The Association of Glomerular Filtration Rate with Coronary Artery Disease in Type 2 Diabetic Patients

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Abstract

Objective: Chronic kidney disease (CKD) and diabetes mellitus can influence coronary artery disease (CAD) independently. The aim of this study was to evaluate the association of glomerular filtration rate (GFR) and CAD in type 2 diabetic patients (T2DM).

Materials and Methods: This cross sectional study evaluated 3624 T2DM patients with clinical presentation of CAD whose documents were registered in angiography center of Shahid Mohammadi Hospital in Bandar Abbas, Iran during 18 months. GFR was measured by MDRD method and divided into 5 subgroups: GFR< 15, 15≤ GFR< 30, 30≤ GFR< 60, 60≤ GFR< 90 and GFR≥ 90. Then the association of 5 subgroups of GFR with coronary angioplasty in T2DM patients was evaluated. T-test was used to compare the mean of quantitative variables, and chi-squared test for qualitative variables. Using SPSS- 22 the collected data were analyzed and *P*-value< 0.05 was significant.

Results: Among 3624 T2DM patients, 36% had GFR< 60 (ml/min/1.73m^2).The highest frequency percentage of coronary angioplasty (53%) was observed in the GFR stage 3 (30-60) ml/min/1.73m^2. A significant inverse association was observed between the GFR of T2DM patients and the frequency of CAD. (*P*-value< 0.001). There was also a significant association between GFR< 60 and history of hypertension and dyslipidemia. (*P*-value< 0.001).

Conclusion: A reduced GFR in patients with diabetes has associations with CAD.

Keywords: Coronary artery disease, Glomerular filtration rate, Diabetes mellitus

Introduction

Diabetes mellitus is one of the most important risk factors for chronic kidney disease (CKD). About 20%-40% of diabetic patients can develop CKD (1-3). It is often manifested with persistent albuminuria or other manifestations of renal dysfunction (1,4).

CKD can manifest itself 10 years after the diagnosis in patients with type 1 diabetes, and at the time of diagnosis in T2DM. This disease

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can eventually progress to End Stage Renal Disease (ESRD), and it is one of the factors leading to kidney transplant worldwide (5).

CKD and diabetes independently increase the risk of CAD (6,7). Compared to patients without diabetes, those with diabetes have a higher risk of CAD (8).

In addition, CKD in patients with diabetes can independently increase the risk of cardiovascular diseases (9,3). Various studies have demonstrated a significant relationship between different degrees of CKD and increased risk of cardiovascular diseases in the general population (10-14). A relationship has also been observed among patients with diabetes (12). The relationship between GFR and CAD is more studied in developed countries (13,14) and there is need for it to be more studied in developing countries to prevent CAD mortality in diabetic patients.

The present study examined the relationship between GFR and CAD in patients with diabetic kidney disease. The existence of a significant relationship can result in the early diagnosis and treatment of CAD by using GFR in patients with diabetic nephropathy.

Materials and Methods

This cross-sectional study evaluated 3624 patients with type 2 diabetes in angiography center of Shahid Mohammadi Hospital during 18 months from June 1st, 2017 to December 1st, 2018.Patients with type 2 diabetes were selected based on inclusion and exclusion criteria and their documents were studied in the registry of the angiography center of Shahid Mohammadi Hospital. All T2DM patients who met the inclusion and exclusion criteria entered the study, so we used the survey method for sampling.

CAD was defined as T2DM patients with clinical presentation of CAD (nonfatal myocardial infarction or coronary angioplasty or the patients who had CAD due to clinical, laboratory or electrocardiogram findings according to cardiologist). The documents of the patients were registered in the registry of angiography center of Shahid Mohammadi Hospital, Bandar Abbas, Iran.

GFR was calculated by MDRD method (18):

GFR= 175 (or 186) x Serum creatinine -1,154 x Age - 0,203

(The value is multiplied by 0,742 in women, by 1,212 in black people.)

GFR was divided into 5 subgroups: GFR< 15, 15≤ GFR<30, 30≤ GFR<60, 60≤ GFR<90 and GFR≥ 90 ml/min/1.73m^2 based on KIDGO classification of CKD (19). Then the association of 5 subgroups of GFR with coronary angioplasty in T2DM patients was examined. The association between age, sex, hypertension, and dyslipidemia with 5 subgroups of GFR was also studied.

Inclusion criteria: patients diagnosed with T2DM by an endocrinologist or an internist according to ADA criteria (7), age≥ 40 y/o with clinical presentation of coronary artery disease (nonfatal myocardial infarction or coronary angioplasty or the patients who had CAD due to clinical, laboratory or electrocardiogram findings) whose documents were registered in the registry of angiography center of Shahid Mohammadi Hospital during 18 months of June 1st, 2017 to December 1st, 2018. Dyslipidemia and hypertension were diagnosed by an endocrinologist or internist according to ADA criteria (7).

Exclusion Criteria: patients who were on dialysis or renal transplant, who had severe liver disease or heart failure, known neoplastic or psychiatric diseases, a history of acute kidney injury or taking contrast and the patients with GFR< 15 ml/min/1.73m^{2}were excluded from the study.

The blood samples were analyzed using Bs800 mindray system. The analyses were performed in Shahid Mohammadi Hospital laboratory on the day of blood collection. All the data were registered in the registry of angiography center of Shahid Mohammadi Hospital of Bandar Abbas, Iran.

T-test was used to compare the mean of quantitative variables, and chi-squared test for qualitative variables. Using SPSS vs22 the

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collected data were analyzed and *P*-value< 0.05 was significant.

Ethical considerations

The protocol of this study was approved by the institutional ethics committee of Cardiovascular Research Center and Clinical Research Development Center of Shahid Mohammadi Hospital, Bandar-Abbas (Code: IR.HUMS. REC.1398.058).

Results

In this study, 3624 patients with diabetes, with the mean age of 58 (± 12) years (54% men and 46% women) were examined. The prevalence of dyslipidemia in this population was 28%. The frequency of hypertension was reported as 53% in the patients with diabetes. Moreover, the frequency of coronary angioplasty was 27% in the patients.

The GFR of the patients was calculated based on the MDRD criteria. The frequency of patients' GFR classification is presented in Table 1.The highest frequency of GFR (59%) was seen in stage 2 (60-89 ml/min/1.73m^2). This study also showed that 36% of the patients had GFR lower than 60 (ml/min/1.73m^2).

In the age group higher than 65 years, 38% of patients had GFR< 60 ml/min/1.73m^2 while in the age group lower than 65 years, GFR< 60 ml/min/1.73m^2 was reported only in 14% of the patients. This difference between the two groups was statistically significant. (*P*-value< 0.01) (Table 3). It was also shown that 17% of patients had a GFR <60 ml/min/1.73m^2 in male patients, whereas 25% had a GFR< 60 ml/min/1.73m^2 in female patients. This difference between the two groups was statistically significant. (*P*-value< 0.001) (Table 3).

The highest frequency of coronary angioplasty (53%) was observed in the GFR stage 3(30-60) ml/min/1.73m^2. A significant inverse association was observed between the GFR of T2DM patients and the frequency percentage of coronary angioplasty. (*P*-value< 0.001) (Table 2). In the group with a history of dyslipidemia, 25% of the patients had a GFR< 60 ml/min/1.73m^2, while in the group without a history of dyslipidemia, 21% of the patients had GFR<60 ml/min/1.73m^2 (*P*-value< 0.01) (Table 3).

The frequency of GFR< 60 ml/min/1.73m^2 was 29% in the group with a history of hypertension, and 14% in the group without a history of hypertension (*P*-value< 0.01) (Table 3).

Discussion

In the present study, 3624 patients with diabetes were investigated. GFR was less than 60 ml/min/1.73m^2 in 22% of these patients. This study showed that reduced GFR is significantly associated with increased coronary angioplasty in T2DM patients.

Table 1. Frequency of GPR classification in patients

GFR	Number	Percentage
Class 1: ≥90 ml/min/1.73m^2	647	17
Class 2: 60-89 ml/min/1.73m^2	2143	59
Class 3A: 45-59 ml/min/1.73m^2	639	17
Class3B: 30-44 ml/min/1.73m^2	165	4
Class4: 15-29 ml/min/1.73m^2	20	7.6
Class 5: <15 ml/min/1.73m^2	15	7.4

Table 2. The relationship between GFR and the frequency of angioplasty

GFR classification	Angioplasty	
	No	Yes
Class1: ≥90 ml/min/1.73m^2	485 (75%)	162 (25%)
Class 2: 60-89 ml/min/1.73m^2	1526 (71%)	617 (29%)
Class 3A: 45-59 ml/min/1.73m^2	453 (71%)	186 (29%)
Class 3B: 30-44 ml/min/1.73m^2	126 (76%)	39 (24%)
Class 4: 15-29 ml/min/1.73m^2	14 (70%)	6 (30%)
Class 5: <15 ml/min/1.73m^2	10 (66%)	5 (34%)

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Table 3. The relationship between age, sex, hypertension, and dyslipidemia with GFR

Variables		GFR Class 1:≥90 ml/min/1.73m^2	GFR Class 2:89-60 ml/min/1.73m^2	GFR Class3A:59-45 ml/min/1.73m^2	GFR Class 3B:44-30 ml/min/1.73m^2	GFR Class4:29-15 ml/min/1.73m^2	GFR Class5:<15 ml/min/1.73m^2	*P*-value
Sex	Male	392 (20%)	1153 (60%)	276 (13%)	63 (3%)	5 (0.5%)	5 (5%)	*P*< 0.01
	Female	256 (14%)	989 (57%)	363 (99%)	102 (5%)	15 (0.6%)	10 (4%)	
Age	<65	589 (23%)	1535 (60%)	295 (11%)	66 (2.3%)	9 (0.02%)	14 (0.5%)	*P*< 0.01
	65≥	58 (5%)	67 (54%)	344 (29%)	99 (8%)	11 (9%)	1 (0.01%)	
Dyslipidemia	Yes	169 (16%)	584 (56%)	199 (19%)	59 (0.5%)	6 (0.6%)	4 (0.4%)	*P*< 0.01
	No	478 (18%)	1548 (58%)	438 (16%)	106 (4%)	17 (0.6%)	11 (0.04%)	
Hypertension	Yes	296 (13%)	1088 (54%	442 (22%)	128 (6%)	17 (0.6%)	13 (0.4%)	*P*< 0.001
	No	380 (23%)	1044 (61%)	195 (11%)	36 (2.7%)	0.2%	0.1%	

This relationship was significant only for the patients with GFR less than 60 ml/min/1.73m^2. Similar studies have reported a CKD frequency percentage of 20%-38% in patients with diabetes. For instance, the study by Lou Aynl (2010) on 16814 patients with diabetes reported the prevalence of CKD to be 34.6% (15).

Similar studies have reported the prevalence of ischemic heart diseases. Benjamin et al. showed about one third of all cases of death is due to CAD in patients over age 35. (20) The incidence rate of ischemic heart disease in hemodialysis patients was reported 21.7% by Nikparvar et al. (21)In Iran. Diabetic Kidney Disease (DKD) leading to ESRD had an increased percentage from 16% in 1997 to 31% in 2006 showed by Aghighi et al. (22)

The higher prevalence of ischemic heart diseases in patients with diabetes and CKD compared to non-CKD patients has been reported in several studies. In the first post-hoc analysis of the ACCORD study, the effect of CKD on cardiovascular morbidity and mortality was studied in 10142 patients with diabetes. It was shown that the risk of cardiovascular events and death was significantly higher in patients with CKD compared to those without CKD (16).

Weerarathna T et al. in a cross sectional study showed that there is a significant association between GFR and asymptomatic CAD in T2DM patients. They also showed that GFR is more accurate than microalbuminuria to predict coronary artery disease in patients with type 2 DM (17).

In many studies, a reduction in the GFR of patients with diabetes has been reported as an independent and predicting factor of ischemic heart diseases. The majority of these studies have been conducted in developed countries (13,14), while this point has been rather neglected in developing countries.

A study by Zhang (2018) on 1914 patients with diabetes demonstrated that the risk of cardiovascular diseases is significantly increased in patients with diabetes and CKD (14).

In our study, the regression analysis showed that a reduction in GFR can be considered as an independent factor to predict the frequency percentage of coronary angioplasty in patients with diabetes.

This study had several strengths and limitations. The strengths include a large sample size, and studying the association between five levels of GFR with CAD. One of the limitations of this study was that, we used a registry and the microalbuminuria of the patients was not recorded as a diagnostic criterion for CKD, so diagnosis of CKD (class 1) at a GFR level of≥ 90 ml/min/1.73m^2 was not so accurate.

Conclusions

A reduced GFR in patients with diabetes has association with increased CAD. Thus, it is recommended that an intervention study with a placebo group be conducted in which therapeutic factors effective in the reduction of GFR are examined.

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Conflict of Interest

The authors declared that they have no conflict of interests.

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