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Long-Term Renal Function Consequences Following Coronary Angiography and Contrast-Enhanced Computed Tomography: Assessing the Influence of Contrast-Induced Nephropathy

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ABSTRACT

Background: Contrast-induced nephropathy (CIN) is kidney damage caused by contrast media in medical procedures like angiography and CT scans. It is linked to acute kidney injury and can affect long-term renalfunction. Factors like pre-existing kidney issues, diabetes, and heart failure increase the risk. CIN's impact on renal function in Bangladesh needs attention due to rising cardiovascular diseases and imaging procedures. Research explores CIN's mechanisms, risk factors, prevention, and management. Research conducted in other locations has demonstrated a correlation between CIN and both chronic kidney disease (CKD) and end-stage renal disease (ESRD). Understanding CIN's impact in Bangladesh is crucial for preventive strategies and better patient care.

Aim of the study: This study aims to investigate CIN's impact on renal function in Bangladeshi patients undergoing angiography, and CT scans to improve clinical decision-making and outcomes.

Methods: This is a prospective comparative study, a total of 207. Patients were enrolled and analyzed in this study. The study was conducted at the Department of Cardiology, Apollo Imperial Hospitals, Chittagong, Bangladesh. Between March 2022 and March 2023, we examined the alterations in renal function subsequent to coronary angiography or contrast-enhanced computed tomography (CT). In this study we divided patients into two groups; Group A and Group B. A total of 72 patients with Coronary Angiography were in Group A and a total of 135 patients with contrast-enhanced computed tomography were in Group B.

Result: The study population consisted of 195 patients, who were divided into two groups. The analysis comparing renal function at the time of coronary angiography and contrast-enhanced CT (eGFR ≥30 ml/min/1.73 m2 and eGFR ≤1.73 m2) revealed no significant difference in the occurrence of contrast-induced nephropathy (CIN). Age and diabetes mellitus, along with pre-existing renal dysfunction, were identified as factors associated with the two-year prognosis of renal function.

Conclusion: Contrary to previous beliefs, the presence of contrast-induced nephropathy (CIN) does not pose a long-term risk to renal prognosis following coronary angiography or contrast-enhanced CT scans. Moreover, individuals with pre-existing renal dysfunction, including those with an eGFR <30 ml/min/1.73 m², do not face an elevated risk of developing CIN. These findings have significant implications, as they assure that patients with kidney disease requiring contrast-enhanced testing can undergo appropriate examinations without undue concern.

Keywords: Renal Function, Coronary Angiography, Contrast-Enhanced Computed Tomography and Contrast-Induced Nephropathy.

INTRODUCTION

The contrast-induced nephropathy (CIN) is a well-recognized complication associated with the use of iodinated contrast media during various medical procedures, including coronary angiography and contrast-enhanced computed tomography (CT). It denotes a type of acute kidney injury (AKI) distinguished by a rapid deterioration in kidney function subsequent to the utilization of contrast agents. CIN has been a subject of extensive research due to its potential impact on long-term renal function and overall patient outcomes. Coronary angiography and contrast-enhanced CT are commonly performed diagnostic procedures in cardiology and radiology, respectively, allowing for

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detailed visualization of blood vessels and organ structures. The use of contrast agents is essential to enhance image quality and provide accurate diagnostic information. There are several clinical factors that can raise the risk of contrast-induced nephropathy (CIN). Several factors contribute to this, such as pre-existing kidney dysfunction, underlying kidney impairment with diabetes mellitus, advanced congestive heart failure, intravascular volume depletion, administration of large quantities of contrast media, and high-osmolar contrast media [1-5]. However, the nephrotoxic effects of contrast media can pose a significant challenge, particularly in patients with preexisting renal impairment or other risk factors. In the context of Bangladesh, where cardiovascular diseases are on the rise and imaging procedures involving contrast media are increasingly performed, understanding the implications of CIN on long-term renal function is of utmost importance. The country has witnessed a significant increase in the prevalence of chronic kidney disease (CKD) over the years, attributed to factors such as diabetes, hypertension, and lifestyle changes. As a result, the potential impact of CIN on the renal function of the Bangladeshi population warrants investigation. Numerous studies have delved into exploring the correlation between contrast-induced nephropathy (CIN) and the enduring renal function following coronary angiography and contrast-enhanced CT scans. These studies have aimed to understand the underlying mechanisms of CIN, identify risk factors, and explore strategies for prevention and management. The implications of CIN on long-term renal outcomes have important implications for patient care, as renal dysfunction can significantly impact overall morbidity and mortality. An example would be thestudy carried out by Tsai et al. (2019), where a retrospective cohort design was employed to explore the lasting effects on kidney function among individuals in Taiwan who underwent coronary angiography and developed contrast-induced nephropathy (CIN) [6]. The study found that patients with CIN had a higher risk of developing CKD and end-stage renal disease (ESRD) compared to those without CIN. Furthermore, a meta-analysis by Huanget al. (2020) analyzed the long-term renal outcomes in patients with CIN after contrast-enhanced CT scans [7]. The study encompassed a diverse patient population from various countries and revealed that CIN was associated with an increased risk of CKD progression and ESRD. However, there is a scarcity of research specifically addressing theimpact of CIN on long-term renal function in the context of Bangladesh. Understanding the magnitude of this issue within the local population is crucial for healthcare providers to develop appropriate preventive strategies and optimize patient care. While the exact pathophysiology of CIN is not completely understood, it is believed to involve a combination of direct toxic effects, ischemic injury, and oxidative stress on the renal tubules. Additionally,underlying patient-related factors such as advanced age, preexisting renal impairment, diabetes mellitus, and volumedepletion contribute to the susceptibility of developing CIN. Hence, the objective of this research is to examine how contrast-induced nephropathy affects the renal function in the long-term following coronary angiography andcontrast-enhanced computed tomography among individuals in Bangladesh. By evaluating the long-term renal outcomes of patients who develop CIN, this research intends to contribute to the existing body of knowledge and provide insights that can guide clinical decision-making and improve patient outcomes in Bangladesh.

METHODOLOGY & MATERIALS

This is a prospective comparative study, a total of 195 patients were enrolled and analyzed in this study. The study was conducted at the Department of Cardiology, Apollo Imperial Hospitals, Chittagong, Bangladesh. In our research, we examined the alterations in renal function following coronary angiography or contrast-enhanced computed tomography (CT) procedures conducted from March 2022 to March 2023. The patient cohort was divided into two distinct groups: Group A and Group B. A total of 72 patients with Coronary Angiography were in Group A and a total of 135 patients with contrast-enhanced computed tomography were in Group B. Patients at risk for CIN, defined as an eGFR <60 mL/ min/1.73 m2 on coronary angiography or an eGFR <45 mL/min/1.73 m2 contrast- enhanced CT, were eligible.

Inclusion criteria:

- Patients aged at least 20 years.

Exclusion criteria:

- Patients with allergy to contrast media.
- Renal replacement therapy.
- Pregnant women.
- Patients with severe liver dysfunction.
- Patients' hyperthyroidism.

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The attending doctor had the authority to administer serum saline loading before and after giving contrast media, based on their discretion. Prior to the study, a range of evaluations were conducted, including patient information such as age, gender, presence of diabetes, cardiovascular disease, and smoking history. Examination conditions,such as the amount of contrast media and supplemental fluid volume, as well as the patients' medication history (diuretics, RAS inhibitors), were also taken into account. Blood tests were conducted to evaluate kidney function before administering contrast and at various time intervals following coronary angiography or contrast-enhancedCT: 3 days, 1 month, 3 months, 1 year, and 2 years. The criteria for contrast-induced nephropathy (CIN) were defined as an increase in serum creatinine level exceeding 0.5 mg/dL or a 25% increase from the previous value within 72 hours of iodine contrast administration, as specified in the guidelines. *Renal cholesterol crystal embolism* was defined as the presence of cholesterol crystals in a renal biopsy or the manifestation of symptomssuch as blue toe, rapidly progressive renal dysfunction, reticular plaques in the lower limbs, or eosinophilia(>500/μL). The study's primary objective was to assess the long-term prognosis of renal function after CIN, defined as either a twofold increase in serum creatinine or the initiation of dialysis within two years. Secondary objectives included evaluating the presence of renal cholesterol crystal embolism, mortality, and an exploratory assessment of risk factors associated with a twofold increase in serum creatinine or the need for dialysis at the two-year mark. The primary analyses focused on examining the occurrence of CIN and its associations with outcomes at the two-year follow-up within the entire study population. Subgroup analyses were also performed, categorizing participants based on baseline renal function and comorbidities. Patients were allocated into groups according to their comorbidities, and their characteristics were compared using statistical methods such as analysis of variance or chi- square tests for categorical variables. Bonferroni analysis was employed to determine the significance of differences among the groups. All statistical analyses were carried out using the SPSS software package.

RESULT

The study population consisted of 195 patients, who were divided into two groups. Table 1 presents the characteristics of the patients in both groups. In Group A, the average age of patients was 71.5 years, with mean serum creatinine and eGFR values at enrollment measuring 1.96 mg/dl and 30.4 ml/min/1.73 m2, respectively. In Group B, the average age was 73.3 years, and the mean serum creatinine and eGFR were 1.69 mg/dl and 34.5 ml/min/1.73 m2, respectively. The distribution of genders in the study population is depicted in Figure 2, where male patients were more prevalent than female patients in both groups. Regarding comorbidities, Group A had a higher percentage of patients with cardiovascular disease, accounting for 40.48% of the group, followed by diabetes at 33.33%. In Group B, the majority of patients (37.78%) had diabetes mellitus, while 32.59% were smokers (Figure2). The analysis comparing renal function at the time of coronary angiography and contrast-enhanced CT (eGFR ≥30 ml/min/1.73 m2 and eGFR ≤1.73 m2) revealed no significant difference in the occurrence of contrast-induced nephropathy (CIN) (Table 2). Furthermore, there was no significant association between the occurrence of CIN and the deterioration of renal function over a period of two years. The absence of a significant association between CIN occurrence and the two-year prognosis of renal function was also observed in the contrast-enhanced computed tomography group (Table 3). Factors contributing to the deterioration of renal function at two years were the presence of cardiovascular disease (specifically myocardial infarction, angina pectoris, and chronic heart failure), as well as pre-existing renal dysfunction at the time of coronary angiography (Table 4). Age and diabetes mellitus, along with pre-existing renal dysfunction, were identified as factors associated with the two-year prognosis of renal function (Table 5).

Table 1: Patients characteristics of both groups.

Variables	Mean±SD	
	Group A (N=72)	Group B (N=123)
Age group (years)	71.5±11.9	73.3±10.8
Systolic blood pressure (mmHg)	122±13.5	130±10
Diastolic blood pressure (mmHg)	78±8	82±8
Blood urea nitrogen (mg/dl)	27.9±5.3	21.1±5.4
Creatinine (mg/dl)	1.96±0.71	1.69±0.74
Estimated glomerular filtration rate (ml/min/1.73m^2)	30.4±10.0	34.5±9.1
Albumin (g/dl)	2.9±0.4	3.3±0.4
Hemoglobin (g/dl)	13.6±2.2	10.8±1.8
Eosinophil count (/μl)	233±21	377±63
Volume of saline infused (ml)	844±232	569±40
Volume of contrast media administered (ml)	34±21	81±32

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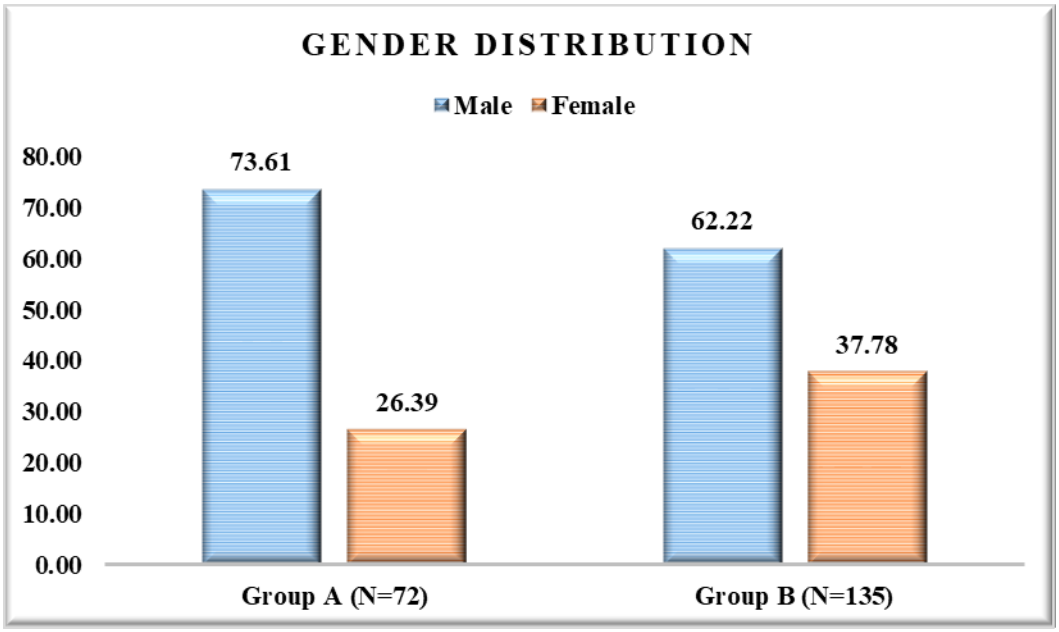

Figure 1: Gender distribution of the study groups.

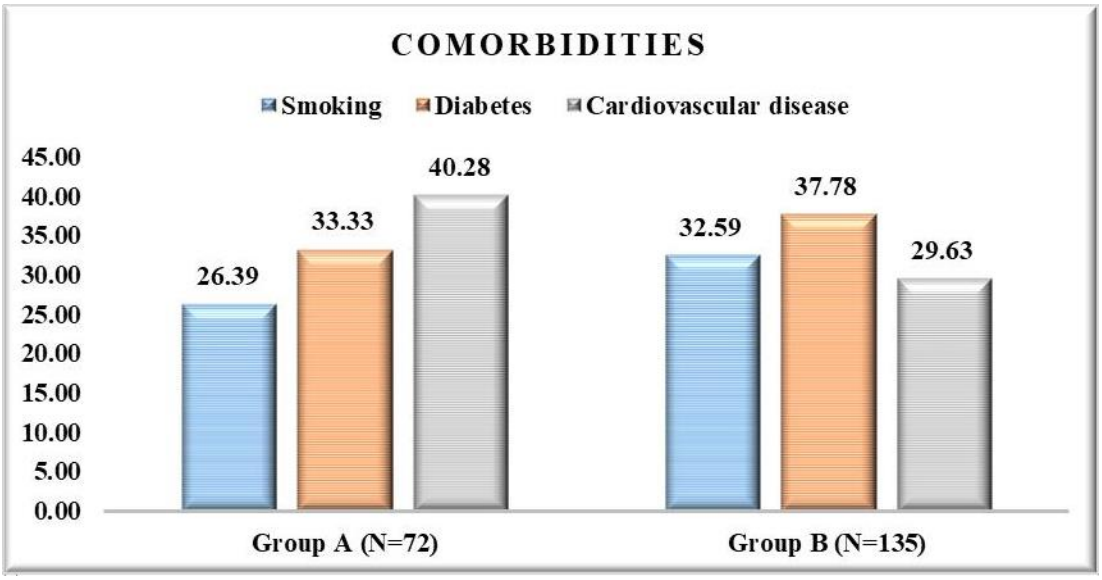

Figure 2: Comorbidities of the study population based on groups.

Table 2: Relationship between the occurrence of CIN and renal function at contrast media administration of both groups.

CIN	Group A (N=72)				Group B (N=135)			
	Renal function at contrast media administration (eGFR)							
	≥30 ml/min/1.73m2 (N=37)		<30 ml/min/1.73m2 (N=35)		≥30 ml/min/1.73m2 (N=76)		<30 ml/min/1.73m2 (N=59)	
	N	%	N	%	N	%	N	%
Positive	2	5.41	2	5.71	2	2.63	3	5.08
Negative	35	94.59	33	94.29	74	97.37	56	94.92
P-value	0.231				0.321			

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Table 3: Relationship between occurrence of contrast-induced nephropathy and worsening of renal function at 2 years of both groups.

CIN	Group A (N=72)				Group B (N=135)			
	Worsening of renal function							
	≥30 ml/min/1.73m2 (N=11)		<30 ml/min/1.73m2 (N=61)		≥30 ml/min/1.73m2 (N=9)		<30 ml/min/1.73m2 (N=126)	
	N	%	N	%	N	%	N	%
Positive	1	9.09	3	4.92	1	11.11	4	3.17
Negative	10	90.91	58	95.08	8	88.89	122	96.83
P-value	0.302				0.099			

Table 4: Factors associated with worsening renal function after coronary angiography; Group A (n=72).

Group A (N=72)					
Variables	Frequency	Percentage	Worsened renal function		
			N	%	P-value
Diabetes					
Positive	24	33.33	7	9.72	0.089
Negative	48	66.67	18	25.00	
Cardiovascular disease					
Positive	28	38.89	3	4.17	0.001
Negative	44	61.11	22	30.56	
Diuretics					
Positive	14	19.44	9	12.50	0.269
Negative	58	80.56	22	30.56	
Renin angiotensin system inhibitors					
Positive	45	62.50	12	16.67	0.621
Negative	27	37.50	10	13.89	
Serum creatinine (mg/dl)					
<1.5	40	55.56	1	0.72	0.001
1.5-2.5	21	29.17	14	10.08	
2.5>	11	15.28	39	28.08	
Estimated glomerular filtration rate (ml/min/1.73m2)					
<45	17	23.61	2	1.44	0.001
30-45	34	47.22	6	4.32	
30>	21	29.17	24	17.28	
Age					
<80	17	23.61	19	13.68	0.053
60-80	40	55.56	6	4.32	
60>	15	20.83	12	8.64	
Volume of contrast media administered (ml)					
<25	40	55.56	8	5.76	0.112
25-50	22	30.56	10	7.20	
50>	10	13.89	22	15.84	
Saline infusion					
Positive	23	31.94	11	15.28	0.739
Negative	49	68.06	9	12.50	

Table 5: Factors correlated with renal function deterioration in the contrast-enhanced CT; Group B (n=135).

Group B (N=135)					
Variables	Frequency	Percentage	Worsening renal function		
			N	%	P-value
Diabetes					
Positive	97	71.85	5	3.70	0.001

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Negative	38	28.15	18	13.33	
Cardiovascular disease					
Positive	114	84.44	6	4.44	0.125
Negative	21	15.56	19	14.07	
Diuretics					
Positive	118	87.41	7	5.19	0.127
Negative	17	12.59	16	11.85	
Renin angiotensin system inhibitors					
Positive	97	71.85	8	5.93	0.529
Negative	38	28.15	10	7.41	
Serum creatinine (mg/dl)					
<1.5	93	68.89	0	0.00	0.001
1.5-2.5	28	20.74	19	14.07	
2.5>	14	10.37	45	33.33	
Estimated glomerular filtration rate (ml/min/1.73m2)					
30-45	106	78.52	4	2.96	0.001
30>	29	21.48	26	19.26	
Age					
<80	17	12.59	28	20.74	0.002
60-80	89	65.93	5	3.70	
60>	29	21.48	7	5.19	
Volume of contrast media administered (ml)					
<25	8	5.93	17	12.59	0.132
25-50	107	79.26	6	4.44	
50>	20	14.81	17	12.59	
Saline infusion					
Positive	111	82.22	8	5.93	0.56
Negative	24	17.78	11	8.15	

DISCUSSION

In previous times, there was concern that the use of contrast media could potentially worsen kidney function. However, a recent study maintains that contrast-induced nephropathy (CIN) is not a prognostic risk factor for long- term chronic kidney disease following coronary angiography or Contrast-enhanced CT scans [8]. Individuals with pre-existing renal dysfunction and an estimated glomerular filtration rate (eGFR) below 30 ml/min/1.73 m² do not face an increased risk of CIN. Contrast-induced acute kidney injury occurs when renal function declines within threedays of intravascular administration of iodinated contrast material. This injury is characterized by vasoconstriction, causing a temporary reduction in renal blood flow, direct toxicity to the renal tubular epithelium, and tubular obstruction due to protein precipitates [8]. Generally, arteriography poses a higher risk of contrast-induced acute kidney injury than venography (e.g., contrast-enhanced CT) due to the higher concentration of contrast material delivered to the kidneys during angiography and the higher risk associated with patients requiring such procedures [9]. Several studies have also reported that even patients with an eGFR below 30 ml/min/1.73 m² do not face a riskof CIN [10-13]. Nonetheless, the risk of CIN remains elevated in coronary angiography. This study discovered that the risk of CIN was not significantly influenced by renal function at the time of angiography, even in patients withan eGFR below 30 ml/min/1.73 m². Similarly, no risk of CIN was observed in contrast-enhanced CT scans for patients with an eGFR below 30 ml/min/1.73 m². Recent studies have suggested that the risk of acute kidney injury caused by contrast material is overestimated [14-18]. The rate of CIN observed in this study is lower than in previous studies, even though only patients with pre-existing renal dysfunction were included. Contrast media- induced renal dysfunction in coronary angiography and contrast-enhanced CT scans is a risk factor for long-term renal dysfunction. However, this study found no significant association between CIN and pre-existing renal dysfunction in coronary angiography or contrast-enhanced CT scans. Furthermore, even if CIN occurs, it does not appear to impact the long-term prognosis of renal function. These findings support the need for reconsidering the "realism" where patients are discouraged from undergoing contrast studies due to the fear of developing CIN, despite the necessity of such studies. However, it is important to note that pre-existing chronic kidney disease

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remains the most significant patient-related risk factor for long-term renal prognosis, regardless of the occurrence of CIN. Additionally, this study identified a link between a history of cardiovascular disease and long-term renal prognosis in coronary angiography. Given that most patients with cardiovascular disease undergo coronary angiography, assessing cardiac function before the procedure is crucial. In this study, administering saline before and after angiography or the amount of contrast media used did not reduce the risk of CIN. However, it is important to consider the limited sample size as a possible reason for this lack of effect. Cholesterol crystal embolism occurs when cholesterol crystals from atherosclerotic foci in large vessels, such as the aorta, disintegrate and cause systemic organ embolism. This condition has a poor prognosis. In the general population, the probability ofcholesterol crystal embolism following cardiac catheterization is approximately 0.06% [19]. However, it is important to note that the occurrence rate of cholesterol crystal embolism in this study, which focuses on patients with pre-existing renal dysfunction, cannot be directly compared to previous reports. The current trend in coronary angiography is primarily through the radial artery, which is expected to lower the occurrence of cholesterol crystal embolism compared to the past. Nevertheless, when renal function deteriorates after coronary angiography, it is crucial to monitor not only changes in serum creatinine but also eosinophil count and symptoms in the lower limbs.

Limitations of the study: Like any hospital-based study, the present study has its own set of limitations. These limitations have been acknowledged and are worth considering. Multiple factors constrain the current study. Firstly, the sample size was relatively small, which may limit the generalizability of the findings to a larger population**.** Secondly, the study was conducted at a single center, which may limit the ability to generalize the results to other settings or populations. Thirdly, due to the random assignment of serum saline by the attending physician's judgment, it was difficult to accurately determine the effectiveness of preoperative administration. To address these limitations and obtain more robust conclusions, a larger clinical study in the future is necessary.

CONCLUSION AND RECOMMENDATIONS

Contrary to common belief, CIN does not pose a risk factor for long-term renal prognosis following coronary angiography or contrast-enhanced CT scans. Even in patients with pre-existing renal dysfunction and an eGFR of less than 30 ml/min/1.73 m^2, the risk of CIN is not elevated. These significant findings provide valuable insights, indicating that patients with kidney disease requiring contrast-enhanced testing can confidently undergo appropriate screening measures.

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