

Glomerular filtration rate rather than Serum Creatinine should be used for recognizing patients at risk for development of Contrast induced nephropathy

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ABSTRACT

Objective: Serum Creatinine (SCr), widely used for renal function assessment is not an accurate measurement. SCr can be within normal range even when there is substantial nephropathy. The objective was to observe the incidence of contrast induced nephropathy (CIN) with normal SCr and low glomerular filtration rate (GFR).

Methodology: This was a cross-sectional, observational study involving patients undergoing coronary angioplasty. During a period of 6 months, 64 patients having SCr \leq 1.4mg/dl and a GFR of $<$ 80ml/min were selected who underwent elective coronary angioplasty. SCr was measured again after 48 hours of the procedure. CIN was defined as a $>$ 25% increase in SCr from the pre-procedure level. For statistical analysis, SPSS version 10 was used to calculate one way Anova was used for comparing variables between CIN and No-CIN groups, while paired t-test was applied for comparison between pre and post procedure SCr.

Results: Out of 64 patients, CIN was seen in 14 patients (21.8%). After the procedure, significant difference was seen in the mean creatinine levels ($p < 0.001$). The before and after experiment creatinine values also showed a significant difference ($p < 0.05$).

Conclusions: SCr along with calculated GFR should be used to assess patients for underlying renal insufficiency undergoing contrast procedures like coronary angioplasty. Patients with low GFR and normal SCr have a significant risk of developing CIN. Identifying such patients before hand can help us decrease the overall incidence of CIN by administering timely prophylactic measures.

KEY WORDS: Creatinine, Glomerular filtration rate, Coronary angioplasty, Contrast induced nephropathy.

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INTRODUCTION

Contrast Induced Nephropathy (CIN) is a common cause of acute kidney injury that develops after exposure to intravascular contrast media. It is one of the leading causes of hospital acquired renal failure being the third leading cause.¹ Although reported very frequently in patients undergoing percutaneous coronary intervention (PCI), patients undergoing diagnostic left heart catheterization or other radiological studies involving contrast media are also at increased risk.

Since CIN is not a benign disease and is associated with prolongation of hospital stay and increased

morbidity and mortality², multiple strategies have been developed and proposed to minimize its development. Multiple risk factors have been identified in the development of CIN; decreased renal function is one of the major among them.^{1,3} Other factors include diabetes mellitus, volume depletion, heart failure and volume and type of contrast used.^{4,5}

Incidence of CIN in patients undergoing cardiac catheterization varies from 2 to 50 %⁶⁻⁹, depending on the criteria used to define CIN. The more widely acceptable definition is an increase in SCr of > 0.5mg/dl or a > 25% increment in Cr from its baseline.⁶⁻¹⁰

Majority of centers use serum creatinine (SCr) as an assessment of renal function, however it is not an accurate measurement of renal function as other factors like patient's age, sex and weight also influence the renal status of a patient.¹¹ It is also known that SCr can be within normal range even when there is substantial nephropathy. In our recent study, underlying nephropathy in our population was found to be 34% with normal SCr.¹²

The aim of this study was to see the incidence of CIN in patients with normal SCr and low GFR as calculated by Cockcroft and Gault formula.

METHODOLOGY

A cross sectional, observational study was undertaken involving patients undergoing coronary angioplasty over a six month period from September 2010 to March 2011 at our hospital. The ethical review committee provided the necessary ethical approval. An informed written consent was taken from all the patients enrolled for study purposes. Venous blood sample was drawn from each patient and analyzed on Dimension RXL Max of Dad Behring using modified Jaffe Kinetic reaction method to measure SCr. The inclusion criterion was to include patients having a SCr of ≤1.4mg/dl before undergoing angiography.

During the study period, 348 patients with the set SCr level underwent coronary angioplasty. Out of these, 69 underwent Primary PCI and were

therefore, excluded. For the remaining 279 patients, the parameters noted were age in completed years, gender, diabetes mellitus, hypertension and weight in kgs was measured using a standard bathroom scale. GFR has been considered to be a predictor of CIN even with normal creatinine levels.¹³ Therefore, GFR was calculated for each patient using the following Cock-croft Gault (C-G) equation:

$$(140\text{-age}) \times (\text{weight in kg}) / \text{SCr (mg/dl)} \times 72 \times (0.85 \text{ if female}) = \text{GFR ml/min}$$

Hence, a final total of 64 patients were selected having a GFR of <80ml/min who subsequently underwent elective coronary angioplasty. Iopamidol, a non-ionic contrast medium was used in all patients. Venous blood samples were drawn again after 48 hours of the procedure to measure SCr using the same method. CIN was defined as a >25% increase in SCr from the pre-procedure level.

The data was entered in SPSS version 10; frequencies were calculated for gender, diabetes and hypertension. Mean and standard deviation was calculated for age, weight, GFR, and SCr levels. One way Anova was used for comparing variables between diseased (CIN) and non-diseased (No CIN) groups, while paired t-test was used for comparison between pre and post procedure creatinine values. P-value <0.05 was considered significant.

RESULTS

A total of 64 patients were selected, 46 males and 18 females, mean age was 58.83±10.37 years, age range 42 to 80 years. The average age for males was 58.78±10.26 years, and for females was 58.94±10.96 years. The mean weight for all patients was 64.52±11.08 kgs, weight range 40 to 92 kgs. The average weight for males was 65.59±9.99 kgs and for females was 59.22±12.24 kgs. Table-I shows comparison of variables between diseased and non-diseased groups. CIN was seen in 14 patients (21.8%). A significant difference has not been noted for pre-procedure GFR between diseased and non-diseased groups (p=0.165).

Table-I: Comparison of variables between diseased and non diseased groups.

| | No CIN (n=50) | CIN (n=14) | p-value |
|-----------------|---------------|---------------|---------|
| GFR | 63.38 (12.06) | 58.21 (12.56) | 0.165 |
| Diabetes | 9 (18%) | 6 (42.9%) | 0.007 |
| Hypertension | 29 (58%) | 10 (71.4%) | 0.120 |
| Pre-Creatinine | 1.11 (0.18) | 1.16 (0.24) | 0.395 |
| Post-Creatinine | 1.08 (0.19) | 1.68 (0.32) | < 0.001 |

The frequency of diabetes has been observed to be more significant in CIN group 42.9%, $p=0.007$. The mean creatinine levels before procedure are not significantly different, whereas after the procedure, significant difference could be seen in the mean creatinine levels ($p<0.001$). The before and after experiment creatinine values were also analysed for all 64 patients, and t-test showed a significant difference between them ($p<0.05$).

DISCUSSION

Impaired renal function is an established independent risk factor for the development of CIN. Most studies looking for CIN take into account SCr as a marker of renal function and a normal SCr is generally considered as indicating normal renal function. A significant number of patients can have renal impairment but their Cr might still be in normal range. Multiple studies have reported an incidence of 13.9%¹⁴ - 34.1%¹² of reduced GFR in patients that had normal SCr.

Prophylaxis for the prevention of CIN is usually given for patients at high risk, one of the factors being renal insufficiency. Usually patient with normal SCr are not given any prophylaxis, even if they have lower GFR, as usually SCr and not GFR is taken as a risk factor.

Our study showed that this subgroup of patients is at significant risk of developing CIN. In our study 21.8% of patients developed CIN undergoing elective PCI, which is worthy of note. Most of these patients were also diabetic as shown in the Table-I. These results are very similar to the results shown by Ghani AA in which they also found renal insufficiency and diabetes as the strongest predictor for developing CIN.¹⁵

The $<80\text{ml}/\text{min}$ 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.¹⁶ Also, as mentioned above in our previous study done in our population¹², a prevalence of 34% was noted to be having a GFR $<80\text{ml}/\text{min}$ and thus such patients were subsequently selected for our study to determine whether they were at increased risk of developing CIN.

In a recent study involving similar patients, a 23% incidence of contrast nephropathy was shown in patients undergoing coronary intervention, which is very similar to our results. The same study states that the criterion of $> 25\%$ increment in SCr from baseline diagnosed small increments in plasma Cr and was a more sensitive marker.¹³

We used a very inexpensive method of calculating GFR by using C-G formula, and tried to highlight that underlying renal insufficiency, not apparent by a rise in SCr is a significant risk factor for the development of CIN which has a strong impact on prolongation of hospital stay and long term morbidity and mortality.

Previous trends of utilizing MRI with gadolinium in patients with pre-existing renal failure has declined after its association with nephrogenic systemic fibrosis, a severe life threatening condition. Consequently, iodinated contrast media is now utilized more frequently in patients with renal impairment predisposing them to higher risk for the development of CIN.¹⁷

Hence, physicians and cardiologists should be aware and vigilant in identifying these patients so that prophylactic measures can be applied to this group of patients as well. Our study has some limitations. We did not take into account volume status or drugs as a cause of renal failure and also atheroembolic disease causing renal failure could not absolutely be ruled out.

CONCLUSIONS

SCr along with calculated GFR should be used to assess patients for underlying renal insufficiency undergoing contrast procedures like coronary angioplasty. Patients with low GFR and normal SCr have a significant risk of developing CIN. Identifying such patients before hand can help us decrease the overall incidence of CIN by administering timely prophylactic measures.

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Sumbal Nasir Mahmood: Drafting the article and interpretation of data.

Tariq Ashraf: Drafting the article and proof reading it.

Qudsia Anjum: Study design and analysis of data.