



The prognostic value of kidney failure based on glomerular filtration rate in predicting long in-hospital outcomes in patients with unstable angina

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Abstract

Objectives: Numerous recent studies have emphasized the role of kidney failure in developing ischemic heart disease (IHD) and the resulting adverse consequences. The purpose of the present study was to quantitatively assess the effect of kidney failure based on glomerular filtration rate (GFR) in predicting clinical outcomes in patients with unstable angina (U/A).

Methods: This retrospective cohort study included 129 patients with unstable angina with preserved left ventricular function. Serum creatinine levels were specified at the beginning of their admission. The GFR at admission time was determined based on the MDRD index. Based on the GFR value, patients were classified into two groups, i.e., normal GFR (>60) and decreased GFR (<60).

Results: The frequency of one-month mortality in <60 GFR and >60 GFR was 3.2% and 0.0%, respectively. Furthermore, the prevalence of 6-month mortality in <60 GFR and >60 GFR was 8.1% and 0.0%, respectively. The frequency of readmission in <60 GFR and >60 GFR was 29% and 11%, respectively. Likewise, the frequency of revascularization through coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI) in <60 GFR and >60 GFR was 25.8% and 8.9%, respectively. According to the multivariate logistic regression model, <60 GFR increased the risk of 6-month mortality up to 0.2 times (probability ratio of 2.081, P-value of 0.023). Regarding readmission, <60 GFR increased the need for readmission up to 2.4 times (probability ratio of 2.433, P-value of 0.049). On the other hand, the risk of CABG or PCI recurrence following initial intervention was 2.8 times higher in patients with <60 GFR than in the >60 GFR group (probability ratio 2.882, p-value .03).

Conclusions: The study revealed that <60 GFR compared to higher values of GFR is associated with an increased risk of 6-month mortality, increased readmission, and increased revascularization in patients with unstable angina.

Keywords: Kidney Failure; Glomerular Filtration Rate; Unstable Angina

Introduction

Kidney failure and cardiovascular disease are common diseases worldwide, affecting patients, physicians, and healthcare systems. Kidney failure is a condition

in which blood urea nitrogen levels exceed 30 mg/dL and creatinine levels exceed 1.5 mg/dL. Damage to the kidneys is likely to be characterized by structural changes, blood or urine

markers, or impaired imaging tests (1). A glomerular filtration rate (GFR) is highly recommended to check how well the kidneys are working and how much kidney function you have (2).

Some other underlying disorders, i.e., unstable angina (acute coronary heart attack) and kidney failure are associated with high mortality risk in patients with acute kidney failure, also called an acute renal failure or acute kidney injury. In the last 15 years, the morbidity and mortality rates caused by cardiovascular diseases have increased significantly in society. Nevertheless, the pathogenicity of the diseases in patients with kidney failure remains intact. We can attribute it to the fact that the effect of kidney failure on cardiovascular functioning has not been clinically specified (3). However, kidney failure has been indicated to be a distinguished predictor of mortality in patients experiencing Coronary artery bypass graft surgery (CABG) or coronary angioplasty(4).

In some investigations, patients with kidney failure accept less treatment for acute coronary syndrome than those without kidney failure. In other words, kidney failure patients tend to receive less aspirin, beta-blockers, thrombolytics, coronary angiography, and even angioplasty than other patients. This is evidence of greater side effects in these patients (5).

Some other studies have revealed that a 10-unit decrease in GFR is associated with a 15% increase in mortality, which will be worsened if routine cardiac treatments are not provided (6, 7). In a study of 130000 elderly patients with acute myocardial infarction, mild kidney failure (serum creatinine 1.5 to 2.4) or moderate (serum creatinine 2.5 to 3.9) were shown as risk factors for mortality (8). Some studies have shown that kidney failure is not only a marker for heart failure exacerbations, but also a factor in cardiovascular injury caused by an inflammatory cascade (9, 10). Overall, both kidney failure and heart failure indicators are mutually effective in the severity and consequences of each other. Little is known about the prognostic role of different degrees of kidney failure in the consequences of acute kidney failure (10).

Studies on the risk role of kidney failure in ischemic heart disease have been conducted in a limited sample or in critically ill patients and therefore cannot be generalized to the general public. On the other hand, in many cases, the evaluation of kidney function was determined based on serum creatinine level, which was not very accurate and efficient due to the possibility

of changing this index based on age, sex, race, and body mass index. Consequently, today, the American Kidney Disease Association (AKDA) has proposed the use of glomerular filtration rate (GFR) as a more accurate indicator to assess kidney failure instead of serum creatinine levels. Consequently, the present study aimed to quantitatively evaluate the effect of kidney failure based on GFR value in predicting clinical outcomes in patients with the acute coronary syndrome (ACS).

Materials and Methods

This study was a retrospective cohort study approved by the ethics committee of Urmia University of Medical Sciences with the ethics code IR.UMSU.REC.11394.152 in 2018.

Participants

The study population included patients admitted to Taleghani Hospital diagnosed with unstable angina pectoris. Inclusion criteria included patients with unstable angina (U/A) with preserved left ventricular function (preserved LVEF) based on clinical evidence, cardiac enzymatic changes, echocardiography, and electrocardiogram evidence. Exclusion criteria included increased cardiac enzymes and diagnosis of Acute MI (NSTEMI-STEMI) in patients with a previous history of myocardial infarction (MI) or a history of diagnostic and therapeutic interventions related to cardiovascular disease. The participants were selected from all the available patients. According to the study by Nabias et al., the prevalence of six-month mortality in patients with GFR less than 60 years and above 60 years was estimated to be 37.2% and 12.1%, respectively. Considering the 95% confidence interval and the study power of 90%, the sample size required for the study in each group with and without kidney failure was 43, and considering the 30% attrition, the inclusion criteria included patients with unstable angina (U/A) with preserved left ventricular function (preserved LVEF) based on clinical evidence, cardiac enzymatic changes, echocardiography, and electrocardiogram evidence.

Data Collection Instruments

The researcher used a researcher-developed questionnaire, including demographic information and information related to the disease. Each patient file was used to collect data on demographics, medical records, medications, and history of medical procedures, as well as information on in-hospital patient mortality and

morbidity. The data were documented on the study checklist. Patients were followed up by telephone, and their six-month outcome was assessed through phone calls. Serum creatinine levels were determined at the beginning of the admission. The GFR value of patients at the admission time was determined based on the MDRD index:

Estimated GFR (ml per minute per 1.73 m² of body surface area) = $186 \times (\text{serum creatinine [mg / dl]})^{-1.154} \times (\text{age [in years]})^{-0.203}$. (This value is multiplied by 0.742 in women).

Based on the value of GFR, patients were divided into two groups: normal GFR (above 60) and decreased GFR (below 60) (the sample size for each group was 60 patients). Length of hospital stay, hospital mortality, and cardiovascular complications from acute coronary syndrome were documented. All patients were followed up by phone calls and assessed constantly regarding mortality, the occurrence of ischemic heart disease, readmission, and the need for coronary revascularization (CABG) (PCI). Finally, nosocomial complication and the 1- and 6-month assessments were compared between the two groups with and without kidney failure. Results were expressed as mean and standard deviation (mean \pm SD) for quantitative variables and as a percentage for stratified qualitative variables. T-

test was employed to compare quantitative variables. And chi-square was used to compare qualitative variables. The multivariate logistic regression model was used to determine the relationship between renal failure and disease progression in the presence of confounding factors. SPSS software version 21 was used for statistical analysis of the data and the level of significance was considered less than 0.05.

Results

This study included a total of 62 patients in the < 60 mL/min GFR groups and 67 patients in the > 60 mL/min GFR groups. With respect to gender frequency, 25 male and 37 female patients were in the < 60 mL/min GFR group and 37 male and 30 female patients were in the > 60 mL/min GFR group. The number of patients was not different in the two groups ($p = 0.315$). The mean age in the <60 ml/min GFR and >60 ml/min GFR groups were 36.8 ± 62.11 and 6.6 ± 55.12 years, respectively, and the difference was significantly significant ($P = 0.001$).

In terms of risk factors for heart disease, the prevalence of hypertension in the <60 ml/min GFR and the >60 ml/min GFR groups was 88.7% and 50.7%, respectively, which was statistically significant ($P = 0.001$) Fig 1.

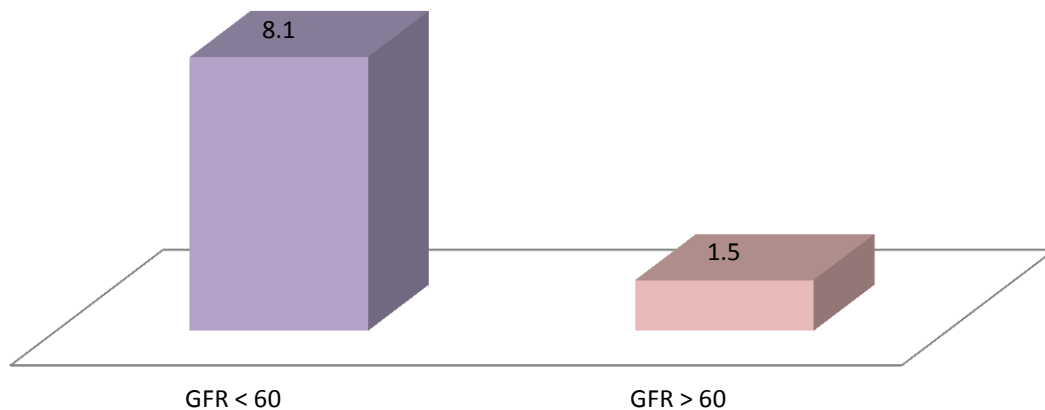


Figure 1. Frequency distribution of hospital mortality in the <60 ml/min GFR and the >60 ml/min GFR groups

The prevalence of smoking in the <60 ml/min GFR and the >60 ml/min GFR groups was 19.4% and 25.4%, respectively, yet the difference was not statistically significant ($P = 0.415$). The prevalence of diabetes in the <60 ml/min GFR and the >60 ml/min GFR groups was 25.8% and 13.4%, respectively, but the difference was not statistically

significant ($P = 0.080$). The prevalence of hyperlipidemia in the <60 ml/min GFR and the >60 ml/min GFR groups was 14.5% and 4.4%, respectively, with a statistically significant difference (P -value = 0.048). The prevalence of myocardial infarction and stroke in the < 60 mL/min GFR and > 60 mL/min GFR groups was

1.6% and 0.0%, respectively, which was statistically significant ($p = 0.001$). In terms of treatment outcomes, the prevalence of in-hospital mortality was 8.1% and 1.5%, respectively, in the <60 ml/min GFR and the >60 ml/min GFR groups Fig.1.

The difference was significantly higher in the former ($P = 0.050$). The frequency of one-month mortality (excluding in-hospital death) was 3.2% and 0.0%, respectively, in the <60 ml/min GFR and the >60 ml/min GFR groups with no difference between the two groups ($P = 0.140$) Fig 2.

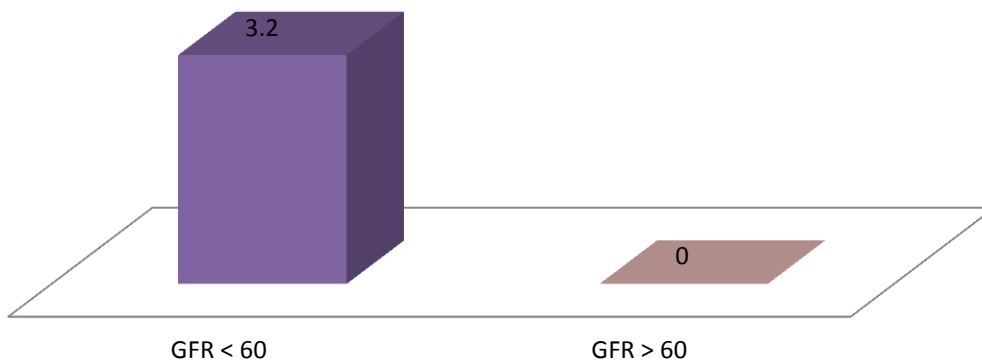


Figure 2. Frequency distribution of one-month mortality in the <60 ml/min GFR and the >60 ml/min GFR groups

Likewise, the six-month mortality rate was 8.1% and 0.0%, respectively, in the <60 ml/min GFR and the >60 ml/min GFR groups, with a

significantly higher value in the former ($P=0.018$) Fig 3.

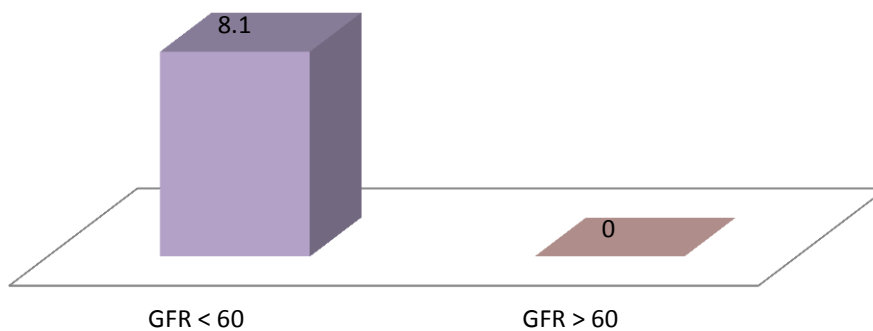


Figure 3. Frequency distribution of six-month mortality in the <60 ml/min GFR and the >60 ml/min GFR groups

The frequency of readmission was 29% and 11.9% in the <60 ml/min GFR and the >60

ml/min GFR groups, respectively, with a much higher value in the first group ($P=0.017$) Fig 4.

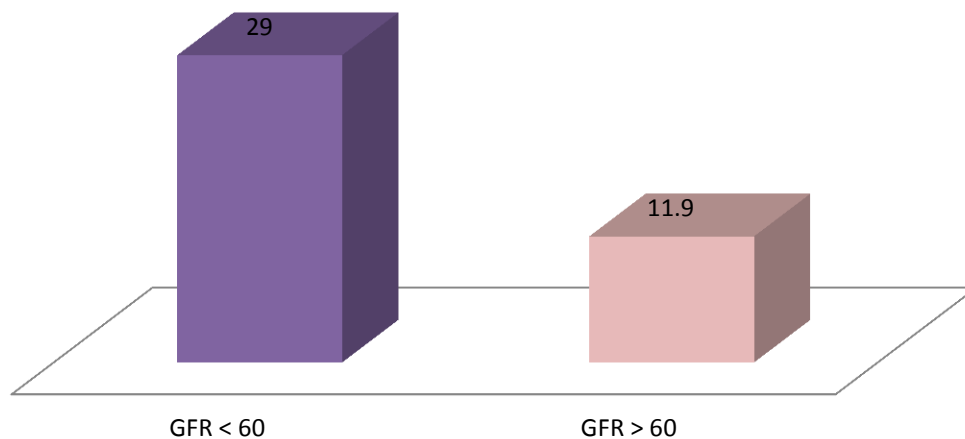


Figure 4. Frequency distribution of readmission in the <60 ml/min GFR and the >60 ml/min GFR groups

Additionally, the frequency of revascularization through CABG or PCI was 25.8% and 8.9% in the <60 ml/min GFR and the >60 ml/min GFR groups, respectively, which was significantly higher in the former ($P=0.048$).

The multivariate logistic regression model indicated that the <60 ml/min GFR was not a risk factor for nosocomial mortality (with a probability ratio of 5.405, 95% confidence interval of 0.614 to 47.619, $P = 0.115$). Nevertheless, concerning 6-month mortality, the <60 ml/min GFR increased the risk of 6-month mortality by 0.2-fold (with a probability ratio of 2.081, 95% confidence interval of 1.739 to 2.488) ($P=0.03$). Concerning readmission, the <60 ml/min GFR increased the need for readmission up to 2.4 times (probability ratio of 2.433, 95% confidence interval of 0.987 to 5.988, P -value=0.049). On the other hand, the risk of CABG or PCI recurrence following initial intervention in the <60 ml/min GFR was 2.8 times higher than the >60 ml/min GFR group (probability ratio of 2.882, 95% confidence interval of 1.060, 7.812, P -value=0.32).

Discussion

This study evaluated the impact of kidney failure related to the GFR assay on outcomes. In this study, the primary outcomes were evaluated through an examination of in-hospital mortality and long-term outcome during one-month and six-month mortality periods, and the need for reintervention, myocardial infarction, or stroke, and the need for readmission. The results of this study revealed that the prevalence of cases such as old age, hypertension, and hyperlipidemia in terms of the incidence of underlying cardiac risk

factors for the group with reduced GFR was much higher than those with normal GFR. This high prevalence rate is associated with the risk of kidney failure development and exacerbation, on the one hand, and adverse outcomes in patients, on the other hand. Likewise, kidney failure in patients was associated with patients' 6-month mortality, readmission, and the need for revascularization. In fact, it appears that the kidney failure development and exacerbation, mostly accompanied by progressive renal failure, will aggravate the adverse and unexpected consequences in patients.

In this regard, many studies agree on the effect of kidney failure on the outcome of patients with the acute coronary syndrome. Karki et al. indicated that there was a significantly positive relationship between decreased GFR (less than 45 ml/min) and patients' mortality(11). Lin et al. showed that the <60 ml/min GFR was associated with higher morbidity, and patient survival in IGFR patients was much lower than in other patients. Eventually, IGFRs experienced higher mortality than other patients (12). El-Menyar et al., like others, asserted that patients with kidney failure were older and had a higher prevalence of hypertension and dyslipidemia. Compared with the normal GFR group, mild, moderate, and severe GFR groups were more associated with mortality and increased the risk of mortality by 2.2-fold, 6.7-fold, and 12-fold, respectively (13). Likewise, Al Suwaidi et al. showed that MI-induced mortality was significantly higher in patients with kidney failure than in those without such a condition at both 30- and 180-day intervals. Creatinine clearance (CrCl) was

associated with mortality risk as well as mortality ratio to non-fatal myocardial infarction within 180 days (14). In a study, Nabais et al. reported that the relative risk of mortality was directly related to a decreased GFR. In this regard, the relative mortality risk was 2.7 for mild kidney failure, 7.5 for moderate, and 8.1 for severe cases (15). Similarly, Sooklim et al. revealed that the risk of one-year death in patients with the acute coronary syndrome was significantly associated with a decrease in GFR to less than 60 ml/min (16). Another study, Anavekar et al., indicated that the risk of death, recurrence of MI, heart failure, stroke, or cardiac arrest increased as GFR lessened (17).

Overall, all studies have highlighted the increased risk of mortality as well as morbidity caused by kidney failure in patients with acute coronary syndrome. The increased mortality and other postoperative complications can be accounted for in two ways. First, as most studies have demonstrated, the prevalence of some risk factors for cardiovascular diseases, i.e. old age, hypertension, hyperlipidemia, and even diabetes, is much higher in patients with kidney failure. Second, kidney failure is an influential and documented risk factor in patients with the acute coronary syndrome. Third, studies stated that given the nature of kidney failure, patients with this condition are incapable of receiving many cardiac drugs; therefore, the outcome of treatment in these patients will be affected by this different treatment protocol.

Limitation

The first limitation of the study is the small number of samples. Another limitation is that this study was done in one center and is not generalizable to other populations.

It is suggested that future studies be conducted

with a larger sample and in multiple centers. It is suggested that future studies be conducted with a larger sample and in multiple centers.

Highlights study

Increased risk of CHD is associated with low GFR in the general population. These findings can have implications for further understanding CHD and targeting cardio protective interventions.

In this study, we evaluated the primary outcomes by examining hospital mortality and long-term outcomes during one-month, and 6-month mortality periods, along with the need for re-intervention, myocardial infarction or stroke, and the need for readmission.

Conclusion

To sum up, the present study indicated that the <60 ml/min GFR is associated with an increased risk of 6-month mortality, increased readmission, and increased revascularization in patients with acute coronary syndrome compared to higher values of GFR.

Cardiovascular and kidney diseases are linked to a common cause and result in a very poor prognosis. Physicians should carefully predict cardiovascular disease in patients with low GRF and take appropriate measures to reduce patient risk, and work with the patient to promote healthy living and adherence to prescribed medications.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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References

1. M C Foster, D E Weiner, A G Bostom, et al. Filtration markers, cardiovascular disease, mortality, and kidney outcomes in stable kidney transplant recipients: the FAVORIT trial. *Am J Transplant.* 2017;17(9):2390-2399.
2. Levey AS, Coresh J, Tighiouart H, et al. Measured and estimated glomerular filtration rate: current status and future directions. *Nat Rev Nephrol.* 2020;16(1):51-64.
3. Ying T, Gill J, Webster A, et al. Canadian-australasian randomised trial of screening kidney transplant candidates for coronary artery disease—a trial protocol for the CARSK study. *Am Heart J.* 2019;214:175-183.
4. Sarnak MJ, Amann K, Bangalore S, et al. Chronic kidney disease and coronary artery disease: JACC

- state-of-the-art review. *J Am Coll Cardiol*. 2019;74(14):1823-1838.
5. Chen J, Budoff MJ, Reilly MP, et al. Coronary artery calcification and risk of cardiovascular disease and death among patients with chronic kidney disease. *JAMA Cardiol*. 2017;2(6):635-643.
 6. Al-Naher A, Wright D, Devonald MAJ, et al. Renal function monitoring in heart failure—what is the optimal frequency? A narrative review. *Br J Clin Pharmacol*. 2018;84(1):5-17.
 7. Jenkins R, Mandarano L, Gugathas S, et al. Impaired renal function affects clinical outcomes and management of patients with heart failure. *ESC Heart Fail*. 2017;4(4):576-584.
 8. Shlipak MG, Heidenreich PA, Noguchi H, et al. Association of renal insufficiency with treatment and outcomes after myocardial infarction in elderly patients. *Ann Intern Med*. 2002;137(7):555-62.
 9. Thakar CV, Christianson A, Freyberg R, et al. Incidence and outcomes of acute kidney injury in intensive care units: a Veterans Administration study. *Crit Care Med*. 2009;37(9):2552-8.
 10. Mullens W, Damman K, Testani JM, et al. Evaluation of kidney function throughout the heart failure trajectory—a position statement from the heart failure association of the European Society of Cardiology. *Eur J Heart Fail*. 2020;22(4):584-603.
 11. Karki P, Agrawaal K, Lamsal M, et al. Predicting outcomes in acute coronary syndrome using biochemical markers. *Indian Heart J*. 2015;67(6):529-37.
 12. Lin T-H, Hsin H-T, Wang C-L, et al. Impact of impaired glomerular filtration rate and revascularization strategy on one-year cardiovascular events in acute coronary syndrome: data from Taiwan acute coronary syndrome full spectrum registry. *BMC Nephrol*. 2014;15(1):1-9.
 13. El-Menyar A, Zubaid M, Sulaiman K, et al. In-hospital major clinical outcomes in patients with chronic renal insufficiency presenting with acute coronary syndrome: data from a registry of 8176 patients. *Mayo Clin Proc*. 2010 ;85(4):332-40.
 14. Al Suwaidi J, Reddan D, Williams K, et al. Prognostic implications of abnormalities in renal function in patients with acute coronary syndromes. *Circulation*. 2002;106(8):974-80.
 15. Nabais S, Rocha S, Costa J, et al. Prognostic impact of moderate renal dysfunction in acute coronary syndromes. *Rev Port Cardiol*. 2008 ;27(3):303-12.
 16. Sooklim K, Srimahachota S, Boonyaratavej S, et al. Renal dysfunction as an independent predictor of total mortality after acute coronary syndrome: the Thai ACS Registry. *J Med Assoc Thai*. 2007;90(1):32-40.
 17. Anavekar NS, McMurray JJ, Velazquez EJ, et al. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. *N Engl J Med*. 2004;351(13):1285-95.