

## Original Article

### **Assessment of Renal insufficiency in patients with normal serum creatinine levels undergoing angiography**

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#### **Abstract**

**Objective:** To determine the frequency of patients with underlying renal insufficiency having normal serum creatinine level proceeding for coronary angiography.

**Methods:** A total of 693 patients from September 2009 to February 2010 undergoing diagnostic coronary angiography at the National Institute of Cardiovascular Diseases (NICVD) with normal serum creatinine  $\leq 1.5$ mg/dl were selected. Glomerular filtration rate (GFR) was calculated for each patient using the Cockcroft-Gault (C-G) equation and a GFR  $< 80$ ml/min was labeled as renal insufficiency.

**Results:** The mean age of males was  $51.86 \pm 10.19$  years and  $51.52 \pm 9.80$  years for females. Almost one-third ( $n=236$ , 34.1%) of patients had GFR  $< 80$ ml/min; comparison between male ( $n=168$ , 31.2%) and female ( $n=68$ , 43.9%) was significant ( $p$ -value 0.003). Age group breakdown showed majority of patients ( $n=196$ ; 83.05%) with GFR  $< 80$  ml/min ranged between 40-69 years ( $p$ -value 0.001).

**Conclusion:** This study has shown that most of the patients with normal serum creatinine have abnormal GFR. Serum creatinine, which is considered to be an important screening test in patients with renal impairment, might remain in the normal range despite the renal function being significantly impaired. Therefore, GFR should be considered as an estimate of renal insufficiency, regardless of serum creatinine levels being in normal range (JPMA 60:915; 2010).

#### **Introduction**

The high global burden of cardiovascular disease (CVD) has resulted in a large number of patients requiring cardiac catheterization and percutaneous coronary intervention (PCI). This is particularly relevant to South Asian countries Pakistan, which are in the midst of a CVD epidemic.<sup>1</sup> CVD is strongly associated with co-morbid conditions like Diabetes mellitus

(DM) and hypertension (HTN), which might affect renal function, leading to a large pool of patients with impaired renal function undergoing angiography or PCI, thereby increasing the risk of Contrast induced nephropathy (CIN).<sup>2</sup> The ever expanding use of contrast media-based imaging techniques especially with an aging population and increasing procedural complexity, CIN remains a serious concern for interventional

cardiologists.<sup>3</sup> Studies have shown that renal insufficiency at baseline is the most important risk factor for CIN.<sup>1,4,5</sup> Many physicians rely on serum creatinine (SCr) as a screening test for renal impairment, however SCr levels could remain within the normal range even when normal renal function is significantly impaired.<sup>6</sup> In contrast, Glomerular filtration rate (GFR) has been traditionally considered the best overall index of kidney function in health and disease.<sup>7</sup> A more accurate approximation of renal function can be obtained using formulae such as the Cockcroft-Gault equation<sup>8-11</sup> to calculate GFR from SCr. In a study, it was found that 13.9% of patients with normal SCr levels had substantially abnormal calculated GFR with C-G values  $\leq 50$  ml/min.<sup>12</sup> In addition, an estimated 29.9% adult population of urban Pakistan have been reported to have reduced GFR. It is evident that using GFR estimating equations for evaluation of reduced GFR in South Asians would be better.<sup>13</sup>

Since GFR decreases with increasing age inspite of normal SCr levels, screening patients undergoing coronary angiography with GFR estimating equation like the C-G equation will help identify underlying renal insufficiency and subsequently decrease the risk of CIN.

The objective of this study was to determine the frequency of patients with underlying renal insufficiency having normal serum creatinine level proceeding for coronary angiography.

## Patients and Methods

Six hundred ninety three (693) patients with SCr  $\leq 1.5$  mg/dl who underwent coronary angiography from September 2009 to February 2010 at the National Institute of Cardiovascular Diseases were included in the study.

The only exclusion criterion was not to enroll patients with SCr  $> 1.5$  mg/dl. An informed verbal consent was taken from all the patients enrolled. Venous blood sample from each patient was drawn and analyzed on Dimension RXL Max of Dad Behring using modified Jaffe Kinetic reaction method. Patient's age was noted and weight in kg was measured using a standard bathroom scale. The Cockcroft-Gault (C-G) equation:  $(140 - \text{age}) \times (\text{weight in kg}) / \text{serum creatinine Cr (mg/dl)} \times 72 \times (0.85 \text{ if female})$  was applied to calculate each patient's GFR in ml/min.

The data was entered and analyzed using SPSS version 10.0 (SPSS Inc, Chicago, US). Mean and standard deviation were calculated for continuous variables and frequencies were computed for categorical variables.

Patients having GFR  $< 80$  ml/min were labeled as having underlying renal insufficiency. Statistical significance was considered at a p-value  $< 0.05$ .

## Results

A total of 693 patients undergoing coronary angiography

**Table-1: Age and weight according to gender.**

| Variables |        | n   | Mean  | S.D.  | P-Value |
|-----------|--------|-----|-------|-------|---------|
| Age       | Male   | 538 | 51.86 | 10.19 | 0.709   |
|           | Female | 155 | 51.52 | 9.80  |         |
| Weight    | Male   | 538 | 70.95 | 12.34 | 0.001   |
|           | Female | 155 | 64.32 | 13.49 |         |

**Table-2: GFR according to gender and age groups.**

|            |                 | No. of subjects | GFR ml/min  |             | p-value |
|------------|-----------------|-----------------|-------------|-------------|---------|
|            |                 |                 | $< 80$      | $> 80$      |         |
| Gender     | Male            | 538             | 168 (31.2%) | 370 (68.8%) | 0.003   |
|            | Female          | 155             | 68 (43.9%)  | 87 (56.1%)  |         |
| Age groups | $< 40$ years    | 67              | 7 (10.4%)   | 60 (89.6%)  | 0.001   |
|            | 40-49 years     | 208             | 32 (15.4%)  | 176 (84.6%) |         |
|            | 50-59 years     | 238             | 81 (34.0%)  | 157 (66.0%) |         |
|            | 60-69 years     | 142             | 83 (58.5%)  | 59 (41.5%)  |         |
|            | $\geq 70$ years | 38              | 33 (86.8%)  | 5 (13.2%)   |         |

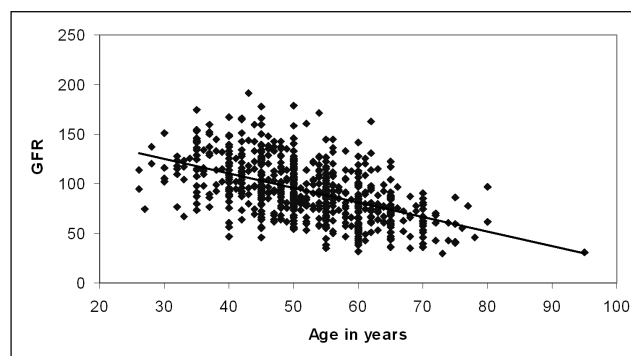


Figure: Correlation of GFR and age.

with SCr  $\leq 1.5$  mg/dl were included in this study and GFR was calculated for each patient using the C-G equation.

Gender wise distribution, mean and standard deviation for age and weight is shown in (Table-1). Mean creatinine for males was  $0.96 \pm 0.20$  (mg/dl) and  $0.82 \pm 0.20$  (mg/dl) for females ( $p = 0.001$ ). Mean GFR for males was  $95.12 \pm 28.28$  (ml/min) and  $86.13 \pm 27.77$  (ml/min) for females ( $p = 0.001$ ). Overall, 236 (34.1%) patients had a GFR  $< 80$  ml/min, out of which 168 (31.2%) were males and 68 (43.9%) females ( $p = 0.003$ ). Age group breakdown showed majority of patients (196; 83.05%) with GFR  $< 80$  ranged between 40-69 years ( $p = 0.001$ ) (Table-2). As anticipated, correlation of GFR and age showed a decreasing GFR trend with increasing age ( $p < 0.05$ ) (Figure).

## Discussion

Renal function is usually assessed by checking SCr because of its simplicity and being economical. However, SCr does not give accurate information about the GFR. In two

different studies, a considerable number of patients ranging from 13.9-29.9% have shown to have low GFR with normal SCr.<sup>12,13</sup> If SCr alone was to be considered as a marker of renal function, there is a likely chance of missing a significant number of patients who actually have underlying renal insufficiency, who would subsequently develop CIN. For measuring GFR, several formulae have been developed to estimate GFR from SCr considering the patient's age, sex and weight. The C-G and MDRD (Modification of Diet in Renal Disease) equations are the most widely used that give a close estimate of the GFR.<sup>11</sup> These creatinine-based formulae being cost effective and easy to manage can be a useful tool for identifying patients with underlying renal insufficiency and thus preventing the subsequent development of CIN.

In the present era, where radiological procedures involving contrast agent are being commonly performed in diagnosing CVD, the incidence of CIN is expected to rise, with an existing prevalence of 3.3 to 16.5%.<sup>4,14</sup> CIN is an important cause of acute renal failure associated with high morbidity, extended hospital stay and high mortality.<sup>4,15,16</sup>

The C-G formula has been shown to correlate well with [<sup>99m</sup>Tc] -DTPA measured GFR over the GFR range of 14-100ml/min, with a correlation coefficient of 1.01,  $r=0.92$ .<sup>17</sup> According to National Kidney Foundation (NKF) guidelines, a GFR of 60-89ml/min indicates renal damage.<sup>18</sup> The <80ml/min cutoff was used in this study to label a patient as renal insufficient considering that GFR decreases with increasing age is in accordance with the Baltimore Longitudinal Study.<sup>19</sup> Another study revealed that a normal patient with a GFR of 120ml/min at age 30 could still have a GFR of >80ml/min at age 80.<sup>20</sup>

In Pakistan, a study conducted in 2005 estimated the prevalence of reduced GFR at 29.9% in individuals aged 40 and above which is comparable to our results.<sup>13</sup>

The present study has some limitations. First, the estimation of abnormal GFR is based on a single measurement of SCr that may not be accurate which might lead to over or under estimating patients with abnormal GFR. Secondly, we used calculated GFR and not measured GFR to diagnose renal insufficiency which is not the gold standard.

This study highlighted the importance of measuring GFR in patients undergoing radiological procedures involving the use of contrast agent. Most cardiologists rely on SCr levels being in the normal range and do not calculate the GFR, thus exposing patients with underlying renal insufficiency to high risk of CIN. Whether this specific subgroup is at increased risk of developing CIN or should preventive protocols be applied to them still needs to be established. Nonetheless, it is

recommended that calculated GFR instead of SCr be used especially in patients undergoing procedures involving use of radio-contrast agents like coronary angiography.

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