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Research Article

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Chronic Kidney Disease and Risk of Coronary Artery Disease, A Prospective Study

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Abstract: Background: Reduced glomerular filtration rate (GFR) is associated with increased cardiovascular risk in adult-aged individuals. Associations with cardiovascular disease and mortality in such people are less clearly established. We aimed to determine the predictive value of the GFR for mortality and morbidity using data from the 106 participants randomized in the Prospective Study of Chronic Kidney Disease and Risk of Coronary Artery Disease. Aim of the study is to determine the predictive value of the GFR for mortality and morbidity using data from the (106) patients randomized in the Prospective Study. Patient and Methods: Glomerular filtration rate was estimated (eGFR) using the Modification of Diet in Renal Disease equation and was categorized in the ranges <60 mL • min−1 per 1.73 m2 and ≥ 60 ml/min/1.73 m2. Baseline risk factors were analyzed by category of eGFR, with and without adjustment for other risk factors. The associations between reduced eGFR and morbidity and mortality outcomes, accrued after the studied patients in the emergency department, were investigated using Cox proportional hazard models adjusting for traditional risk factors. We analyzed the declining eGFR and mortality risks in a patient with chronic kidney disease and have had coronary artery disease, including risk factors (P=0.000) for risk of coronary artery disease and (p=0.0024) for mortality risks. Low eGFR was independently associated with risk of all-cause mortality, vascular mortality, and other noncancer mortality and with fatal and nonfatal coronary and heart failure events. Results: study included (106) men (54) and women (52) between the ages of 16 and 87 years, mean age (54.9±15.2). The eGFR data are calculated for all randomized study patients with eGFR <60ml/min/1.73 m287 (82%) and a group of patients with eGFR ≥60ml/min/1.73 m2 19 (18%). Patients were divided into the following three categories by estimated GFR (eGFR) at baseline: ≥90 (n = 4), 60 to 90 (n = 7), and <60 (n = 95) ml/min/1.73 m2. The outcome and death rates of this study among patients. Were analyzed. Overall (106) patients there was (44) death 42% mortality risk, patient with depress e GFR is 68 (78%) had positive history of (CAD) and 19 (22%) had negative history of (CAD), while in patients with eGFR ≥60 ml/min/1.73 m2 19 (18%), positive history of (CAD) is3 (15.8%) and negative history of (CAD) is16 (84.2%, P=0.000). group with depressed eGFR <60 ml/min/1.73 m2 and positive history of (CAD) 42 (48.2%), and with negative history is 45 (51.8%). In the eGFR ≥60 ml/min/1.73 m2 group and positive history of (CAD), the mortality rate is 2 (10.5%), and in the negative history (CAD) group is 17 (89.5%).The p=0.0024, $\chi 2$= 9.1.GFR Conclusion: This study established that impaired GFR in an adult population is independently associated with significant levels of increased risk of all-cause mortality and of fatal and nonfatal coronary and heart failure events; e-gfr change over time adds prognostic information to traditional mortality risk predictors among patients with CKD. The utility of incorporating e-GFR trends into patient-risk assessment should be further investigated

Keywords: Chronic kidney disease, coronary artery disease.

INTRODUCTION

Coronary artery diseases are a leading cause of death in a patient with end-stage renal failure {1}. Chronic kidney diseases have been associated with striking excess of cardiovascular and all causes of mortality {2,8}. Strong associations have also been reported between non-dialysis dependent chronic kidney disease and such outcomes in patients with ischemic heart diseases, heart failure, and high blood pressure {3,4,5}. Such observations have led to recommendations by scientific and professional bodies that patients with manifest cardiovascular diseases should be screened for evidence of kidney diseases and that all patients with chronic kidney diseases should be regarded as at a very high risk of coronary artery diseases {6,7}. This study was done to determine the predictive value of the GFR for mortality and morbidity using data from the (106) patients randomized in the Prospective Study.

PATIENTS AND METHODS

Design: The Prospective cross-sectional study **Setting:** Emergency Medicine Department/ Baghdad Teaching Hospital, AL-Imam Ali General Hospital **Duration:** Data was collected between November 2022 to November 2023. **Inclusion criteria:** pre-existing coronary artery diseases (CAD) or increased risk of such disease because of smoking, hypertension, or diabetes. Laboratory tests include serum creatinine, which

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was measured by kinetic alkaline picrate standard U.K. Kit with blood urea and packed cell volume (PCV%), blood sugar and serum potassium and chest radiograph and Electrocardiography (EKG) that available as an emergency investigation done in where Ethics committees approved the protocol. All patients in the randomized study provided informed consent.

METHODS

GFR was estimated using the (MDRD) Modification of Diet in Renal Disease equation;{9}.

$$\mathrm{eGFR} = 186 \times \mathrm{Scr}^{(-1.154)} \times \mathrm{age}^{(-0.203)} \times 0.742 \ [\text{if female}],$$

Where S.cr. Denotes serum creatinine level (mg/dl). The primary outcome of the basic study was the combined endpoint of death from CAD, nonfatal myocardial infarction, assessed in the entire cohort. All deaths were recorded. Outcomes studied in this report include death from vascular causes, the composite outcome of coronary heart disease death or nonfatal myocardial infarction, and the composite of death or hospitalization due to heart failure during follow-up.

All study data were processed and analyzed; characteristics was based on a comparison among subgroups based on ranges of eGFR according to stages of (CKD) in three categories adjusted for the potentially confounding effects of study inclusion criteria (histories of vascular disease, diabetes, hypertension, and current smoking status, all categorized as yes/no) as well as age and gender and weight in kilogram. 82% of patients had eGFR <60 ml/min/1.73 m2, and further subdivision at the different levels of the eGFR range.

The e GFR <60 mL · min−1 per 1.73 m2 is selected as the cutoff value for the definition of CKD because it represents a reduction by more than half of the normal value of ≈125 mL · min−1 per 1.73 m2 in young men and women, and this level of GFR is associated with the onset of laboratory abnormalities characteristic of kidney failure, including increased prevalence and severity of several CVD risk factors {3}.

Statistical Analysis: Continuous variables are summarized by means and standard deviations and compared by one-way analysis of variance or covariance as appropriate with the calculation of a p-value for the general test of heterogeneity among the eGFR categories. Categorical variables are summarized by counts and percentages and compared using logistic regression analyses, with a general test of heterogeneity among the categories of eGFR with and without adjustment for the confounding factors.

A corresponding approach was used for estimating expected proportions for the categorical variables. The relationships between baseline and eGFR in each clinical outcome were assessed using Cox proportional hazards models with eGFR. GFR was subdivided by categories, and a group with eGFR ≥ 60 ml/min/1.73 m2 as the referent. Evidence of treatment by eGFR interaction was investigated with eGFR as a continuous variable to maximize statistical power. All analyses reported were adjusted for the following baseline confounders: sex (male or female); smoking (current or not current); age; histories (yes/no) of each of hypertension, diabetes, and vascular diseases; systolic blood pressure (SBP); diastolic blood pressure (DBP); body mass index (BMI); plasma glucose concentration. To explore the influence of inflammation on the results.

RESULTS

Study included (106) men (54) and women (52) between the ages of 16 and 87 years, and the mean age (54.9±15.2) lived in Baghdad. The design, baseline characteristics of the patients and the primary study results have been done. Baseline characteristics for the entire cohort are presented in Table (1):

The eGFR data are calculated for all randomized study patients. The number (percentage) of patients in collecting data with different (CKD) stages when the eGFR <60ml/min/1.73 m287 (82%), and a group of patients with eGFR ≥60ml/min/1.73 m2 19 (18%). Patients were divided into the following three categories by estimated GFR (eGFR) at baseline: ≥90 (n = 4), 60 to 90 (n = 7), and <60 (n = 95) ml/min/1.73 m2. The outcome of this study among patients is illustrated in Figures (2.3.4):

Overall (of 106) patients, there was (44) deaths with 42% mortality risk. Most of them with preceding (CRF) chronic renal failure history (76) {71.6%} on hemodialysis or peritoneal dialysis, and in those associations of hypertension, DM, cigarette smoking and all of them have had (CAD), with different types of (CAS) coronary artery

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syndrome including heart block. In those with mild to moderate (CKD), the number of deaths is (1) patient 0.944%, and only six patients with stage 1 and stage 2 (CKD), while this rate in such group of patients is16.66%.Generally, when eGFR is depressed, it is strongly impacted on the risk of (CAD) and death. In this study, of a patient with depressed e GFR is, 68 (78%) had a positive history of (CAD) and 19 (22%) had an adverse history of (CAD), while in patients with eGFR ≥60 ml/min/1.73 m2 19 (18%), positive history of (CAD) is3 (15.8%) and negative history of (CAD) is16 (84.2%), P=0.000.

The death rates in this study participants group with depressed eGFR <60 ml/min/1.73 m2 and a positive history of (CAD) 42 (48.2%), and with an adverse history is 45 (51.8%). In the eGFR ≥60 ml/min/1.73 m2 group and positive history of (CAD), the mortality rate is 2 (10.5%), and in the negative history (CAD) group is 17 (89.5%).

The p=0.0024, $\chi 2$= 9.1.GFR impaction on mortality risk in patients with (CAD). This indicates that GFR is a strongly associated risk factor for (CAD) in those patients in whom whether had a history or had no history of (CKD).

Table 1: Distribution of the studied group according to demographic Characters

Baseline patient characteristics	**Overall (n=106)**
Age	54.9±15.2
Male	51%
Female	49%
HT	80%
CRF	63.2%
Obesity	22.6%
IHD	67%
DM	41.5%
Smoking	52.8%
GFR (< 60 ml/min)	82% Mean=27.9±25
Bl. Urea (>40 mg/dl)	87.8% Mean=150.1±88
S. Creatinine (>1.3mg/dl)	83% Mean=4.2±2.9

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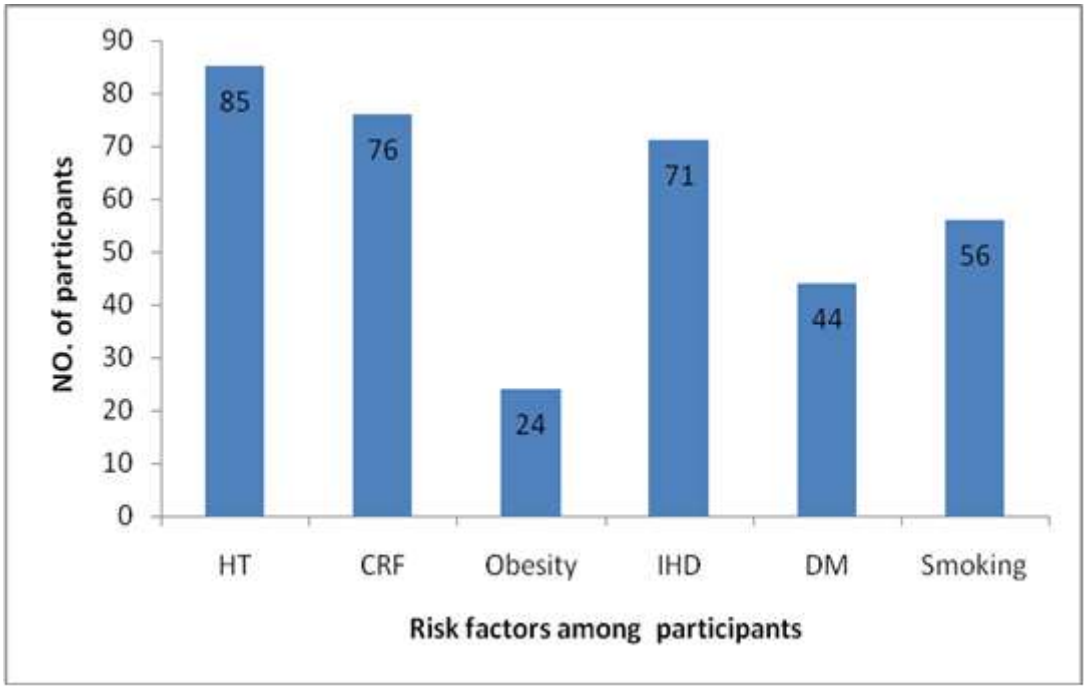

Figure 1: Distribution of the studied group according to Risk factors

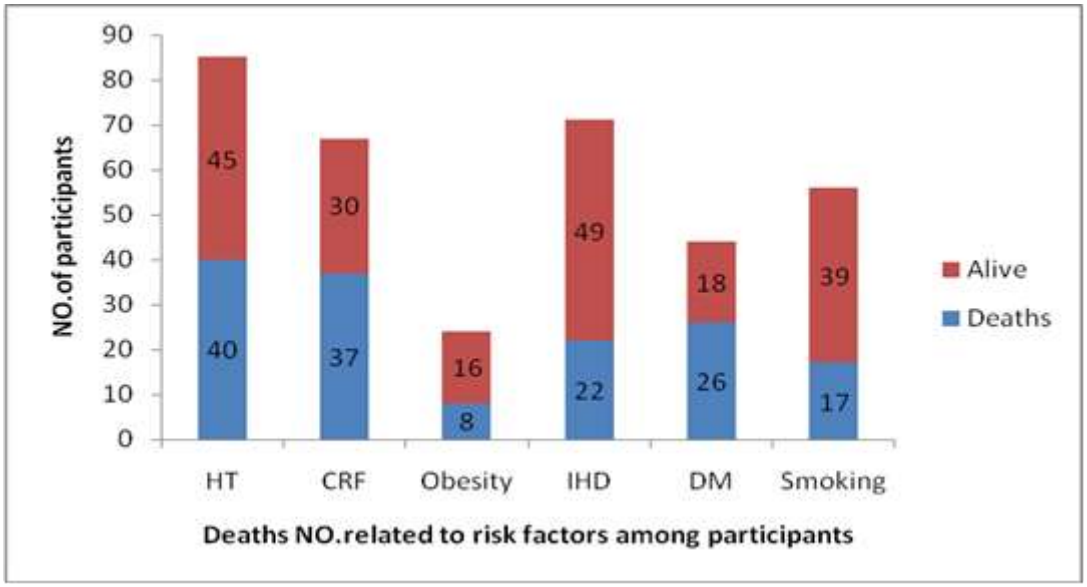

Figure (2): Distribution of the studied group according to death rate related to Risk factors

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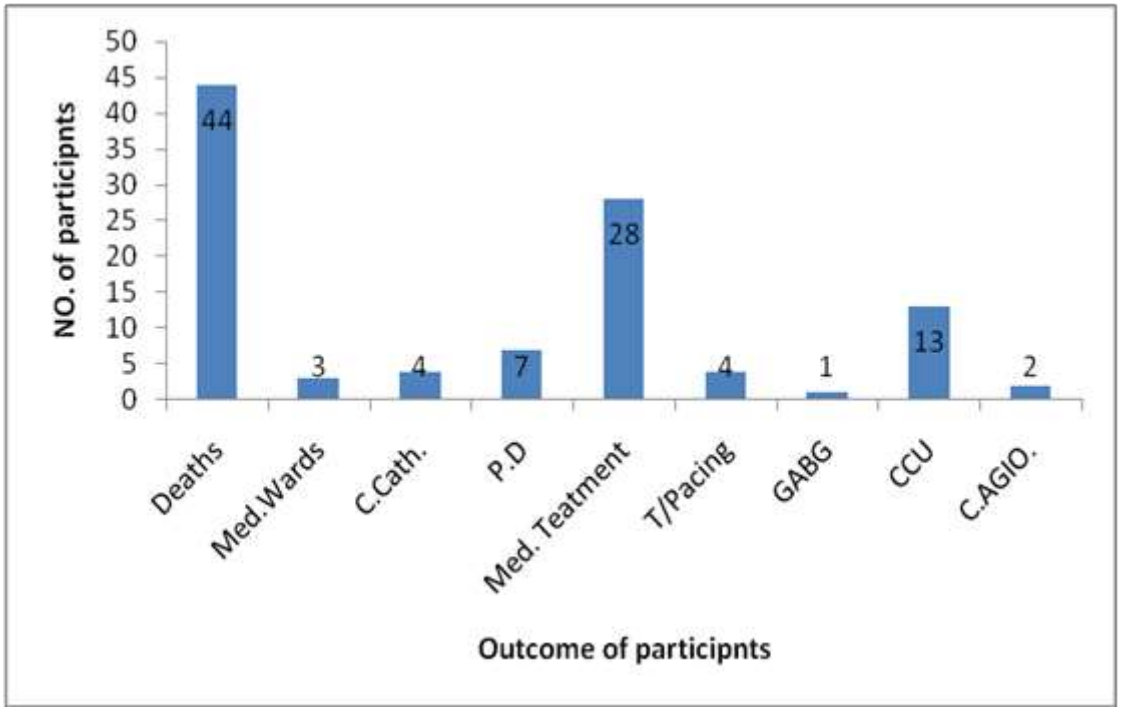

Figure (3): Distribution of studied group according to outcome

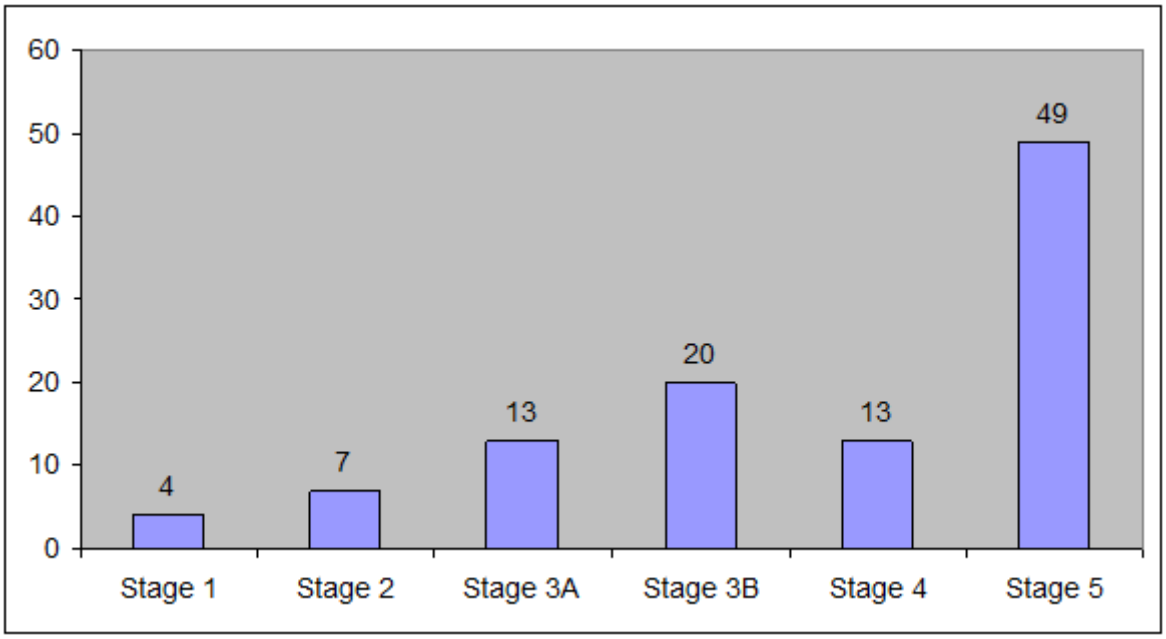

Figure (4): Distribution of the studied group according to CKD stages

Table (2): Association between reduction in GFR and history of IHD.

Reduced GFR eGFR <60ml/min/1.73 m^2.	**History of IHD**		**Total**
	Positive	Negative	
	no. (%)	no. (%)	no. (%)
Positive	68 (78%)	19 (22%)	87 (82%)
Negative	3 (15.8%)	16 (84.2%)	19 (18%)
Total	71 (67%)	35 (33%)	106 (100%)

$\chi 2$= 27.4 P = 0.000

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Table (3): Impact of elevated blood urea on mortality risk among participants.

Elevated blood urea	Mortality risk		Total
	Positive	Negative	
	no. (%)	no. (%)	no. (%)
Positive	42 (45%)	51 (55%)	93 (87.8%)
Negative	2 (15%)	11 (85%)	13 (12.8%)
Total	44 (41.5%)	62 (58.5%)	106 (100%)

χ^2=4.17 P =0.041 (blood urea is more than 40 mg/dl Elevated)

Table (4): Impact of elevated S. Creatinine on mortality risk among

Elevated S. Creatinine	**Mortality risk**		**Total**
	Positive	Negative	
	no. (%)	no. (%)	no. (%)
Positive	43 (48.8%)	45 (51.2%)	88 (83%)
Negative	1 (5.5%)	17 (94.5%)	18 (17%)
Total	44 (41.5%)	62 (58.5%)	106 (100%)

χ^2= 11.5 P =0.00063 (Elevated S. Creatinine is more than 1.3mg/dl)

Table (5): Impact of reduction in GFR on mortality risk among participants.

Reduction in GFR	**Mortality risk**		**Total**
	Positive	Negative	
	no. (%)	no. (%)	no. (%)
Positive	42 (48.2%)	45 (51.8%)	87 (82%)
Negative	2 (10.5%)	17 (89.5%)	19 (18%)
Total	44 (41.5%)	62 (58.5%)	106 (100%)

χ^2= 9.1 P =0.0024 (Reduction in GFR is less than 60ml)

DISCUSSION

This study showed significant independent associations of reduced e GFR (below 60ml/min/1.73 m2) with all-cause mortality, vascular deaths, coronary heart disease events (coronary death or nonfatal myocardial infarction), and for heart failure death or hospitalization in an adult population with vascular disease or vascular disease risk factors. There appeared to be a strong gradient of effect, with risks greatest in those with e GFR in the range (below 60) ml/min/1.73 m2, although significant increases in the incidence of these adverse events were also seen in the mild to moderate (CKD). In comparison to the reference group (eGFR ≥ 60 ml/min/1.73 m2) for any of the outcomes studied.

Analyses of baseline cardiovascular medications revealed no evidence that participants with impaired renal function were less well treated. In middle-aged individuals with vascular disease, the e GFR is predictive of all-cause, coronary heart disease, and vascular mortality.

There are a number of potential mechanisms by which low GFR may be associated with an increased risk of adverse outcomes. Low GFR is associated with vascular risk factors, including a history of hypertension and, an unfavorable lipid profile, and an increased burden of underlying coronary atheroma. This is likely to increase the risk of myocardial infarction and of death in those who have a coronary event.

Hence, low eGFR could merely be a marker for cardiovascular risk rather than being causally implicated. However, in some situations, low GFR may be a direct cause of vascular events or death. In heart failure, kidney disease is associated with impaired intra-cardiac conduction and progressive deterioration of diastolic function.

There are also associations with left ventricular hypertrophy. Further, inflammation, endothelial dysfunction, hypercoagulability, and raised homocysteine may play a role. There are a number of limitations to this study. We were restricted in our measures of renal function to e GFR. Cystatin-C may be a better predictor of outcomes and have no measure of albuminuria and lipid profile in the emergency department. The patients in this study were selected for a clinical trial with specific inclusion and exclusion criteria. They may not fully represent related data with vascular disease or vascular risk factors. There is the possibility that, despite careful adjustment, associations or the lack thereof between e-GFR and baseline factors could be biased. Strengths of this study include

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assiduous follow-up and rigorous methods of classification of deaths and nonfatal clinical events. Halpern SM *et al*., (2005) Albert Einstein College of Medicine, Bronx, New York U.S.A found that:

The risk of IHD death increased progressively as the GFR decreased. Hazard ratio for IHD mortality for each 10-unit reduction of estimated GFR below the normal threshold of >or=90 ml/min per 1.73 m was 1.33 (95% confidence interval 1.17, 1.50; P<0.001).

In a recent analysis of the USRDS that examined patients initiated on dialysis more recently, outcomes were slightly improved, but mortality was still quite high. One, 2-, and 3-year survival rates for ESRD patients presenting with ACS were 61%, 39%, and 27%, respectively. In the subgroup of these patients with MI, survival was 52%, 29%, and 20%, respectively, at these time points.

Dr. Robert M. Perkins *et al*., (2005) 1*Center for Health Research and 2. Nephrology Department, Geisinger Medical Center, Danville, Pennsylvania.

A total of 15,465 patients were followed for a median of 3.4 years. Median rates of eGFR change by those in the lower, middle, and upper tertiles of the e-GFR slope were −4.8, −0.6, and 3.5 ml/min per 1.73 m2/yr, respectively. In Cox proportional hazard modeling for time to death, adjusted for baseline proteinuria, changes in nutritional parameters, and episodes of acute kidney injury during follow-up (among other covariates), the hazard ratio for those in the lower (declining) and upper (increasing) e GFR tertiles (relative to the middle, or stable, tertile) was 1.84 and 1.42, respectively. Longitudinal changes in nutritional status, as well as episodes of acute kidney injury, attenuated the risk only modestly. These findings were consistent across subgroups, according to Charles Bankhead, Staff Writer, Med Page Today (2011). In patients with STEMI and NSTEMI, the probability of survival declined with worsening GFR (*P*<0.0001). Regardless of whether they had revascularization procedures (*P*<0.0001).

CONCLUSION

This study established that impaired GFR in an adult population is independently associated with significant levels of increased risk of all-cause mortality and of fatal and nonfatal coronary and heart failure events; e-gfr change over time adds prognostic information to traditional mortality risk predictors among patients with CKD. The utility of incorporating e-GFR trends into patient-risk assessment should be further investigated.

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