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Article

The Estimated Glomerular Filtration Rate in the Prediction of Major Adverse Cardiovascular Events in Patients with Normal Renal Function after Coronary Artery Bypass Grafting: A Single-Center Retrospective Cohort Study

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Abstract

Background: The estimated glomerular filtration rate (eGFR) has emerged as a risk factor for coronary artery disease (CAD), but there are currently insufficient data on the association of eGFR with the postoperative prognosis in patients undergoing coronary artery bypass grafting (CABG). This study aimed to investigate the potential utility of eGFR as a prognostic indicator for major adverse cardiovascular events (MACE) in patients with normal renal function after CABG. **Methods**: This study included a total of 222 consecutive patients with normal renal function (eGFR $\geq$90 mL/min/1.73 m^2) who underwent CABG between June 2018 and December 2019. These patients were divided into two groups based on the occurrence of MACE: without MACE group (n = 202) and with MACE group (n = 20). The eGFR was calculated from serum creatinine (SCr). The eGFR (mL/min/1.73 m^2) = 175 $\times$ SCr (mg/dL) $^{-1.234}$ $\times$ age (year) $^{-0.179}$ $\times$ 0.79 (in the case of females). Kaplan–Meier survival curve analysis was conducted followed by the log-rank test. Cox proportional hazards regression models were used to explore the association between the eGFR and MACE. Receiver operating characteristics (ROC) curve analysis was performed to assess the predictive performance of the eGFR and identify the optimal cutoff point. **Results**: A progressively lower eGFR was associated with an increasingly higher cumulative incidence of MACE (log-rank test, p = 0.017). The hazard ratio (95% CI) of MACE was 0.068 (0.005–0.941) in tertile 3 of the eGFR and 0.204 (0.051–0.817) per SD increase in the eGFR. The AUC of the eGFR was 0.678 (p = 0.009) and the optimal cut-off value to predict MACE was >118.3 mL/min/1.73 m^2. **Conclusion**: The eGFR may be an independent prognostic determinant in patients with normal renal function undergoing CABG surgery. In patients with normal renal function, MACE was more likely to occur in patients with lower eGFR compared with those with higher eGFR. The eGFR may have an important predictive value in predicting MACE in patients with normal renal function undergoing CABG surgery.

Keywords

estimated glomerular filtration rate; major adverse cardiovascular events; coronary artery bypass grafting

Background

Advances in medical science and technology have led to significant advances in our understanding of the causes, prevention, diagnosis, and treatment of coronary artery disease (CAD). However, despite these advances, CAD remains the leading cause of death, disability, and healthcare resource utilization world-wide [1,2]. Coronary artery bypass grafting (CABG), a major surgical intervention for the treatment of CAD, has been widely used in clinical practice for more than five decades [3]. To date, CABG has been widely recognized as one of the leading surgical procedures performed worldwide for the treatment of CAD. Nevertheless, patients undergoing coronary artery bypass grafting (CABG) are faced with the possibility of recurrent postoperative ischemia [4–6]. Therefore, the search for reliable indicators of major adverse cardiovascular events (MACE) after coronary artery bypass grafting (CABG) has become an important topic in clinical research.

The present prevalence of chronic kidney disease (CKD) is approximately 10% in the general population, but it can reach 30–50% in high-risk categories such as individuals with diabetes, hypertension, or cardiovascular disease [1,7–9]. A decrease in estimated glomerular filtration rate (eGFR) is a widely recognized as a risk factor for early cardiovascular events, particularly CAD [10,11], which is the primary cause of morbidity and mortality in individuals with CKD [12–14]. There is a clear and strong connection between the decrease in eGFR and the occurrence of atherosclerotic cardiovascular events. This association has been documented in several studies [15–17].

While it is widely accepted that an eGFR level below 60 mL/min/1.73 m^2 indicates CKD and is strongly linked to an increased risk of death, it remains uncertain whether a normal renal function with an eGFR level of 90 mL/min/1.73 m^2 or higher is associated with a higher (shouldn't this be lower) risk of death in patients who have undergone CABG [12,18–20]. The aim of this study was to investigate the potential utility of eGFR as a prognostic indicator for MACE in patients with normal renal function who underwent CABG.

Methods

Study Population

The study was approved by the Ethics Review Committee of Shandong Provincial Hospital, and followed the criteria outlined in the Helsinki Declaration. The patients provided written consent, authorizing their de-identified health data to be used for research purposes. This was done in accordance with the Ethics Committee's guidelines.

This study was a retrospective cohort analysis that included patients who had undergone CABG at Shandong Provincial Hospital. Between June 2018 and December 2019. A total of 452 individuals who had received a CABG underwent screening. Among the total number of patients, 68 individuals were not included in the study because they had undergone additional procedures, specifically valve surgery or congenital heart surgery. In addition, one patient was eliminated from the study due to a prior history of CABG, and three patients were omitted because they had malignancies. Another 16 individuals were removed from the analysis because they lacked the necessary data to calculate the eGFR. A total of 364 patients met all the specified criteria for inclusion and underwent telephone follow-up between January 2024 and April 2024. The average follow-up time in our study was 58 months, with a dropout rate of 12.6%. The final 318 patients, representing 87.4% of the total, were removed for patients with eGFR below 90 mL/min/1.73 m^2 (n = 96), resulting in a total of 222 patients included in the final data analysis (Fig. 1).

Data Collection and Definitions

The clinical data were collected from medical records by clinicians who had received specialized training. The data consisted of factors related to the patients' overall health, such as age, sex, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), and left ventricular ejection fraction (LVEF). In addition, it included cardiovascular risk factors such as current alcohol consumption and smoking habits, high blood pressure, diabetes mellitus (DM), high cholesterol levels, previous myocardial infarction (MI), previous stroke, percutaneous coronary artery intervention (PCI), family history of coronary artery disease (FH-CAD), and disease in the left main artery (LMD). Details about the surgical technique, such as the length of the operation, endarterectomy and the number of grafts were also reported. The ICU data included the duration of respiratory support, duration of ICU stay, 24-h postoperative drainage, total ICU drainage and whether high-flow oxygen therapy was administered. The laboratory tests included the measurement of fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), estimated glomerular filtration rate (eGFR), uric acid (UA), albumin, red blood cell count and hemoglobin. Peripheral venous blood samples were obtained in the early morning following a minimum 8-hour period of fasting. The Body Mass Index (BMI) was computed by dividing the weight (in kilograms) by the square of the height (in square meters). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were assessed using a sphygmomanometer, following established protocols. These protocols involved refraining from smoking and consuming coffee for a minimum of 30 minutes, and resting in a calm atmosphere for at least 5 minutes. Hypertension was characterized as having a systolic blood pressure (SBP) of 140 mmHg or higher and/or a diastolic blood pressure (DBP) of 90 mmHg or higher, or the utilization of antihypertensive medication. Diabetes mellitus (DM) was characterized by a fasting plasma glucose (FPG) level of 7.0 mmol/L or higher, a random blood glucose (RBG) level of 11.1 mmol/L or higher, a 2-hour plasma glucose level after an oral glucose tolerance test (OGTT) of 11.1 mmol/L or higher, or the administration of insulin or oral hypoglycemic medications. Hyperlipidemia was classified as matching the criteria specified by the ICD-10 classification E78, which includes the use of lipid-lowering medicines or having a total cholesterol (TC) level equal to or greater than 240 mg/dL [21]. Myocardial infarction (MI) was diagnosed using clinical symptoms, ECG results, and cardiac biomarkers [22]. FH-CAD was deemed to be present if there was a documented occurrence of coronary artery disease in a first-degree relative who had CAD prior to the age of 55 years (for males) or 65 years (for females). The eGFR was determined using the Chinese modified Modification of

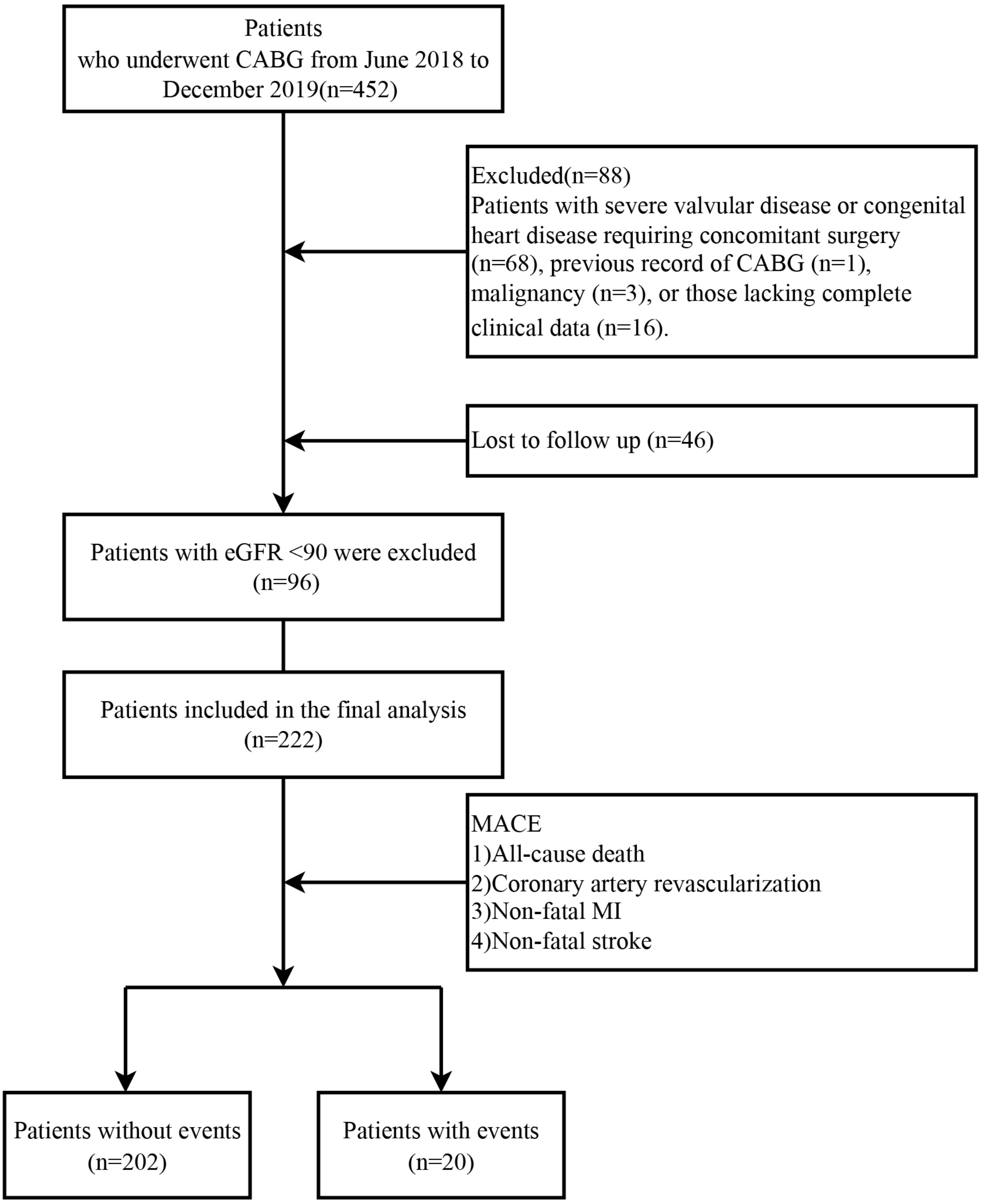

Fig. 1. Flow diagram of patient selection. CABG, coronary artery bypass grafting; MACE, major adverse cardiovascular events; MI, myocardial infarction; eGFR, estimated glomerular filtration rate.

Diet in Renal Disease equation, which takes into accounts serum creatinine (SCr) levels and other factors. The equation is expressed in the following manner: The estimated glomerular filtration rate (eGFR) in milliliters per minute per 1.73 square meters is calculated using the following formula: eGFR = 175 multiplied by the serum creatinine (SCr) level in milligrams per deciliter, minus 1.234 multiplied by the age in years, minus 0.179, and multiplied by 0.79 if the individual is a female [23]. We define "normal renal function" as an eGFR $\geq$90 mL/min/1.73 m^2, based on the current guidelines for kidney function classification, such as those provided by Kidney Disease: Improving Global Outcomes (KDIGO) [9].

Endpoints

The main objective of this study was to determine the frequency of MACE, which includes a combination of mortality from any cause (cardiovascular or non-cardiovascular), non-fatal MI, coronary artery revascularization (either CABG or PCI), and stroke. In the case of patients experiencing numerous clinical events, MACE was defined as the first event recorded together with its time of occurrence. The secondary outcomes included all-cause mortality, non-fatal MI, coronary artery revascularization, and stroke. The diagnosis of non-fatal MI was made in accordance with the Fourth Universal Definition of Myocardial Infarction [24].

Statistical Analysis

The statistical analysis was performed using SPSS version 27.0 (SPSS, Chicago, IL, USA), GraphPad Prism version 8.0.2(263) (GraphPad Software, Inc., San Diego, CA, USA), and R software version 4.2.2 (R Foundation for Statistical Computing, Auckland, New Zealand). The participants were classified according to the presence of MACE that were observed during the subsequent follow-up period. The study employed continuous variables, which were presented as either mean ± standard deviation (SD) or median with the 25th and 75th percentiles, depending on the data's distribution. Statistical comparisons were performed using the Student's t-test for variables that followed a Gaussian distribution, and the Mann-Whitney U test was used for variables that did not follow a Gaussian distribution. We employed chi-square tests to compare categorical variables. ANOVA was employed for continuous variables that followed a normal distribution, whereas the Kruskal-Wallis H test was utilized for continuous variables that exhibited skewed values. We generated Kaplan-Meier event-free survival curves and assessed their statistical significance using log-rank testing. The variables were analysis using univariate Cox regression analysis. A multivariate Cox proportional hazards regression analysis was undertaken to determine the connection between eGFR and MACE, specifically focusing on independence. Three regression models were built, each incorporating more confounding variables. Model 1 was calibrated for age and sex. Model 2, the partially adjusted model, incorporated factors that had a significance level of less than 0.05 in the univariate analysis. Model 3, which is the completely adjusted model, incorporated modifications for Age, Sex, BMI, LVEF, Current drinking, Current smoking, Hypertension, Diabetes mellitus, Previous MI, Previous stroke, Left main disease, Duration of surgery, Endarterectomy, Respiratory support, Duration of ICU stay, 24-h postoperative drainage, Total ICU drainage, High flow oxygen, FPG, TC, TG, LDL-C, HDL-C, UA, Albumin. The eGFR was incorporated into the models as both continuous and categorical variables, namely as the tertile of the eGFR. The eGFR was further standardized to evaluate the predictive importance of each standard deviation increase in the eGFR. To address the potential influence of multicollinearity on the results, we calculated the variance inflation factor (VIF) for the variables included in the models. The models did not exhibit any signs of collinearity, as indicated by the VIF being below 5 [25]. The study utilized receiver operating characteristic (ROC) curves to evaluate the prediction efficacy of the eGFR. The predictive value was determined using the area under the curve (AUC). Data was considered to be statistically significant when the p value was <0.05.

Results

Baseline Characteristics

The study had a cohort of 222 patients, with a mean age of 62.27 ± 7.62 years. 156 individuals, accounting for 70.27% of the sample, were classified as males. Table 1 displays the fundamental characteristics of individuals who developed a MACE and those who did not. The incidence of a cardiovascular event was found to have a strong correlation with many parameters, such as Age ($p < 0.001$) and Previous stroke ($p = 0.025$). Significant statistical differences were observed for the Duration of ICU stay ($p = 0.002$), 24-h postoperative drainage ($p = 0.025$), Total ICU drainage ($p = 0.048$), TG levels ($p = 0.036$), and Albumin levels ($p = 0.025$). Furthermore, according to the data shown in Table 1, patients who developed a MACE exhibited a significantly reduced eGFR in comparison to those who did not encounter any events.

Patients were categorized into three groups according to their eGFR Tertiles. Tertile 1 included patients with an eGFR less than 106.89 (n = 74), Tertile 2 included patients with an eGFR between 106.89 and 121.34 (n = 74), and Tertile 3 included patients with an eGFR equal to or more than 121.34 (n = 74). Statistically significant differences were observed among the variables, namely eGFR, Sex, Previous MI, 24-h postoperative drainage, Total ICU drainage, FPG, and UA. The major endpoints demonstrated a statistically significant difference between the groups, as indicated by MACE (Table 2).

Predictive Value of the eGFR

Within our study group, the median follow-up time was 60 months, with an interquartile range of 55 to 64 months. During this period, a total of 20 patients, accounting for 9.0% of the cohort, experienced MACE. 11 patients died from all causes, which accounts for 5.0% of the total cohort. Among these cases, 2 individuals experienced cardiac-related deaths, while 9 individuals succumbed to other causes. Additionally, there was 1 instance (0.5%) of non-fatal myocardial infarction, 8 instances (3.6%) of non-fatal stroke, and 1 instance (0.5%) of repeat revascularization. The patients were classified into three groups based on their admission eGFR level. Fig. 2 illustrates the Kaplan-Meier curves that show the cumulative incidences grouped based on the eGFR tertiles. Fig. 2 demonstrates that the cumulative incidence of MACE decreases progressively as the

Table 1. Baseline characteristics of the study population according to the occurrence of MACE.Baseline characteristics of the study population according to the occurrence of MACE.

Variables	Total (n = 222)	Without MACE (n = 202)	With MACE (n = 20)	*p*-value
General conditions				
Age (years)	62.27 ± 7.62	61.81 ± 7.67	66.90 ± 5.33	**<0.001**
Male, n (%)	156 (70.27)	141 (69.80)	15 (75.00)	0.628
BMI (kg/m^2)	25.46 ± 3.18	25.55 ± 3.19	24.55 ± 3.01	0.182
SBP (mmHg)	136.15 ± 20.76	135.86 ± 20.66	139.15 ± 22.05	0.500
DBP (mmHg)	79.82 ± 11.51	79.96 ± 11.57	78.45 ± 11.02	0.578
LVEF (%)	57.55 ± 5.33	57.67 ± 5.31	56.35 ± 5.54	0.292
Risk factors, n (%)				
Current drinking	76 (34.23)	69 (34.16)	7 (35.00)	0.940
Current smoking	95 (42.79)	86 (42.57)	9 (45.00)	0.834
Hypertension	131 (59.01)	118 (58.42)	13 (65.00)	0.568
Diabetes mellitus	87 (39.19)	78 (38.61)	9 (45.00)	0.577
Previous MI	34 (15.32)	29 (14.36)	5 (25.00)	0.350
Previous stroke	34 (15.32)	27 (13.37)	7 (35.00)	**0.025**
Family history-CAD	34 (15.32)	30 (14.85)	4 (20.00)	0.776
Left main disease	35 (15.77)	30 (14.85)	5 (25.00)	0.386
Surgical procedure				
Duration of surgery (min)	206.51 ± 32.25	205.59 ± 32.47	215.75 ± 29.12	0.180
Endarterectomy, n (%)	30 (13.51)	27 (13.37)	3 (15.00)	1.000
Number of grafts	4 (4.00–5)	4 (4–5)	4 (4–5)	0.789
ICU data				
Respiratory support (hour)	10.00 (7.00–13.50)	10.00 (6.50–13.50)	10.25 (7.50–13.25)	0.293
Duration of ICU stay (hour)	69.00 (45.50–97.88)	68.00 (45.00–94.00)	94.50 (91.38–110.50)	**0.002**
24-h postoperative drainage (mL)	410 (300–550)	400 (300–538)	500 (408–600)	**0.025**
Total ICU drainage (mL)	790 (640–1000)	780 (633– 990)	930 (800–1125)	**0.048**
High flow oxygen, n (%)	11 (4.95)	8 (3.96)	3 (15.00)	0.065
Laboratory test				
FPG (mmol/L)	6.45 (5.01–8.96)	6.37 (4.98–8.96)	6.78 (5.24–8.88)	0.634
TC (mmol/L)	3.74 ± 1.25	3.78 ± 1.26	3.32 ± 1.09	0.116
TG (mmol/L)	1.21 (0.87–1.76)	1.25 (0.91–1.79)	0.90 (0.65–1.24)	**0.036**
LDL-C (mmol/L)	2.20 (1.63–2.79)	2.20 (1.63–2.79)	2.20 (1.63–2.79)	0.521
HDL-C (mmol/L)	1.03 ± 0.31	1.02 ± 0.23	1.12 ± 0.74	0.547
UA (µmol/L)	290.54 ± 83.29	291.25 ± 83.37	283.35 ± 84.29	0.687
Albumin (g/L)	38.10 (34.82–40.90)	38.40 (35.08–41.05)	35.50 (33.08–38.32)	**0.025**
Red blood cell (10^{12}/L)	4.06 ± 0.73	4.08 ± 0.72	3.87 ± 0.80	0.220
Hemoglobin (g/L)	123.36 ± 21.50	124.14 ± 21.27	115.50 ± 22.82	0.086
eGFR (mL/min/1.73 m^2)	116.88 ± 18.85	117.85 ± 19.06	107.09 ± 13.27	**0.015**

Continuous variables were given as mean ± SD or median with interquartile range. Categorical variables were given by frequency and percentage as n (%).

p-values in bold are <0.05.

MACE, major adverse cardiovascular event; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; CAD, coronary artery disease; ICU, intensive care unit; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; UA, uric acid; eGFR, estimated glomerular filtration rate.

eGFR tertiles increase. This trend is statistically significant with a Log-rank *p* value of less than 0.017.

We utilized univariate Cox regression analysis to determine the variables that are associated with MACE. The risk factors for MACE were identified in Table 3 as Age, Previous stroke, High flow oxygen, and Albumin. The unadjusted HR with a 95% CI for the risk of MACE associated with a one SD increase in the eGFR was 0.96 (0.93–0.99) and 0.47 (0.25–0.87), respectively. The multivariate Cox proportional hazards regression analysis revealed that the eGFR, whether considered as categorical or continuous, remained statistically significant even when accounting for

Table 2. Baseline characteristics of the study population based on tertiles of eGFR.

Variables	Tertile 1 (n = 74)	Tertile 2 (n = 74)	Tertile 3 (n = 74)	*p*-value
eGFR (mL/min/1.73 m^2)	98.57 ± 4.74	113.78 ± 4.18	138.28 ± 14.89	**<0.001**
General conditions				
Age (years)	63.20 ± 6.98	62.46 ± 8.12	61.14 ± 7.68	0.248
Male, n (%)	60 (81.08)	54 (72.97)	42 (56.76)	**0.004**
BMI (kg/m^2)	25.68 ± 3.18	25.75 ± 3.38	24.94 ± 2.96	0.229
SBP (mmHg)	135.49 ± 19.23	137.36 ± 21.00	135.61 ± 22.17	0.828
DBP (mmHg)	80.16 ± 10.47	79.81 ± 11.41	79.49 ± 12.69	0.939
LVEF (%)	56.59 ± 6.52	57.69 ± 5.03	58.36 ± 4.07	0.125
Risk factors, n (%)				
Current drinking	29 (39.19)	28 (37.84)	19 (25.68)	0.162
Current smoking	36 (48.65)	35 (47.30)	24 (32.43)	0.087
Hypertension	46 (62.16)	46 (62.16)	39 (52.70)	0.402
Diabetes mellitus	27 (36.49)	23 (31.08)	37 (50.00)	0.052
Previous MI	16 (21.62)	14 (18.92)	4 (5.41)	**0.013**
Previous stroke	12 (16.22)	12 (16.22)	10 (13.51)	0.870
Family history-CAD	9 (12.16)	13 (17.57)	12 (16.22)	0.637
Left main disease	10 (13.51)	11 (14.86)	14 (18.92)	0.643
Surgical procedure				
Duration of surgery (min)	211.01 ± 34.59	204.59 ± 29.40	203.92 ± 32.52	0.338
Endarterectomy, n (%)	7 (9.46)	8 (10.81)	15 (20.27)	0.111
Number of grafts	4 (4–5)	4 (4–5)	4 (4–5)	0.340
ICU data				
Respiratory support (hour)	9.25 (6.50–13.38)	10.50 (7.12–14.00)	10.00 (6.62–13.00)	0.397
Duration of ICU stay (hour)	69.00 (46.12–97.25)	68.50 (44.25–106.00)	69.00 (61.00–96.62)	0.587
24-h postoperative drainage (mL)	500 (400–608)	400 (300–498)	365 (258–478)	**<0.001**
Total ICU drainage (mL)	850 (725–1045)	720 (594–950)	750 (630–1000)	**0.039**
High flow oxygen, n (%)	5 (6.76)	4 (5.41)	2 (2.70)	0.634
Laboratory test				
FPG (mmol/L)	5.71 (4.88–7.90)	5.99 (5.11–8.54)	7.79 (5.40–10.32)	**0.023**
TC (mmol/L)	3.67 ± 1.30	3.72 ± 1.20	3.82 ± 1.25	0.762
TG (mmol/L)	1.19 (0.86–1.76)	1.33 (0.91–1.89)	1.17 (0.88–1.67)	0.753
LDL-C (mmol/L)	2.16 (1.61–2.75)	2.20 (1.51–2.75)	2.25 (1.75–2.85)	0.717
HDL-C (mmol/L)	1.05 ± 0.42	1.03 ± 0.23	1.01 ± 0.24	0.756
UA (µmol/L)	311.09 ± 77.73	297.93 ± 87.07	262.58 ± 78.12	**0.001**
Albumin (g/L)	37.85 (34.78–41.10)	39.05 (35.88–41.65)	37.85 (34.12–40.08)	0.112
Red blood cell (10^{12}/L)	4.14 ± 0.79	4.08 ± 0.71	3.96 ± 0.67	0.315
Hemoglobin (g/L)	125.07 ± 22.77	124.81 ± 21.91	120.22 ± 19.65	0.305
MACE	12 (16.22)	6 (8.11)	2 (2.70)	**0.015**

Continuous variables were given as mean ± SD or median with interquartile range. Categorical variables were given by frequency and percentage as n (%).

p-values in bold are <0.05.

MACE, major adverse cardiovascular event; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; CAD, coronary artery disease; ICU, intensive care unit; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; UA, uric acid; eGFR, estimated glomerular filtration rate.

confounding factors (Table 4). Model 2 demonstrated a significant 49.5% reduction in the risk of MACE for each SD increase in the eGFR. The HR and 95% CI were 0.505 (0.279–0.914). When comparing patients with the lowest eGFR values, the partially adjusted HR for MACE was 0.567 (0.209–1.542) in the middle tertile and 0.166 (0.037–0.744) in the highest tertile. There was a notable and meaningful decrease in the risk of MACE when comparing the second tertile to the third tertile for the eGFR. A significant reduction in risk was observed for the eGFR (*p* for trend = 0.011). The fully adjusted model demonstrated a comparable pattern in the correlation between the eGFR and the

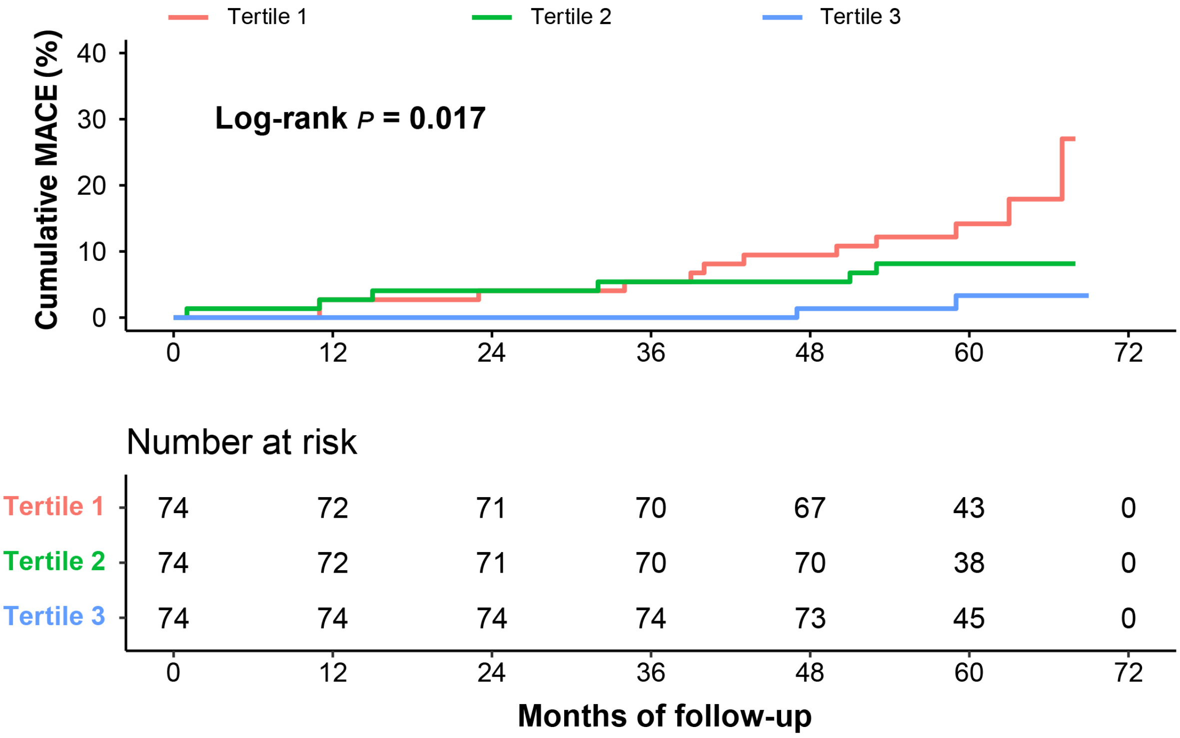

Fig. 2. Kaplan–Meier survival curves for MACE across the eGFR tertiles. The cumulative incidence of MACE during follow-up grouped according to the eGFR tertiles was analyzed by Kaplan-Meier curves. The *p* value was calculated with the log-rank test.

outcome of interest. Each SD increase in the eGFR was associated with a HR of 0.204 (95% CI 0.051–0.817). The HR in the second tertile was 0.366 (95% CI 0.056–2.376), while in the third tertile, it was 0.068 (95% CI 0.005–0.941). The *p*-value for the trend was 0.034.

To thoroughly evaluate the prediction accuracy and prognostic importance of the eGFR, we performed receiver operating characteristic (ROC) analysis (Fig. 3). The ROC study showed that the eGFR had an optimal cutoff value of 118.3 for predicting MACE. Upon evaluating the prediction capacities, it was determined that the eGFR had an area under the curve (AUC) value of 0.678 (95% CI, 0.564–0.791) as indicated in Table 5. Moreover, it was established that an eGFR of 118.3 is the optimal threshold for identifying MACE, with a sensitivity of 90.0% and a specificity of 43.1%.

Discussion

The main conclusions of our analysis are as follows: (1) eGFR may be an independent prognostic determinant in patients with normal renal function undergoing CABG surgery. (2) In patients with normal renal function, MACE was more (should this be less) likely to occur in patients with higher eGFR compared with those with lower eGFR. eGFR may have an important predictive value in predicting MACE in patients with normal renal function undergoing CABG surgery.

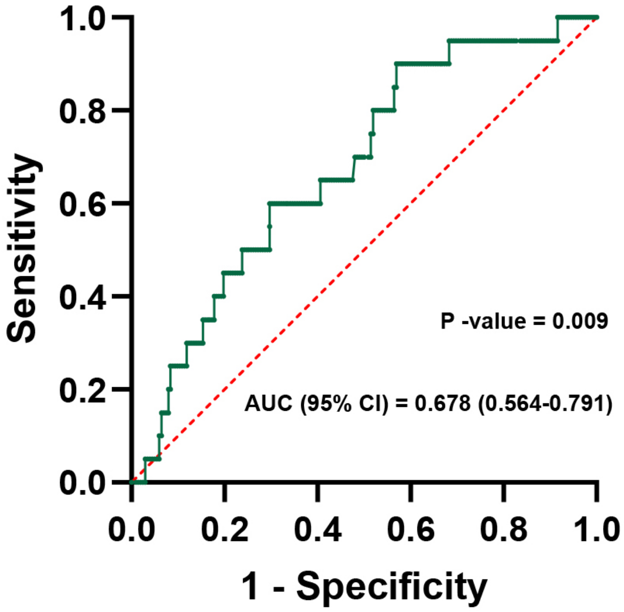

Fig. 3. ROC curves of the eGFR for the prediction of MACE. ROC curves, receiver operator characteristic curves; MACE, major adverse cardiovascular event; eGFR, estimated glomerular filtration rate.

CKD has been identified as a significant risk factor for CAD and death. It also increases the probability of death from any cause in patients with severe CAD [26]. Several epidemiologic studies have demonstrated that an eGFR be-

Table 3. Univariate Cox regression analyses for MACE.

Variables	HR	95% CI	*p*-value
Age	1.11	1.03–1.20	**0.004**
Sex	1.31	0.48–3.60	0.604
BMI	0.92	0.79–1.06	0.228
SBP	1.01	0.99–1.03	0.392
DBP	0.99	0.95–1.03	0.639
LVEF	0.97	0.90–1.03	0.322
Current drinking	1.03	0.41–2.59	0.942
Current smoking	1.10	0.46–2.67	0.825
Hypertension	1.43	0.57–3.62	0.447
Diabetes mellitus	1.35	0.56–3.25	0.509
Previous MI	1.86	0.68–5.12	0.230
Previous stroke	3.60	1.42–9.13	**0.007**
Family history-CAD	1.48	0.50–4.44	0.481
Left main disease	1.67	0.60–4.60	0.980
Duration of surgery	1.01	1.00–1.02	0.178
Endarterectomy	1.20	0.35–4.10	0.772
Number of grafts	1.14	0.60–2.14	0.693
Respiratory support	0.99	0.96–1.03	0.740
Duration of ICU stay	1.01	1.00–1.01	0.050
24-h postoperative drainage	1.002	1.00–1.00	0.071
Total ICU drainage	1.00	1.00–1.00	0.208
High flow oxygen	4.70	1.36–16.27	**0.015**
FPG	1.03	0.90–1.19	0.632
TC	0.71	0.48–1.06	0.093
TG	1.27	1.00–1.62	0.053
LDL-C	1.03	0.63–1.67	0.908
HDL-C	2.19	0.84–5.67	0.107
UA	1.00	0.99–1.00	0.755
Albumin	0.90	0.82–0.98	**0.016**
Red blood cell	0.68	0.37–1.24	0.210
Hemoglobin	0.98	0.96–1.00	0.084
eGFR	0.96	0.93–0.99	**0.016**
eGFR (Per SD)	0.47	0.25–0.87	**0.016**

p-values in bold are <0.05.

MACE, major adverse cardiovascular event; HR, Hazard ratio; CI, Confidence interval; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; CAD, coronary artery disease; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; UA, uric acid, eGFR, estimated glomerular filtration rate.

tween 60–89 mL/min/1.73 m^2 is an independent risk factor for CAD [27,28]. The presence of hyperalgesia may lead to early cardiac remodeling and calcification, which could explain this observation [28]. Our data further support the finding that individuals with normal renal function who receive a CABG are at a significantly higher risk of MACE. Furthermore, the ESC 2021 guideline advise routine screening for albuminuria and eGFR in the general population [29]. To prevent the initial progression of renal impairment, it is necessary to screen for normal renal function early and implement strong interventions to protect against CKD in CAD patients, as a significant number of these patients have normal renal function.

Several mechanisms may explain the protective role of higher eGFR against MACE. Enhanced renal function is indicative of better overall cardiovascular health, reflecting lower levels of systemic inflammation, oxidative stress, and endothelial dysfunction—all factors contributing to cardiovascular events [30,31]. Specifically, inflammation plays a crucial role in the pathogenesis of atherosclerosis and subsequent cardiovascular events. Patients with higher eGFR tend to have lower levels of inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6), which are known to be associated with adverse cardiovascular outcomes [32]. Oxidative stress and endothelial dysfunction are interrelated processes that contribute to the progression of cardiovascular disease. Improved renal function helps mitigate these conditions, reducing the likelihood of MACE.

Moreover, higher eGFR may correlate with more efficient clearance of cardiovascular risk factors, such as uremic toxins and advanced glycation end-products, further mitigating the risk of MACE [33,34]. Uremic toxins, which accumulate in patients with impaired renal function, have been shown to promote vascular calcification and endothelial dysfunction, both of which are pivotal in the development of cardiovascular disease. By maintaining a higher eGFR, patients can effectively clear these harmful substances, thereby protecting their cardiovascular system.

In this study, we categorized eGFR values into tertiles to assess the potential relationship between renal function and the incidence of MACE. The use of tertiles, a widely adopted statistical method for dividing continuous variables, enabled us to explore non-linear trends across the data. This approach was selected based on the distribution of eGFR values within our cohort, rather than on predefined clinical cut-offs. We considered alternative classification methods, such as dichotomizing the data or using quartiles, but chose tertile groupings because they offered a balance between model fit and interpretability. Dichotomization, while simplifying the analysis, risks overlooking nuanced associations, whereas quartiles, though providing more granularity, did not significantly improve model performance in our cohort. Future studies could further explore the impact of alternative grouping strategies on MACE prediction. However, in our analysis, the tertile approach was found to be the most effective in capturing the relationship between eGFR and MACE risk.

The identification of an optimal eGFR cutoff value of 118.3 for predicting MACE underscores the potential of eGFR as a valuable marker in clinical practice. This threshold offers high sensitivity, albeit with moderate specificity, suggesting its utility in screening and risk stratification of

Table 4. Multivariate Cox regression analyses for MACE.

Indexes		HR (95% CI)		
		Model 1	Model 2	Model 3
eGFR	Per 1 Unit increase	0.967 (0.936–0.999) *	0.964 (0.935–0.995) *	0.919 (0.854–0.989) *
	Per 1 SD increase	0.527 (0.285–0.972) *	0.505 (0.279–0.914) *	0.204 (0.051–0.817) *
	Tertile 1	Reference	Reference	Reference
	Tertile 2	0.521 (0.195–1.390)	0.567 (0.209–1.542)	0.366 (0.056–2.376)
	Tertile 3	0.190 (0.042–0.854) *	0.166 (0.037–0.744) *	0.068 (0.005–0.941) *
	p for trend	**0.017**	**0.011**	**0.034**

Model 1: adjusted for Age and Sex.

Model 2: adjusted for variables with p-value < 0.05 in univariate analysis, including Age, Previous stroke, High flow oxygen and Albumin.

Model 3: adjusted for Age, Sex, BMI, LVEF, Current drinking, Current smoking, Hypertension, Diabetes mellitus, Previous MI, Previous stroke, Left main disease, Duration of surgery, Endarterectomy, Respiratory support, Duration of ICU stay, 24-h postoperative drainage, Total ICU drainage, High flow oxygen, FPG, TC, TG, LDL-C, HDL-C, UA, Albumin.

MACE, major adverse cardiovascular event; eGFR, estimated glomerular filtration rate; HR, Hazard ratio; CI, Confidence interval; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; UA, uric acid.

p values in bold are <0.05

* $p < 0.05$.

Table 5. AUC of eGFR for predicting MACE among study populations.

Variables	Total				
	Sensitivity (%)	Specificity (%)	Cutoff value	AUC (95% CI)	p-value
eGFR	90.0	43.1	>118.3	0.678 (0.564–0.791)	**0.009**

p-values in bold are <0.05.

eGFR, estimated glomerular filtration rate; AUC, area under the curve; CI, confidence interval.

patients undergoing CABG. By integrating eGFR into routine preoperative assessments, clinicians can better identify high-risk individuals and tailor perioperative management strategies accordingly. For instance, patients identified as high-risk based on their eGFR could benefit from more intensive monitoring and proactive management of potential complications, ultimately improving their outcomes.

Furthermore, understanding the relationship between eGFR and MACE can guide therapeutic interventions aimed at optimizing renal function. For example, strategies to improve renal perfusion and function, such as adequate hydration, avoidance of nephrotoxic agents, and careful management of comorbid conditions like diabetes and hypertension, could be emphasized in the perioperative care of CABG patients. This proactive approach may help preserve renal function and, reduce cardiovascular risk.

Despite the strengths of our study, several limitations warrant consideration. First, the retrospective design inherently introduces potential biases, including selection bias and information bias. Retrospective studies rely on existing records, which may not always be comprehensive or accurate, potentially affecting the validity of our findings. Additionally, our findings are based on a single-center cohort, which may limit the generalizability of the results. Future prospective, multicenter studies are needed to validate our findings and establish more robust clinical guidelines.

Second, while we adjusted for multiple confounders in our analyses, residual confounding cannot be entirely ruled out. Factors such as medication use, lifestyle modifications, and genetic predispositions, which were not comprehensively captured, may influence the observed associations. For example, patients' adherence to prescribed medications or their engagement in lifestyle interventions such as diet and exercise could significantly impact their cardiovascular outcomes, yet these factors were not fully accounted for in our study. Moreover, the relatively short follow-up period may not fully capture the long-term impact of eGFR on cardiovascular outcomes. Longer follow-up periods are necessary to better understand the enduring effects of renal function on cardiovascular health.

Further research should aim to elucidate the underlying biological mechanisms linking eGFR and MACE in patients with normal renal function. Exploring the molecular pathways and genetic factors involved in this association could provide deeper insights into potential therapeutic targets. Additionally, exploring the interplay between eGFR and other emerging biomarkers, such as novel inflammatory markers and genetic variants, could provide a more comprehensive risk assessment framework. Identifying specific biomarkers that interact with eGFR to influence cardiovascular risk could enhance the precision of risk stratification models.

Randomized controlled trials investigating interventions targeting renal function improvement in the perioperative setting may also yield valuable insights into reducing cardiovascular risk in CABG patients. For instance, studies evaluating the efficacy of pharmacological agents aimed at enhancing renal function or reducing renal injury in the perioperative period could inform best practices for managing these patients. Moreover, interventions such as preoperative renal optimization programs, which include measures to improve hydration status and manage comorbid conditions, could be explored to assess their impact on postoperative cardiovascular outcomes.

Lastly, integrating advanced imaging techniques to assess renal perfusion and function in the context of cardiovascular risk could provide a more nuanced understanding of the relationship between renal health and MACE. Techniques such as magnetic resonance imaging (MRI) and positron emission tomography (PET) scans offer detailed insights into renal blood flow and tissue characteristics, potentially identifying early signs of renal dysfunction that are not captured by eGFR alone. These imaging modalities could complement eGFR measurements, offering a more holistic assessment of renal and cardiovascular health.

Conclusion

In conclusion, our study highlights the significant predictive value of eGFR for MACE in patients with normal renal function following CABG. Higher eGFR levels are associated with a lower risk of MACE, underscoring the importance of renal function assessment in this patient population. Integrating eGFR into preoperative evaluation protocols could enhance risk stratification and improve clinical outcomes. Future research should focus on validating these findings and exploring targeted interventions to optimize renal and cardiovascular health in CABG patients.

Abbreviations

CAD, Coronary artery disease; CABG, Coronary artery bypass grafting; MACE, Major adverse cardiovascular event; CVD, cardiovascular disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; FH-CAD, Family history of CAD; PCI, percutaneous coronary intervention; OPCABG, off-pump coronary artery bypass grafting; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; UA, uric acid; eGFR, estimated glomerular filtration rate; VIF, variance inflation factor; SD, standard deviation; AUC, area under the curve; ROC, receiver operating characteristic; HR, hazard ratio; CI, confidence interval.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

QZ, ZW and XS drafted, revised the manuscript and contributed to the conception and design of this article. XS and ZW were responsible for the statistical analysis. DG, YZ and RZ contributed to the case collection and database establishment. XS, DG and QZ interpreted the results. All authors approved the final manuscript. All authors contributed to editorial changes in the manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Review Committee of the Shandong Academy of Medical Sciences and complied with the Declaration of Helsinki, approval number: KYLL-202207-028-1. All participants provided written informed consent. Clinical Trial Registration URL: https://www.chictr.org.cn/; Unique Identifier: ChiCTR2200065233.

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Conflict of Interest

The authors declare no conflict of interest.

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