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**Original Research Article**

# Detection Relationship between VEGF Gene Expression in Patient Which Coronary Artery and Comparison Result with Control Group

Dhuha Abdullah Abbas[1*], Zainab Falih Dakhil[2], Shahad Ali Mahdi[3]

[1]Department of Pathological Analysis, Al-Qadisiyah University, College of Science, Iraq
[2]Department of Biology, College of Science, Al-Qadisiyah University, Al Diwaniyah province, Iraq
[3]Dept Pathological Analysis, Collage of Science, Al-Qadisiyah University, Iraq

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**Abstract:** ***Background****:* Coronary artery disease ("CAD") is the most frequent kind of cardiovascular disease and one of the primary causes of morbidity and death in different cultures. Several risk factors for this condition have been found so far. For many years, researchers have researched problems such as old age, gender, smoking, diabetes mellitus, hyperlipidemia, higher body mass index, and a good family history. Various research on the risk factors for this illness have shown disparate and conflicting findings, suggesting that achieving a consistent and rational reaction might aid in the prevention and treatment of cardiovascular disease. Although identifying risk factors has the potential to lower CAD dramatically. Several genes and associated proteins have been recognized in relation to cardiovascular illness. The purpose of this research was to identify and compare the expression of the VEGF gene in the positive angiography and control groups. ***Method*****:** The target group is 20 people, 10 of whom are healthy and 10 of whom have cardiovascular disease who undergo angiography. In this work, RNA was extracted from the samples, cDNA was produced, and Real Time PCR was used to quantify and qualitatively measure gene expression. SPSS was used to do statistical analysis. Considered significant was a significance level of.05. ***Results*****:** Based on quantitative data obtained from Real Time PCR, VEGF expression was significantly increased in the angio-positive group compared to the "control group" ($P < 0.05$). Statistical analysis showed a significant relationship between demographic factors Current smoker, DM, HTN, Education level, Male, Age and vascular stenosis ($P > 0.05$) There was also a significant relationship between biochemical factors LDL-C, HDL-c, Triglyceride, Total cholesterol, No FBS and stenosis ($P > 0.05$). ***Conclusion*****:** This study showed that the expression of VEGF in people with coronary artery disease is statistically significantly increased. It also showed that coronary artery disease has no significant relationship with demographic and biochemical factors.

**Keywords:** VEGF ،CAD، Angiography.



## INTRODUCTION

In many areas, "coronary artery disease" ("CAD") "is the most prevalent type of cardiovascular disease and the major cause of morbidity and death". As of this writing, a slew of risk variables have been discovered. For many years, researchers have examined the effects of growing older, being a man, smoking, diabetes, hyperlipidemia, and a higher BMI. Different research have shown conflicting findings when it comes to determining risk factors for this illness. A consistent and rational approach may help prevent and cure cardiovascular disease, according to some researchers. Additional study is necessary, even though recognizing risk factors dramatically decreases the probability of developing CAD. This field's future diagnostic and therapeutic advancements will be aided by research into the genetics of coronary artery disease (CAD) and its linked genes. Cardiovascular disease has been linked to a number of genes and proteins, and their research may help determine a person's risk of developing the condition. Endothelial cells and megakaryocytes produce von Willebrand protein, a polypeptide. The production of fibrin and the prevention of bleeding are both dependent on factor 8 delivery to the injured region.

Vascular Endothelial Growth Factor" ("VEGF") is a 7-minute signaling protein in plasma

***Corresponding Author:** Dhuha Abdullah Abbas
Department of Pathological Analysis, Al-Qadisiyah University, College of Science, Iraq

produced by cells that stimulate angiogenesis. When a fetus is developing, VEGF's primary job is to stimulate the "formation of new blood vessels". Vascular endothelial cells-5 VEGF isoforms are highly mitogenic. The VEGF gene undergoes sporadic splicing to produce this growth factor. Biol's molecular weight and characteristics are very diverse. So the goal of this research was to identify and compare VEGF gene expression in persons with negative angiography, positive angiography, and healthy people in the general population. Patients at high risk for coronary artery disease" may be identified if the link between VEGF gene expression and coronary artery disease is demonstrated.

People die from cardiovascular disease every year in greater numbers than from any other cause. Cardiovascular disease is the world's most common killer. More than one-third of all fatalities in 2012 were caused by the illness, which killed 5.17 million people globally, including 4.7 million from coronary heart disease and 7.6 million from other causes. Heart attacks and strokes have been responsible for this condition. Cardiovascular illness accounts for 33 to 39.3 percent of fatalities in Iran, with 5.19 percent attributed to heart attacks and 3.9% to strokes, according to official figures from the Ministry of Health and Medical Education. Atherosclerosis may be prevented by learning more about MCP1 and CCR2. Studies by Hans-Franz Albert (2002) found that Atrovastatin medication lowered plasma levels of the gene VEGF in individuals with coronary heart disease. It was first thought that Andrew Ballon had endothelial damage, which was a precursor to atherosclerosis. In order to repair or replace injured cells, these cells need to repopulate and expand. Endothelial cells may be affected by the angiogenic factor VEGF, which was evaluated by ELISA in this study. CAD patients had higher levels of VEGF than those in the control group.

Sangar *et al*., (1983) discovered a protein termed the vascular permeability factor that greatly improved vascular permeability (VPF). In 1989, Ferrara and Hansel identified "vascular endothelial growth factor", an endothelial cell-specific mitogen (VEGF). The inclusion of VPF and VEGF in the model was confirmed by further DNA simulations. Five interrelated human proteins (VEG.A, VEG.B, VEGFD and placental growth factor) and one monoclonal protein (VEGF.E), which is derived from two different receptor families, have been part of the VGF family since its inception. They help endothelium cells grow, migrate, and survive [1-5]. VEGF.A, better known as VEGF, is the most well-known member of this family and will be the focus of this section. Endothelial cell proliferation, skin angiogenesis, specific endothelial cell gene expression, and improved vascular permeability all play a role in wound healing when VEGF is expressed. Microvascular permeability alters the extracellular matrix by increasing the extraction of fibrinogen, fibronectin, and other proteins from the blood plasma [6-10]. VEGF expression is typically lower in the skin than in other large vessels such as the lungs, kidneys, and heart. However, during the first few days after tissue damage, VEGF expression is significantly increased, plasma proteins are excreted, and angiogenesis begins.

**VEGF Structure"**

There are eight exons and seven introns in the VEGF gene. "It is situated on human chromosome 6" (p12). When exons 6 and 7 of the VEGF gene are substituted with noncoding RNA (ncRNA), five protein isoforms containing anywhere from 121 to 206 amino acids are produced (Figure 1.1). Most cell types express "VEGF121 and VEGF165", the two most prevalent isoforms. While other VEGF isoforms have various degrees of heparin binding, VEGF121 does not. Although heterodimers have been discussed, most of the VEGF family's active forms are homodimers [14, 15].

**Regulation of VEGF Production and Activity"**

At both the transcription and post-transcriptional stages, VEGF expression may be controlled. Many transcription factors, such as Sp1, Stat3, AP.1, and Hypoxia Factor-1, bind to the VEGF gene promoter (HIF.1). In addition to platelet-derived growth factor, epidermal growth factor, and beta-growth factor (TGF.b), the mRNA levels of VEGF are influenced by cytokines of the tumor necrosis factor (TNF.a), as well as interleukin 1 beta (IL.1b). First, it seems that substances like cytokines and growth factors are delivered to cells through Sp1, Stat3, and AP.1. VEGF mRNA transcription is also regulated by ras and Wnt mutations. VEGF synthesis is greatly aided by hypoxia. It is hypoxia-dependent that VEGF mRNA expression rises and falls with normoxia. HIF.1 is a highly responsive transcription factor. MrE VEGF expression is reduced to sub-neurocoxic levels in hyperoxia [16, 17]. Additionally, hypoxia stabilizes the 3T (UTR) non-converted section of Mrna VEGF's mRNA by binding HuR, a protein that binds to an AU-rich element in the 3T (UTR) non-converted region. The stability of hypoxia-stimulated mRNA requires additional components in both the 5 and 3 UTRs. It is possible to express distinct VEGF isoforms in different organs by the use of varied mRNA binding conditions. Thus, when the growing capillary network moves closer to the airway epithelium during fetal lung development, the ratio of less soluble VEGF189 to VEGF121 drops. Cells that express VEGF include vascular smooth muscle cells, cartilage cells, liver cells, monocytes, macrophages, neutrophils, pituitary and pancreatic glands, mesenchymal cells, and tumor cells.

**Biological Function of VEGF**

Vasculogenesis and angiogenesis are two of the most important processes in the growth of vascular networks. Vasculogenesis refers to the generation of new vascular tubes from endothelial cells, while angiogenesis refers to the formation of new vascular tubes from

endothelial cells (formation of small vessels and capillaries by sprouting from existing larger vessels). VEGF acts as a survival factor for endothelial cells and encourages proliferation, migration, and tubulogenesis in endothelial cells that line blood vessels and lymphatic vessels. Vascular permeability may be exacerbated by VEGF. Perforation of the endothelium in tiny venules and capillaries seems to be the source of this impact. When it comes to the development of blood vessels, hemangioblast differentiation, bleeding, and vasculogenesis, the VEGF hormone is critical in the developing fetus. One or two VEGF alleles are missing in transgenic mice, and as a result, embryos from these animals die early in pregnancy due to aberrant blood vessel development in the developing fetal body as well as in the yolk sac and placenta.

**VEGF Receptors**

EVGF family members act primarily via two distinct receptor subfamilies (Table 1.1). There are three closely spaced, highly interlinked, seven-domain peptides that resemble extracellular immunoglobulin and two-celled tyrosine kinase (VEGFR) in terms of structure and function. Two of these receptors, VEGFR.1 (also known as flt.1) and VEGFR.2, are the primary targets of VEGF ("known as flk-1 or KDR"). For example, endothelial cell migration is encouraged when VEGF binds to VEGFR.1. VEGFR-1 EVGF and VEGFR.2 are regarded to be the most essential mediators of mitogenic permeability, angiogenesis, and vascular VEGF, and Nir may be the "prey" receptor in certain situations by binding and separating them. Endothelial cell proliferation, migration, and differentiation are all stimulated by VEGFR.2 activation.

**Coronary Artery Disease" (CAD)**

Coronary heart disease ("CAD"), or ischemic heart disease, has many different clinical presentations. Angina pectoris, myocardial infarction, and sudden cardiac death all fall under the category of acute coronary syndrome (ACS). Chronic coronary heart disease, for example. "Complex interactions" "between the coronary circulation and myocardium" characterize these syndromes [26, 27], which are often accompanied with coronary atherosclerosis, the disease's fundamental foundation.

It is the inflammation of the artery wall that causes coronary atherosclerosis (atherosclerosis), a process that results in the production of atherosclerotic plaques (fibroplexes, atheroma) in the coronary arteries that is the primary cause of CAD (Figure 1.2 and 1.3).

In the membrane, there are thick patches known as plaques, which are made up of fibrous tissues, cells, and lipids. An atherosclerotic lesion is formed when blood-soluble substances interact with the artery wall (Figure 1.3). One of the most important causes of plaque formation and progression is endothelial dysfunction or injury. (2) The buildup of monocytes and macrophages; (3) the inflow of T lymphocytes; and (4) the binding of platelets. Proliferation of smooth muscle; (6) increase in plasma LDL input flow; (7) "oxidation of LDL"; (8) fat buildup in foam-shaped cells; (9) foam cell apoptosis. (11) Hemodynamic "effects on blood pressure and blood flow pattern", as well as (10) extracellular fat deposition [28].

VEGF is a mitogen for vascular endothelial cells in addition to its potential to induce permeability in these cells. Endothelial cells are the only cells in the body that have VEGF receptors ("VEGFR.1 and 2"). "VEGFR".1 (FL T) seems to have an abnormally high level of vascular permeability, while VEGFR.2 (FLK.1) seems to play a role in the process of angiogenesis. In addition, VEGF is the factor responsible for the induction of collagenases. These collagenases, in turn, remove the matrix and make it simpler for endothelial cells to migrate and germinate. VEGF is responsible for both of these processes. Angiogenesis is the term that describes this process. In response to a range of stressors, including vascular injury, acute hypoxia, acute ischemia, and chronic cardiac ischemia, myocytes and vascular smooth muscle cells exhibit an increase in the production of VEGF mRNA [30, 31]. In addition to this, it has been demonstrated that VEGF may attenuate the negative effects of CAD by unblocking blood arteries within the thrombus, promoting lateral circulation to protect the heart from ischemia, and enhancing endothelial-dependent vasodilation. All of these mechanisms work together to protect the heart from ischemia. VEGF, or vascular endothelial growth factor, plays a part in the enlargement of blood vessels as well as the control of the integrity of the vascular wall, according to the results of certain studies [35, 36].

According to research, muscle endothelial growth factor, often known as VEGF, is a necessary component of the process of angiogenesis. VEGF is responsible for inducing the migration and proliferation of endothelial cells, as well as increasing vascular permeability and modulating clotting rate. "VEGF.A, VEGF.B, VEGF.C, VEGF.D, VEGF.E", VEGF.F, and placental growth factor are all members of the VEGF family. These growth factors all enhance their activity by connecting with high-affinity tyrosine kinase receptors. Placental growth factor also belongs to this family. The VEGF gene can be found on chromosome 6p21.3 and consists of a 14 kb cryptographic area that is broken up into a total of eight exons and seven introns. It is found to be expressed in a variety of cell types, including endothelial cells, vascular smooth muscle cells, macrophages, and a few distinct kinds of tumor cells. Studies in molecular biology have shown that the production of VEGF is controlled by single mononucleotide polymorphisms (SNPs). These SNPs have different expression patterns depending on the kind of tissue and the age of the subject. In addition, the variety of VEGF genes may be of special significance for a number of disorders that are associated with

angiogenesis. These diseases include malignancies, osteosarcoma, age-related macular degeneration, diabetic retinopathy, and various chronic inflammatory diseases. CAD encourages lateral circulation against cardiac ischemia and enhances endothelium-dependent vasodilation.

# RESEARCH METHOD

The target group is 20 people, 10 of whom are healthy and 10 of whom have cardiovascular disease who have undergone angiography and are referred to the cardiac catheterization department of Ghaaem Hospital (AS) and are angiographed by a cardiologist. To be. The non-probability sampling method is purpose-based and all patients with coronary angiography indication were included in the study. After angiography, those whose angiographic response was positive and had coronary artery disease ("stenosis ≥50%") "as the patient group and those whose angiographic response was negative and had no coronary" artery involvement ("stenosis <50%") "as the control group". Were considered. In both groups, individuals were matched in terms of age and sex. Sampling of patients in the morning angiography in the fasting state of arm vein blood was also performed. Blood samples are taken from 5 cc and stored in a freezer at. 80°C to perform the desired tests on them. Information about blood pressure, personal and family history of cardiovascular disease and hyperlipidemia, diabetes, renal failure, drug use as well as angiographic results of patients were recorded according to standard criteria and provided to the project.

**Measurement of Biochemical Factors**

Biochemical factors were measured in the two groups. Serum concentrations of glucose, triglycerides and total cholesterol were measured enzymatically using Pars Azmoun kits were measured. Also, serum HDL.C concentration was measured enzymatically using the kit of Pishtaz Teb Company and with autoanalyzer (model BT3000). Serum LDL.C concentration was calculated using Frieedewald formula":

$$\text{"LDL-C} = \text{Total Cholesterol"} - (\frac{\text{Trigelyceride}}{5} + \text{"HDL-C)"}$$

**RNA Extraction"**

Isolation of total RNA was accomplished with the assistance of an RNX.PLUS kit and conformance to the method outlined by Mashhad University of Medical Sciences.

**cDNA Synthesis**

8 µl of RNA template was combined with 10 µl of buffer.mix and 2 µl of PARSTOUS kit enzyme mixture and vorteexed for 15 seconds. It was then inceubated for 10 minutes at 25 ° C and 60 minutes at 47 ° C. In order to stop the reaction, the contents were placed at 85 ° C for five minutes.

**Real Time PCR**

Table 3.2 shows the results of bioinformatics analysis for the design of PCR primers. Gene Runner ("version 3.05"), PerIPrimer ("version 1.1.21") and Oligo (version 7.56) were used for this purpose. Also Q plus 2x master mix Green ("Ampliqon, Denmark") along with ROX dye was used for all Real time PCR analyzes.

Glyciraldehyde 3.phosphate dehydrogenase ("GAPDH") expression was used as an internal control. All Real time PCR analyzes were performed by ABI "STEP ONE real time PCR system with the presented conditions": starting at 95 ° C for 15 minutes," amplification for 40 cycles with denaturation at 95 ° C for" 15 seconds and anling at 63 ° C Degrees Celsius for 55 seconds.

**Table 3.3: Design of PCR primers**

| Primer's Name | Sequence |
|---|---|
| VEGF Forward Primer | TGCAGATTATGCGGATCAAACC |
| VEGF Reverse Primer | TGCATTCACATTTGTTGTGCTGTAG |
| GAPDH Forward Primer | ATGGGGAAGGTGAAGGTCG |
| GAPDH Reverse Primer | GGGGTCATTGATGGCAACAATA |

**Statistical Methods in Data Analysis**

The SPSS program was used at every stage of the analytic process. The T-student test was used for analyzing variables with normal distribution. The Mann-Whitney U test was used for analyzing data containing variables that had an irregular distribution. Using GraphPad Prism version8, we evaluated the findings of the RT-PCR.

**Demographic Factors of the Study Population"**

In this study, 20 people were studied, 10 of whom were angiographically positive and had stenosis ≥50% and 10 were angio-negative and had stenosis <50% (control group) according to the results of angiography. The comparison of these factors in the two groups shows that people in the angio-positive group have a higher mean age than the control group, "but this difference was not statistically significant" ("p value = 0.643").

People with stenosis ≥50% were more likely than men to have stenosis <50%, but this difference was not "statistically significant" ("p value = 0.361"). The results showed that the level of education had no significant relationship with the percentage of clogged arteries (p value = 0.243). In the angio-positive group, more people had a history of hypertension than the control group, however, no significant difference was

shown in terms of statistical analysis. (p value = 0.500). Also, the history of diabetes mellitus and hyperlipidemia is not significantly associated with clogged arteries (p value> 0.05).

**Table 4.1: Comparison of demographic information in angio-positive and control group**

| Variables | | Stenosis<50% (n=10) | Stenosis≥50% (n=10) | P value* |
|---|---|---|---|---|
| Age | | 63.20±9.47 | 65.10±8.52 | 0.643 |
| Male (n%) | | 5 (41.7%) | 7(58.3%) | 0.361 |
| Education level (n%) | Illiterate | 7 (77.8%) | 6 (60.0%) | 0.243 |
| | Primary school | 1(11.1%) | 4 (40.0%) | |
| | Bachelor | 1(11.1%) | 0 (0.0%) | |
| HTN history (n%) | | 5 (50.0%) | 6 (60.0%) | 0.500 |
| DM history (n%) | | 4 (40.0%) | 6 (60.0%) | 0.328 |
| HLP history (n%) | | 5 (50.0%) | 7 (70.0%) | 0.325 |
| Current smoker (n%) | | 3 (30%.0) | 2 (20.0%) | 0.500 |

*"Mean±Standard deviation was reported for normal variables and the medium for abnormal variables". "T-student test was used to compare data with normal distribution and" Mann-"Whitney test was used for data with abnormal distribution".

**Biochemical Factors of the Study Population**

Comparison of biochemical factors in the two groups of stenosis ≥ 50% and stenosis <50% "shows that the mean fasting blood sugar", triglycerides, high-"density lipoprotein", low-density lipoprotein, however, these differences were not statistically significant ("p value> 0.05").The results showed that the mean total cholesterol in patients with vascular occlusion was 50% and more than 50% higher than the control group, but this difference Did not show significance ("p value> 0.05"). As shown in Table 4.2, in the study of biochemical factors, fasting blood sugar variables (p value = 0.70), total cholesterol (p value = 0.766), triglycerides (p value = 0.160), lipoprotein with High density (p value = 0.876), low density lipoprotein (p value = 0.769) were homogeneous in the two groups and did not show a statistically significant relationship.

**Table 4.2: Biochemical evaluations in two groups of angio positive and control group**

| Variables | Stenosis<50% (n=10) | Stenosis≥50% (n=10) | P value* |
|---|---|---|---|
| FBS | 114.20±39.36 | 107.56±39.92 | 0.720 |
| Total cholesterol | 120.50±38.10 | 125.70±42.15 | 0.766 |
| Triglyceride | 105.20±51.27 | 79.30±22.21 | 0.160 |
| HDL-C | 33.20±9.99 | 32.50±9.79 | 0.876 |
| LDL-C | 81.67±44.6 | 71.00±9.90 | 0.769 |

*"Mean ±Standard deviation was reported for normal variables and the medium for" abnormal variables. "T-student test was used to compare data with normal distribution and Mann-Whitney test was used for data with abnormal distribution".

**Results of Real Time PCR**

As can be seen in Figure 3.4, the relative level of VEGF in angio-positive individuals increased statistically significantly "compared to controls"("p <0.05").

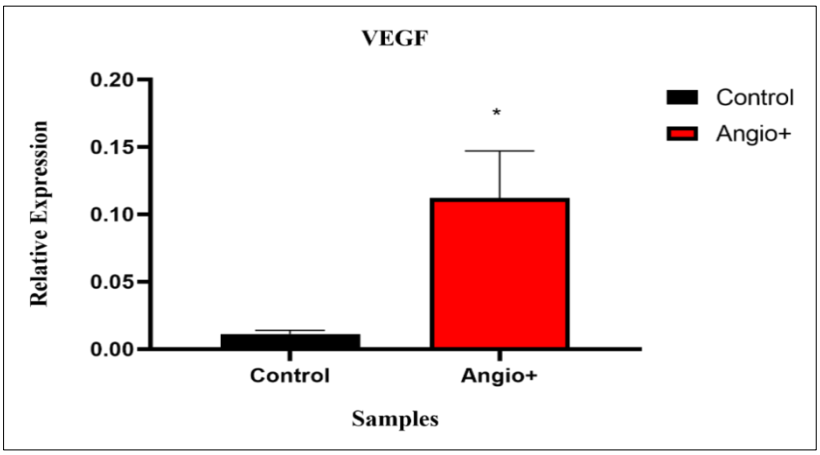


**Figure 4.1: Relative level of VEGF in angio-positive and control group**

## DISCUSSION AND ANALYSIS

Heart disease is one of the leading causes of death throughout the world. As the most common kind of cardiovascular illness, coronary artery disease (CAD) is considered a major contributor to both morbidity and mortality across a wide range of countries. So far, a slew of risk factors have been linked to this illness. Studies have looked at a variety of characteristics, including advanced age, female gender, tobacco use and diabetes mellitus as well as high BMI and good family history. This field will benefit greatly from more research into connected genes' genetic base, even if risk factors can be identified and reduced substantially, since this will lead to new diagnostic and therapeutic approaches in this area. Heart disease may be predicted by looking at many genes and proteins that are linked together, which has been shown to be useful. Endothelial cells in the blood vessels secrete VEGF, which is a vascular permeability factor. Pericytes, macrophages, and T lymphocytes are all examples of vascular permeability factors. Vascular endothelial cells may be induced to become more permeable by VEGF, which is also a mitogen for these cells. Collagen production, angiogenesis, and cell migration are all encouraged by VEGF, which also facilitates the proliferation of endothelial cells. VEGF levels in the blood of patients with acute coronary syndrome have been shown to be higher in many studies. An examination of VEGF expression might be utilized to determine whether or not coronary artery disease is progressing or not (CAD).

People with and without coronary artery disease (CAD) were studied by Ameli *et al*., (2012) for their VEGF expression levels. Participating individuals with coronary artery disease (CAD) who had positive or negative angiographic findings were all included in this study. Patients with coronary artery disease (CAD) have significantly lower levels of VFGF expression than those without CAD. The C allele, VEGF 782578, and the CC genotype were also shown to be more common in those with a confirmed diagnosis of CAD [56].

There are two kinds of tyrosine kinase receptors on endothelial cells: VEGFR1 and VEGFR2. VEGF is a well-known inducer of angiogenesis, and it works via these receptors to produce mitogenic and angiogenic effects. Researchers from Iran conducted a research in 2017 to see whether there was a link between the severity of coronary artery disease and the VEGF rs2010963 polymorphism. According to their angiography results, 374 of the 520 participants in this study were diagnosed with coronary artery disease (CAD), whereas 173 were classified healthy. The C allele of the VEGF rs2010963 polymorphism has been associated to an increased risk of coronary artery disease, according to one study (CAD). So the results of this study showed that the VEGF rs2010963 polymorphism may be linked to CAD, despite the fact that no correlation was discovered with CAD severity and this polymorphism [57].

Numerous studies have shown that VEGF, or vascular endothelial growth factor, plays an important role in the development of atherosclerosis. For this study, Lane *et al*., (2010) looked at two VEGF polymorphisms, namely 405C/G (rs2010963) and 2578C/A (rs699947). Tests were carried out on both of these versions. 309 people with advanced stages of CAD participated in this study. For the purposes of this inquiry, the CVS and diffuse score were used to assess the severity of coronary atherosclerosis (DS). It was also separated into SVD and MVD as two independent parameters for CVS. Results from this study show that the frequency of the + 405C/G genotype is linked to the CVS and DS measurements. The frequency of the + 405C allele is much higher in MVD patients than in the general population [58].

## CONCLUSION

The study's goal was to examine the levels of VEGF gene expression between patients who had positive angiography results and healthy controls. People with coronary artery disease had considerably higher levels of VEGF expression, according to this research. It also revealed that there is no correlation between coronary artery disease and demographic or biochemical markers.

**Study Limitations and Recommendations**

"One of the limitations of this study is the small sample size", so the results cannot be generalized to the general public and more studies are needed for more accurate results.

## REFERENCES

1. Wang S, Li X, Parra M, Verdin E, Bassel.Duby R, Olson EN. Control of endothelial cell proliferation and migration by VEGF signaling to histone deacetylase 7.ProcNatlAcadSci U S A. 2008;105(22):7738–43.
2. Inoue M, Itoh H, Ueda M, Naruko T, Kojima A, Komatsu R. K, Ogawa Y, Tamura N, Takaya K, et al. vascular endothelial growth factor (VEGF) expression in human coronary atherosclerotic lesions. Circulation. 1998;98(20):2108–16.
3. Ferrara N. Molecular and biological properties of vascular endothelial growth factor. J Mol Med (Berl). 1999;77(7):527–43.
4. Tamura K, Amano T, Satoh T, Saito D, Yonei.Tamura S, Yajima H. Expression of rigf, a member of avian VEGF family, correlates with vascular patterning in the developing chick limb bud. Mech Dev. 2003;120(2):199–209.
5. Ruggiero D, Dalmasso C, Nutile T, Sorice R, Dionisi L, Aversano M, Broet P, Leutenegger AL, Bourgain C, Ciullo M. Genetics of VEGF serum variation in human isolated populations of cilento: importance of VEGF polymorphisms. PLoS One. 2011;6(2):e16982.
6. Pantsulaia I, Trofimov S, Kobyliansky E, Livshits G. Heritability of circulating growth factors

involved in the angiogenesis in healthy human population. Cytokine. 2004;27(6):152–8.
7. Al.Habboubi HH, Sater MS, Almawi AW, Al.Khateeb GM, Almawi WY. Contribution of VEGF polymorphisms to variation in VEGF serum levels in a healthy population. Eur Cytokine Netw. 2011;22(3):154–8.
8. Hu GL, Ma G, Ming JH. Impact of common SNPs in VEGF gene on the susceptibility of osteosarcoma. Genet Mol Res. 2015;14(4):14561–6.
9. Xian W, Zheng H, Wu WJ. Predictive value of vascular endothelial growth factor polymorphisms on the risk of renal cell carcinomas. Genet Mol Res. 2015;14(3):7634–42.
10. Gurtner GC, Werner S, Barrandon Y, and Longaker MT: Wound repair and regeneration. Nature 2008; 453:314.
11. Gerhardt H, Golding M, Fruttiger M, et al. : VEGF guides angiogenic sprouting utilizing endothelial tip cell filopodia. J Cell Biol 2003; 161:1163.
12. Brown NJ, Smyth EA, Cross SS, and Reed MW: Angiogenesis induction and regression in human surgical wounds. Wound Repair Regen 2002; 10:245.
13. Jacobi J, Tam BY, Sundram U, et al. : Discordant effects of a soluble VEGF receptor on wound healing and angiogenesis. Gene Ther 2004; 11:302.
14. Shibuya M, Ito N, Claesson.Welsh L. Structure and function of vascular endothelial growth factor receptor.1 and.2. Curr Top MicrobiolImmunol. 1999;237:59–83.
15. Ferrara N, Davis.Smyth T. The biology of vascular endothelial growth factor.Endocr Rev. 1997;18:4–25. doi: 10.1210/edrv.18.1.0287
16. Roskoski R., Jr VEGF receptor protein.tyrosine kinases: structure and regulation. BiochemBiophys Res Commun. 2008;375:287–291. doi: 10.1016/ j.bbrc. 2008.07.121.
17. Christinger HW, Fuh G, de Vos AM, Wiesmann C. The crystal structure of placental growth factor in complex with domain 2 of vascular endothelial growth factor receptor.1. J Biol Chem. 2004;279:10382–10388.
18. Bryant DM, Wylie FG, Stow JL. Regulation of endocytosis, nuclear translocation, and signaling of fibroblast growth factor receptor 1 by E.cadherin.MolBiol Cell. 2005;16:14–23.
19. D'Amore PA. Vascular endothelial cell growth factor.a: not just for endothelial cells anymore. Am J Pathol. 2007;171:14–18.
20. Jones WS, Annex BH. Growth factors for therapeutic angiogenesis in peripheral arterial disease.CurrOpinCardiol. 2007;22:458–463.
21. Ho QT, Kuo CJ. Vascular Endothelial Growth Factor: Biology and Therapeutic Applications. Int J Biochem Cell Biol. 2007; 39(7.8): 1349–1357.
22. Chappell JC, Wiley DM, Bautch VL. Regulation of blood vessel sprouting.Semin Cell Dev Biol. 2011;9:1005–1011
23. Tammela T, Zarkada G, Wallgard E, Murtomäki A, Suchting S, Wirzenius M, Waltari M, Hellström M, Schomber T, Peltonen R, et al. Blocking VEGFR.3 suppresses angiogenic sprouting and vascular network formation. Nature. 2008;454:656–660.
24. Quaegebeur A, Lange C, Carmeliet P. The neurovascular link in health and disease: molecular mechanisms and therapeutic implications. Neuron. 2011;71:406–424.
25. Yeung, SLU., Hung San Lam HS, Mary Schooling C. Vascular Endothelial Growth Factor and Ischemic Heart Disease Risk: A Mendelian Randomization Study. J Am Heart Assoc. 2017 Aug; 6(8): e005619.
26. Global Atlas on Cardiovascular Disease Prevention and Control. Geneva: World Health Organization, 2011.
27. Arciero TJ, Jacobsen SJ, Reeder GS, et al. Temporal trends in the incidence of coronary disease. Am J Med 2004;117:228.33.
28. Sanchis.Gomar F, Perez.Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. Ann Transl Med. 2016 Jul; 4(13): 256.
29. Goyal A, Yusuf S. The burden of cardiovascular disease in the Indian subcontinent. Indian J Med Res 2006;124:235.44.
30. Ladoux, A., and C. Frelin. Hypoxia is a strong inducer of vascular endothelial growth factor mRNA expression in the heart. Biochem. Biophys. Res. Commun. 195: 1005–1010, 1993.
31. Li, J, Brown LF, M. Hibberd G, Grossman JD, Morgan JP, Simons M. VEGF, flk.1, and flt.1 expression in a rat myocardial infarction model of angiogenesis. Am. J. Physiol. 270 (Heart Circ. Physiol. 39): H1803–H1811, 1996.
32. Ferrara N. Molecular and biological properties of vascular endothelial growth factor. J Mol Med (Berl). 1999;77(7):527–43.
33. Coultas L, Chawengsaksophak K, Rossant J. Endothelial cells and VEGF in vascular development. Nature. 2005;438(7070):937–45.
34. Grunewald M, Avraham I, Dor Y, Bachar. Lustig E, Itin A, Jung S, Chimenti S, Landsman L, Abramovitch R, Keshet E. VEGF.induced adult neovascularization: recruitment, retention, and role of accessory cells. Cell. 2006;124(1):175–89.
35. Azambuja AP, Portillo.Sanchez V, Rodrigues MV, Omae SV, Schechtman D, Strauss BE, Costanzi.Strauss E, Krieger JE, Perez.Pomares JM, Xavier.Neto J. Retinoic acid and VEGF delay smooth muscle relative to endothelial differentiation to coordinate inner and outer coronary vessel wall morphogenesis. Circ Res. 2010;107(2):204–16.
36. Kliche S. Waltenberger J. VEGF receptor signaling and endothelial function. IUBMB Life. 2001;52(1–2):61–6.
37. Grosskreutz CL, Anand.Apte B, Duplaa C, Quinn TP, Terman BI, Zetter B, D'Amore PA. Vascular endothelial growth factor.induced migration of

vascular smooth muscle cells in vitro. Microvasc Res. 1999;58(2):128–36.
38. Howell WM, Ali S, Rose.Zerilli MJ, Ye S. VEGF polymorphisms and severity of atherosclerosis. J Med Genet. 2005;42(6):485–90.
39. Eaton CB, Gramling R, Parker DR, Roberts MB, Lu B, Ridker PM. Prospective association of vascular endothelial growth factor.a (VEGF.A) with coronary heart disease mortality in southeastern New England. Atherosclerosis. 2008;200(1):221–7.
40. HUANG, Anan, et al. Serum VEGF: diagnostic value of acute coronary syndrome from stable angina pectoris and prognostic value of coronary artery disease. Cardiology research and practice, 2020, 2020.
41. AMOLI, Mahsa M., et al. VEGF gene mRNA expression in patients with coronary artery disease. Molecular biology reports, 2012, 39.9: 8595.8599.
42. RAMOS, Catarina, et al. Prognostic value of VEGF in patients submitted to percutaneous coronary intervention. Disease markers, 2014, 2014.
43. WANG, Maojing, et al. MiR.206 suppresses the progression of coronary artery disease by modulating vascular endothelial growth factor (VEGF) expression. Medical science monitor: international medical journal of experimental and clinical research, 2016, 22: 5011.
44. AWATA, Takuya. Vascular endothelial growth factor gene polymorphisms in susceptibility to coronary artery disease. American journal of hypertension, 2010, 23.9: 938.939.
45. KALAYI NIA, Samira, et al. The impact of vascular endothelial growth factor+ 405 C/G polymorphism on long-term outcome and severity of coronary artery disease. Journal of clinical laboratory analysis, 2017, 31.4: e22066
46. BARALE, Cristina; RUSSO, Isabella. Influence of cardiometabolic risk factors on platelet function. International journal of molecular sciences, 2020, 21.2: 623
47. LIN, Tsung. Hsien, et al. Vascular endothelial growth factor polymorphisms and extent of coronary atherosclerosis in Chinese population with advanced coronary artery disease. American journal of hypertension, 2010, 23.9: 960.966
48. MIHCI, Ebru, et al. VEGF polymorphisms and serum VEGF levels in Parkinson's disease. Neuroscience letters, 2011, 494.1: 1.5.
49. SHIBATA, Yohei, et al. Balance between angiogenic and anti.angiogenic isoforms of VEGF.A is associated with the complexity and severity of coronary artery disease. Clinica chimica acta, 2018, 478: 114.119
50. STEHR, A., et al. VEGF: a surrogate marker for peripheral vascular disease. European Journal of Vascular and Endovascular Surgery, 2010, 39.3: 330.332.
51. SCHIMANSKI, Carl C., et al. VEGF.D correlates with metastatic disease in gastric cancer patients undergoing surgery. World journal of surgery, 2011, 35.5: 1010.1016.
52. ZAFAR, Mohammad Ishraq, et al. Association between the expression of vascular endothelial growth factors and metabolic syndrome or its components: a systematic review and meta.analysis. Diabetology & metabolic syndrome, 2018, 10.1: 1.17.
53. WIECZÓR, Radosław, et al. Overweight and obesity versus concentrations of VEGF.A, sVEGFR.1, and sVEGFR.2 in plasma of patients with lower limb chronic ischemia. Journal of Zhejiang University.SCIENCE B, 2016, 17.11: 842.849.
54. SUN, Li, et al. VEGF genetic polymorphisms may contribute to the risk of diabetic nephropathy in patients with diabetes mellitus: a meta.analysis. The Scientific World Journal, 2014, 2014.
55. ANDERSON, Christopher E., et al. The association of angiogenic factors and chronic kidney disease. BMC nephrology, 2018, 19.1: 1.8.
56. Amoli, M.M., Amiri, P., Alborzi, A. et al. VEGF gene mRNA expression in patients with coronary artery disease. Mol Biol Rep 39, 8595–8599 (2012).
57. Kalayi Nia, S., Ziaee, S., Boroumand, M.A., et al. The impact of vascular endothelial growth factor +405 C/G polymorphism on long-term outcome and severity of coronary artery disease. JCLA 31, e22066 (2017).
58. Lin, T.H., Su, H.M., Wang, C.L., et al., Vascular Endothelial Growth Factor Polymorphisms and Extent of Coronary Atherosclerosis in Chinese Population with Advanced Coronary Artery Disease. Am J Hypertens 23, 960.966 (2010).

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