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Original Article

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Examination of Glutathione S-Transferase (GST) enzyme levels and some biochemical parameters in coronary artery patients

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Abstract

***Background & Aims*:** Heart diseases stand out as a leading cause of death. Specific enzymes are active eliminators of toxic substances from the body. One of the crucial enzymes in this process is Glutathione S-Transferase (GST). In this study, GST activities were determined in individuals with and without coronary artery, and the relationship between some biochemistry tests and GST activity was examined.

Materials & Methods: This case-control study was conducted on 54 patients with CAD and 54 people without CAD with matched age and sex as control group. Biochemical parameters were measured on an autoanalyzer, and GST enzyme activity was measured on a spectrophotometer. All parameters were examined statistically in line with the data obtained. Data were analyzed by SPSS v.20. A p-value less than 0.05 was considered statistically significant

Results: Accordingly, while there was a statistically significant difference in the GST enzyme activity and HDL-C levels, there was no statistically significant difference in total cholesterol, triglycerides, LDL-C, urea, creatinine and CRP levels. GST enzyme activity level, total cholesterol, triglycerideç LDL-C and CRP levels were found to be higher in thr patient group than the control group, while HDL-C, urea and creatinine levels were found to be higher in the control group than the patient group (*Ps <0.05*).

Conclusion: The results obtained indicate that determining the GST enzyme activity level, in addition to routine cardiac markers for the diagnosis of CAD, is important in the diagnosis of CAD-related conditionsç Also ıt will elucidate the mechanisms that constitute the main cause of these diseases.

***Keywords*:** Artery, Coronary, Enzyme, Glutathione S-Transferase

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Introduction

Coronary artery disease (CAD) undeniably affects society, particularly impacting the elderly population and significantly diminishing overall quality of life on a global scale. This reality escalates both the economic strain of CAD and the demand for healthcare services, rendering it a pressing social issue warranting attention (1, 2). CAD develops due to the accumulation of plaque on the inner walls of the arteries that supply blood to the heart, leading to the narrowing or complete blockage of

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these vessels. Consequently, this impedes the proper flow of blood to the heart, resulting in insufficient oxygen supply to the heart muscle (3). Plaques typically form from accumulations of cholesterol deposits. The buildup of plaque leads to the narrowing of the inner walls of arteries over time, initiating the process of arteriosclerosis known as atherosclerosis. CAD that arises from the blockage of coronary arteries with atherosclerotic plaque is characterized by various symptoms resulting from decreased blood flow to the heart and insufficient oxygen supply to the cardiac muscle (4). The clinical picture of CAD generally includes insufficient oxygen supply to the heart muscle, chest pain of cardiac origin, blockage of the coronary arteries, heart failure, and cases of sudden death (5). Unhealthy and inadequate diet, obesity, and stress, along with hypertension, hyperlipidemia, smoking, and lack of exercise, are commonly recognized risk factors for CAD. Managing CAD involves lifestyle changes, minimizing risk factors, and implementing effective pharmacological treatments early in the process to control the condition (3). Therefore, the treatment of early diagnosed CAD holds significant importance for an individual's health and quality of life (6). Lifestyle modifications, especially in advanced age and for individuals with genetic predispositions, are of vital importance for those at high risk of CAD (7).

Glutathione (GSH) is formed by the linkage of the carboxyl group of glutamic acid with the amino group of cysteine through a peptide bond, and the carboxyl group of cysteine is also linked to the amino acid glycine through a peptide bond (8). Glutathione synthesis occurs in the liver (9). Reactive oxygen species (ROS) are neutralized by the tripeptide structure of GSH, which acts as an antioxidant (10). GSH's high solubility in water and its significant role in the defense system are facilitated by its structure, which contains numerous hydrophilic (water-attracting) groups and has a low molecular weight (11). GSH plays significant roles in organisms, including amino acid transport, enzyme regulation, peroxidase metabolism, and xenobiotic metabolism. Both an increase and a decrease in GSH levels are crucial for maintaining cellular functions (12). In situations where antioxidants cannot adequately counter excessive free radicals, oxidative stress occurs. The occurrence of oxidative stress leads to oxidative damage at the levels of DNA, lipids, and proteins, resulting in tissue damage and deterioration (13). GSH acts as an antioxidant by neutralizing the effects of damage caused by ROS in various tissues. It interacts with both peroxides and free radicals to eliminate oxidative damage induced by ROS, thereby protecting tissues and cells against oxidative stress (14). Furthermore, the removal of toxic metabolites from the cell is known as one of the most important functions of glutathione. The continuity of sulfhydryl groups within cells is maintained through the reduced form of glutathione. GSH also serves as the main cofactor for enzymes such as GST (15).

Glutathione S-transferases (GSTs; E.C.2.5.1.18) represent a superfamily of multifunctional enzymes that play significant roles in the biosynthesis of certain metabolites, cellular detoxification, regulation of proliferation, and apoptosis mechanisms (15, 16). Furthermore, they are known as detoxification enzymes that catalyze the formation of metabolites (xenobiotic and endobiotic), each consisting of two subunits, which have a lower toxic effect due to conjugation with glutathione (GSH) and gain solubility in water, making them more easily excreted from the body (17). Therefore, GSTs constitute an enzyme family that catalyzes the conjugation of endogenous (internal) and exogenous (external) elecrophilic and hydrophobic compounds with glutathione (18). GSTs are found in various tissues in the body, particularly in the liver. These enzymes play a significant role in removing toxic substances from the body and protecting cells from the effects of various harmful compounds. They typically facilitate the transformation of substances into metabolites that are more easily excreted and less toxic. The activity of GSTs can vary among individuals due to genetic factors and environmental influences (19). Due to the entry of exogenously derived xenobiotics into the body of organisms and the resulting impact on tissues, there is an increase in GST levels in these areas. Additionally, GSTs create a defense mechanism against

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lipid peroxidation of membrane constituents (15). Due to the catalysis of detoxification of harmful toxins by all GST isoenzymes, GSTs are known as natural protectors (20).

Through the balance between ROS and antioxidants, cells can perform their normal functions. The basal level of ROS is crucial for cells to function healthily. However, excessive ROS can lead to damage and necrosis in cells, followed by apoptosis. Increased ROS levels can reduce nitric oxide (NO) levels, leading to vasoconstriction and consequently arterial hypertension. Similarly, elevated ROS negatively affects myocardial calcium utilization, leading to arrhythmias, and triggers cardiac issues through cellular apoptosis. Additionally, ROS exhibits pro-atherosclerotic properties by promoting the formation of atherosclerotic plaques (21, 22). The relationship between oxidative stress and atherosclerosis involves situations where antioxidant systems fall short. The antioxidant system attempts to limit the effects of oxidative stress by neutralizing ROS in cells. However, when this balance is disrupted, oxidative stress increases and can elevate the risk of atherosclerosis. Modern research and literature support the significant role of oxidative stress in the pathogenesis of atherosclerosis (23).

Although the etiopathogenesis of arterial atherosclerosis is still not fully known, there is evidence showing that oxidative stress, which occurs due to the disruption of the balance between antioxidant defense and reactive oxygen species production, plays a vital role in the pathogenesis of coronary atherosclerosis and its complications. It is predicted that the formation of ROS may contribute to the development of atherogenesis through mechanisms such as oxidation of LDL, endothelial dysfunction, growth of vascular smooth muscle cells and migration of monocytes (24). As a result, many studies have shown that oxidative stress is closely related to the development and progression of atherosclerosis (25).

Glutathione S-transferase enzyme is responsible for the detoxification of intracellular carcinogens and harmful organic substances. Some studies have reported that polymorphism in this enzyme may initiate or accelerate the development of cancer and atherosclerosis. In addition to routine cardiac markers, lipid profile, some biochemical parameters and inflammatory markers for the diagnosis of CAD, determining the GST enzyme activity level is thought to be important in the diagnosis of CAD-induced atherosclerotic conditions, as well as to help elucidate the mechanisms that constitute the main cause of this disease.

The aim of this study was to evaluate the levels of GST enzymes in individuals diagnosed with coronary artery disease compared to those without coronary artery disease. Additionally, the study aims to investigate the relationship between GST enzyme levels and certain biochemical parameters (total cholesterol, triglycerides, LDL-C, HDL-C, urea, creatinine, CRP) in both groups of individuals.

Materials & Methods

Place of Research:

By using the random selection method among the volunteers who agreed to participate in the study, selection was made among individuals diagnosed with CAD who applied to the cardiology outpatient clinic of Kars Kafkas University Faculty of Medicine Health Research and Application Hospital or were admitted to the cardiology service.

Population and Sample of the Research :

Patients living in the center of Kars apply to Kars Kafkas University Faculty of Medicine Health Research and Application Hospital. The research was carried out with male and female patients who applied to Kars Kafkas University Faculty of Medicine Health Research and Application Hospital Cardiology Polyclinic.

Collection and Processing of Blood Samples:

The study collected blood samples from individuals who provided voluntary consent and accepted the informed consent form for the examination of GST enzyme activity. Blood samples from the patient and control groups were collected into hemogram tubes with purple caps containing ethylenediaminetetraacetic acid (EDTA), with 2 mL volume each. After complete blood counts were performed on the blood samples, the tubes

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were centrifuged at 2500xg for 15 minutes. The plasma and leukocyte layer remaining at the top of the centrifuged tubes were carefully collected using a dropper, and the erythrocyte pellet at the bottom of the tubes was washed three times with 1% (isotonic) NaCl solution. Each washing process was performed at 2500xg for 15 minutes, and the obtained erythrocytes were hemolyzed with five times their volume of ice-cold water. To remove erythrocyte cell membranes from the hemolysate, the hemolysate was centrifuged at 20000xg for 30 minutes at +4°C. The supernatant containing the hemolysate was carefully transferred into capped tubes and stored at -20°C for further analysis, while the sediment was discarded.

Additionally, blood samples were collected from individuals who accepted the informed consent form for the examination of their biochemical parameters, using red-capped gel biochemistry tubes. Each tube contained 2 mL of blood. The blood samples from both the patient and control groups were centrifuged at 4000xg for 10 minutes at +4°C in the Biochemistry Laboratory of Kafkas University Health Research and Application Hospital. This process resulted in obtaining clear serum samples. Biochemical parameters (total cholesterol, triglycerides, HDL-C, LDL-C, urea, creatinine, CRP) were analyzed from the serum samples using an automatic biochemical analyzer (Beckman Coulter Chemistry Analyzer AU5800, Japan).

The Characteristics of Included/Excluded Individuals in the Study:

A total of 54 individuals (27 females - 27 males) aged between 30 and 80 years, diagnosed with coronary artery disease, who applied to the cardiology outpatient clinic and/or were admitted to the cardiology service at the Health Research and Application Center of Kafkas University Faculty of Medicine, were included in the study. Individuals who did not provide voluntary informed consent, patients under 30 years of age, pregnant individuals, patients with liver disease, those with active malignancy, and those with a history of stroke were not included in the study. In the control group, individuals under 30 years of age and those with symptoms or signs of heart disease were excluded from the study.

GST Activity Assay:

The GST enzyme activity assay was conducted using a modified version of the method described by Habig et al. (26). GST activity was measured at 25°C using 1-chloro-2,4-dinitrobenzene (CDNB) as a model substrate. The assay system included a phosphate buffer (pH 6.5), GSH (20 mM), and CDNB (25 mM). A spectrophotometer was used to estimate the changes in absorbance at 340 nm for 3 min. One unit of activity is defined as the formation of 1.0 µmol product per minute.

Analysis of Data:

The laboratory results were imported into the 'Statistical Package for Social Sciences' (IBM SPSS Statistics 20) software for analysis. Descriptive statistics were computed for categorical variables and expressed as mean, number (n), and percentage (%). The Wilcoxon Mann-Whitney U test was utilized to assess the relationship between categorical variables. Seroprevalence values were reported with a 95% confidence interval. A significance level of 5% was applied in the calculations, and a p-value less than 0.05 was considered statistically significant.

Results

Statistical analysis revealed a significant difference in the age distribution between genders in both the control and CAD-patient groups ($p<0.05$). When evaluating the mean ages of women and men in the control and CAD-patient groups, it was found that the average age of men was lower in both groups (Table 1).

Table 1. Gender distribution in control and CAD diagnosed patient groups.

Gender	Control Group	CAD Patients Group	p
	Mean ± SD	Mean ± SD	
Female	65.96 ± 11.38	66.11 ± 7.44	0.000
Male	58.15 ± 11.53	57.07 ± 8.84	

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Statistical analysis revealed a significant difference in gender distribution by age in the CAD diagnosed patient group ($p<0.05$). Additionally, in both male and female individuals within the CAD diagnosed patient group, the average age of individuals aged 30-59 was lower than the average age of individuals aged 60 and above (Table 2).

Table 2. Distribution of gender according to age groups in the patient group diagnosed with CAD

Age Group	Female	Male	p
	Mean ± SD	Mean ± SD	
30-59	53.00 ± 3.83	51.06 ± 5.43	0.000
60 and older	68.39 ± 5.18	65.82 ± 4.12	

Wilcoxon Mann-Whitney U test was utilized to determine whether there was a significant difference in GST enzyme activity levels between patients diagnosed with CAD and those without. In other words, the investigation aimed to ascertain whether CAD had a significant effect on GST enzyme activity. Upon examination of GST enzyme activity levels between the groups, the GST enzyme activity level was found to be significantly higher in the patient group compared to the control group ($p<0.05$) (Table 3).

The study also investigated whether CAD had a significant effect on certain biochemical parameters. For this purpose, the distribution of lipid parameters (total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol) as well as urea, creatinine, and CRP levels between the control and CAD patient groups was statistically analyzed.

Upon statistical examination of lipid parameters (total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol) between the groups, the data revealed that there was no significant difference in serum total cholesterol ($p>0.05$), serum triglyceride ($p>0.05$), and serum LDL cholesterol levels ($p>0.05$). However, a significant difference was observed in serum HDL cholesterol levels ($p<0.05$). Additionally, while the serum total cholesterol, serum triglyceride, and serum LDL cholesterol levels of the CAD patient group were found to be higher compared to the control group, the serum HDL cholesterol level was higher in the control group compared to the patient group (Table 3).

According to the statistical analysis conducted on the biochemical parameters including urea, creatinine, and CRP levels between the CAD diagnosed patient group and the control group, no significant differences were found in urea ($p>0.05$), creatinine ($p>0.05$), and CRP ($p>0.05$) levels. However, it was determined that the CRP levels of the CAD diagnosed patient group were higher than those of the control group, while the levels of urea and creatinine were higher in the control group compared to the patient group (Table 3).

Table 3. Comparison of all parameters between the groups included in the study

Lipid Parameters	Control Group	CAD Patients Group	p
	Mean ± SD	Mean ± SD	
GST (U/mL)	5.63 ± 2.06	6.98 ± 2.59	0.000
Total cholesterol (mg/dL)	143.87 ± 37.04	154.41 ± 50.36	0.396
Triglyceride (mg/dL)	111.48 ± 29.36	143.48 ± 111.32	0.341
HDL-C (mg/dL)	47.20 ± 6.39	42.54 ± 8.39	0.002
LDL-C (mg/dL)	59.46 ± 22.46	83.37 ± 44.19	0.011
Urea (mg/dL)	35.46 ± 9.43	36.69 ± 11.81	0.477
Creatinine (mg/dL)	0.93 ± 0.33	0.89 ± 0.19	0.374
CRP (mg/dL)	3.18 ± 1.33	7.17 ± 12.86	0.386

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The Spearman correlation analysis was conducted to reveal the relationships between troponin, a routine cardiac parameter included in the CAD diagnosed patient group, and cardiac markers, GST enzyme level, lipid parameters, and biochemical blood parameters (Table 4).

Table 4. Relationship of troponin with GST enzyme activity and biochemical blood parameters (Spearman Correlation Analysis)

		Troponin	GST	Total_C	Triglyceride	HDL_C	LDL_C	Urea	Creatinine	CRP
Troponin	r		·.040	0.009	-0.021	-0.062	0.044	-0.025	-0.046	0.045
	p		0.774	0.946	0.881	0.655	0.754	0.855	0.743	0.746
GST	r			0.145	-0.041	-0.025	0.233	0.099	0.101	-0.097
	p			0.294	0.768	0.858	0.090	0.476	0.468	0.484
Total_C	r				0.395**	0.523**	0.869**	0.090	-0.214	0.177
	p				0.003	0.000	0.000	0.518	0.121	0.200
Triglyceride	r					0.084	0.092	-0.289*	-0.111	0.085
	p					0.547	0.508	0.034	0.424	0.540
HDL_C	r						0.427**	0.056	-0.306*	-0.073
	p						0.001	0.688	0.024	0.598
LDL_C	r							0.148	-0.220	0.232
	p							0.286	0.109	0.091
Urea	r								0.223	-0.068
	p								0.105	0.623
Creatinine	r									-0.250
	p									0.068

** Correlation is significant at 0.01. *Correlation is significant at 0.05.

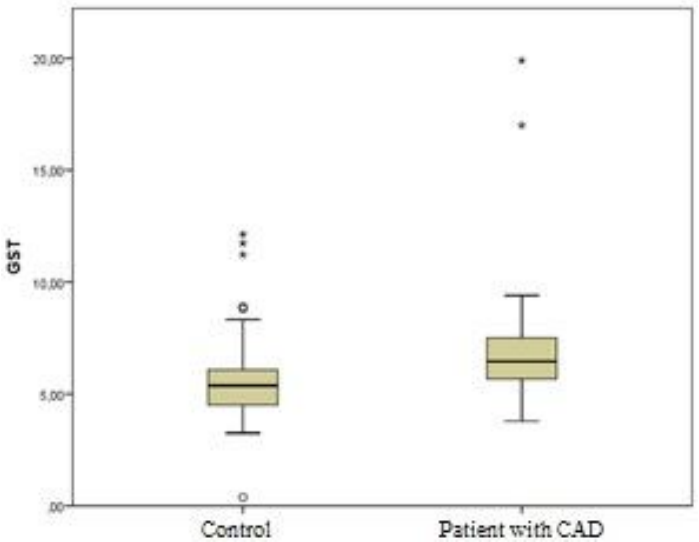

Fig. 1. Distribution of GST enzyme activity level in control and patient groups

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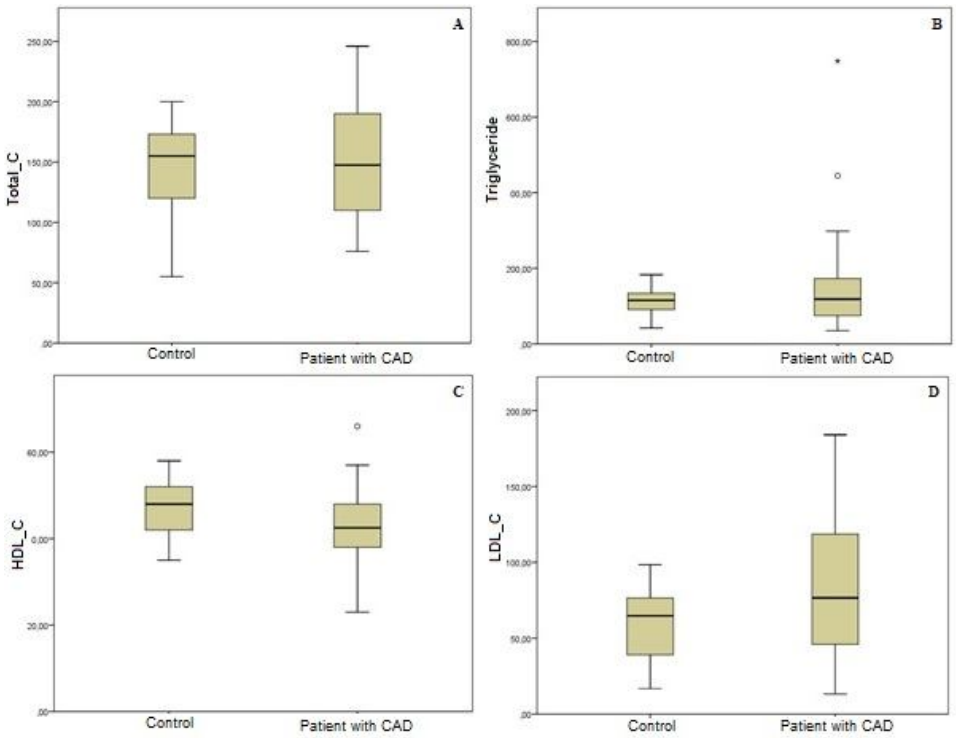

Fig. 2. Distribution of serum total cholesterol (A), triglyceride (B), HDL-C (C) and LDL-C (D) levels in control and patient with CAD groups

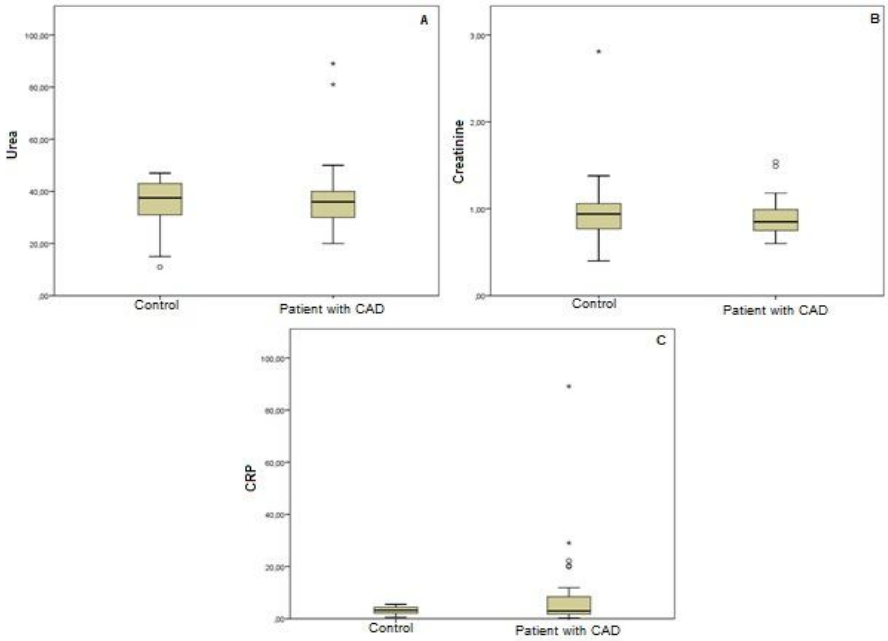

Fig. 3. Distribution of urea (A), creatinine (B) and CRP (C) levels in control and patient with CAD groups

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Discussion

CAD stands as one of the most prevalent heart conditions, arising from atherosclerotic changes in the arteries that supply blood to the heart. CAD, a chronic inflammatory process, is triggered by endothelial damage and influenced significantly by genetic factors, alongside chronic infections, oxidative stress, stress, diabetes, smoking, high cholesterol, and high blood pressure. During the process of endothelial damage, endothelial cells release inflammatory cytokines and become targets for leukocytes, monocytes, and platelets. Monocytes migrate to endothelial cells, transforming into macrophages and loading lipids to form foam cells containing oxidized LDL cholesterol. As a result of smooth muscle cell proliferation, fibrous atheromatous plaques develop (27).

For CAD, besides risk factors that individuals cannot change such as gender, age, genetic predisposition, and race, there are also modifiable risk factors including obesity, sedentary lifestyle, stress, heavy smoking, diabetes, hypertension, high total cholesterol, high triglyceride levels, low HDL cholesterol levels, and elevated LDL cholesterol levels. Both modifiable and non-modifiable risk factors include age and gender, which constitute the fundamental risk factors for CAD (28, 29). In our study, half of the patients diagnosed with CAD were males (50%). The mean age of female patients (66.11 ± 7.44) was higher than that of male patients (57.07 ± 8.84). According to the literature, estrogen hormone in women is known to have a certain protective effect against cardiovascular diseases. After menopause, there is an increase in the frequency of cardiovascular diseases such as hypertension, arterial stiffness, coronary artery diseases, and stroke due to hormonal changes (30). In this context, the higher age and mean age of female patients in our study could be attributed to the decreased protective effect of estrogen after menopause, which is associated with gender. This finding is consistent with the results obtained in previous studies (31). In addition, gender distribution according to age in the patient group diagnosed with CAD was statistically examined and a significant difference was observed ($p < 0.05$). In both men and women in the patient group diagnosed with CAD, the average age of individuals between the ages of 30-59 was determined to be lower than the average age of the male and female groups aged 60 and older.

Many studies have indicated that after endothelial dysfunction, excessive oxidative stress in the plasma and inadequate antioxidant defense system may lead to the development of CAD risk. Although the mechanisms of atherosclerosis formation and development have not been definitively established scientifically, it has also been suggested that it may begin with LDL oxidation and progress with the accumulation of foam cells. Oxidized molecules generally initiate radical chain reactions, leading to the formation of many new oxygen-free radicals, and the effects of such radicals can be quenched by antioxidants (32-34). The excessive production of reactive oxygen species (ROS) represents a significant pathological process in atherosclerosis. It has been evidenced that each component of the atherosclerotic blood vessel, primarily including superoxide anion (O_2^-), contributes to increased ROS production. Key sources of ROS include vascular smooth muscle cells, endothelial cells, fibroblasts, and infiltrating leukocytes. ROS production affects gene transcription by causing damage to DNA and enhances the production of inflammatory transcription factors (35).

Atherosclerosis, which predisposes to cardiovascular risk factors, is also associated with oxidative stress. Several agonistic effects and pathological conditions lead to dysregulation in the functions of oxidant and antioxidant enzymes, and as a result, the free radical load in the vessel increases. Oxidative stress triggers pathological events in cells at every stage of the disease, including the development and progression of atherosclerosis. GSTs, which are found in various tissues in the body, especially in the liver, play an important role in the removal of toxic substances from the body, protecting cells from the effects of various harmful compounds and generally contributing to Phase-II detoxification processes by ensuring the transformation into more easily excreted and less toxic metabolites. In addition, the defense

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mechanism of the structural components of the membrane against lipid peroxidation is created by GSTs (15).

The maintenance of organismal vitality is closely associated with preserving antioxidant capacity within the organism. Many tissues face cellular damage linked to various types of mitochondrial degeneration due to GSH deficiency. Specifically, any disruption in the balance between oxidant-antioxidant systems localized within cellular compartments implies numerous pathophysiological conditions for a normal cell, such as neurodegenerative damage, aging, cancer, and immune disorders. Therefore, many diseases resulting from GSH deficiency can be prevented or reversed through the administration of GSH or GSH precursors. Oxidative stress is recognized as the effects of free radicals generated during normal metabolism or various pathological events. If these radicals are not removed from their environment, they can lead to damage in cells by inactivating many enzymes and proteins, ultimately resulting in necrosis. Hence, free radicals are implicated as causative factors in various conditions like premature aging, cancer, autoimmune diseases, and inflammation (15,18). In a study, the relationship between oxidative stress and inflammation markers with GST gene polymorphism was investigated in patients with coronary artery disease (CAD), and it was found that individuals with the GST T1 or GST M1 null genotype had higher levels of inflammation markers, which increased the risk of CAD. Based on this, it is suggested that the combination of inflammation and lipid peroxidation leads to the disruption of endothelial integrity (36). In another study conducted in 2009, the relationship between GST polymorphism and triglycerides (TG) and HDL cholesterol (HDL-C) levels was investigated. The study involved 1577 individuals, and their triglyceride, HDL cholesterol, and triglyceride/HDL cholesterol ratios were examined. It was found that the GST double null genotype was associated with hypertriglyceridemia and low HDL-C levels. Additionally, the relationship between GST polymorphism and vascular diseases was examined, indicating that having the double null genotype increased the risk of vascular diseases by 1.55 times (37). Statistical analysis of the GST enzyme activity levels in the individuals from both the control and CAD diagnosed patient groups included in this study revealed a statistically significant difference ($p<0.05$) between the GST enzyme activity levels of the control and patient groups. Additionally, the GST enzyme activity level was found to be higher in the patient group compared to the control group. These findings are consistent with the objectives of our study (Figure 1).

The increase in the amount of ROS and/or the decrease in the defense systems that prevent this situation directly causes endothelial dysfunction, as well as causing structural damage in tissues and organs. Glutathione is an agent that is most abundant in cells in antioxidant systems and has many important functions. GSH is responsible for both removing ROS and regenerating oxidized species of other antioxidants. GSH is transformed into GSSG by a reaction catalyzed by the NADPH-dependent glutathione reductase enzyme. Cells help preserve the functions of cells by providing integrity in cells with the ability to maintain glutathione levels. In addition, GSH serves as the main cofactor for enzymes such as GST (38). Studies have shown that there is a relationship between inflammation and lipid peroxidation and GST gene polymorphism. With endothelial dysfunction resulting from inflammation and lipid peroxidation, thrombosis occurs and occlusion in the vessels is observed (39).

In cases of dyslipidemia, the increased accumulation of fat within the arterial walls can lead to narrowed blood flow, resulting in a higher risk of ischemic attacks, heart diseases, strokes, embolic attacks, and other related risks. Lipids, being insoluble in water, are transported in the form of lipoproteins in the blood, hence, hyperlipidemia is often associated with lipoprotein abnormalities. While elevated levels of LDL-C, responsible for transporting cholesterol from the liver to tissues, are commonly linked to cardiac conditions, it's worth noting that individuals with normal LDL-C levels can also experience various cardiac issues (40). This situation can be explained by evaluating non-HDL-C instead of LDL-C. Thus, non-HDL-C is

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included among the determinative lipid parameters in cardiac conditions. The contribution of other lipoproteins besides LDL-C to the atherosclerotic risk factor in the process of atherosclerosis can be cited as the reason for this (41). These are particularly involved in the metabolism of lipoproteins, either by producing intermediate or end products rich in triglycerides, especially in VLDL and chylomicrons. Through reactions catalyzed by lipases, the removal of triglycerides from lipoproteins rich in triglycerides leads to these structures becoming even denser and richer in cholesterol. Particles resulting from triglyceride lipolysis, which are rich in Apo-B48, are known as chylomicrons, which transport dietary fat. VLDL metabolism, which carries endogenously produced triglycerides and has a more complex metabolism compared to others, is expressed as the conversion of VLDL into LDL after the conversion of VLDL to IDL. These particles, which vary in both density and triglyceride/cholesterol ratio, all contain ApoB-100. It is believed that these particles are important risk factors for CVD. This situation can be explained by the uptake of particles that the liver cannot eliminate into arteries, leading to the formation of foam cells, which play a role in atherosclerosis by becoming lipid-laden macrophages (42-44). Based on the data obtained from our study, the levels of total cholesterol, triglycerides, and LDL-C were found to be higher, while HDL-C levels were lower in the group diagnosed with CAD (Figure 2). These findings are consistent with various previous studies conducted on this topic.

Cardiovascular risk factors are highly prevalent in individuals diagnosed with chronic kidney disease (CKD), and their contribution to atherosclerotic vascular disease is particularly significant in the early stages of CKD. In addition to other risk factors, hypertension, insulin resistance/diabetes, dyslipidemia, and smoking not only contribute to atherosclerotic cardiovascular and cerebrovascular diseases but also contribute to the progression of CKD due to their effects on both large (e.g., renal artery stenosis) and smaller (e.g., nephrosclerosis) renal vessels (45). When the creatinine and urea values of the patient and control groups were statistically analyzed, no significant difference was found (Figure 3). However, in the group diagnosed with CAD, these values were determined to be lower (Table 3). Additionally, upon evaluation of the obtained data in line with the literature review, it was observed that the results were consistent with other studies conducted.

Another factor that plays a significant role in all stages of atherosclerosis is inflammation. One of the commonly used clinical markers of inflammation is the CRP level. CRP, an acute-phase protein, is produced in the liver. In response to inflammation, its levels increase, and it is observed among the risk factors for individuals diagnosed with CAD. Elevated levels of CRP are associated with the stage of coronary syndrome in patients with stable CAD. Although the pathogenesis between CRP levels and CAD is not fully understood, the existence of many mechanisms influencing this relationship is anticipated. CRP contributes to the breakdown of fibrinolysis, collagen degradation in monocytes, activation of the complement system, and the uptake of LDL-C by macrophages, thereby converting them into foam cells. Furthermore, inflammation has been identified as a crucial process in the pathogenesis of atherosclerosis (46). The association between inflammation and CVD has been confirmed by significant evidence. (46-48). The inflammatory process is generally associated with the formation of plaques in the presence of atherosclerosis, which may lead to clinical conditions. This process is also highlighted for its potential to cause coronary syndromes (47). The results obtained from prospective studies involving the important inflammatory marker, CRP protein, have revealed that CRP is a predictor independent of subsequent cardiovascular events (49). Numerous studies have examined CRP levels, and it has been concluded that high serum CRP levels in healthy individuals without cardiovascular disease may be an important predictor for cardiovascular events in subsequent years (50, 51). The study revealed that serum CRP levels were higher in the group diagnosed with coronary artery disease compared to the control group (Figure 3). This finding is consistent with the literature.

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The study examined GST enzyme activity levels in patients diagnosed with CAD, revealing higher GST enzyme activity in the patient group compared to the control group. Additionally, total cholesterol, triglycerides, LDL-C, and CRP levels were found to be elevated in the patient group compared to the control group, while HDL-C, urea, and creatinine levels were decreased. Statistical significance was observed in GST enzyme activity and HDL-C levels, whereas no statistically significant differences were observed in total cholesterol, triglycerides, LDL-C, urea, creatinine, and CRP levels. In the light of these data obtained, it was concluded that parameters that were not found to be significant would not provide useful information in the diagnosis of CAD. However, we believe that the finding that the GST enzyme level is significant in patients diagnosed with CAD is a candidate to be an important criterion in the diagnosis of this disease and that this parameter can be used in the diagnosis of patients in the clinic with the data obtained from further studies. More studies with more case and control individuals are recommended to confirm the data obtained in this study.

Acknowledgments

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Authors' Contribution

Conception and design of research: HED, Performed experiments: TS, Analyzed data: TS, Interpretation of the results of experiments: TS, Prepared figures: HED, Drafted the manuscript: HED.

Ethical statement

This study was carried out with the approval of the Ethics Committee of Kafkas University Faculty of Medicine (2020/262). It was conducted in accordance with the principles of the Declaration of Helsinki II. Informed written consent was obtained from all study subjects. (80576354-050-99/262)

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Not applicable.

Conflict of interest

The authors have no conflict of interest in this study.

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