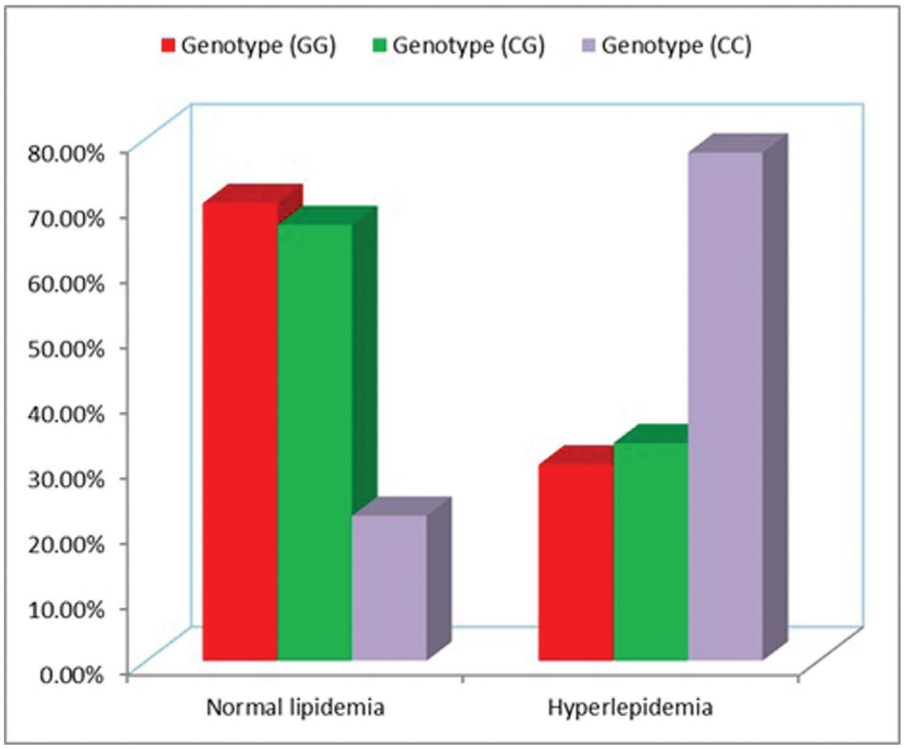
**Financial support and sponsorship**
Nil.

**Figure 5**



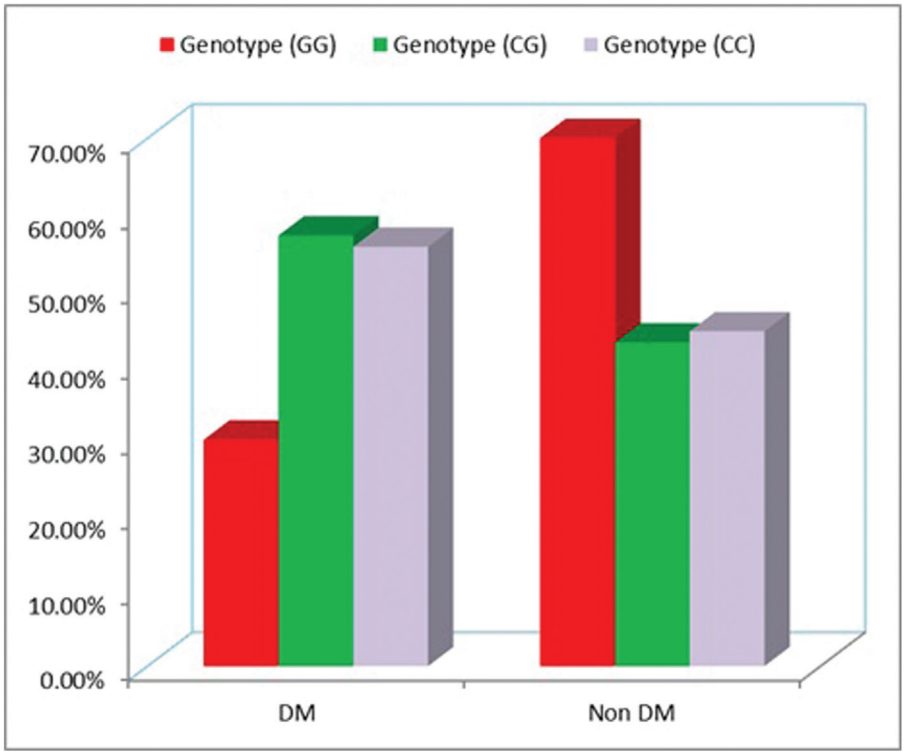

Relation between Patient genotypes and TC.

**Figure 6**




Relation between Patient genotypes and hyperlipidemia.

**Figure 7**




Relation between Patient genotypes and DM.

### Conflicts of interest

There are no conflicts of interest.

## References


1 Giuseppe L, Gianfranco C. The interplay between genetics, epigenetics and environment in modulating the risk of coronary heart disease. *Ann Transl Med* 2016; **4**:460.

2 Katarzyna B, Bartosz H, Mariusz G. The impact of type 2 diabetes mellitus on prognosis in patients with non-ST elevation myocardial infarction. *Kardiochir Torakochirurgia Pol* 2017; **14**:127–132.

3 Laszlo G, Samuel TK, Leo BJ, Mihai GN, Niels PR. Monocyte and macrophage immunometabolism in atherosclerosis. *Semin Immunopathol* 2017; **40**:1–12.

4 Popović D, Nikolajević SJ, Šantl LM, Makuc J, Cokan VA, Reschner H, *et al. PECAM-1* gene polymorphism (rs668) and subclinical markers of carotid atherosclerosis in patients with type 2 diabetes mellitus. *Balkan J Med Genet* 2016; **19**:63–70.

5 Feng YM, Chen XH, Zhang X. Roles of PECAM-1 in cell function and disease progression. *Eur Rev Med Pharmacol Sci* 2016; **20**:4082–4088.

6 Matej Z, Stojan K, Jana M, Maja S, Ines C, Daniel P. PECAM-1 Leu125Val (rs688) polymorphism and diabetic nephropathy in Caucasians with type 2 diabetes mellitus. *Anal Cell Pathol* 2016; **2016**:3152967.

7 Yanmin S, Qunfang L, Lili L, Ning Z, Yunhai L. Asn563Ser polymorphism of CD31/PECAM-1 is associated with atherosclerotic cerebral infarction in a southern Han population. *Neuropsychiatr Dis Treat* 2015; **11**:15–20.

8 Hegazy LA, Khaled HM, Abd ElAal AA, Labeeb SA, Amer HM. Association of platelet endothelial cell adhesion molecule-1 gene polymorphisms with coronary artery disease. MD Thesis. *Kasr El Aini Teach Hosp* 2014; **95**.

9 Gang L, Zong LH, He-Gui D, Xia Z, Xiang-Qian K, Xing J. Platelet endothelial cell adhesion molecule-1 gene 125C/G polymorphism is associated with deep vein thrombosis. *Mol Med Rep* 2015; **12**:2203–2210.

10 Tao X, Xin L, Chang JD, Xin J, Xiang QK, Gang L. Association of Leu125Val polymorphisms in the *PECAM-1 gene* with the risk of coronary heartdisease: a meta-analysis. *Int J Clin Exp Med* 2015; **8**:2219–2225.

11 Fang L, Wei H, Chowdhury SH, Gong N, Song J, Heng CK, *et al.* Association of Leu125Val polymorphism of platelet endothelial cell adhesion molecule-1 (PECAM-1) gene & soluble level of PECAM-1 with coronary artery disease in Asian Indians. *Indian J Med Res* 2005; **121**:92–99.