Brief Communication

Investigating the Prevalence of Contrast-associated Nephropathy and the Related Risk Factors in Patients Undergoing Elective Angioplasty

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ABSTRACT

Objective: Contrast-associated nephropathy (CAN) is a sudden decrease in kidney function following contrast media administration. Considering the importance of CAN in the patient's outcome and the high prevalence of this complication in cardiac catheterizing centers, this study was designed to investigate the prevalence and the related risk factors of CAN in patients undergoing angioplasty in Chamran Heart Hospital, Isfahan, Iran, from January 2022 to June 2022. **Methods:** The inclusion criteria were adult patients above 18 admitted for elective percutaneous coronary intervention (PCI). Patient demographic information, underlying diseases and medications, dehydration state, type and amount of contrast media, and serum levels of blood urea nitrogen (BUN) and serum creatinine (SrCr) at 24 and 72 h after contrast injection were all recorded. **Findings:** Out of 340, 128 patients developed CAN after PCI, giving an incidence of 37.64%. Adjusted analysis showed a significant relation between age over 65, the amount of contrast media administered, and the use of furosemide with the incidence of CAN. However, adjusted logistic regression analysis failed to show any significant relationship between the risk of CAN and the hydration status of the patients at 24 and 48 h after receiving contrast media as diagnosed by BUN/SrCr >20. **Conclusion:** The prevalence of CAN in this study was higher than in other studies since this high-risk population was under risk factors such as arterial injection of contrast material and a higher amount of contrast material administration. In addition, advanced age, volume of contrast material, and previous or concurrent furosemide administration were associated with an increased risk of CAN.

KEYWORDS: *Acute renal failure, angioplasty, contrast-associated nephropathy, prevalence*

INTRODUCTION

Contrast-associated nephropathy (CAN) is a sudden decrease in kidney function following contrast media administration. Investigations have shown that even mild declines in renal function that do not lead to overt organ failure are of significant clinical importance and can increase morbidity and mortality.[1] Acute renal failure associated with contrast agents is generally reversible; however, this failure may progress and leave adverse effects.[2] The incidence of contrast-related acute kidney failure in patients with normal renal function has been reported to be 3.3%–14.5%. However, in the presence of some risk factors related to the procedure, such as intraarterial (vs. intravenous [IV]) injection and interventional (vs. diagnostic) process, this percentage might increase up to 27%.[3] The pathogenesis of CAN is complex and not fully understood, but iodinated contrast agents cause severe and prolonged vasoconstriction at the renal corticomedullary junction. In addition, high osmolarity contrast agents directly impair renal autoregulatory capacity through loss of nitric oxide production. These effects, along with the direct tubular

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toxicity of contrast agents, lead to evident acute tubular necrosis and CAN syndrome.[4,5] There is no definitive treatment for established CAN. Therefore, the benefits of performing diagnostic or interventional procedures based on administering contrast material should always be weighed against the risks.[6] Considering the importance of CAN in the patient's outcome and the high prevalence of this complication in cardiac catheterizing centers due to the arterial injection and the interventional nature of the process, this study was designed to investigate the prevalence and the related risk factors of CAN in patients undergoing angioplasty.

Methods

This observational study was conducted in Shahid Chamran Hospital, affiliated with Isfahan University of Medical Sciences, Isfahan, Iran, from January 2022 to June 2022.

The inclusion criteria were adult patients above 18 admitted for elective percutaneous coronary intervention (PCI). Patient's demographic and clinical information, including age, gender, weight, underlying diseases (heart failure, kidney failure, diabetes, history of myocardial infarction [MI]), and previously or concomitantly-used medications (furosemide, statin, angiotensin-converting enzyme inhibitors [ACEI], and angiotensin receptor blockers [ARB]), as well as laboratory findings, for example, the serum level of blood urea nitrogen (BUN), and serum creatinine (SrCr), were all gathered. The type and amount of IV fluid received by the patient for hydration were also extracted from the patient's documents. Information related to the type and volume of the administered contrast media was also recorded. The type of contrast agent prescribed for all patients was iodixanol. Since dehydration is a known risk factor for CAN, the BUN/SrCr ratio was also calculated 24 and 48 h after the contrast media administration to investigate the patient's hydration status. A dehydrated state was defined as a BUN/SrCr ratio of more than 20. To investigate the prevalence of CAN, serum creatinine was also recorded at baseline, 24 and 48 h after receiving the contrast media. We defined CAN as an absolute increment of 0.5 mg/dL or a relative increment of 25% from baseline at 48–72 h following the injection of contrast media, after excluding other causes of nephropathy, such as nephrotoxins, hypotension, urinary obstruction, or atheromatous emboli.[1] Statistical analysis was performed using SPSS 16.0 Software (Statistical Package for the Social Sciences, Version 16, SPSS Inc., Chicago, IL, USA), and the $P < 0.05$ was considered statistically significant.

Results

Three hundred and forty subjects were included in this study. Out of 340, 128 patients developed CAN after PCI, giving an incidence of 37.64%. Chronic kidney disease (CKD) diagnosed by baseline creatinine was present in 150 patients (44.11%). CKD was defined as an estimated glomerular filtration rate <60 ml/min/1.73 m^2 calculated by the CKD-epidemiology equation.[7] The prevalence of CAN was 33.33% in CKD and 41.05% in non-CKD patients. The prevalence of other risk factors of CAN, namely heart failure with reduced ejection fraction (HFrEF), diabetes, and MI, was 83 (24.41%), 158 (46.47%), and 150 (44.11%), respectively. Since the prevalence of CAN in CKD and non-CKD patients was different, we divided our patients into two groups based on the presence of CKD, and the two groups were analyzed separately concerning the related risk factors of CAN in these patients.

Logistic regression analysis (crude and adjusted analysis) was used to estimate the effect of risk factors on the incidence of CAN in CKD and non-CKD patients. As shown in Table 1, the adjusted analysis showed a significant relation between age over 65, the amount of contrast medium administered, and concomitant use of furosemide with the incidence of CAN in patients with CKD. However, adjusted logistic regression analysis failed to show any significant relationship between other factors such as sex, the presence of risk factors (such as HFrEF, diabetes, and MI), the volume of IV fluid used for hydration, and the co-administration of ACEI and ARB medications with the incidence of CAN in both patient with and without CKD.

In addition, there was no significant relationship between the dehydration status of the patients at 24 and 48 h after receiving contrast media (diagnosed by BUN/SrCr >20) and the risk of CAN. However, statistical analysis did not show any significant relationship between the administration of furosemide and BUN/SrCr above 20 at 24 and 48 h after receiving the contrast media.

Discussion

Nephropathy related to the administration of contrast material is one of the most common side effects that has attracted the attention of doctors and researchers in recent years. The occurrence of this complication, in addition to the destructive effect on the kidney and its failure, causes an increase in the length of stay of patients in the hospital and, as a result, an increase in care and treatment costs.[6] With the increasing use of iodinated contrast agents in diagnostic imaging and interventional procedures such as angioplasty, contrast agent-related nephropathy has become an important

Table 1: The relationship between risk factors and the incidence of contrast-associated nephropathy in patients undergoing angioplasty

Risk factors	Crude analysis				Adjusted analysis			
	Without CKD	*P*	With CKD	*P*	Without CKD	*P*	With CKD	*P*
Age >65 years	0.82 (0.43–1.58)	0.56	3.45 (1.41–8.48)	0.007	0.74 (0.37–1.48)	0.39	5.3 (1.62–17.33)	0.005
Sex (male)	0.89 (0.31–2.49)	0.82	0.72 (0.37–1.43)	0.86	0.67 (0.21–2.08)	0.48	0.61 (0.26–1.42)	0.29
BUN/SrCr >20 (24 h)	0.59 (0.23–1.51)	0.27	1.06 (0.48–2.30)	0.89	0.47 (0.15–1.51)	0.20	0.59 (0.14–2.44)	0.47
BUN/SrCr >20 (48 h)	0.89 (0.43–1.89)	0.76	1.34 (0.64–2.82)	0.44	0.96 (0.36–2.52)	0.92	1.31 (0.35–4.85)	0.69
Volume of contrast media	1.00 (0.99–1.01)	0.76	1.005 (1.001–1.008)	0.005	0.99 (0.99–1.00)	0.72	1 (1–1.01)	0.01
NAC administration	4.40 (0.45–5.49)	0.2	1.43 (0.67–3.08)	0.35	6.62 (0.61–72.27)	0.12	0.74 (0.23–2.31)	0.59
Volume of IV fluid	0.66 (0.37–1.18)	0.16	0.84 (0.43–1.69)	0.85	0.71 (0.2–2.62)	0.61	1.49 (0.32–7)	0.61
History of								
Heart failure	1.51 (0.84–2.74)	0.17	1.04 (0.51–2.14)	0.9	1.55 (0.8–3.03)	0.19	0.8 (0.31–2.04)	0.63
DM	0.82 (0.38–1.74)	0.6	0.65 (0.31–1.39)	0.27	0.9 (0.41–2)	0.79	0.47 (0.19–1.18)	0.11
MI	1.78 (0.99–3.20)	0.053	0.72 (0.35–1.44)	0.35	1.77 (0.85–3.67)	0.12	0.47 (0.18–1.24)	0.13
Coadministration of								
Furosemide	1.28 (0.44–3.69)	0.64	4.89 (2.14–11.18)	<0.001	0.91 (0.29–2.87)	0.87	9.02 (2.85–28.59)	<0.001
ACEI/ARB	1.18 (0.66–2.12)	0.57	0.96 (0.48–1.89)	0.91	0.99 (0.5–1.98)	0.97	0.94 (0.39–2.26)	0.88

Data are presented as OR (CI). CKD=Chronic kidney disease, BUN=Blood urea nitrogen, SrCr=Serum creatinine, NAC=N-acetylcysteine, IV=Intravenous, DM=Diabetes mellitus, MI=Myocardial infarction, ACEI=Angiotensin-converting enzyme inhibitor, ARB=Angiotensin receptor blocker, OR=Odds ratio, CI=Confidence interval

factor in hospital-associated morbidity and mortality in high-risk patients. This disease is the third-most common cause of hospital-acquired renal failure and occurs after major surgeries and decreased renal perfusion.[8]

This study investigated the prevalence of CAN and related risk factors in elective angioplasty patients. The prevalence of nephropathy caused by contrast material in this study was reported as 37.64%, much higher than in other studies. The reason for the higher prevalence can be factors such as arterial injection of contrast material, the higher amount of contrast material administration due to the interventional nature of the process, as well as the admission of patients with high-risk features such as diabetes (24.41%), MI (46.47%), heart failure (60.58%), chronic kidney failure (44.11%), and age over 65 years (47%). Increasing age and the volume of received contrast material are known risk factors for CAN, which have also been proven in this study. However, in the present study, no significant relationship was observed between patients' hydration status and the occurrence of CAN. Despite the recommendation in most guidelines,[9] the preventive effect of hydration is not proven, especially in patients with heart failure, and even in some recent studies, its negative impact on CAN (in patients with heart failure) has been proposed.[10] For example, in a survey conducted by Bei *et al*. in 2019 on patients with heart failure, hydration before angioplasty (750 cc of liquid) increased the risk of CAN.[11] Furthermore, another study was conducted on 1307 patients who were candidates for angioplasty and angiography with concomitant kidney and heart failure. The results of this study showed hydration's negative effect on the occurrence of CAN.[12] It might be concluded that physicians should consider preventive hydration strategies on a case-by-case basis.[13] In our study, we noticed a negative impact of furosemide on CAN independent of furosemide-associated dehydration. Since the exact mechanism of nephropathy caused by contrast agents has yet to be well known, there is also controversy regarding the use of Lasix. In addition, it is still unclear whether the increased risk of nephropathy associated with contrast agents is due to the direct nephrotoxicity of furosemide itself or is secondary to its decrement of intravascular volume caused by it. Even though many studies have associated the use of furosemide with an increased risk of CAN,[8] some other studies consider its cautious use, along with liquid administration and controlled diuresis.[12] Considering that the administration of furosemide was reported as a risk factor for CAN in the current study, and since the possible cause of this relationship could be the decrease in intravascular volume caused by furosemide or the nephrotoxicity of furosemide itself, the level of BUN/SrCr of the patients was measured as an indicator of patients' dehydration state, 24–48 h after receiving the contrast agent, and its relationship with the use of furosemide was investigated. In patients with kidney failure, the percentage of patients with BUN/SrCr above 20 (24 and 48 h after the consumption of contrast material) was nonsignificantly higher in patients receiving furosemide compared to others. Furthermore, after statistical analysis, no significant relationship was observed between high BUN/SrCr levels and increased risk of nephropathy caused by contrast material,

which can indicate that the kidney damage caused by furosemide is independent of the dehydration caused by this diuretic. Many studies have been conducted in different populations on the risk factors of CAN and its preventive strategies. However, there still needs to be a consensus among these studies that the main reason for this issue is the unknown exact mechanism (or mechanisms) of this complication. Furthermore, the extent of the role of direct renal toxicity of the contrast material and other risk factors has yet to be well known. For this reason, in recent years, the term "contrast-induced nephropathy" has been changed to "contrast-associated nephropathy."

The prevalence of CAN in this study was higher compared to other studies. The related reasons can be an arterial injection of contrast material, a higher amount of contrast material administration, and the admission of high-risk patients. In addition, age, volume of contrast material, and furosemide were associated with an increased risk of CAN. However, the exact mechanism of CAN still needs to be completely understood, and the effect of related risk factors still needs to be discovered.

Authors' Contribution

M. Dianatkhah and S. Badri developed the research idea and drafted the manuscript. E. Shirvani contributed to patients' selection and clinical interpretation of the gathered data. S. Poursaeid recruited the patients and gathered the needed information. All authors have read and approved the manuscript.

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Conflicts of interest

There are no conflicts of interest.

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