



➔ Original Article



Effect of Glomerular Filtration Rate on the Severity of Coronary Artery Disease in Diabetic Patients Undergoing Angiography

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Abstract

Background: Cardiovascular disease is the leading cause of disability and mortality in individuals with chronic kidney disease. Using the Gensini score, this study examined the impact of glomerular filtration rate on the severity of coronary artery disease in diabetic patients undergoing angiography.

Methods: This cross-sectional study investigated patients undergoing coronary angiography at Seyed al-Shohada Hospital, Urmia (2021–2022). They were categorized into GFR $\geq$ 90, GFR $>$ 90, GFR $\geq$ 60 groups based on eGFR. The extent and severity of coronary heart disease were evaluated by the GSS.

Results: Of 171 patients, 43.3% were male and 56.7% were female. A statistically significant association was observed between smoking and gender ($P=0.000$). The prevalence of mild vascular involvement was higher among female patients with diabetes mellitus for ≤ 5 years (23.7%) compared to males (17.5%). This trend persisted among females with a longer DM history (22.6% vs. 13.5%). There was a strong correlation between the severity of vascular involvement, DM duration, and gender ($P=0.000$). Among individuals with a GFR of 60–90 (mL/min/1.73 m²), 42.6% and 8.18% had DM for > 5 years and ≤ 5 years. Conversely, of those with a GFR above 90 (mL/min/1.73 m²), 49.2% and 21.6% of patients with > 5 and ≤ 5 years of DM maintained an eGFR above 90 (mL/min/1.73 m²).

Conclusion: Reduced GFR values are correlated with significant CAD detected by GSS in stable patients. Renal function plays a crucial role in predicting the presence and severity of angiographic CAD in individuals without severe renal insufficiency.

Keywords: Coronary artery disease, Diabetes, Gensini score, Angiography, Glomerular filtration rate

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Background

Cardiovascular disease (CVD) is an extensive health concern and continues to be the primary cause of disability and mortality globally (1). According to evidence, 18.5 million individuals succumbed to CVDs in 2019, accounting for 32% of all global fatalities (2). CVDs are the foremost cause of death in end-stage renal disease (ESRD) populations worldwide (3). In patients with chronic kidney disease (CKD), cardiovascular risk is, at least partially, influenced by vascular stiffening (4).

CKD is a chronic condition marked by a gradual and progressive decline in kidney function over time, which can progress to ESRD if left unmanaged (5). It is widely recognized that CKD, identified by an estimated glomerular filtration rate (GFR) below 60 mL/min/1.73 m², is a significant risk factor for CVD and cardiovascular mortality (3). GFR is considered the best indicator of kidney function worldwide, determining the stage of CKD (6). Therefore, the precise evaluation of GFR levels

and their longitudinal changes is crucial for detecting CKD, assessing its severity, and making informed decisions regarding diagnosis, prognosis, and treatment (7). A comprehensive meta-analysis has revealed that 30% and 40% reductions in GFR were associated with an increased risk of ESRD and mortality in both individuals with and without diabetes mellitus (DM) (8). CVD and CKD are prevalent comorbidities in patients with type 2 DM (T2DM) (9).

T2DM is also a significant factor contributing to heart failure, peripheral arterial insufficiency, and microvascular complications, significantly impacting the overall quality of life and longevity (10). Due to its association with increased cardiovascular mortality, T2DM has long been considered a “cardiovascular risk equivalent”. This concept was largely based on the results of a Finnish study (11), which reported that T2DM patients without coronary heart disease (CHD) had a similar risk of coronary mortality as non-diabetic

patients with a history of CHD. However, recent research suggests that CHD risk in T2DM is not universally equivalent to that of patients with prior CVD; rather, it exhibits considerable heterogeneity (12). A large population-based cohort study (13) involving 1,586,061 adults aged 30–90 years followed for ten years revealed that the CHD risk was significantly lower among T2DM patients without CHD compared to patients with CHD without DM (hazard ratio: 1.70, 95% confidence interval: 1.66–1.74 versus hazard ratio: 2.80, 95% confidence interval: 2.70–2.85).

GFR is a widely recognized, valuable, readily calculable, and reproducible measure that is employed to assess renal functional status (14). According to research, GFR is a more informative prognostic indicator compared to serum creatinine (15). The present study aims to investigate the impact of GFR on the severity of coronary artery disease (CAD) in diabetic patients undergoing coronary angiography, as assessed by the Gensini Score (GSS). It is expected that the findings of this study will facilitate the potential for angiographic interventions by predicting the extent of coronary artery involvement prior to angiography based on patient risk factors and preparation for addressing potential invasive procedures during angiography.

Methods

This cross-sectional analytical study enrolled consecutive patients who underwent coronary angiography due to positive noninvasive stress testing at Seye al-Shohada Hospital, Urmia, between 2021 and 2022. The study protocol was approved by the Ethics Committee of Urmia University of Medical Sciences (IR.UMSU.REC.1401.095), and informed consent was obtained from all participants. Prior to coronary angiography, height and weight were measured using standard procedures, and body mass index (BMI) was calculated as weight (kg) divided by height (m) squared (kg/m^2). Moreover, blood pressure was assessed by trained technicians using a standard mercury column sphygmomanometer, with systolic and diastolic blood pressure values determined as the average of two measurements. Blood samples were collected for lipid profile analysis, including triglyceride, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol.

Participants were included in the study if they were over 18 years of age and provided informed consent. On the other hand, patients with a history of coronary artery bypass graft surgery, prior myocardial infarction or revascularization procedures, acute heart failure, cardiogenic shock, those on hemodialysis, sepsis cases, and patients with a GFR below 60 were excluded from the study.

Coronary angiography was performed on all patients, and the results were reviewed by at least two interventional

cardiologists. In addition, the severity of CAD was assessed using the GSS system, which was assigned by two independent senior cardiologists. The GSS is calculated by multiplying the location of the lesion by the degree of stenosis, with a higher score indicating a more severe coronary artery lesion. The GSS classifies the narrowing of the coronary artery lumen as mild (GSS below 10), moderate (10 to 40), or severe (more than 40). The score is then multiplied by a factor based on the importance of the coronary artery: 5 for a left main stem lesion, 2.5 for proximal left anterior descending artery (LAD) and proximal circumflex artery (CX) lesions, 1.5 for mid-LAD lesions, 1 for distal LAD, mid/distal CX, and right coronary artery lesions, and 0.5 for other indicators. GFR was estimated, and the relationship between this rate and the severity of coronary artery involvement underwent investigation. Patients were divided into three groups based on their computed GFR into $\text{GFR} \geq 90$, $\text{GFR} > 90$, $\text{GFR} \geq 60$. Eventually, the percentage of patients in each group, the percentage of vascular stenosis severity, and the number of vessels involved in each group were calculated as well.

Sample Size

In this study, based on a previous study (16), the minimum required sample size with 90% confidence and a statistical power test of 75% was estimated to be 171 patients who were randomly selected based on the inclusion criteria.

Statistical Analysis

The data were analyzed using SPSS software (version 21.0 for Windows; SPSS Inc., Chicago, IL, USA). The normality of the distribution of the variables was assessed using the Kolmogorov-Smirnov test. Furthermore, the strength of the association between continuous variables was evaluated using Pearson's correlation coefficient. Additionally, comparisons were made between groups using the Kruskal-Wallis and Mann-Whitney U tests. A chi-square test was also employed to determine whether the distributions of categorical variables differed within groups. In addition, the optimal cutoff value for predicting significant CAD using GFR was determined through receiver operating characteristic analysis, and area under the curve values were calculated. Categorical variables were expressed as percentages. All analyses were stratified based on the severity of CHD, and a *P*-value less than 0.05 was considered statistically significant.

Results

This study was performed on 171 diabetic patients, including 74 (43.3%) males and 97 (56.7%) females, who underwent coronary angiography and met the inclusion criteria. The mean age of the participants was 61.06 ± 9.66 years, with a range of 38–90 years. In addition, the mean ages of male and female patients were 61.04 ± 10.33

years and 60.07 ± 9.17 years, respectively. No significant difference in the mean age was observed between male and female patients ($P=0.983$). The mean BMI of male patients was 29.09 ± 4.5 kg/m², and that of female patients was 30.91 ± 5.10 kg/m². Similarly, there was no significant difference in mean BMI between male and female patients ($P=0.016$). A history of hypertension (HTN) was reported in 129 (75.43%) patients, including 61 (82.4%) males and 68 (91.8%) females. Moreover, no significant association was found between HTN and gender ($P=0.591$). A history of smoking was found in 32 (43%) male and 6 (6%) female patients ($N=38$, 22%). Based on the results, smoking was remarkably more prevalent among male patients compared to female patients ($P=0.000$). Hyperlipidemia was diagnosed in 92 (53.8%) patients, which was calculated indirectly due to the absence of total cholesterol levels in the patient records (Table 1).

Fisher’s Exact Test

The mean GSS of the patients was 26.93 ± 31.36 , with a

Table 1. Baseline Characteristics of Study Participants

Variables	Mean $\pm$ SD/ Number (%)	P value
Gender		
Male	74 (43.3%)	-
Female	97 (56.7%)	
Age (year)	61.06 $\pm$ 9.66	
Male	61.4 $\pm$ 10.33	0.983
Female	60.07 $\pm$ 9.17	
BMI (kg/m2)	30.12 $\pm$ 4.9	
Male	29.09 $\pm$ 4.5	0.06
Female	30.91 $\pm$ 5.10	
Smoking status	38 (22%)	
Male	32 (43%)	0.000
Female	6 (6%)	
Hypertension	129 (75.43%)	
Male	61 (82.4%)	0.591
Female	68 (91.8%)	
Hyperlipidemia	92 (53.8%)	-
TG		
Male	170.6 $\pm$ 116.3	0.069
Female	142.92 $\pm$ 66.10	
LDL		
Male	90.3 $\pm$ 45.56	0.01
Female	70.73 $\pm$ 21.11	
HDL		
Male	44.48 $\pm$ 38.30	0.13
Female	37.51 $\pm$ 12.87	

Note. SD: Standard deviation; BMI: Body mass index; TG: Triglyceride; LDL: Low-density lipoprotein; HDL: High-density lipoprotein.

range of 0–190. Male patients had a higher mean GSS (30.919 ± 35.5405) than female patients (23.89 ± 27.56). Overall, 68 (39.76%), 58 (33.91%), and 45 (26.31%) participants had mild, moderate, and severe CAD, respectively (Table 2). The prevalence of mild CAD was higher among male patients (23%) compared to female patients (13.45%), while that of severe CAD was higher among female patients (25%) compared to male patients (20%). The duration of DM was categorized into two groups: less than 5 years and more than 5 years. The average duration of DM was 2.59 ± 1.099 years and 10.44 ± 4.31 years in the groups with less than 5 years and more than 5 years of DM history, respectively. The proportion of female patients was higher than male patients in both groups (Table 2).

Based on the results (Table 3), the severity of CAD was less prevalent in the early stages of DM. Female patients with less than 5 years of DM and mild CAD were more common (23.7%) than male patients (17.5%). Similarly, the prevalence of female patients with a longer history of DM (more than 5 years) and mild CAD (22.6%) was also higher than male patients (13.5%). Pearson’s correlation test revealed a significant association between the severity of CAD, the duration of DM, and gender ($P=0.000$). The presence of other risk factors (e.g., HTN) was one of the potential reasons for the increased prevalence of CAD among females. Additionally, the severity of CAD increased with the duration of DM. The Pearson coefficient for males, indicating the correlation between the duration of DM and the severity of coronary artery stenosis, was 0.74, demonstrating a strong and statistically significant relationship (standard deviation = 0.00). The results of this test were similar for females, with a Pearson coefficient of 0.743 and a standard deviation of 0.00, indicating a strong and significant relationship.

Using the Pearson correlation test, there was a significant relationship between the angiography score and the duration of DM (0.743 ± 0.00). The angiography score increased with the increase in the duration of DM (Figure 1).

The mean GFR of the 171 patients was 102.65 ± 34.74 mL/min/1.73 m² (Table 4). In addition, the average GFR was 100.99 ± 34.42 mL/min/1.73 m² and 103.92 ± 35.11 mL/min/1.73 m² for male and female patients, respectively. Additionally, 50.8% of the patients (23.3% men and 27.4% women) had a GFR between 60 mL/min/1.73 m² and 90 mL/min/1.73 m². The remaining 49.2% of patients (19.8% men and 29.2% women) had a GFR above 90 mL/min/1.73 m². The Fisher’s exact test indicated that there was no significant relationship between gender and GFR ($P=0.537$). Table 4 provides the results related to GFR distribution among the studied patients.

The mean GFR of the 171 participants was 102.65 ± 34.74 mL/min/1.73 m². In male patients, the mean GFR was 100.99 ± 34.42 mL/min/1.73 m², while in female patients,

Table 2. Mean GSS, Frequency of CAD Severity, and Duration of Diabetes by Gender

	Total	Male	Female	P value
Mean GSS	26.93 ± 31.36	30.91 ± 35.54	23.89 ± 27.56	0.147
CAD severity				
Mild	68 (39.6%)	23 (13.45%)	45 (26.31%)	0.084
Moderate	58 (33.91%)	31 (18.12%)	27 (15.78%)	
Severe	23 (13.45%)	20 (11.69%)	25 (14.61%)	
History of diabetes				
≤ 5	2.59 ± 1.09 (n = 51)	23 (%)	28 (%)	0.095
> 5	10.44 ± 4.31 (n = 120)	51 (%)	69 (%)	

Note. GSS: Gensini score; CAD: Coronary artery disease.

Table 3. Frequency Distribution of Duration of Diabetes With the Severity of CAD by Gender

History of Diabetes CAD Severity	≤ 5		> 5		Total N (%)	P value
	Male n (%)	Female n (%)	Male n (%)	Female n (%)		
Mild	13 (17.5)	23 (23.7)	10 (13.5)	22 (22.6)	68	0.000
Moderate	8 (10.8)	4 (4.1)	23 (31.08)	23 (23.7)	58	
Severe	2 (2.7)	1 (1.03)	18 (24.3)	24 (24.7)	45	

Note. CAD: Coronary artery disease.

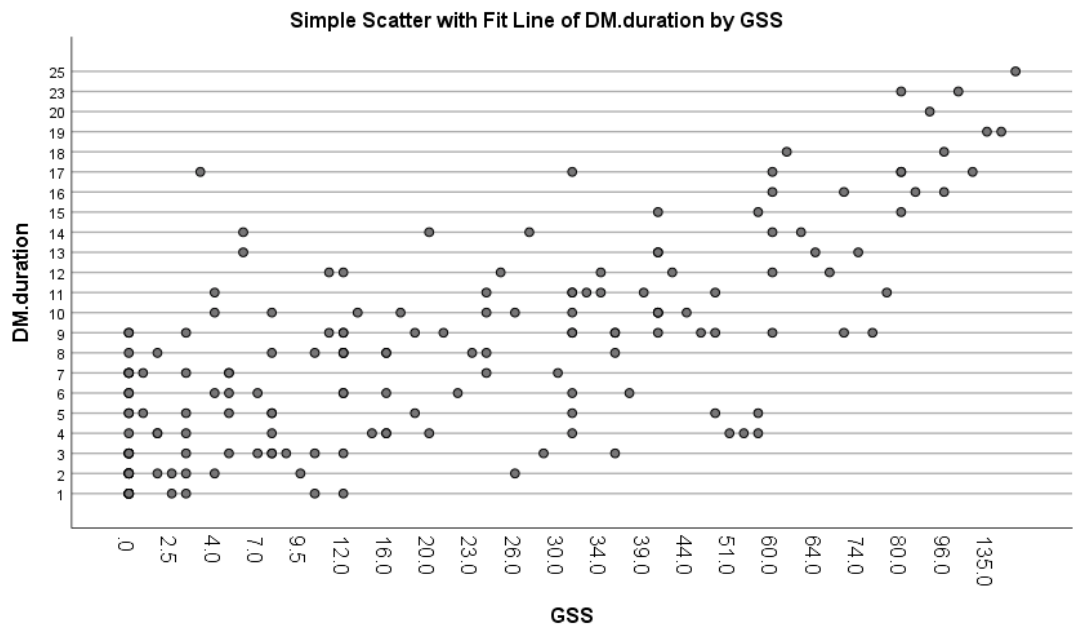


Figure 1. Correlation of the Duration of Diabetes with Gensini Score. Note. DM: Diabetes mellitus; GSS: Gensini score.

it was 103.92 ± 35.11 mL/min/1.73 m². Based on the results of Fisher's exact test, no significant association was found between gender and GFR ($P=0.537$).

Out of 171 patients, 87 (50.8%) had a GFR between 60 mL/min/1.73 m² and 90 mL/min/1.73 m² (Table 4). Of this number, 73 (42.6%) patients had DM for more than 5 years, while 14 (8.18%) had DM for less than 5 years. Of the remaining 84 (78%) patients who had a GFR above 90 mL/min/1.73 m², 47 (49.2%) had DM for more than 5 years, and 37 (21.6%) had DM for less than 5 years. The results of the Pearson correlation test revealed a statistically significant association between the duration

of DM and GFR ($P=0.000$).

In males, a weak but statistically significant negative correlation was observed between the GSS and GFR ($P=0.05$). In general, a significant negative correlation was found between the severity of coronary artery stenosis based on the GSS and GFR ($P=0.00$), suggesting that GFR decreases with an increase in the severity of coronary artery stenosis (Table 4, Figure 2).

Discussion

GFR is a sensitive and valuable indicator of kidney function, which is primarily assessed using creatinine

Table 4. GFR Distribution Among Studied Patients

	Male (76) Mean ± SD	Female (97) Mean ± SD	Total (171)	P-Value	Diabetes (Year)		P-Value
					≤5	>5	
Mean GFR (mL/min/1.73 m²)	100.99 ± 34.42	103.92 ± 35.11	102.62 ± 34.4				
60-90	40 (23.3%)	47 (27.4%)	87 (50.8%)	0.537	14 (8.18%)	73 (42.6%)	0.000
>90	34 (19.8%)	50 (29.2%)	7 (49.2%)		7 (21.6%)	47 (49.2%)	

Note. DM: Diabetes mellitus; GFR: Glomerular filtration rate.

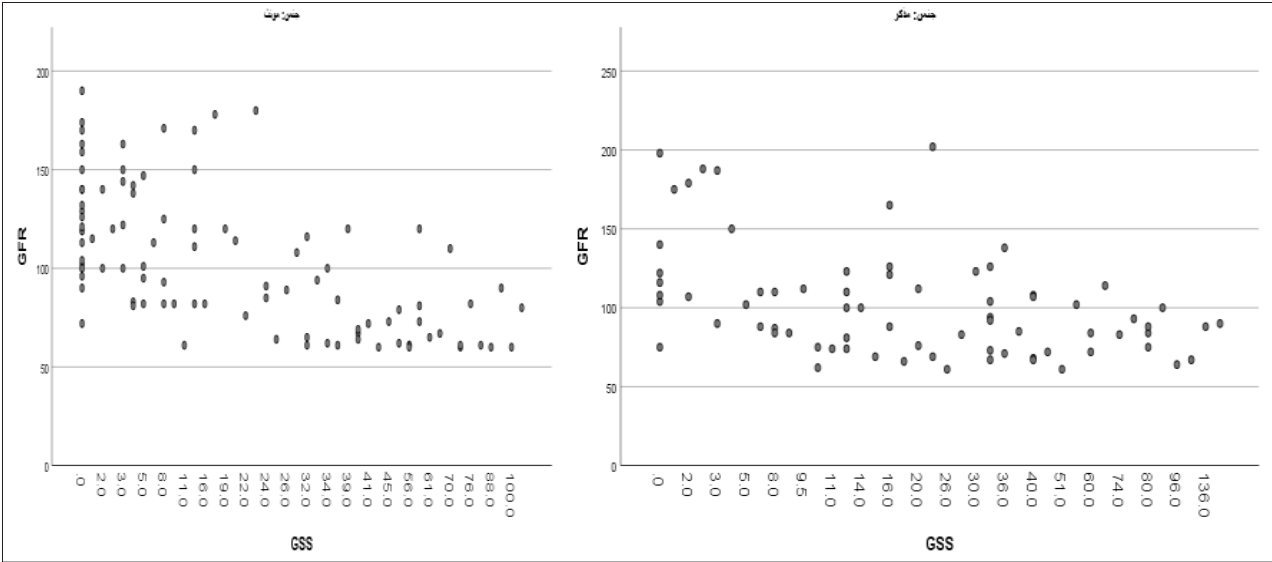


Figure 2. The Relationship Between GFR and GSS in Both Genders. Note. GFR: Glomerular filtration rate; GSS: Gensini score.

clearance or inulin clearance measurements (17). In addition, it is an independent risk factor for CAD (18). Previous studies have demonstrated that mortality is associated with both the GFR level and creatinine level at admission in patients with acute coronary syndrome (19). Several investigations have shown that even mild GFR decline can predict CVD or stroke, while moderate kidney disease consistently predicts cardiovascular mortality in community-based cohorts (19, 20). This study investigated the impact of GFR on the severity of CAD in diabetic patients who underwent angiography based on the GS.

Previous research has provided contradictory results regarding the association between mild-moderate kidney disease and the severity of CAD (21). Budoff et al (22) reported a link between low GFR and increased prevalence of coronary artery calcification, while Ix et al (23) observed no similar independent association. Similarly, Beddhu et al (24) found no difference in the progression rates of total atheroma volume and percentage atheroma volume in patients with GFRs below and above 60 mL/min per 1.73 m².

The underlying mechanisms linking diminished GFR to atherosclerosis remain unclear, but several potential factors may be involved in this process (19). Individuals with renal dysfunction often exhibit an elevated burden of CAD risk factors, including aging, HTN, DM,

metabolic syndrome, and dyslipidemia (25). Studies have shown that reducing low-density lipoprotein cholesterol levels significantly decreased the occurrence of major atherosclerotic events across a broad range of patients with advanced CKD (26). Renal dysfunction has emerged as a significant determinant of mortality and morbidity among individuals who have undergone coronary artery bypass grafting and those recovering from acute coronary syndrome (27).

DM is a significant modifiable cardiovascular risk factor, and the length of time a person has DM is linked to varying levels of CAD (28). Our findings confirmed that both the duration of DM and GSs were significantly associated with gender, though the association was stronger among female patients compared to male patients. Additionally, both factors were found to be much higher among older patients (over 60 years of age), and the association was stronger in older patients. Previous studies reported a close relationship between GFR and other prognostic factors, such as insulin resistance, DM, HTN, and hypercholesterolemia (29). Based on our results, low GFR was associated with advancing age, female gender, and non-smoking habits. It was revealed that multivessel disease is linked to advancing age, female gender, non-smoking habits, and HTN. The average angiography score was reported to be higher in male patients compared to female patients in

our study. Multiple studies indicated gender differences in angiographic findings among men and women with myocardial infarction. Mehta et al (30) studied a large group of patients with acute myocardial infarction and discovered that women had higher mortality rates.

Moreover, 39.76%, 33.91%, and 26.31% of patients had mild, moderate, and severe CAD, respectively. A significant correlation was observed between CAD severity and the duration of DM, with CAD severity increasing with longer DM duration. Previous research indicated a direct link between DM duration and adverse cardiovascular events (31). The Framingham Heart Study found that each 10-year increase in DM duration led to a 1.38-fold higher risk of CAD and a 1.86-fold increased risk of cardiovascular death (32). In the Verona Diabetes Study, ischemic heart disease was the primary cause of cardiovascular-related deaths in men, and the mortality rate increased with increasing DM duration. Moreover, a recent analysis by the British Regional Heart Study revealed that only DM with a duration of at least 10 years was considered a CHD risk equivalent (33).

Our findings demonstrated no significant correlation between gender and GFR, which aligns with the results of a recent meta-analysis investigating the relation between GFR and renal and cardiovascular outcomes by gender (34). The meta-analysis revealed no gender difference in the long-term progression to ESRD for a given GFR, taking into account cardiovascular risk behaviors between men and women. This suggests that the higher renal metabolic burden observed in men with a given GFR is likely attributable to common cardiovascular risk factors, such as BMI.

Early changes in GFR in people with DM may reflect the body's return to normal GFR after initial hyperfiltration, rather than the progression of CKD, thereby indicating their lack of association with future clinical outcomes (35). Based on the results of this study, 50.8% of patients with GFR between 60 mL/min/1.73 m² and 90 mL/min/1.73 m² had DM for more than 5 years, while 8.18% had DM for less than 5 years. Additionally, 78% of patients with GFR above 90 mL/min/1.73 m² had DM for more than 5 years, and 21.6% had DM for less than 5 years, implying a correlation between longer DM duration and higher GFR. This finding conforms to the results of a study by Matsushita et al, showing that GFR at discharge for patients with CHD was within the normal range but tended toward a lower normal value (36). This could be attributed to the longer duration of DM in these patients, as prolonged DM has been shown to worsen renal function (37). The normal GFR at discharge for patients with CHD who were admitted for hyperglycemia treatment indicates that kidney function may improve with short-term hyperglycemia management (38).

Limitations of the Study

Our study had several limitations, including its cross-sectional design and single-center approach. Additionally, patients were not subjected to intravascular ultrasonography to evaluate coronary atherosclerotic plaque burden. Another limitation was the absence of albuminuria data, which may influence the cardiovascular effects of renal dysfunction. Accordingly, future studies should employ larger sample sizes and investigate other controversial factors to refine the cutoff points with improved sensitivity and specificity. Moreover, inflammatory markers (e.g., high-sensitivity C-reactive protein and cardiac enzymes) should be measured and compared to the Sex Hormone–Binding Globulin scoring system in future research.

Conclusion

Our findings revealed that lower GFR values are linked to the presence of significant CAD, as assessed by the GSS in stable patients. Renal function plays a crucial role in predicting the presence and severity of angiographic CAD in individuals without severe kidney impairment. Both the duration of DM and the GFRs exhibited statistically significant associations based on gender. Finally, the severity of CAD was directly correlated with the duration of DM, such that the severity of CAD increased with longer DM duration.

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Authors' Contribution

Conceptualization: Roghaiyeh Afsargharehbagh, Alireza Rostamzadeh.

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Competing Interests

The authors declare that they have no competing interests relevant to the content of this article.

Consent to Participate

Informed consent was obtained from all individual participants included in this study.

Ethical Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Urmia University of Medical Sciences (No. IR.UMSU.REC.1401.095).

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