Original Article

Incidence and risk factors of contrast-induced nephropathy in acute stroke patients undergoing computed tomography angiography: A single-center study

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ABSTRACT

الأهداف: دراسة مدى انتشار وعوامل الخطر المحتملة المرتبطة باعتلال الكلية الناجم عن التباين في هذه الفئة المحددة من المرضى، بهدف ضمان أعلى جودة من الرعاية السريرية.

المنهجية: أجريت دراسة على جميع المرضى الذين وصلوا لقسم الطوارئ بمستشفى الملك فهد بجدة بأعراض جلطة دماغية حادة خلال الفترة من مارس 2022م حتى نوفمبر 2022م وخضعوا لأشعة مقطعية للأوعية الدموية الدماغية، وكانت معايير التضمين في الدراسة كما يلي: أن تكون نتائج الكرياتينين الأساسية وإجراء الأشعة المقطعية للأوعية الدموية الدماغية تم إجراؤها في غضون 24 ساعة من ظهور الأعراض ونتائج الكرياتينين المتاحة في وقت مبكر (أقل من 5 أيام بعد إجراء الأشعة).

النتائج: من بين 246 مريضًا وصل للطوارئ، خضع 182 مريض لأشعة مقطعية للأوعية الدموية الدماغية في الدماغ وكان لدى 8.24% اعتلال الكلى الناجم عن استخدام الصبغة. المرضى الذين وجد لديهم نزيف دماغي زاد من نسبة خطورة حصول اعتلال الكلى بسبعة اضعاف (OR=6.7; 95% CI: 1.23-33.3). زاد وجود معدل غير طبيعي لوظائف الكلى الخطورة بنسبة 8 اضعاف (OR=7.8; 95% CI: 1.74-35.1). ارتفاع ضغط الدم يضاعف من خطر الإصابة باعتلال الكلى (OR=2.1; 95% CI: 1.26-6.98).

الخلاصة: كانت نسبة حدوث اعتلال الكلى الناجم عن استخدام الصبغة 8.2%، وقد كانت النسبة أكثر ارتفاعاً لدى المرضى الذين وجد لديهم نزيف دموي دماغي ومصابين بارتفاع ضغط الدم وكان معدل وظائف الكلى لديهم مرتفع وتم علاجهم بإعطائهم مذيب منشط البلازمينوجين النسيجي، وهذه العوامل تستدعي الانتباه من الممارسين الصحيين أثناء التعامل مع حالات الجلطات الدماغية الحادة.

Objectives: To investigate the prevalence and risk factors linked to contrast-induced nephropathy in this specific patient population, aiming to ensure the highest quality of clinical care.

Methods: In a retrospective analysis, all patients who presented with an acute stroke to King Fahad Hospital, Jeddah, Emergency Department from March until November 2022 and underwent Computed Tomography Angiography (CTA) brain, Inclusion criteria were as follows: a baseline creatinine results and CTA examination performed within 24 hours of symptom onset and an available early (<5 days after CTA) follow-up creatinine result.

Results: Among 246 stroke patients in the emergency, 182 underwent brain CTA and 8.24% had Contrast-Induced Nephropathy (CIN). intracerebral hemorrhage (ICH) increased CIN risk 7-fold (OR=6.7; 95% CI: 1.23-33.3). Abnormal baseline raised CIN risk 8-fold (OR=7.8; 95% CI: 1.74-35.1). hypertension doubled the risk for CIN (OR=2.1; 95% CI: 1.26-6.98)

Conclusion: The incidence of CIN was 8.2%, particularly elevated in patients with ICH, hypertension, tissue plasminogen administration, and abnormal baseline, necessitating vigilance in managing acute stroke cases.

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Contrast-induced nephropathy (CIN) is a medical condition characterized by an acute decline in kidney function that typically occurs within 48 to 72 hours of injection with contrast media in order to do

brain CT Angiogram. A range of definitions has been proposed to describe Contrast-induced nephropathy. the Kidney Disease Improving Global Outcomes (KDIGO) definition is among the most commonly used. According to KDIGO, Contrast-induced nephropathy is defined as an increase in the level of serum creatinine (SCr) by over 25% of the baseline or an absolute increase of at least 44 µmol/L (0.50 mg/dl) that occurs after intravenous administration of contrast media with absence of any other plausible explanation. serum creatinine usually returns to baseline within 14 days; however, some patients may progress to acute or chronic renal disease requiring dialysis in context.[1] In acute stroke patient care, neuroradiological imaging is crucial to ensuring optimal patient outcomes, often involving both Non-Contrasted Head Computed Tomography (NHCT) and a Brain CT Angiogram which assesses the extracranial and intracranial vessels to detect any large vessel occlusion.[2-3] New studies show a low incidence of Contrast-induced nephropathy and waiting for creatinine levels in the emergency setting leads to a delay in the acute management of acute stroke.[4-5] Therefore, it is important to examine the prevalence and potential risk factors linked to Contrast-induced nephropathy in this specific patient population, aiming to ensure the highest quality of clinical care.

Methods. We performed a retrospective analysis of patient records to investigate the incidence and risk factors associated with CIN in patients with acute stroke who underwent brain CT angiography (CTA) at King Fahad Hospital in Jeddah, Kingdom of Saudi Arabia. We included all patients who presented with acute stroke to the emergency department between March 2022 and November 2022 and underwent CTA within 24 hours of symptom onset and had baseline creatinine results with an available early follow-up creatinine result (<5 days after CTA). We excluded patients with end-stage renal disease, on dialysis or with missing data. Patient demographics, stroke severity (as assessed by the National Institutes of Health Stroke Scale [NIHSS]), baseline kidney function, use of tissue plasminogen activator (TPA), and development of CIN within 72 hours of CTA were collected. The definition of CIN utilized in this study was in accordance with criteria established by the KDIGO, with the baseline serum creatinine level at the time of admission being considered as the reference point and baseline creatinine.[6] Demographic information, including known risk factors for CIN (such as the presence of diabetes, known renal disease, and use of metformin) was collected. Follow-up creatinine results were collected from day 1 to day 5 after the baseline CTA. The CTA procedure followed the institutional protocol of administering 75 to 100 mL of ioversol (Optiray 320), a nonionic and low-osmolar contrast agent. The study received approval from the Institutional Review Board of King Fahad Hospital, Jeddah, Saudi Arabia, and informed consent was waived since the study was retrospective in nature (IRB Log No: A01571). The confidentiality and anonymity of patient data were maintained throughout the study. Data analysis was performed using the Statistical Package for the Social Sciences version 21 (SPSS: An IBM Company), and all statistical tests were two-tailed with a significance level of 0.05, indicated by a *p*-value of less than or equal to 0.05. The prevalence of CIN among all patients who presented with acute stroke and underwent CT angiography was graphed. Descriptive analysis was conducted by prescribing frequency distribution and percentage for study variables, including patient demographic and clinical data. Cross Tabulation was used to identify characteristics of CIN in stroke patients who underwent CTA, using the Pearson chi-square test for significance and exact probability test if there were small frequency distributions. we have conducted a multiple regression analysis to comprehensively assess the impact of multiple variables on the occurrence of CIN. The multiple regression analysis takes into consideration the interplay between various variables and their potential interactions, allowing us to draw more robust and accurate conclusions.

Results. At King Fahad General Hospital in Jeddah, a total of 287 stroke patients were admitted to the Emergency Department. Out of these, 246 underwent Non-Contracted Head Computed Tomography (NCHCT) imaging. Among them, 182 patients met the inclusion criteria and were followed up for at least 72 hours after undergoing CTA (**Figure 1**). Of the patients included in our study, 8.24% developed contrast-induced acute kidney injury (**Table 1**). Patients who received TPA had a 7 times higher risk of developing CIN compared to those without TPA (OR=7.15; 95% CI: 1.73-29.5). Additionally, the presence of hypertension in stroke patients doubled the risk of CIN (OR=2.1;

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Table 1 - Bio-demographic characteristics of acute stroke patients developing contrast-induced nephropathy following CT angiography brain.

Data	Total	CIN		*P*-value
		Yes	No	
	No (%)	No (%)	No (%)	
Incidence of CIN	182	15 (8.24)	167 (91.8)	
Age in years				
< 40	14 (7.7)	1 (7.1)	13 (92.9)	.322
40-59	80 (44.0)	4 (5.0)	76 (95.0)	
60+	88 (48.4)	10 (11.4)	78 (88.6)	
Gender				
Male	120 (65.9)	9 (7.5)	111 (92.5)	.613
Female	62 (34.1)	6 (9.7)	56 (90.3)	
Risk factors				
Diabetes Mellitus	93 (51.1)	7 (7.5)	86 (92.5)	
Hypertension	109 (59.9)	10 (9.2)	99 (90.8)	
Smoking	21 (11.5)	0 (0.0)	21 (100.0)	
Ischemic heart disease	34 (18.7)	3 (8.8)	31 (91.2)	.049**$
Epilepsy	4 (2.2)	0 (0.0)	4 (100.0)	
Atrial fibrillation	5 (2.7)	0 (0.0)	5 (100.0)	
Heart failure	4 (2.2)	0 (0.0)	4 (100.0)	
CKD	4 (2.2)	2 (50.0)	2 (50.0)	
Unknown	38 (20.9)	3 (7.9)	35 (92.1)	
Large vessel occlusion				
Yes	44 (24.3)	4 (9.1)	40 (90.9)	.824$
No	137 (75.7)	11 (8.0)	126 (92.0)	
Thrombectomy				
Yes	33 (18.1)	2 (6.1)	31 (93.9)	.615$
No	149 (81.9)	13 (8.7)	136 (91.3)	
TPA				
Yes	39 (21.4)	7 (17.9)	32 (82.1)	.013*$
No	143 (78.6)	8 (5.6)	135 (94.4)	

P - Pearson X^2 test, $ - Exact probability test * p<0.05 (significant), CIN - Contrast Induced Nephropathy, CKD - Chronic Kidney Disease, TPA - tissue plasminogen activator

Table 2 - Multiple logistic regression analysis for predictors of developing contrast-induced nephropathy among acute stroke patients underwent brain CT angiography.

Factors	B	S.E.	*P*-value	OR_A	95% CI	
					Lower	Upper
Age in years	0.04	0.03	.123	1.04	0.99	1.10
Male gender	0.21	0.71	.769	1.23	0.31	5.10
Diabetes Mellitus	-0.67	0.72	.353	0.51	0.13	2.10
Hypertension	0.69	0.03	.045*	2.10	1.29	6.98
Smoking	-0.55	1.27	.664	0.57	0.05	6.99
Ischemic heart disease	-0.25	0.89	.778	0.78	0.13	4.48
Large vessel occlusion	0.35	0.93	.711	1.41	0.23	8.79
Thrombectomy	-0.73	1.04	.481	0.48	0.06	3.69
TPA	1.97	0.72	.007*	7.15	1.73	29.59
ICH	1.92	0.87	.027*	6.66	1.23	33.31
fever	-0.38	1.24	.760	0.69	0.06	7.76
Abnormal baseline	2.06	0.77	.007*	7.82	1.74	35.11
Seizures	0.12	1.06	.910	1.13	0.14	9.07

B - regression coefficient, SE - Standard error, ORA - Adjusted odds ration, CI - Confidence interval,*p< 0.05 (significant), ICH - intracerebral hemorrhage, TPA - tissue plasminogen

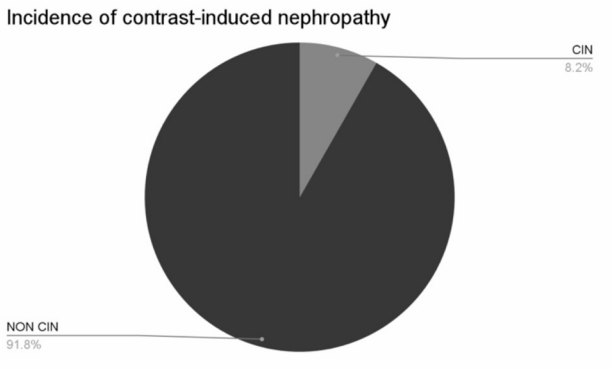

Figure 1 - Incidence of acute stroke patients developing Contrast-Induced Nephropathy (CIN) following CT angiography brain.

95% CI: 1.26-6.98). Intracerebral hemorrhage (ICH) increased the risk of CIN nearly 7 times (OR=6.7; 95% CI: 1.23-33.3). Moreover, an abnormal baseline assessment raised the risk of CIN among stroke patients by approximately 8 times (OR=7.8; 95% CI: 1.74-35.1) (**Table 2**). Furthermore, patients who developed CIN had significantly higher NIHSS scores in the emergency room than those who did not (17.0±6.4 vs. 9.7±6.7, respectively; p=.001). Lastly, the incidence of in-hospital mortality was significantly higher among patients who developed CIN (53.3%) compared to those who did not (12.6%) (p=.001) (**Table 3**).

Discussion. The present study investigated the incidence and risk factors of CIN among patients presented to the emergency room with acute stroke symptoms within 24 hours of symptom onset and underwent brain CT angiography in the emergency setting. The incidence of CIN in our study was found to be 8.24%. This incidence is consistent with previous studies that have reported an incidence of CIN after contrast-enhanced CT ranging from 7% to 11%, depending on the patient population studied.[7-9] We found that patients with abnormal level of SCr were at a higher risk of developing CIN and raised the risk of CIN among stroke patients by approximately 8 times. This is in line with a lot of studies that reported that chronic kidney disease (CKD) and abnormal abnormal level of SCr was a significant risk factor for CIN in

Table 3 - Clinical data characteristics of acute stroke patients developing contrast-induced nephropathy following CT angiography brain.

Clinical data	Total	CIN		*P*-value
		Yes	No	
	No (%)	No (%)	No (%)	
Diagnosis				
ICH	19 (10.4)	4 (21.1)	15 (78.9)	
Ischemic stroke	134 (73.6)	10 (7.5)	124 (92.5)	.150
Mimics	9 (4.9)	0 (0.0)	9 (100.0)	
TIA	20 (11.0)	1 (5.0)	19 (95.0)	
Fever 1st 48 hours				
Yes	5 (2.9)	0 (0.0)	5 (100.0)	.487
No	170 (97.1)	15 (8.8)	155 (91.2)	
Abnormal serum creatinine baseline				
Yes	21 (11.6)	5 (23.8)	16 (76.2)	.006*
No	160 (88.4)	10 (6.3)	150 (93.8)	
Seizures				
Yes	15 (8.2)	2 (13.3)	13 (86.7)	.454
No	167 (91.8)	13 (7.8)	154 (92.2)	
Length of hospital stay				
1-6 days	71 (39.0)	4 (26.7)	67 (40.1)	
7-14 days	54 (29.7)	6 (40.0)	48 (28.7)	
15-30 days	27 (14.8)	3 (20.0)	24 (14.4)	.655
>30 days	30 (16.5)	2 (13.3)	28 (16.8)	
At hospital death				
Yes	29 (15.9)	8 (53.3)	21 (12.6)	
No	146 (80.2)	7 (46.7)	139 (83.2)	.001*
Unknown	7 (3.8)	0 (0.0)	7 (4.2)	
Other factors		Mean±SD		*p*-value #
NIHSS score in ER	10.3±7.0	17.0±6.4	9.7±6.7	.001*
ECHO – Ejection fraction	55.3±10.7	51.6±15.0	55.5±10.3	.322
Hemoglobin	13.9±9.6	11.8±2.4	14.1±9.9	.360
Highest WBCs count 1st 48 hours	9.9±4.6	11.1±4.9	9.8±4.5	.279
HbA1c	7.1±2.1	6.7±2.1	7.2±2.1	.620
Highest glucose level	220.1±152.3	305.3±155.7	214.7±151.1	.049*
LDL	102.5±49.7	111.4±54.1	101.9±49.7	.652

P- Exact probability test, # - independent t-test *$p<0.05$ (significant), ICH - intracerebral hemorrhage, TIA - transient ischemic attack, NIHSS - National Institutes of Health Stroke Scale, WBC - White Blood Cells, LDL - low-density lipoprotein

patients undergoing contrast-enhanced imaging.[10-14] Multiple predisposing risk factors for the development of CIN have been identified, the most important predictor is history of hypertension (HTN), the presence of hypertension in stroke patients doubled the risk of developed CIN; Several studies have indicated an elevated incidence of CIN among patients with a documented HTN.[5,15] Patients with impaired baseline kidney function may have reduced renal reserve and be less able to handle the additional stress imposed by contrast agents and those who receive TPA may be at increased risk for developing CIN after CTA. One observational study reported an increased incidence of CIN among patients who received TPA but did not show any significant difference between the 2 groups (35.5% in TPA treated vs 33.89% in non-TPA treated patients developed AKI).[16,17] This increase in CIN incidence could be explained by complications that could happen among patients who have received TPA. The precise mechanism behind this heightened risk remains less clear; however, it might stem from the interplay between TPA-triggered fibrinolysis and contrast-induced vasoconstriction. Alternatively, it could be attributed to compromised renal function due

to atheroembolic renal disease, a possibility particularly relevant in patients with vascular risk factors. Therefore, it is important to closely monitor kidney function in patients who receive TPA and undergo CTA.[18] Furthermore, our study found that patients with Intracerebral hemorrhage ICH were at a higher risk of developing CIN. Intracerebral hemorrhage increased the risk of CIN nearly 7 times (OR=6.7; 95% CI: 1.23-33.3). This is consistent with previous studies which reported that patients with ICH had a higher incidence of AKI compared to those with ischemic stroke.[19-21] And in line with a meta-analysis conducted in 2018 reported a general prevalence of AKI in acute ischemic stroke patients was 12.9% (95% CI 10.3-15.5), and 19.0% (95% CI 8.3-29.7) in patients with ICH.[20] Our study also found that stroke severity, as measured by the NIHSS score, was significantly higher in patients who developed AKI compared to those who did not. This may suggest that patients with more severe stroke are at increased risk for AKI after CTA, and this consistent with the results of A PRISMA-compliant meta-analysis which reported AKI is a common complication after stroke and high NIHSS score on admission was the critical risk factor for AKI after stroke. However, further studies are needed to confirm this association and to investigate the underlying mechanisms.[19-23] In our study, CIN was associated with a significantly higher incidence of in-hospital mortality among patients who developed CIN (53.3%) compared to 12.6% who did not develop CIN. These results are similar to previous publications which have demonstrated that CIN is a strong and independent predictor of both in-hospital and long-term mortality after stroke.[22-24] Our study investigated several potential risk factors for CIN. We examined whether the presence of fever or seizures within the first 48 hours or an increase in white blood cell count during this period, was associated with an increased risk of CIN. However, our analysis did not reveal any significant correlations between these factors and CIN incidence. Similarly, we found that age and gender were not significantly associated with CIN risk, except for patients over 60 years old who may be at a higher risk. Interestingly, we did not observe any association between CIN incidence and large vessel occlusion stroke or undergoing thrombectomy, despite the latter procedure involving a higher amount of contrast exposure. However, our findings must be interpreted within the context of several limitations. This is an observational study of a single center without a control group, with the intrinsic deficiency of potentially limited external validity and intrinsic bias. In addition, we did not have data on the exact volume of contrast agent used in every patient, which may also be an important predictor of CIN. Further prospective studies with larger sample sizes and more detailed data collection are needed to confirm and expand on our findings. Another non-quantified variable was the volume of intra-arterial or venous hydration during the procedure, although all patients received fluids for the duration of the procedure.

Conclusions. In conclusion, our study found that the incidence of CIN in acute stroke settings was 8.2%, and this incidence was higher in patients with HTN, utilization of Tissue Plasminogen Activator (TPA), and abnormal baseline creatinine levels. Therefore, clinicians managing acute stroke cases should be vigilant of these risk factors. our study adds to the body of evidence indicating that CKD, TPA use, ICH, abnormal baseline creatinine levels, and high NIHSS score are factors that increase the risk of CIN in stroke patients undergoing CTA. While CTA is a vital diagnostic tool in the management of acute stroke, healthcare providers must carefully consider the benefits and risks of contrast administration. Clinicians should be mindful of these risk factors and take appropriate steps to prevent CIN, such as monitoring renal function closely in high-risk patients. Future research is needed to identify other potential risk factors and develop strategies for preventing CIN in stroke patients.

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