



Original Research Article

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PHYSICIANS' AWARENESS OF CONTRAST-ASSOCIATED NEPHROPATHY IN SAUDI ARABIA

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ABSTRACT

Objectives: Iodinated contrast-enhanced computed tomographic scans and angiographies are frequently performed in current medicine, making iodinated contrast medium (CM) one of the inevitably prescribed agents in diagnosing various diseases. There are several complications of CM; one of them is contrast-associated nephropathy (CAN). CAN is one of the most important complications of CM, which is a sudden deterioration of renal function resulting from intravenous (IV) or intra-arterial (IA) administration of contrast media.

Materials and Methods: We conducted a cross-sectional study using an online self-administered questionnaire, guided by the study objectives, was performed in 2020 on 281 physicians who frequently ordered image-based CM for diagnosis in Riyadh, Saudi Arabia, including general physicians, emergency department, internal medicine, general surgery, obstetrics/gynecology, radiologists, and interventional radiologists.

Results: The study showed variations in physicians' awareness regarding the risk factors, definition, and other aspects of contrast-associated nephropathy (CAN). The most common definition chosen by the respondents was an increase in serum creatinine by >25% or by 0.5 mg/dL from baseline within 48 hours (61.9%). Additionally, the result showed a high variability of the awareness of the CM complications and management among different medical subspecialties and physicians' experience years and gender. In addition, the results showed decreased awareness regarding the effect of hemodialysis on CAN. The majority thought that the side effects were commonly observed with arterial injections (69.8%), and preexisting chronic kidney disease was chosen as a risk factor (88.3%). For protocol management, most departments chose "50 mg

prednisone given orally 13 hours, 7 hours, and one hour before the imaging study" for patients at high risk of CAN.

Conclusion: The study showed a lack of knowledge, awareness, complications, and management before and after the use of intravascular iodine contrast agents. A high effort is needed to increase the level of awareness of CAN among physicians by using social media and doing more discussions, seminars, workshops among the residents and physicians, as well as distributing pamphlets for further reading.

Keywords: Contrast, Nephropathy, Awareness, Iodinated, Physician

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INTRODUCTION

Iodinated contrast-enhanced computed tomographic scans or angiographies are frequently performed in current medicine, making iodinated contrast medium (CM) one of the inevitably prescribed agents in diagnosing various diseases. Intravenous contrast material is used to enhance tissue conspicuity and to expand diagnostic ability and accuracy.

Its benefits should be considered in addition to risks when using intravenous iodinated contrast. CM has several adverse effects, ranging from mild like nausea, vomiting, thyroid dysfunction, or severe due to hypersensitivity reactions, such as urticaria, laryngeal edema, bronchospasm, hypotension, and anaphylactic shock [1].

The term "contrast-induced nephropathy (CIN)" has been changed to "contrast-associated nephropathy" or "contrast-associated acute kidney injury (CAN)" [2].

CAN is a clinically asymptomatic but important complication of CM, manifesting as a sudden deterioration of renal function following intravenous (IV) or intra-arterial (IA) administration of CM [3]. CAN is the 3rd most common cause of hospital-acquired

acute renal injury after impaired renal perfusion and nephrotoxic management [4]. It occurs due to toxic complications within renal tubular cells directly caused by CM [5]. CAN has been reported since over 50 years ago, and the number of patients at high risk of CAN is increasing over time due to expanding indications for contrast media use [6].

CAN is defined based on The Kidney Disease Improving Global Outcomes (KDIGO) guidelines as an increase in serum creatinine (SCr) levels of 1.5 times or more over the baseline within seven days after the administration of CM, or an increase in SCr levels by at least 0.3 mg/dL (26.5 μ mol per liter) above the baseline value within 48 hours after administration of CM [7]. Moreover, CAN may be suspected with a urinary volume of less than 0.5 mL/kg of a person's body weight/h that continues for at least 6 h after contrast exposure [2].

Mehran et al. developed a risk-profiling score for CM administration based on the amount of contrast administered, baseline GFR, hemodynamic instability, congestive heart failure, age, anemia, and diabetes. The 4 categories of risk in the score are based on the

sum of recorded points. The incidence of CAN increases from 8% to 57% as the risk category increases [8].

Many other factors make patients more susceptible to CAN, including diabetes mellitus (DM), dehydration, congestive heart failure, multiple myeloma, and concurrent use of nephrotoxic medications (non-steroidal anti-inflammatory drugs [NSAIDs], angiotensin-converting enzyme inhibitors, aminoglycosides, sulfonamides, amphotericin B cyclosporin A, tacrolimus, and platinum-based drugs) [6]. Among the mentioned risk factors, chronic kidney disease is the most important and most common risk factor for CAN [6].

From a physician's purview, it is important to make a clinical judgment regarding the feasibility of CM use when ordering ancillaries. This decision should consider any preexisting conditions mentioned above. The presence of multiple risk factors can increase the risk of CAN [2].

To prevent CAN, an efficient protocol is to use pre-hydration with 9% normal saline or a combination of sodium bicarbonate and low iso-osmolality contrast [2-9].

A previous study reported that physicians who often use contrast have adequate awareness of CAN [10].

However, there are not enough studies in the literature that discuss clinician knowledge of CAN. In this study, we aimed to assess physicians' knowledge regarding CAN and its consequences.

From a physician preview, it is important to make a clinical judgment on the use of iodinated contrast media; this consideration should include the preexisting conditions mentioned above. The presence of multiple

risk factors can increase the risk of contrast-associated nephropathy [11].

No studies have been conducted in Saudi Arabia regarding physician awareness of CAN, and the previous studies on this topic were focused on either radiologist mindfulness or patient consequences. In this study, we aimed to assess physicians' knowledge regarding CAN and its implications.

MATERIALS AND METHODS

Institutional Review Board (IRB) approval was obtained from King Fahad Medical City, the authors' institutional IRB committee (IRB log number: 20-470E). We conducted a cross-sectional study among physicians in Saudi Arabia whose specializations often required ordering contrast media for diagnosis, including those in general practice, emergency department, internal medicine, general surgery, obstetrics/gynecology, radiology, and interventional radiology. This study focused on physician knowledge regarding CAN and its consequences. We excluded any other specialty other than those mentioned above, along with students' responses. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all participants included in the study (before continuing to the questionnaire link, they were asked if they agreed to participate).

Due to the recent change in CAN terminology, which was previously called

contrast-induced nephropathy (CIN), we decided to use the phrase CIN in the questionnaire to avoid any confusion with the newly introduced terminology.

Data were collected using an online self-administered questionnaire containing 20 close-ended questions guided by the study objectives and review of the literature. Data were collected between August 1, 2020, and September 30, 2020.

Statistical analyses were performed using the R statistical software v 3.6.3 (The R Foundation, Vienna, Austria). Counts and percentages were used to summarize the responses to categorical variables and Likert-scale items. The median and interquartile ranges were used to summarize the distribution of patients with CAN during the previous 12 months. The mean and standard deviation were used to summarize the distribution of responses to the 3-point-Likert scale items. Bar plots were used to visualize answers.

Statistical analysis was performed to compare the distribution of knowledge across various departments to assess the different specialties. Counts and percentages were used to summarize the responses. The chi-square test of independence was used to assess whether the distribution of responses was significantly different between departments. Specialty analysis was restricted to departments with more than 10 respondents. Radiologists and interventional radiologists were combined into a single category. Hypothesis testing was performed at a 5% significance level.

RESULTS

Descriptive statistics for the study sample

The study sample included 281 physicians. Males represented 67.3% and females, 32.7% of the study sample. Saudi physicians accounted for 86.8% of the study sample. Physicians from the government represented 82.9% and the private sector, 8.54% of the study sample. Regarding years in practice, approximately half of the respondents (49.8%) had 3–5 years of experience, and more than one quarter (29.5%) had 6–10 years of experience. The remaining physicians had 11–20 years (16%) or >21 years of experience (4.63%). Residents represented half of the included physicians, while consultants represented slightly less than one-fifth (18.1%) of the respondents' Specialists represented 19.6%, and assistant consultants, 9.25% of the included physicians.

Respondents from the internal medicine and general surgery departments each represented 22.1% of the study sample, while general practitioners represented 17.4%. Other represented departments included obstetrics-gynecology (12.8%) and emergency departments (12.5%). See Table 1 and Figure 1.

Awareness regarding CAN

The most common definition chosen by the respondents was an increase in SCr >25% by 0.5 mg/dL from baseline within 48 hours (61.9%). An increase in SCr >50% or 1 mg/dL was chosen by 20.6% of the respondents (20.6%).

Physicians chose all suggested protocols to avoid allergic reactions. However, the most common pre-treatment protocol, suggested

by approximately half of the physicians (47.3%), was 50 mg prednisolone administered orally 13 h, 7 h, and 1 h before imaging. Responses showed varying levels of awareness regarding the estimated risk of renal injury in patients who received contrast injections. The two extreme responses (2%–8% and >90%) were chosen by 35.9% and 36.3% of respondents. Responses also showed somewhat low awareness regarding the adverse effects of oral contrast injection. Slightly less than half (45.6%) of the included physicians thought that oral contrast had the same adverse effects as IV contrast injection.

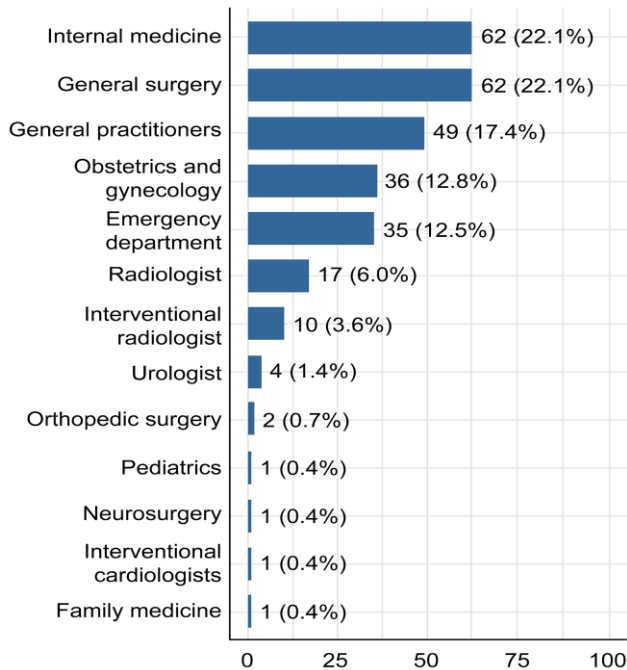


Figure. 1 Distribution of the included physicians across departments. Respondents from the internal medicine and general surgery departments each represented 22.1% of the study sample, while general practitioners represented 17.4%. Other represented departments included obstetrics, gynecology, and emergency departments (12.8% and 12.5%, respectively).

Table 1. Descriptive statistics for the study sample

Demographic Data	
N=281	
Age	
20-29	123 (43.8%)
30-39	107 (38.1%)
40-49	38 (13.5%)
50-59	13 (4.6%)
Gender	
Female	92 (32.7%)
Male	189 (67.3%)
Nationality	
Non-Saudi	37 (13.2%)
Saudi	244 (86.8%)
Work	
Government sector	233 (82.9%)
Private sector	24 (8.5%)
Both	24 (8.5%)
Years in practice	
3-5 years	140 (49.8%)
6-10 years	83 (29.5%)
11-20 years	45 (16.0%)
+21 years	13 (4.6%)
Position:	
Resident	149 (53%)
Specialist	55 (19.6%)
Assistant consultant	26 (9.25%)
Consultant	51 (18.1%)

The results also showed a low level of awareness regarding the effect of hemodialysis on CAN. The majority of the physicians thought that the investigation/treatment should be delayed if the patient is at high risk (62.3%). In comparison, 16.4% thought that the treatment/investigation should be delayed, irrespective of the risk of adverse reactions. The majority of respondents (69.8%) thought that side effects were more commonly observed with arterial injections. Susceptible groups, as perceived by respondents, included: Hay fever patients (79%), ischemic heart disease patients (48%), asthmatic patients (38.1%), patients receiving metformin (25.6%), and diabetic patients with normal renal function (17.1%). Table 2

More than half of the respondents had never encountered any case of CAN (53.7%, n = 151), while 35.2% (n = 99) encountered 1–5

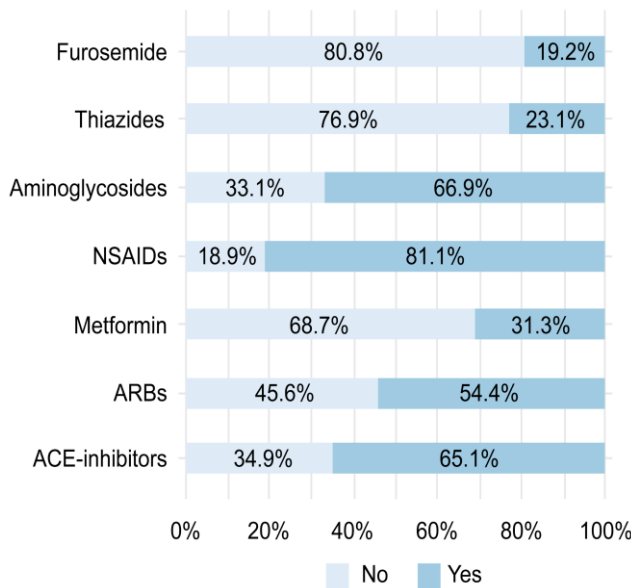


Figure. 2 Medications identified by physicians as nephrotoxic

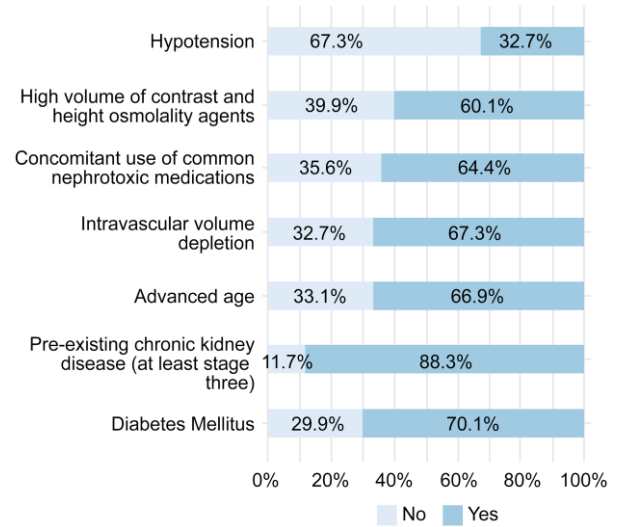


Figure. 3 Factors associated with a high risk of contrast-associated nephropathy

patients during the past 12 months. Only 11% (n = 31) of the respondents encountered 5+ CAN cases during the past 12 months.

On the other hand, 81.1% of the respondents chose NSAIDs as nephrotoxic medication, whereas aminoglycoside was chosen in 66.9%. Other medications were chosen in different percentages, as shown in Figure 2.

The majority of respondents chose preexisting chronic kidney disease as a risk factor for CAN (88.3%). Other risk factors identified by respondents included DM (70.1%), advanced age (66.9%), IV volume depletion (67.3%), and concomitant use of nephrotoxic medications (64.4%; Figure 3).

Approximately three-quarters of the respondents, 71%, agreed that CAN is a rare event associated with contrast media use. More than half of the respondents disagreed that CAN is transient, and half 53% agreed that CAN occurs more frequently than often believed. One-half of the respondents chose "Neutral" as a response to whether CAN was

Recommend protocol as pre-treatment to avoid allergic reaction:		N (%)	
30 mg prednisone 12 hours and 2 hours before the administration of contrast media.		32 (11.4%)	
30 mg prednisone, given orally 72, 48, and 24 hours before contrast media administration.		18 (6.4%)	
50 mg prednisone given orally 13 hours, 7 hours, and 1 hour before the imaging study for patients at high risk.		133 (47.3%)	
Administration of intravenous hydrocortisone a few minutes before the contrast medium injection as appropriate pre-medication.		39 (13.9%)	
If there is no risk, there is no need to give pre-treatment.		59 (21.0%)	
Groups susceptible to chemotoxic or anaphylactic ADR ^a			
Asthma	222 (79%)	DM with normal renal function	48 (17.1%)
Hay fever	107 (38.1%)	IHD	135 (48%)
Food allergy	197 (70.1%)	Metformin with normal renal function	72 (25.6%)
The estimated rate of risk of renal injury in diabetic patients who take contrast injection			
2–8%	101 (35.9%)	10–40%	54 (19.2%)
60–80%	24 (8.5%)	More than 90%	102 (36.3%)
Delay investigation/treatment if suspect ADR to contrast:			
Depends on the severity of the case	12 (4.3%)	Yes, I will wait in both situations. (High and low risk)	46 (16.4%)
No, I will not wait	22 (7.8%)	Yes, if the patient is at high risk, I will wait.	175 (62.3%)
		Yes, if the patient is at low risk, I will wait.	26 (9.25%)
More side effects is observed with:			
Arterial injection contrast	196 (69.8%)	Venus injection contrast	85 (30.2%)
		No	Yes
Oral contrast has the same adverse effect as intravenous contrast injection:	153 (54.4%)	128 (45.6%)	
Hemodialysis after the injection of contrast will decrease the risk of CAN	164 (58.4%)	117 (41.6%)	

Table 2. Responses for multiple choice questions regarding contrast-associated nephropathy

^aOnly responses with n > 1 are shown in the table

ADR, adverse drug reaction

CAN, contrast-associated nephropathy

DM, diabetes mellitu

IHD, ischemic heart disease.

associated with increased mortality and morbidity rates of 44% and 45%, respectively, as shown in Figure 4.

Regarding protocol management, most departments have chosen "50 mg prednisone given orally 13 hours, 7 hours and 1 hour before the imaging study for patients at high risk", with obstetrics and gynecology in the lead at 66.7% followed by the Emergency medicine department (62.9%), general surgery department (51.6%), General Practitioner (46.9%), Radiology department (37.0%), and lastly, the internal medicine department (32.3%).

The majority of the Internal Medicine department has chosen "If there is no risk, there is no need to give pre-treatment." The least chosen protocol was "30 mg prednisone, given orally 72, 48 and 24 hours before contrast media administration". It was selected by 9% of internal medicine, 7.4% radiology, 6.45% general surgery, 6.12% general practitioner, 5.6% obstetrics and gynecology, and none of the emergency department physicians ($P = 0.002$).

Regarding the risk of CAN in diabetic patients, 63.9% of obstetricians and gynecologists picked the rate of $> 90\%$, followed by emergency physicians (45.7%) and general practitioners (42.9%). The lowest percentage was 3%, among the radiologists. Most responders believe that hemodialysis after contrast use will not decrease the risk of CAN and had chosen to delay the investigation/treatment if the patient is at a high risk of CAN.

DISCUSSION

CAN is a serious complication that a physician should consider before requesting

any procedure in which CM should be used, such as a CT scan, particularly if the patient is at increased risk. In this study, we used a contemporary online survey conducted on Saudi and non-Saudi physicians with different specialties, reflecting the perceptions and awareness of CAN among them. Our sample reflects a huge range of physician opinions regarding CAN across Saudi Arabia. Moreover, it was randomly distributed among physicians of different specialties with a good response rate.

More than half of the respondents (54.4%) believed that there was no difference between oral contrast and intravenous contrast injection in terms of the risk of developing CAN. In contrast, 69.8% thought that the arterial injection contrast had the greatest risk. An article has found that radiologists believe that intra-arterial injections have a greater risk of CIN (20%) [6].

Surprisingly, 35.9% of the respondents believed that diabetic patients had only a 2%–8% risk of developing CAN. On the other hand, 36.3% believed that there was more than 90% risk of developing CAN. In one study of patients with diabetic nephropathy undergoing coronary angiography, 50% developed CAN (despite the use of low osmolar CM and adequate hydration) [11].

Most responses (58.4%) believed that there was no need for hemodialysis (HD) after contrast injection, while 41.6% thought that patients should undergo HD to lessen the side effects of CAN. An article has found that HD immediately after contrast injection is favorable for two groups of patients: chronic HD and very high-risk contrast nephropathy patients [12]. In 13 patients with serum creatinine levels of 2.4–7.4 mg/dl, HD was

carried out within 1–18 h of the injection. No patient showed an increase in serum creatinine levels within 15 days. The authors concluded that HD is likely to be helpful in preventing CAN. However, there was no control group in that study, which makes these results difficult to interpret [13]. Multiple studies have recommended that although HD eliminates contrast medium effectively, it may not influence the incidence or outcome of CAN [12].

In our results, most responders believed that some medications could cause nephrotoxicity more than others. The most common answer was NSAIDs (81.1%), followed by aminoglycosides (66.9%). Most of the responders' answers were compatible with the available evidence on common drugs causing nephrotoxicity [14].

In our questionnaire, preexisting chronic kidney disease was chosen first by 88.3% as a risk factor for CAN, followed by diabetes mellitus (70.1%). Intravascular volume depletion and advanced age occurred in the third and fourth places by 67.3% and 66.9%, respectively. This reflects a good awareness among our physicians regarding risk factors for CAN, as evident from previous trials [11,15,16].

CONCLUSION

This is a cross-sectional study among physicians with knowledge of CAN, which is one of the most important complications of contrast media and the third cause of acquired hospital acute kidney injury. The results varied remarkably, but it showed that most respondents agreed that there is no need for dialysis after CM injection; however,

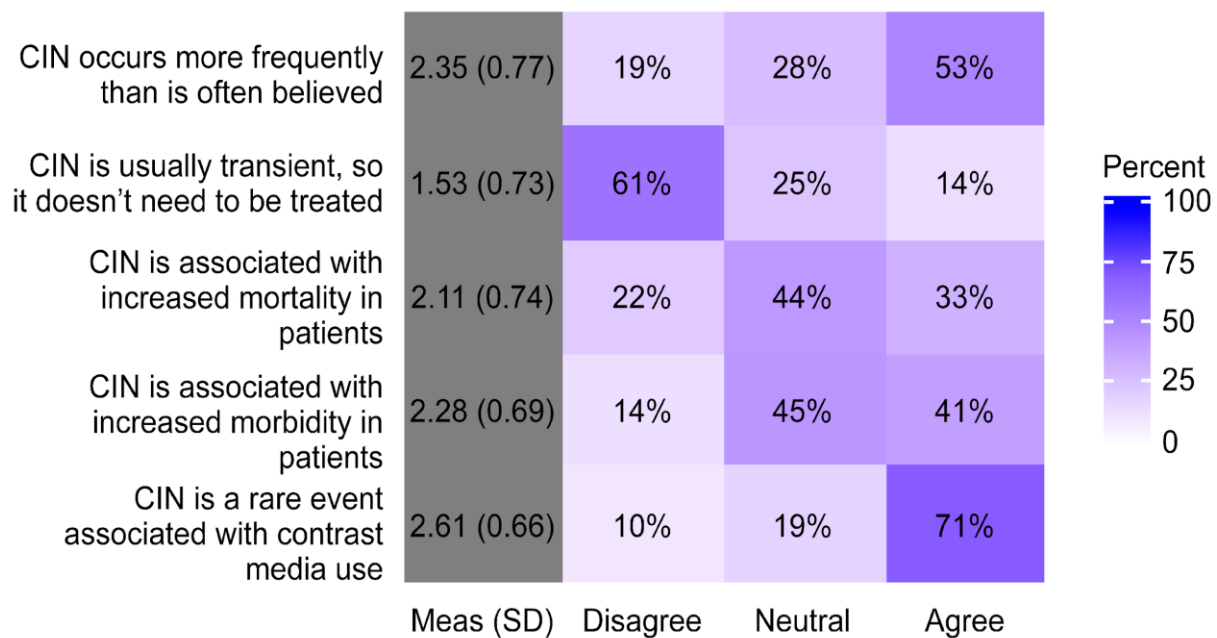


Figure. 4 Physicians' opinions on the incidence and impact of contrast-associated nephropathy Responses were based on a scale of 1–3 where 1 = Disagree, 2 = Neutral, 3 = Agree.

medications that can cause nephrotoxicity and multiple risk factors must be kept in mind during patient evaluation. Unfortunately, we noticed a lack of knowledge, awareness, complications, and management regarding CAN as a result a high effort is needed to increase the level of awareness of CAN among physicians by using social media and doing more discussions, seminars, workshops among the residents and physicians, as well as distributing pamphlets for further reading.

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