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ORIGINAL RESEARCH ARTICLE

STUDY OF CARDIAC BIOMARKERS IN CHRONIC KIDNEY DISEASE PATIENTS IN A TERTIARY CARE CENTRE

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ABSTRACT

Background: There has been increasing evidence of association between cardiovascular and chronic kidney disease. Most of complications and mortality in these patients are due to development of cardiovascular disease (CVD) rather than due to chronic kidney disease (CKD) by itself. Though cardiac biomarkers are available but due to lack of clinical symptoms in early stages and delayed diagnosis mortality rate has increased. The present study was conducted to detect the cardiovascular dysfunction measured by various cardiac biomarkers like serum Cardiac high sensitivity Troponin I, Creatinine kinase and creatinine Kinase MB with eGFR in CKD patients to correlate the association of cardiovascular dysfunction in patients with CKD for early detection and initiation of aggressive treatment to reduce mortality.

Methods: The present cross-sectional study was conducted on 110 patients of chronic kidney disease (CKD) at tertiary care hospital, Hyderabad. Cardiac HS Troponin I, Creatine Kinase (CPK) and Creatine Kinase- MB (CK-MB) were analysed and correlated with e-GFR, Urea and creatinine levels.

Results: There was statistically significant association between Hs Troponin I, CK-MB and CPK with Chronic kidney disease. There was negative corelation of cardiac biomarkers with eGFR and positive correlation with Urea and creatinine. Multivariate regression analysis for predictors of cardiac dysfunction was done using ANOVA with renal parameters in patients with CKD which showed strong association between e-GFR and cardiac markers.

Conclusion: High morbidity and mortality in patients with CKD is observed due to Cardiovascular disease. It is important to diagnose CVD with high index of suspicion and evaluate with commonly available biochemical cardiac markers. In our study there was significant elevation in Hs Trop I, CK MB and CPK in CKD patients which correlated negatively with eGFR. Routine use of these markers during follow-up of CKD patients helps in risk assessment, prevention of complications and timely interventions.

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Keywords: Cardiovascular Disease, Cardiac Biomarkers, Chronic Kidney Disease, Hs-Troponin I

INTRODUCTION

Cardiovascular dysfunction and renal dysfunction have been well recognised causes of morbidity and mortality worldwide. In chronic kidney disease (CKD) spectrum of CVD includes ischaemic heart disease, congestive heart failure, arrhythmias and peripheral vascular disease.[1] It is also known that chronic kidney disease patients experience premature mortality due to impaired cardiac function. In India CKD is very frequent due to multitude of causes including congenital kidney disease to nephropathy. Poverty, pollution, lack of sanitation, overcrowding, and nephrotoxins like heavy metals and plant toxins can cause glomerular and interstitial kidney diseases.[2] Also increased in cases of hypertension, diabetes, and other diseases that are risk factors for chronic kidney disease is also driving growth in prevalence of chronic kidney disease, putting enormous pressure on health-care resources.[3]

The prevalence of CVD in renal dysfunction is as high as 73%. Interpretation of cardiac biomarkers in CKD can be difficult, as elevated levels may not indicate either myocardial injury or may be due to decreased urinary clearance with retention of solutes and/or overall CKD-associated chronic inflammation. Appropriate diagnosis of disease in CKD is important. [4] Early detection of CVD in these patients can help prevent the complications and mortality. cardiac biomarkers are necessary for timely and accurate diagnosis and prompt management of heart failure and acute coronary syndrome in CKD patients. Most patients present at very late stage when eGFR is <15ml/min per 1.73 m2 due to many reasons like poor resources, in-affordability to health care, delay in start of Renal Replacement Therapy (RRT), and financial crisis. [5] National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) 2000 guidelines define and classifies CKD as follows: Stage 0/1 CKD was defined as eGFR > 90 mL/min/1.73 m2; stage 2 CKD as eGFR 60–89 mL/min/1.73 m2; stage 3 CKD as eGFR 30–59 mL/min/1.73 m2; stage 4 CKD as eGFR 15–29 mL/min/1.73 m2; and stage 5 CKD as eGFR < 15 mL/min/1.73 m2 or if the participant was on dialysis. [6] Cardiovascular mortality rate in End stage kidney disease patients is about 10–20 times that of the general population. Many patients of CKD with Acute coronary syndrome (ACS) present atypically like silent myocardial infarction (MI), nonspecific electrocardiogram changes due to comorbidities such as left ventricular hypertrophy or electrolyte abnormalities are commonly noticed. CKD patients who present with acute chest pain have non-ST elevation MI (NSTEMI) more than twice as often as patients with normal kidney function.[7] In 1974, Lindner et al. [8] first pointed out that patients treated by chronic renal replacement therapy are exposed to cardiovascular problems and suffer from accelerated and severe atheromatosis. Hence it is important to evaluate CKD patients with cardiac markers for early management. Heart failure is also common in CKD. Uraemia induced fatigue in CKD patients causes confounding effect leading to delayed diagnosis and management of CVD. In these high-risk patients, Cardiac biomarkers like Cardiac Troponins, N-terminal pro-B-type natriuretic peptide, Creatine Kinase MB and Creatine Kinase have been proven to be of great use.[9] Cardiac troponins and Creatine kinase are routinely used in clinical practice for diagnosis of cardiopulmonary conditions. Several studies are available on N-terminal pro-B-type natriuretic peptide, high sensitivity Troponin T and certain novel markers of heart failure like growth differentiation factor-15, soluble ST2, and galectin-3. [10] However these are not available in most clinical settings for routine screening. Hence, we wanted to find the association of cardiac biomarkers like cardiac high sensitivity Troponin I, Creatinine Kinase and

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Creatinine Kinase MB among Patient with CKD with or without cardiac symptoms. Estimated-GFR is a very simple and useful marker of progression and stage of Renal dysfunction. The main objective of the present study was to correlate the association of cardiovascular dysfunction measured by various cardiac biomarkers including serum Cardiac high sensitivity Troponin I, Creatine kinase and Creatine Kinase MB with eGFR in patients with CKD for early detection and initiation of aggressive treatment to reduce mortality.

MATERIALS & METHOD

The present cross-sectional study was conducted on 110 patients of age >18 years with chronic kidney disease diagnosed clinically as per the KDIGO 2012 CKD guideline that defines CKD as abnormalities of kidney structure or function, present for a minimum of 3 months, with implications for health. The study was conducted between February to April 2024 after obtaining institutional ethical clearance. Informed consent was taken from patients. Patients with acute kidney injury, history of myocardial infarction, coronary artery stent implantation, or arteriovenous fistula; history of Acute coronary Syndrome, malignant hypertension, surgery, trauma, blood infusion, erythropoietin treatment, history of malignancy, active tuberculosis, inflammatory diseases, or diabetic ketoacidosis were excluded from the study.

Serum samples were collected under aseptic precautions and processed to analyse Serum Creatinine, Serum Urea, Serum Creatine Kinase in AU 480 Fully automated chemistry analyser by Urease-GLDH Method, IDMS traceable Modified Jaffe's method and Modified IFCC Method. Creatine Kinase-MB, high sensitivity Troponin I were estimated in Access 2 Immunoassay Analyser by CLIA method. Estimated- Glomerular Filtration rate(e-GFR) was calculated using CKD-EPI Creatinine Equation. The results presented as the means ± SD. The significance of any differences in the means and proportions were tested with student's t-test and ANOVA using SPSS version 29.0 statistical software. p-values < 0.05 were considered stastically significant. Correlations between cardiac and renal function tests in CKD was done by using multivariate logistic regression analysis.

RESULTS

Among 110 patients in our study, 38% were females and 62% were males indicating predominance of CKD in male population. The mean age of the study population was 63.56±12.25. Mean values of biochemical parameters tested are as shown in the Table 1. Serum creatinine was normal in 32% of patients with CKD at the time of presentation. They were previously diagnosed with CKD. eGFR was calculated and it was observed that 8 % were in stage I CKD, 18% in Stage II, 40% in Stage III, 14% in Stage IV and 20 % in Stage V Chronic kidney disease. Cardiac markers were found to be elevated among patients with CKD in all of the above stages. None of these study patients had previous history of cardiac illness. Family history of Cardio vascular disease was present in 21% patients. statistical analysis including correlation analysis was done by determining Karl Pearson's correlation coefficient for a positive and negative correlation between various parameters. Pearson's correlation showed positive correlation of hSTrop I, CPK and CKMB with Urea and creatinine but negative correlation with eGFR (Table 2 and Graph 1a, Graph 1b, Graph 1c). Students' t test showed statistically significant increase in cardiac markers including Creatine kinase, CK-MB and high sensitivity Troponin I with decreasing eGFR and increasing Urea and creatinine among CKD patients($p<0.05$) as shown in Table 3. Multivariate regression analysis for predictors of cardiac dysfunction was done using ANOVA with renal parameters in patients with CKD (Table 4) which showed strong association between e-GFR and cardiac markers.

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Variables	Mean ±SD
AGE	63.56±12.254
Sex	Females n=42, Males n=68
CPK	935.864±1225.1410
CK-MB	133.570±91.9943
TROP-I	11666.386±38596.1509
UREA	58.56±35.809
CREATININE	2.734±2.5444
E-GFR	41.36±26.862

Table 1: Baseline characteristics of study population, (n=110)

Variables	hsTroponin I		CPK		CK-MB	
	Correlation Coefficient (r value)	p-value (2-tailed)	Correlation Coefficient (r value)	p-value (2-tailed)	Correlation Coefficient (r value)	p-value (2-tailed)
Age	-0.125	0.386	-0.081	0.578	-0.020	0.890
e-GFR	-0.187	0.193	-0.168	0.242	-0.055	0.706
Urea	0.256	0.072	0.270	0.058	0.091	0.531
Creatinine	0.131	0.365	0.058	0.689	-0.041	0.778
**. Correlation is significant at the 0.01 level (2-tailed).						
*. Correlation is significant at the 0.05 level (2-tailed).						

Table 2: Pearsons's correlation in patients with CKD between cardiac markers and tests for renal function

Renal markers	Mean ±SD	Biological Reference Interval	Cardiac markers	Biological Reference Interval	Mean ±SD	t value	P value
Urea	58.56±35.809	15-45mg/dl	CPK	24-170IU/L	935.86 ± 1225.14	-5.10	**<0 .001***
			TROP-I	0-11.6pg/mL	11666.38 ± 38596.15	-2.13	**0.038***
			CK-MB	0 - 6.3ng/mL	133.57 ± 91.99	-5.55	**< 0.001***
Creatinine	2.734±2.5444	Female:0.5-1.2mg/dl Male: 0.6-1.5mg/dl	CPK	24-170IU/L	935.86 ± 1225.14	-5.39	**<0 .001***
			TROP-I	0-11.6pg/mL	11666.38 ± 38596.15	-10.04	**< 0.001***
			CK-MB	0 - 6.3ng/mL	133.57 ± 91.99	-2.14	**0.038***
e-GFR	41.36 ± 26.86	≥ 90mL/min/1.73m^2	CPK	24-170IU/L	935.86 ± 1225.14	-5.14	**< 0.001***
			TROP-I	0-11.6pg/mL	11666.38 ± 38596.15	-6.71	**<0 .001***
			CK-MB	0 -	133.57 ±	-2.13	**0.038***

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				6.3ng/mL	91.99		

Table 3: Statistical analysis using Student's t test showing relation between cardiac and renal biochemical parameters (*p<0.005 statistical significance)

Model Summary					
Model1	**Dependent Variable**	**R**	**R Square**	**Adjusted R Square**	**Std. Error of the Estimate**
Predictors: (Constant), hsTROP-I, CK-MB, CPK	**e-GFR**	0.189	0.036	-0.027	27.225
	Urea	0.284	0.080	0.020	35.441
	Creatinine	0.171	0.029	-0.034	2.5874

ANOVA						
Model 1 Predictors: (Constant), hs TROP-I, CK-MB, CPK		**Sum of Squares**	**df**	**Mean Square**	**F**	**Sig.**
e-GFR	Regression	1260.113	3	420.038	0.567	0.640
	Residual	34095.407	106	741.204		
	Total	35355.520	109			
Urea	Regression	5052.103	3	1684.034	1.341	0.273
	Residual	57778.217	106	1256.048		
	Total	62830.320	109			
Creatinine	Regression	9.267	3	3.089	0.461	0.711
	Residual	307.945	106	6.694		
	Total	317.212	109			

Table 4: Regression Analysis and correlation by ANOVA between cardiac and renal parameters.

Coefficients							
Model 1			Unstandardized Coefficients		Standardized Coefficients	t	Sig.
			B	Std. Error	Beta		
a.	**e-GFR**	**(Constant)**	42.683	6.877		6.207	0.000
		CPK	-0.001	0.008	-0.064	-0.172	0.864

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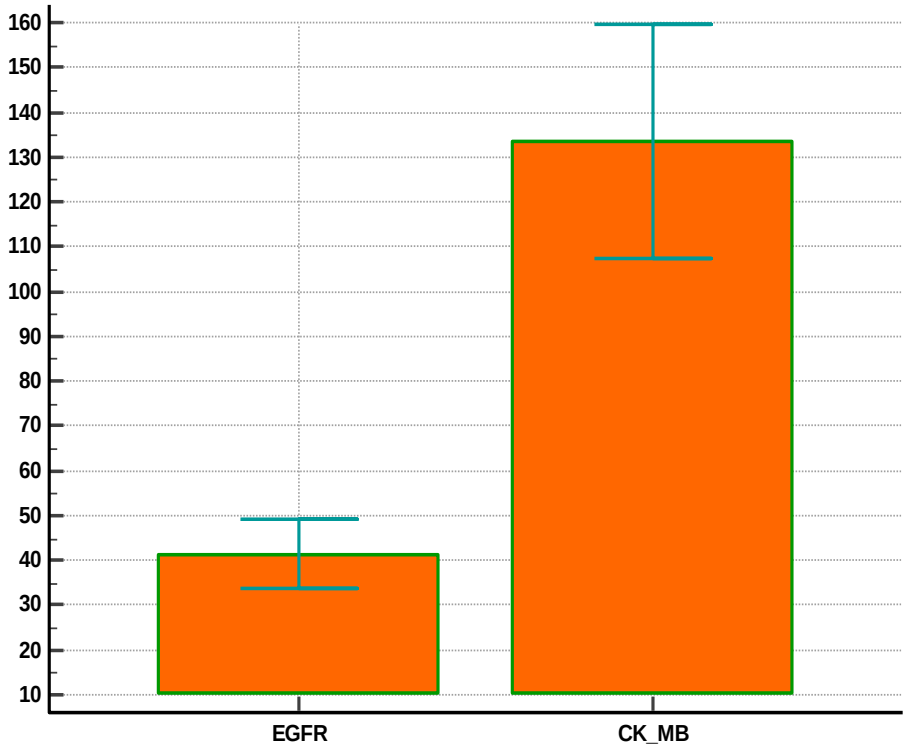
		CK-MB	0.009	0.059	0.029	0.145	0.885
		TROP-I	-9.836E-5	0.000	-0.141	-0.444	0.659
B	**Urea**	**(Constant)**	55.057	8.952		6.150	0.000
		CPK	0.009	0.011	0.312	0.855	0.397
		CK-MB	-0.039	0.077	-0.101	-0.514	0.610
		TROP-I	1.968E-5	0.000	0.021	0.068	0.946
C	**Creatinine**	**(Constant)**	2.968	0.654		4.541	0.000
		CPK	0.000	0.001	-0.169	-0.451	0.654
		CK-MB	-0.001	0.006	-0.034	-0.170	0.866
		TROP-I	1.894E-5	0.000	0.287	0.900	0.373



Graph 1a: Shows correlation between eGFR levels with CK-MB levels

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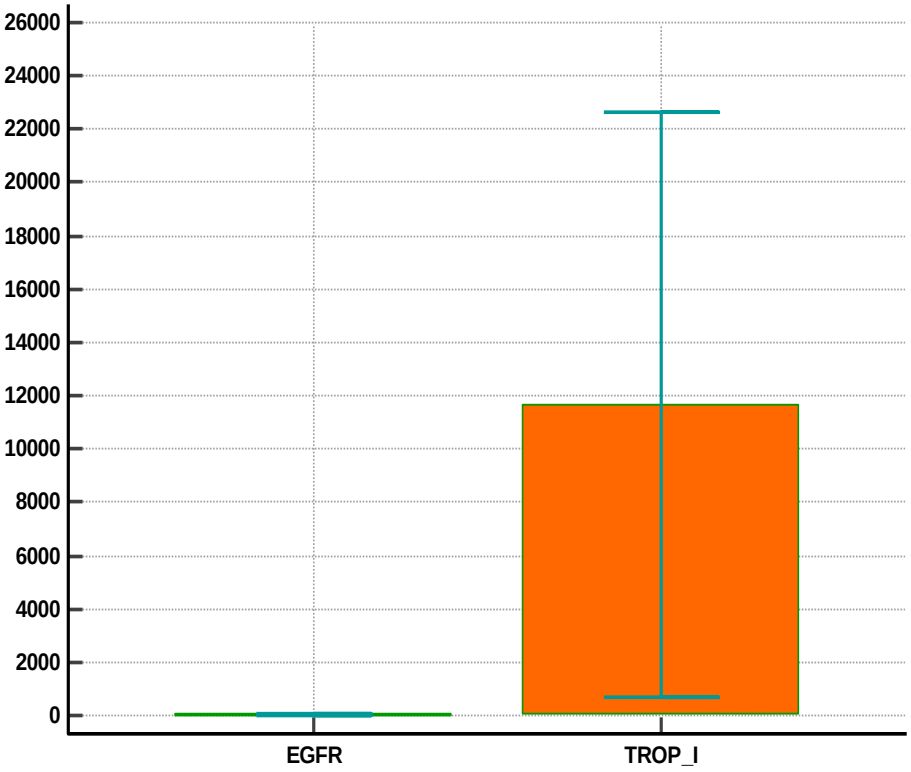
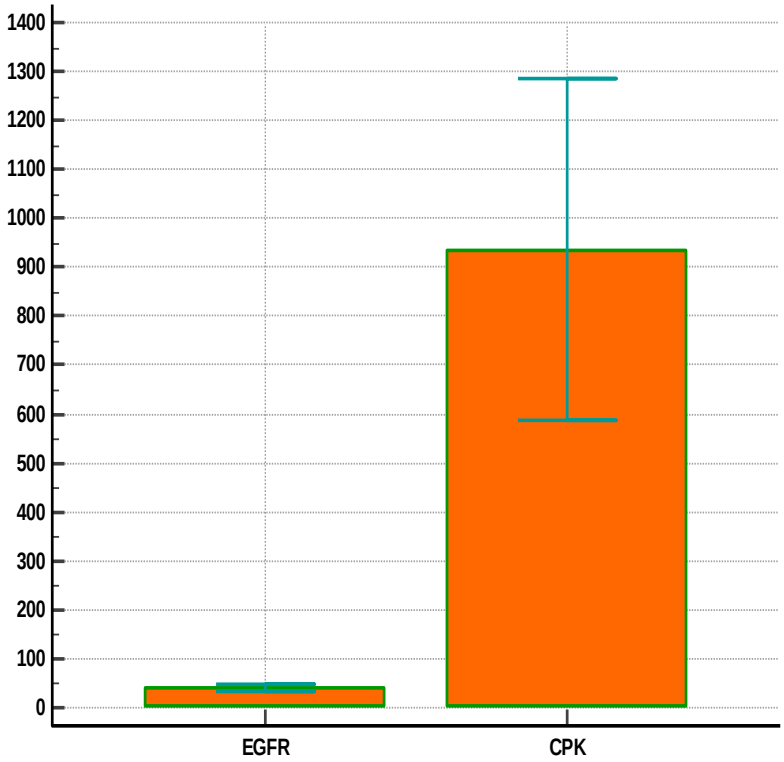


Graph 1b: Shows correlation between eGFR levels with hsTrop I



Graph 1c: Shows correlation between eGFR levels with Creatine kinase

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DISCUSSION

Cardiovascular damage occurs at much early stage in patients with CKD. The fact that CVD and CKD can initiate and sustain one another created term cardiorenal syndrome. [12] The exact reasons and mechanism behind such increased risk of cardiovascular events in CKD patients is not clear. Most people with CKD die prematurely due to cardiovascular disease rather than due to CKD progression and with ESRD risk increases by 20 to 30 times than the general population. [13] Some traditional risk factors like increasing age, hypertension, dyslipidaemia, diabetes, smoking and obesity are common for CVD as well as CKD. Some other risk factors associated are anaemia, oxidative stress, altered mineral metabolism, endothelial dysfunction, inflammation, hyperparathyroidism, metabolic bone disease, hyper homocysteinaemia, malnutrition, apolipoprotein isoforms, albuminuria, electrolyte disturbances, cardiac hypertrophy and myocardial fibrosis which predispose to early cardiovascular dysfunction causing complications. The various risk factors traditional and non-traditional tend to have an additive effect and hasten atherosclerosis and progression of CKD. [14,15,16] However, unless symptomatic, cardiac evaluation by biomarkers gets delayed. In our study we highlight the significance of biochemical cardiac markers in risk stratification for cardiovascular dysfunction and increased mortality in patients with CKD. Irrespective of cause, the presence of CKD remains an important independent risk factor for CVD. Numerous studies have examined the association of different cutoff values of serum creatinine with risks of death from cardiovascular causes and death from any cause. [17-26] However there is limited information on changes in estimated glomerular filtration rate (eGFR) and coexisting conditions like CVD. Go et al. [27] demonstrated that reduced kidney function is an independent risk factor for mortality using single estimates of retrospectively calculated GFR. Our findings suggested elevations in these biomarkers may provide new insight into key pathways involved in the pathogenesis of CVD in CKD patients and may be used to guide development of new therapies. Assessment of markers of cardiac stress and inflammation helps to risk-stratify CKD patients who have poor clinical outcomes. By assessing cardiac biomarker levels in CKD patients as done in our study we can assess risk and target therapy to reduce Cardiac complications in CKD patients.

In CKD patients, however, troponin levels are higher than would be expected probably due to decreased renal clearance as shown in previous studies. Many studies have shown mechanisms like inflammation and chronic myocardial injury to be the cause for increased cardiac markers. In our study irrespective of levels of creatinine there was elevation in cardiac markers suggesting subclinical myocardial injury and warrants early and prompt treatment by correlation with eGFR to decrease cardiac related mortality in these patients both with and without dialysis. [28]

NT-proBNP has been shown to be a predictor of cardiovascular morbidity and mortality in the general population as well as in patients with CAD as indicated in some studies. [29-31] However CK-MB, cTnI and cTnT are the preferred biomarkers for the evaluation of myocardial injury, and are recommended for routine clinical use. [32] CPK, CK-MB and hs-cTnI were significantly and inversely associated with eGFR in our study. Irrespective of the cause whether due to decreased renal clearance or chronic myocardial injury it prompts further evaluation.

CONCLUSION

Cardiovascular disease is an increasing cause of morbidity and mortality in patients with CKD. Having a great burden of CKD, in developing countries like India with multiple etiologies and risk factors, it is important to diagnose with high index of suspicion and evaluate with commonly available biochemical cardiac markers. In our study there was significant elevation in Hs Trop I, CK MB and CPK in CKD patients which correlated negatively with eGFR. Routine use of these

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markers during follow-up of CKD patients helps in risk assessment, prevention of complications and timely interventions.

REFERENCES

1. Subbiah AK, Chhabra YK, Mahajan S. Cardiovascular disease in patients with chronic kidney disease: a neglected subgroup. Heart Asia. 2016 Nov 7;8(2):56-61.
2. Varughese S, Abraham G. Chronic Kidney Disease in India: A Clarion Call for Change. Clin J Am Soc Nephrol. 2018 May 7;13(5):802-804.
3. Ene-Iordache B, Perico N, Bikbov B, Carminati S, Remuzzi A, Perna A, Islam N, Bravo RF, Aleckovic-Halilovic M, Zou H, Zhang L, Gouda Z, Tchokhonelidze I, Abraham G, Mahdavi-Mazdeh M, Gallieni M, Codreanu I, Togtokh A, Sharma SK, Koirala P, Uprety S, Ulasi I, Remuzzi G. Chronic kidney disease and cardiovascular risk in six regions of the world (ISN-KDDC): a cross-sectional study. Lancet Glob Health. 2016 May;4(5): e307-19.
4. Savoj J, Becerra B, Kim JK, Fusaro M, Gallieni M, Lombardo D, Lau WL. Utility of Cardiac Biomarkers in the Setting of Kidney Disease. Nephron. 2019;141(4):227-235.
5. Varughese S, John GT, Alexander S, Deborah MN, Nithya N, Ahamed I, Tamilarasi V, Jacob CK. Pre-tertiary hospital care of patients with chronic kidney disease in India. Indian J Med Res. 2007 Jul;126(1):28-33.
6. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International (2024) 105 (Suppl 4S), S117–S314.
7. Twerenbold R, Badertscher P, Boeddinghaus J, Nestelberger T, Wildi K, Puelacher C, Sabti Z, Rubini Gimenez M, Tschirky S, du Fay de Lavallaz J, Kozhuharov N, Sazgary L, Mueller D, Breidthardt T, Strebel I, Flores Widmer D, Shrestha S, Miró Ò, Martín-Sánchez FJ, Morawiec B, Parenica J, Geigy N, Keller DI, Rentsch K, von Eckardstein A, Osswald S, Reichlin T, Mueller C. 0/1-Hour Triage Algorithm for Myocardial Infarction in Patients With Renal Dysfunction. Circulation. 2018 Jan 30;137(5):436-451.
8. Ryan TP, Fisher SG, Elder JL, Winters PC, Beckett W, Tacci J, Sloand JA. Increased cardiovascular risk associated with reduced kidney function. Am J Nephrol. 2009;29(6):620-5.
9. Bansal N, Zelnick L, Go A, Anderson A, Christenson R, Deo R, Defilippi C, Lash J, He J, Ky B, Seliger S, Soliman E, Shlipak M. Cardiac Biomarkers and Risk of Incident Heart Failure in Chronic Kidney Disease: The CRIC (Chronic Renal Insufficiency Cohort) Study. J Am Heart Assoc. 2019 Nov 5;8(21): e012336.
10. Gürgöze MT, van Vark LC, Baart SJ, Kardys I, Akkerhuis KM, Manintveld OC, Postmus D, Hillege HL, Lesman-Leegte I, Asselbergs FW, Brunner-la-Rocca HP, van den Bos EJ, Orsel JG, de Ridder SPJ, Pinto YM, Boersma E. Multimarker Analysis of Serially Measured GDF-15, NT-proBNP, ST2, GAL-3, cTnI, Creatinine, and Prognosis in Acute Heart Failure. Circ Heart Fail. 2023 Jan;16(1):e009526.
11. Levey AS, Beto JA, Coronado BE, Eknoyan G, Foley RN, Kasiske BL, Klag MJ, Mailloux LU, Manske CL, Meyer KB, Parfrey PS, Pfeffer MA, Wenger NK, Wilson PW, Wright JT Jr. Controlling the epidemic of cardiovascular disease in chronic renal disease: what do we know? What do we need to learn? Where do we go from here? National Kidney Foundation Task Force on Cardiovascular Disease. Am J Kidney Dis. 1998 Nov;32(5):853-906.
12. Anavekar NS, Pfeffer MA. Cardiovascular risk in chronic kidney disease. Kidney Int Suppl. 2004 Nov;(92): S11-5.
13. Braam B, Joles JA, Danishwar AH, Gaillard CA. Cardiorenal syndrome--current understanding and future perspectives. Nat Rev Nephrol. 2014 Jan;10(1):48-55.

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14. Collins AJ, Li S, Gilbertson DT, Liu J, Chen SC, Herzog CA. Chronic kidney disease and cardiovascular disease in the Medicare population. Kidney Int Suppl. 2003 Nov;(87): S24-31.
15. Gansevoort RT, Correa-Rotter R, Hemmelgarn BR, Jafar TH, Heerspink HJ, Mann JF, Matsushita K, Wen CP. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. Lancet. 2013 Jul 27;382(9889):339-52.
16. Levey AS, Beto JA, Coronado BE, Eknoyan G, Foley RN, Kasiske BL, Klag MJ, Mailloux LU, Manske CL, Meyer KB, Parfrey PS, Pfeffer MA, Wenger NK, Wilson PW, Wright JT Jr. Controlling the epidemic of cardiovascular disease in chronic renal disease: what do we know? What do we need to learn? Where do we go from here? National Kidney Foundation Task Force on Cardiovascular Disease. Am J Kidney Dis. 1998 Nov;32(5):853-906.
17. Wannamethee SG, Shaper AG, Perry IJ. Serum creatinine concentration and risk of cardiovascular disease: a possible marker for increased risk of stroke. Stroke. 1997 Mar;28(3):557-63.
18. Culleton BF, Larson MG, Wilson PW, Evans JC, Parfrey PS, Levy D. Cardiovascular disease and mortality in a community-based cohort with mild renal insufficiency. Kidney Int. 1999 Dec;56(6):2214-9.
19. Mann JF, Gerstein HC, Pogue J, Bosch J, Yusuf S. Renal insufficiency as a predictor of cardiovascular outcomes and the impact of ramipril: the HOPE randomized trial. Ann Intern Med. 2001 Apr 17;134(8):629-36.
20. Shlipak MG, Heidenreich PA, Noguchi H, Chertow GM, Browner WS, McClellan MB. Association of renal insufficiency with treatment and outcomes after myocardial infarction in elderly patients. Ann Intern Med. 2002 Oct 1;137(7):555-62.
21. Garg AX, Clark WF, Haynes RB, House AA. Moderate renal insufficiency and the risk of cardiovascular mortality: results from the NHANES I. Kidney Int. 2002 Apr;61(4):1486-94.
22. Wannamethee SG, Shaper AG, Perry IJ. Serum creatinine concentration and risk of cardiovascular disease: a possible marker for increased risk of stroke. Stroke. 1997 Mar;28(3):557-63.
23. Culleton BF, Larson MG, Wilson PW, Evans JC, Parfrey PS, Levy D. Cardiovascular disease and mortality in a community-based cohort with mild renal insufficiency. Kidney Int. 1999 Dec;56(6):2214-9.
24. Mann JF, Gerstein HC, Pogue J, Bosch J, Yusuf S. Renal insufficiency as a predictor of cardiovascular outcomes and the impact of ramipril: the HOPE randomized trial. Ann Intern Med. 2001 Apr 17;134(8):629-36.
25. Shlipak MG, Heidenreich PA, Noguchi H, Chertow GM, Browner WS, McClellan MB. Association of renal insufficiency with treatment and outcomes after myocardial infarction in elderly patients. Ann Intern Med. 2002 Oct 1;137(7):555-62.
26. Drey N, Roderick P, Mullee M, Rogerson M. A population-based study of the incidence and outcomes of diagnosed chronic kidney disease. Am J Kidney Dis. 2003 Oct;42(4):677-84.
27. 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 Sep 23;351(13):1296-305.
28. Kendrick J, Chonchol MB. Nontraditional risk factors for cardiovascular disease in patients with chronic kidney disease. Nat Clin Pract Nephrol. 2008 Dec;4(12):672-81.
29. Wang K, Zelnick LR, Anderson A, Cohen J, Dobre M, Deo R, Feldman H, Go A, Hsu J, Jaar B, Kansal M, Shlipak M, Soliman E, Rao P, Weir M, Bansal N; CRIC Study Investigators.

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Cardiac Biomarkers and Risk of Mortality in CKD (the CRIC Study). Kidney Int Rep. 2020 Sep 10;5(11):2002-2012.

30. Claudel SE, Waikar SS, Gopal DM, Verma A. Association of cardiac biomarkers, kidney function, and mortality among adults with chronic kidney disease. medRxiv [Preprint]. 2023 Dec 14:2023.12.12.23299886.
31. Chesnaye NC, Szummer K, Bárány P, Heimburger O, Magin H, Almquist T, Uhlin F, Dekker FW, Wanner C, Jager KJ, Evans M. Association Between Renal Function and Troponin T Over Time in Stable Chronic Kidney Disease Patients. J Am Heart Assoc. 2019 Nov 5;8(21): e013091.
32. Ryan TP, Fisher SG, Elder JL, Winters PC, Beckett W, Tacci J, Sloand JA. Increased cardiovascular risk associated with reduced kidney function. Am J Nephrol. 2009;29(6):620-5.