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Original Article

How does clinical profile and outcome differ in patients with Chronic Kidney Disease undergoing percutaneous coronary revascularization according to the severity of CKD? – CHANNEL Study

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ABSTRACT

Background: Chronic kidney disease (CKD) is an independent risk factor for the development of coronary artery disease. We evaluated outcomes amongst patients of CKD undergoing percutaneous coronary intervention (PCI) as assessed on severity of CKD based on estimated glomerular filtration rate (eGFR) at the time of PCI.

Method and materials: We analyzed 100 consecutive CKD patients who underwent PCI and were followed up for 1 year; an observational, prospective, open-label study. Multivariate and Receiver operator characteristics (ROC) analysis was used to determine the cut point ofeGFR for predicting 4-P major adverse cardiac events (MACE) outcomes defined as the composite of Cardiovascular (CV) mortality, heart failure hospitalization (HHF), repeat revascularization and non-fatal MI over 1 year follow up.

Results: According to eGFR cut-off value derived from ROC, patients were divided in to two groups based on eGFR cut-off of 36.25 mL/min/1.73 m^2. Majority of patients (79%) were in Group 1 (eGFR >36.25 mL/min/1.73 m^2). Group 2 had Lower HbA1C, hemoglobin and elevated level of urea as compared to group:1 (p=0.002,<0.0001 respectively). All-cause mortality had trend forbeing higher (6.3 vs. 19%) in group:2, but statistically non-significant ($p = 0.17$). Lower baseline LVEF (39 ± 10.08%) across the cohort was independent predictor of higher risk for HHF. eGFR <36.25 mL/mim/1.73 m^2 was the most robust predictor of MACE, carrying a 3-fold increase in risk of 4-P MACE with significant association (0.69, CI 0.59 to 0.78, $p = 0.0009$).

Conclusions: Lower baseline eGFR was associated with higher incidence of 4 P MACE with best cut-off being eGFR <36.25 mL/min/1.73 m^2. Lower Baseline LVEF was independent predictor from HHF across the cohort.

1. Introduction

Chronic kidney disease (CKD) is emerging as an important chronic disease globally.[1] In India which a country of more than 1 billion, the rising incidence of CKD is likely to pose a major problem for both healthcare and the economy in future. It has been recently estimated that the age-adjusted incidence rate of end-stage renal disease (ESRD) in India is 229 per million populations,[2] and >100,000 new patients enter renal replacement programs annually.[3] Recent studies suggest that CKD is associated with increased risk of cardiovascular (CV) morbidity and mortality in a manner independent of DM.[4,5] This association is even more evident in patients with ESRD, where CV mortality accounts for 45% of all-cause mortality.[6]

By the time patients reach ESRD, left ventricular hypertrophy (LVH) is almost universal and left ventricular (LV) mass has been correlated with survival in these patient population. ESRD also causes cardiac fibrosis resulting in LV systolic and diastolic dysfunction, contributing to increased incidence of sudden death.[7]

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Patients with CKD are also more likely to experience higher rates of bleeding, drug-related adverse events, strokes, and need for dialysis, apart from longer hospital stay and increased mortality following coronary revascularization as compared to patients with normal kidney function.[8] Also, it is imperative to note that, coronary angiography (CAG) itself carries a high risk of contrast-induced nephropathy (CIN) and worsening renal function in these subgroup of patients.

The impact of PCI in patients with various stages of CKD is not very well studied amongst Asian Indians.[9,10] Reduced effectiveness of PCI is anticipated in the CKD population because of diffuse nature of vascular disease, extensive vascular calcification, smaller vessel diameter, high diabetes prevalence, and, possibly, increased prothrombotic activity.[11]

Although the efficacy of PCI in reducing adverse events has been shown in several randomized controlled trials of the general population, the benefit of PCI in patients with CKD,[12,13,14,] has been understudied or not found significant from certain studies, and hence remains controversial.

The objective of our study was to analyze the clinical profile and outcomes at 1 year in CKD patients for pre-defined 4 point major cardiovascular events (MACE) defined as a composite of hospitalization for heart failure (HHF), non-fatal MI, repeat revascularization and CV mortality amongst our cohort of CKD patients who underwent PCI vis-à-vis their eGFRat the time of PCI.

2. Materials & methods

A Total of 102 patients who underwent PCI in CKD were observed in a prospective, all comer fashion at tertiary cardiac care hospital from December 2016 to December 2018.2 patients who were lost to follow up were excluded. 100 patients who completed 1 year follow up with a mean of 365.43 ± 49.1 days were analyzed for their baseline characteristics and outcomes.

All events were captured in predefined datasheet in Microsoft excel format for all 102 CKD patients who underwent PCI with special focus on pre-defined 4-point MACE which was composite of CV mortality, need for repeat revascularization, hospitalization for Heart failure (HHF) and non-fatal MI. Inclusion criteria defined participant to be a patient of CKD with EGFR <60 mL/min/1.73 m^2 as calculated by MDRD method who underwent PCI for any coronary angiographic lesion more than >70% diameter which was amenable to PCI. Written consent was obtained for inclusion in the study. We Excluded CKD patients with eGFR >60 mL/min/1.73 m^2 by MDRD method and patients with life expectancy less than 1 year. Ethical clearance was obtained from the Institutional Ethics committee.

2.1. Data analysis

All statistical analysis was performed using SPSS v 24.0 (Chicago, IL, USA). Continuous variables were compared using the unpaired student's *t*-test or one-way analysis of variance. Continuous variables were summarized as mean ± standard deviation (SD) whereas categorical variables were expressed as percentage of the sample. Multivariate analysis and regression analysis was done for all the continuous variables. Receiver operator characteristics (ROC) analysis was performed to determine a cut-off point for eGFR to provide a cut-off value with equivalent sensitivity and specificity for predicting 4-P MACE outcomes. Group differences associated with a p value < 0.05 were considered statistically significant.

3. Results

Present study involved 102 patients out of which 100 cases that completed 1 year follow up are reported here. Data was analyzed for these 100 patients. 79% were males and 21% were females. Baseline characteristics of patients are summarized in Table 1. On the basis of eGFR (MDRD method), majority patients (85%) were in stage 3 (eGFR between 30 and 60 mL/min/1.73 m^2), 9% in stage 4 (eGFR between 15 and 30 mL/min/1.73 m^2), while 6% in stage 5 (eGFR less than 15 mL/min/1.73 m^2).

A Receiver Operator Characteristic (ROC) analysis was performed to determine a cut point for eGFR which yielded a value of ≤36.25 mL/min/1.73 m^2 for predicting 4 P- MACE outcome with 96.55% specificity as shown in Fig. 1. Value of eGFR ≤36.25 mL/min/1.73 m^2 is associated with significantly higher 4-P major adverse cardiac events (MACE) outcomes defined as composite of Cardiovascular (CV) mortality, heart failure hospitalization (HHF), repeat revascularization and non-fatal MI.

Majority of patients (79%) in our cohort were in Group 1 (eGFR>36.25 mL/min/1.73 m^2), while only 21% were in Group 2 (eGFR≤36.25 mL/min/1.73 m^2). Group comparison of the baseline characteristics is shown in Table 2. Patients were matched for age in group:2 with patients in group:1 (57.48 ± 11.58 vs. 60.77 ± 10.39 years, $p = 0.21$). There was no significant difference in LVEF between two groups (39.37 ± 10.48 and 37.62 ± 8.46; $p = 0.48$). Patients in group:1 and group:2 had previous history of PCI (3.8% and 9.5%), prior MI(2.5 and 14.3%) but these were not statistically significant between two groups (P 0.61,0.1). Patients with single, double and triple vessel disease were present in 35.4%, 43% and 20.3% in group:1 and 28.6%, 52.4% and 9.5% in group:2 respectively. Multivariate regression analysis showed that there was trend towards higher prevalence of double vessel disease in both groups, but not reaching statistical significance ($p = 0.74$, 0.60 and 0.41). The difference may be insignificant due to smaller sample size.

Patients in group 2 had higher Urea and lower hemoglobin and HBA1C in group:2 as compared to patients in group 1. These were statistically significant between these 2 groups as analyzed for their

Table: 1
Baseline characteristics.

	N = 100
Male (%)	79
Female	21
Age (in years)	60.08 ± 10.68
Hypertension	54
Diabetes Mellitus-II	38
Number of stent/s	
1	76
2	23
3	1
Systolic Blood pressure (SBP in mmHg)	137.59 ± 29.50
Diastolic Blood pressure (DBP in mmHg)	79.28 ± 17.77
Heart rate (beats per minute)	84.15 ± 16.09
HBA1c (gm%)	7.73 ± 1.82
Urea (mg%)	51.27 ± 35.23
Hemoglobin (gm%)	11.74 ± 2.00
Previous MI	5
Previous Bypass	2
Previous PCI	5
Stable CAD	10
Unstable angina	45
Non-ST Elevation Myocardial infarction (NSTEMI)	30
ST Elevation Myocardial infarction (STEMI)	15
LVEF (%)	39 ± 10.08
Stage 3	85
Stage 4	9
Stage 5	6

*LVEF, left ventricular ejection fraction.

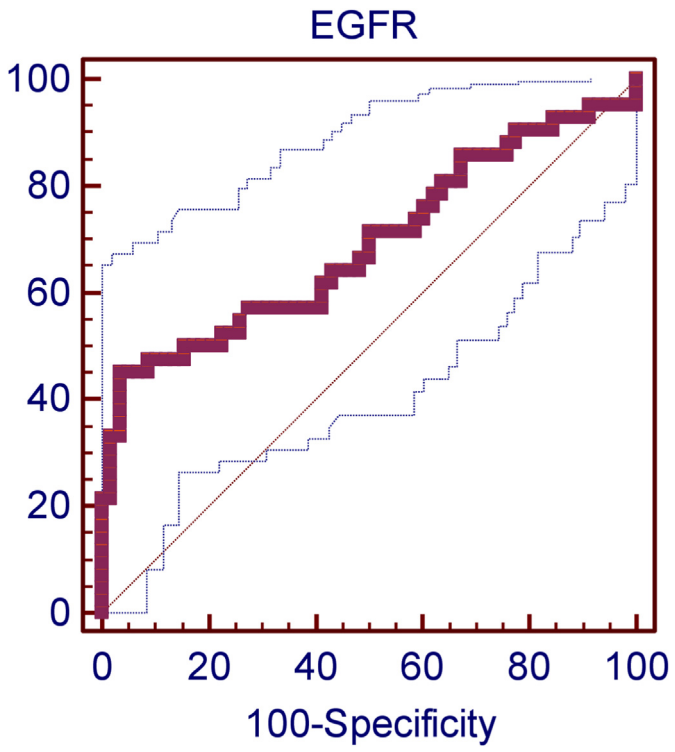

Fig. 1. Receiver operator characteristics (ROC) curve of eGFR for predicting 4-P major adverse cardiac events (MACE).

eGFR based groups (7.99 ± 1.85 vs. 6.65 ± 1.23; $p = 0.002$ for HbA1C and 12.16 ± 1.80 vs. 10.18 ± 1.99; P= <0.0001 for hemoglobin).

The overall in hospital complications like cardiogenic shock (7%) and unstable angina (3%) was present in the overall cohort. There was no significant difference for these outcomes between the groups in our cohort ($p = 0.32, 0.85$).

Over the follow-up period of 365.43 ± 49.1 days of these 100 patients, 58 patients had event free survival and while 42 patients had major cardiovascular events (MACE) as shown in table no.3. There was 9% all-cause mortality seen in the cohort. 23% patients were readmitted for HHF, 2% patients were readmitted for HHF and revascularization and 7% were readmitted for only revascularization. HHF was significantly higher in group:2 (15.2 vs. 52.4%; $p = 0.0009$). 4 P-MACE as a composite endpoint was statistically higher in group 2 as compared to group1 for eGFR cut-off value as derived by ROC suggesting worse outcomes for patients with lower eGFR. As shown in Table 3, individually none of the components of 4 P-MACE i.e. all-cause mortality, HHF and repeat revascularization seen in group:2 as compared to group:1, was not statistically significant ($p = 0.17, 0.06$ and 0.98). On multivariate analysis, the lower baseline LVEF (39 ± 10.08%) across the cohort was independent predictor of higher risk for hospitalization for heart failure (HHF) but the difference between the groups was not statistically significant ($p = 0.48$).

The number of stents used during PCI showed no significant difference in 4 P-MACE. There was no significant impact of age, gender and previous history of Diabetes mellitus II, Hypertension, Stable or unstable CAD, Past or present history of Myocardial Infarction, or past history of PCI or CABG on 4 P-MACE in our study cohort. However, this may be confounded by the smaller sample size.

4. Discussion

Our findings from the study for baseline characteristics showed that amongst the patients of CKD who underwent PCI, patients with group:2 tended to be younger, had lower baseline hemoglobin and HBA1C and higher Urea levels. There was no significant difference between the groups of CKD with regards to other baseline characteristics like mean blood pressure, resting heart rate, past history of AMI or CABG, baseline LVEF and number of vessels involved. Group:2 were more likely to have need for 1 stent as compared to Group:1 but this was statistically not significant.

Table:2
Baseline characteristics according to eGFR groups.

Variables	Group:1(>36.25) N = 79	Group:2(<=36.25) N = 21	P value
Male (%)	66 (83.5)	13 (61.9)	0.06
Female	13 (16.5)	8 (38.1)	
Age (in years)	60.77 ± 10.39	57.48 ± 11.58	0.21
Number of stent/s			
1	58 (73.4)	18 (85.7)	0.38
2	21 (26.6)	2 (9.5)	0.17
3	0	1 (4.8)	0.47
HBA1c (gm%)	7.99 ± 1.85	6.65 ± 1.23	**0.002***
Urea (mg%)	44.36 ± 24.67	77.25 ± 53.59	**<0.0001***
Hemoglobin (gm%)	12.16 ± 1.80	10.18 ± 1.99	**<0.0001***
Previous MI	2 (2.5)	3 (14.3)	0.1
Previous Bypass	1 (1.3)	1 (4.8)	0.89
Previous PCI	3 (3.8)	2 (9.5)	0.61
Stable CAD	7 (8.9)	3 (14.3)	0.74
Unstable angina	38(48.1)	7 (33.33)	0.19
Non-ST Elevation Myocardial infarction (NSTEMI)	26 (32.91)	4 (19.05)	0.33
ST Elevation Myocardial infarction (STEMI)	12 (15.19)	3 (14.29)	0.81
SVD	28 (35.4)	6 (28.6)	0.74
DVD	34 (43)	11 (52.4)	0.60
TVD	16 (20.3)	2 (9.5)	0.41
LVEF	39.37 ± 10.48	37.62 ± 8.46	0.48
In-hospital complication			
Cardiogenic shock	4 (5.1)	3 (14.3)	0.32
Unstable angina	2 (2.5)	1 (4.8)	0.85

*p-value < 0.05 shows statistically significance; †SBP, systolic blood presser; ‡DBP, diastolic blood presser; §MI, myocardial infraction; || PCI, percutaneous coronary intervention; #SVD, single vessel disease; **DVD, Double vessel disease; ††TVD, Triple vessel disease; ‡‡LVEF, left ventricular ejection fraction.

Table: 3
Outcome within 1 year of PCI.

Variables	Group: 1 N = 79	Group: 2 N = 21	P value
All-cause Mortality	5 (6.3)	4 (19)	0.17
Event free survival	56 (70.9)	2 (9.5)	**<0.0001**[a]
Readmission for LVF	12 (15.2)	11 (52.4)	**0.0009**[a]
Readmission for LVF and Revascularization	0	2 (9.5)	0.06
Readmission for revascularization	5 (6.3)	2 (9.5)	0.98
4 points MACE	23 (29.1)	19 (90.5)	**<0.0001**[a]

[a] *p*-value <0.05 shows statistically significance; †LVF, left ventricular failure; ‡MACE, major adverse cardiovascular event, § HHF- Hospitalization for heart failure.

In our cohort, LV systolic dysfunction and lower eGFR were associated independently with an increased risk of 4 P-MACE on multivariate analysis. Previous studies have shown that renal impairment is a significant prognostic predictor of mortality in patients with coronary artery disease.[14,15]

Group:2 had higher incidence of 4 P MACE whereas; readmission for acute heart failure was significantly higher in Group:2 patients as compared to group:1 of the cohort as assessed by ROC based cut-offs. Previous studies have shown that renal impairment is a significant prognostic factor for mortality in patients with coronary artery disease. Lower eGFR was the strongest predictor of 4 P-MACEand this is similar to data from Manjunath et al[16] which also demonstrated that eGFR is an independent risk factor for atherosclerotic cardiovascular disease and related outcomes.

Another study done by Furberg CD et al and Beattie JN et al showed that in post-myocardial infarction patients, an increase in creatinine above the upper reference limit is associated with an increase in the overall mortality.[17,18] In our study, we have demonstrated that eGFR is a strong predictor of MACE in patients undergoing PCI and the risk of mortality increases as renal function deteriorates.

The difference in LVEF across CKD group was not statistically different as shown in Table 2. The difference in values may be due to higher prevalence of dialysis, anemia (though statistically not significant) which may have confounded the estimation of LVEF. HHF following PCI was related to a higher risk in the subgroup of patients who had lower baseline LVEF as compared to those not having HHF across the cohort irrespective of Stage of CKD. Even though, the difference in baseline LVEF between various stages of CKD were not statistically different, across the cohort of 100 patients, those with lower baseline LV systolic dysfunction (EF 36.31 ± 9.24) had significantly higher MACE ($p = 0.02$) as compared to those with mild LV systolic dysfunction or fair LV function (40.95 ± 10.28). Lower baseline LV systolic function (EF <35%) has been shown as a robust predictor of mortality in our series as well (HR = 4.04, 95% CI: 2.16–7.59) as compared to moderate and mild LV systolic dysfunction in patients of CKD undergoing PCI and corroborates with other studies with similar results.[14,16,18]

Other cardiovascular risk factors such as diabetes, hypertension did not show a significant difference in 4 P-MACE between the ROC derived groups. These findings are partially consistent with those of Best et al.[19] The prevalence of diabetes amongst our patients was similar to the study done by Best et al[19,24](20.4–50.0%). Bevc et al[20] also investigated mortality in CKD patients undergoing PCI, where they had additionally included a control arm comprising of patients with normal renal function. Their multivariate analysis showed hypertension and diabetes to be not significantly associated with mortality. Furthermore, Goldenberg et al[21] studied a population with non-ST-segment elevation ACS and renal impairment and correlated renal function to outcomes. In their study also, presence of hypertension and diabetes did not significantly correlate with mortality.

However, it is believed that coexisting conditions and comorbidities such as diabetes mellitus, hypertension, may contribute to adverse outcomes in patients with renal impairment.[22,23] In our study, CKD (eGFR) remained the major predictor even after adjusting for the above variables as analyzed by ROC derived 2 groups, indicating an independent influence of eGFR in PCI outcomes in CKD patients.

We found cardiogenic shock at presentation and unstable angina as predictors of in-hospital adverse events but they did not reach statistical significance between the 2 groups. This is probably explained by the small sample size of the cohort. Previous studies have shown cardiogenic shock to be a strong predictor of in hospital death with 40–50% mortality in the studies.[24]

ISCHEMIA-CKD study had shown no benefit in outcomes between conservatively arm as compared to invasive arm in CKD patients with moderate to large ischemia documented by non-invasive assessment. However, the sub-group analysis showed that invasive strategy was better in patients with large ischemia but not in moderate ischemia sub-group. However, the study didn't have significant number of Asian ethnicity population.[25]

In addition, our study shows that the number of treated vessels, previous myocardial infarction, previous PCI, previous CABG was not significantly associated with 4-P MACE though smaller sample size may account for the non-significant outcomes. It seems that renal impairment is a robust determinant of mortality that may obscure other 'classical' prognostic factors like diabetes and hypertension. It is well known that CKD is strongly associated with coronary artery disease and has a major impact on outcomes.

4.1. Conclusion

Our results show that the lower baseline eGFR was associated with higher incidence of 4 P MACE in patients of CKD undergoing PCI at 1 year follow up with the best cut-off being eGFR <36.25 mL/min/1.73 m^2 for the cohort. Lower Baseline LVEF was anindependent predictor from HHF within 1-year of follow-up.

Key message – To the best of our knowledge, this is the largest prospective study evaluating 4 P MACE amongst Asian Indian ethnicity CKD patients undergoing PCI based on their eGFR.

4.2. Limitation

The study is limited by the lower number of patients in group 2 as compared to group 1, due to sampling study design which was based on the consecutive, prospective 100 cases of CKD that underwent PCI. A future randomized stratified sampling based study may help to overcome this limitation of this study and studies comparing PCI outcomes in CKD with AMI as compared with those with normal renal functions may throw additional light on the subject. Lower eGFR may have mandated more conservative approach for CAD in sicker CKD patients thus causing the survival bias at the enrollment.

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Compliance with ethical standards

This study is approved by institutional ethics committee. All patients gave written inform consent for enrollment in this study.

Statement of human rights

The study involves human participants; authors should include a statement that the studies have been approved by the appropriate institutional ethics committee (UNMICRC/CARDIO/2016/18) and have been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Declaration of competing interest

There is no conflict of interest.

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References

1. Ruggenenti P, Schieppati A, Remuzzi G. Progression, remission, regression of chronic renal diseases. *Lancet*. 2001;357(9268):1601–1608.
2. Modi GK, Jha V. The incidence of end-stage renal disease in India: a population-based study. *Kidney Int*. 2006;70(12):2131–2133.
3. Kher V. End-stage renal disease in developing countries. *Kidney Int*. 2002;62(1):350–362.
4. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med*. 2004;351(13):1296–1305.
5. Gansevoort RT, Correa-Rotter R, Hemmelgarn BR, et al. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. *Lancet*. 2013;382(9889):339–352.
6. Papachristidis A, Lim WY, Voukalis C, Ayis S, Laing C, Rakhit RD. Determinants of mortality in patients with chronic kidney disease undergoing percutaneous coronary intervention. *CardiorenalMed*. 2016;6(3):169–179.
7. Berl T, Henrich W. Kidney-heart interactions: epidemiology, pathogenesis, and treatment. *Clin J Am Soc Nephrol*. 2006;1(1):8–18.
8. Gupta R, Birnbaum Y, Uretsky BF. The renal patient with coronary artery disease: current concepts and dilemmas. *J Am Coll Cardiol*. 2004;44(7):1343–1353.
9. Gruberg L, Dangas G, Mehran R, et al. Clinical outcome following percutaneous coronary interventions in patients with chronic renal failure. *Catheter CardiovascInterv*. 2002;55(1):66–72.
10. Rubenstein MH, Harrell LC, Sheynberg BV, Schunkert H, Bazari H, Palacios IF. Are patients with renal failure good candidates for percutaneous coronary revascularization in the new device era? *Circulation*. 2000;102(24):2966–2972.
11. Paloian NJ, Giachelli CM. A current understanding of vascular calcification in CKD. *Am J Physiol Ren Physiol*. 2014;307(8):F891–F900.
12. Shroff GR, Solid CA, Herzog CA. Long-term survival and repeat coronary revascularization in dialysis patients after surgical and percutaneous coronary revascularization with drug-eluting and bare metal stents in the United States. *Circulation*. 2013;127(18):1861–1869.
13. Tsai TT, Messenger JC, Brennan JM, et al. Safety and efficacy of drug-eluting stents in older patients with chronic kidney disease: a report from the linked CathPCI Registry–CMS claims database. *J Am Coll Cardiol*. 2011;58(18):1859–1869.
14. Parikh PB, Jeremias A, Naidu SS, et al. Impact of severity of renal dysfunction on determinants of in-hospital mortality among patients undergoing percutaneous coronary intervention. *CatheterCardiovascInterv*. 2012;80(3):352–357.
15. Wańha W, Kawecki D, Roleder T, et al. Long-term percutaneous coronary intervention outcomes of patients with chronic kidney disease in the era of second-generation drug-eluting stents. *CardiorenalMed*. 2017;7(2):85–95.
16. Manjunath G, Tighiouart H, Ibrahim H, et al. Level of kidney function as a risk factor for atherosclerotic cardiovascular outcomes in the community. *J Am Coll Cardiol*. 2003;41(1):47–55.
17. Furberg CD, Byington RP. What do subgroup analyses reveal about differential response to beta-blocker therapy? The Beta-Blocker Heart Attack Trial experience. *Circulation*. 1983;67(6 Pt 2):I98–I101.
18. Beattie JN, Soman SS, Sandberg KR, et al. Determinants of mortality after myocardial infarction in patients with advanced renal dysfunction. *Am J Kidney Dis*. 2001;37(6):1191–1200.
19. Best PJ, Lennon R, Ting HH, et al. The impact of renal insufficiency on clinical outcomes in patients undergoing percutaneous coronary interventions. *J Am Coll Cardiol*. 2002;39(7):1113–1119.
20. Bevc S, Penko M, Kanic V, Hojs R. Mortality of patients with renal dysfunction after percutaneous coronary intervention. *Angiology*. 2010;61(1):24–30.
21. Goldenberg I, Subirana I, Boyko V, et al. Relation between renal function and outcomes in patients with non–ST-segment elevation acute coronary syndrome: real-world data from the European Public Health Outcome Research and Indicators Collection Project. *Arch Intern Med*. 2010;170(10):888–895.
22. Thambyrajah J, Landray MJ, McGlynn FJ, Jones HJ, Wheeler DC, Townend JN. Abnormalities of endothelial function in patients with predialysis renal failure. *Heart*. 2000;83(2):205–209.
23. Kronenberg F, Kuen E, Ritz E, et al. Lipoprotein (a) serum concentrations and apolipoprotein (a) phenotypes in mild and moderate renal failure. *Clin J Am Soc Nephrol*. 2000;11(1):105–115.
24. De Luca L, Olivari Z, Farina A, et al. Temporal trends in the epidemiology, management, and outcome of patients with cardiogenic shock complicating acute coronary syndromes. *Eur J Heart Fail*. 2015;17(11):1124–1132. https://doi.org/10.1002/ejhf.339.
25. Bangalore S, Maron DJ, O'Brien SM, et al. On behalf of the ISCHEMIA-CKD Research group. Management of coronary disease in patients with advanced kidney disease. *N Engl J Med*. 2020;382(17):1608–1618.