

Chronic Kidney Disease And Risk Of Coronary Artery Disease, A Prospective Study

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Abstract

Background: Reduced glomerular filtration rate is associated with increased morbidity in patients with coronary artery disease.

Objectives : To analyze the declining eGFR and mortality risks in a patients with Chronic Kidney Disease and have had Coronary Artery Disease including risk factors .

Patients and Methods : The study included (160) patients between the ages of 16 and 87years. Glomerular filtration rate was estimated (eGFR) using the Modification of Diet in Renal Disease equation and was categorized in the ranges $<60 \text{ mL} \cdot \text{min}^{-1} \text{ per } 1.73 \text{ m}^2$ and $\geq 60 \text{ mL} \cdot \text{min}^{-1} \text{ per } 1.73 \text{ m}^2$. Baseline risk factors were analyzed by category of eGFR.,The studied patients in emergency department, were investigated using Cox proportional hazard models adjusting for traditional risk factors.

Results: The study included (106) male (54) and female (52) between the ages of 16 and 87Years mean age (54.9±15.2). The eGFR data are calculated for all randomized studied Patients eGFR $<60 \text{ mL} \cdot \text{min}^{-1} \text{ per } 1.73 \text{ m}^2$ 87 (82%), and group of patients with eGFR

$\geq 60 \text{ mL} \cdot \text{min}^{-1} \text{ per } 1.73 \text{ m}^2$ 19(18%). Overall there was (44) death 42% mortality risk. Patients with eGFR $\geq 60 \text{ mL} \cdot \text{min}^{-1} \text{ per } 1.73 \text{ m}^2$ 19(18%), positive history of (CAD) is 3 (15.8%) and negative history of (CAD) is 16 (84.2%, $P=0.0001$). group with reduced eGFR $<60 \text{ mL} \cdot \text{min}^{-1} \text{ per } 1.73 \text{ m}^2$ and positive history of (CAD) 42(48.2%), and with negative history is 45(51.8%). In eGFR $\geq 60 \text{ mL} \cdot \text{min}^{-1} \text{ per } 1.73 \text{ m}^2$ group and positive history of (CAD), the mortality rate is 2 (10.5%) and in negative history (CAD) group is 17 (89.5%)

Conclusion:

This study concluded that impaired GFR, in an adult population, is independently associated with significant levels of increased risk of mortality of fatal and nonfatal coronary events ,e GFR change over time adds prognostic information to traditional mortality risk predictors among patients with chronic kidney disease.

Key Words:

chronic kidney disease , end-stage renal disease, coronary artery disease .

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Introduction

Coronary artery diseases(CAD) are a leading cause of death in patients with end stage renal disease (ESRD)⁽¹⁾.Chronic kidney diseases(CKD) have been associated with striking excess of cardiovascular and all cause of mortality⁽²⁾. Strong association have also been reported between non-dialysis dependent CKD and such outcome in patients with ischemic heart diseases(IHD), heart failure, and high blood pressure^{(3),(4),(5)}.Such observations have lead to recommendations by scientific and professional bodies that patients with manifested cardiovascular diseases should be screened for evidence of kidney diseases and that all patients with CKD should be regarded at very high risk of CAD^{(6),(7)}.

Furthermore, CKD might increase the risk of the onset of acute coronary syndrome^{(8),(9)}.

In general adult population, however,CKD often goes undiagnosed because it is largely asymptomatic⁽¹⁰⁾. Annual cardiovascular mortality in patients with CKD, is much higher than in general populations⁽¹¹⁾. Data from the general population cannot simply be extrapolated to the ESRD population, because ESRD patients are subjected not only to traditional risk factors but also, more importantly, kidney disease-related risk factors, such as inflammation, increased calcium phosphorus product, uremic toxins, anemia, and fluid overload⁽¹¹⁾.

. According to recent data from the USRDS, cardiac disease is the leading cause of mortality, accounting for 43% of all-cause mortality in patients receiving hemodialysis or

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peritoneal dialysis (PD). The incidence of death attributable to cardiac arrest/cause unknown or arrhythmia is high in ESRD patients, accounting for ≈25% of all mortality^(12, 13).

An increase in creatinine concentration of 1.0 mg/dl raises the risk of death among patients with CAD by 15–35%⁽¹⁴⁾.

AIM OF THE STUDY

To evaluate the predictive value of the GFR for mortality and morbidity in patients with CKD who had CAD.

Patients and Methods

Design: The prospective cross sectional study of (106) patients, (54%) male and (52%) female

Between the ages of 16 and 87 years, mean ages (54.9±15.2)

Setting: Emergency Medicine Department/Baghdad Teaching Hospital

Duration: Data was collected between November 2010 to November 2011.

Inclusion criteria: pre-existing coronary artery diseases (CAD) or increased risk of such disease because of smoking, hypertension, or diabetes, full clinical examinations including detailed history taken from patients. Laboratory tests include serum creatinine was measured by kinetic alkaline picrate standard U.K. Kit with blood urea and blood sugar and serum potassium and (EKG) were available as an emergency investigations done.

Ethical committee approved the protocol, by a consent for all patients

Methods: GFR was estimated using the (MDRD) Modification of Diet in Renal Disease equation^(15,16).

$$eGFR = 186 \times Scr^{(-1.154)} \times age^{(-0.203)} \times 0.742$$

The e GFR <60 mL · min⁻¹ per 1.73 m² is selected as the cutoff value for 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⁾.

Outcomes studied include death from the composite outcome of coronary heart disease or nonfatal myocardial infarction, and the composite of death or hospitalizations due to heart failure during follow up.

The study data were processed and analyzed, comparison among subgroups based on ranges of eGFR according to stages of (CKD) in two categories adjusted for the potentially confounding effects of study inclusion criteria [diabetes (Hba1c >7), hypertension (BP>140 mmhg systolic, >90 mmhg diastolic) and current smoking status, all categorized as yes or no] as well as age and gender and weight in kg.

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. These 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. and group with eGFR ≥ 60 ml/min/1.73 m² as the referent.

Results:

This study included (106) male (54) and female (52) ages range was 16 and 87 years, mean age (54.9±15.2). The design, baseline characteristics of the patients and the primary study results were done. Baseline characteristics for the entire cohort are presented in, Table (1).

Generally when eGFR reduced it is strongly impacted on risk of (CAD) and death. In this study, patient with reduced 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) is 3 (15.8%) and negative history of (CAD) is 16 (84.2%, P=0.0001), Table (2).

The death rates in study patients group with reduced eGFR <60 ml/min/1.73 m² and

positive history of (CAD) 42(48.2%), and with negative history is 45(51.8%). In eGFR ≥ 60 ml/min/1.73 m² group and positive history of (CAD), the mortality rate is 2 (10.5%) and in 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 indicate GFR is strongly associated risk factor for (CAD) in those patients in whom whether had history or had no history of (CKD), Table (3).

The elevated BU and serum creatinine also have an impact on mortality risk and burden on creatinine 88(83%) mortality risk were 43(48.8% P = 0.00063) Table(4), while in case of BU 93(87.8%) and mortality death was 42(45% P =0.04) Table(5). Increases in BUN and creatinine are highly prevalent in patients with (CAS). This add thinking

elevated these measures have prognostic significant in evaluating a patients in whom they are (CKD) with (CAS) and need further studies to find which was of them more affect the outcomes. In this study as a result, the calculation of the risk in the patient based on the serum creatinine level will be more accurate.

We built Multiple Linear Regression (MLR) model to differentiate between the dependent and independent risk factors regarding the outcome of included samples, in which we found that Age, DM, HT, Obesity, and Cigarette smoking were dependent factors and have no direct effect on outcomes in death or follow up while CKD has been proved to have independent relationship with outcomes $P < 0.05$ as shown in Table (6).

Table (1); Distribution of patients according to demographic characters.

Base line patient characteristics	Overall(n=106)
<i>Age</i>	54.9±15.2
<i>Male</i>	54%
<i>Female</i>	52%
<i>Hypertension</i>	80%
<i>Obesity</i>	22.6%
<i>Coronary Artery Syndrome</i>	67%

<i>Diabetes Mellitus</i>	41.5%
<i>Smoking</i>	52.8%
<i>GFR(< 60 ml/min)</i>	82% Mean=27.9±25
<i>Blood Urea(>40 mg/dl)</i>	87.8% Mean=150.1±88
<i>Serum Creatinine(>1.3mg/dl)</i>	83% Mean=4.2±2.9

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

Reduced 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 = 0.001

Table (3): Impact of reduction in GFR on mortality risk among patients.

Reduction in GFR eGFR <60ml/min/1.73 m ²	Mortality risk		Total
	Positive	Negative	
	no.(%)	no.(%)	n .(%)
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%)

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

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

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%)

$\chi^2= 11.5$ P =0.00063 Elevated S.Creatinine is more than 1.3mg/dl

Table (5): Impact of elevated blood urea on mortality risk among patients.

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%)

$\chi^2=4.17$ P =0.041Elevatedblood urea is more than 40 mg/dl Table

Table (6) Multiple Linear Regression Model for the Outcome
Coefficients^a

	Unstandardized Coefficients		Standardized Coefficients	t	P value.
	B	Std. Error	Beta		
age	.000	.003	-.016	-.143	0.887
DM	-.107	.077	-.141	-1.393	0.167
HT	.062	.106	.066	.585	0.560
CKD	-.131	.079	-.168	-1.666	0.047
obesity	-.049	.091	-.055	-.536	0.593
smoking	-.029	.077	-.038	-.373	0.710

a. Dependent Variable: outcome

Discussion:

There are a number of potential mechanisms by which low GFR may be associated with 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(12).

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.

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.

In adult individuals with vascular disease the e GFR is predictive of cause, in coronary heart disease and vascular mortality.

There are also associations with left ventricular hypertrophy. Further, inflammation, endothelial dysfunction, hyper coagulability, 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, and have no measure of albuminuria and lipid profile in emergency department. The patients in this study were selected for a clinical trial with specific inclusion and exclusion criteria, and may not be fully representative of related data with vascular disease or vascular risk factors. There is the possibility that, despite careful adjustment, associations or the lack there of between e GFR and baseline factors could be biased. Strengths of this study include assiduous follow-up and rigorous methods of classification of deaths and nonfatal clinical events. Hailpern 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 ≥ 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 CAD 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.(12,13)

Conclusion:

This study concluded that impaired GFR, in an adult population, is independently associated with significant levels of increased risk of mortality and of fatal and nonfatal coronary 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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