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Contrast-associated acute kidney injury following intravenous contrast media computed tomography; new concept and future directions: A systematic review study on emergencies patients

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ABSTRACT

Introduction: Computed tomography (CT) is a key method for various disorders. Image can be more quality with intravenous contrast media, however in some cases may be accompanied by a risk of kidney impairment.
Objectives: This study aimed to investigate the association between acute kidney injury incidence and intravenous contrast media for CT in emergency patients.
Methods and Materials: Search strategies were performed using standard keywords across international databases such as Web of Science, Scopus, Cochrane, PubMed, and Embase. Dimension, OpenGrey, DOAJ, CINAHL, and Google Scholar search engines were searched for a complete search. Additionally, manual searching was conducted using the references of related articles. Studies that reported the correlation between acute kidney injury incidence and intravenous contrast media were included in this systematic review.
Results: First, 1185 studies were identified. After duplication, 533 studies remained and 417 were excluded. Out of 116 evaluated studies for retrieval, 49 were eliminated and 67 were assessed for eligibility. Ultimately, 28 studies with 48878 patients were included in the final review. Most of the studies were retrospective cohorts and have found no significant correlation between the incidence of acute kidney injury and intravenous contrast media administration (ICMA) for CT.
Conclusion: Intravenous contrast media with a conventional dose for CT does not cause acute kidney injury unless in the presence of a particular condition.
Registration: This study was compiled following the PRISMA checklist and its protocol was registered on the PROSPERO (CRD42023448461) and Research Registry (UIN: reviewregistry1690) websites.

Implication for health policy/practice/research/medical education:
In this systematic review of studies that investigated the incidence of acute kidney injury following intravenous contrast media for computed tomography in emergency patients, we found that intravenous contrast media with a usual dose for computed tomography does not cause acute kidney injury unless in the presence of a particular condition such as older age, diabetes mellitus, hypotension, anemia, hypoalbuminemia, estimated glomerular filtration rate < 30 mL/min, and pre-contrast creatinine >1.5 mg/dL.

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Review

Introduction

Computed tomography (CT) due to its high sensitivity and specificity is a practical method in the diagnosis of various disorders (1). There are several benefits to using CT imaging, including its quick availability, lower expenses, shorter scan durations, non-invasively, and improved patient comfort and tolerability (2). To increase the CT image quality, contrast-enhanced computed tomography (CECT) form is developed, which is crucial for diagnosing and treating many urgent medical conditions often seen in emergencies (3). Annually, more than 80 million doses of iodinated contrast media are given globally for performing CT scans, making it one of the most frequently prescribed agents in all fields of medicine (4). One drawback of utilizing a CECT-based imaging system is the potential safety risks associated with the iodinated contrast agents utilized for imaging purposes (2).

Renal failure is a common outcome caused by intravenous contrast media administration (ICMA) and is known as contrast-induced nephropathy (CIN) (5). Post-contrast acute kidney injury (AKI), historically known as CIN (6) is a common form of renal failure that occurs within 48 to 72 hours after ICMA (7). Despite their clinically valuable and widespread use of CECT, deciding whether to administer contrast media can be complicated due to concerns about causing AKI (4). Although with intravenous contrast agent administration image quality can be improved, the risk of AKI is a main consideration (6). This study investigates the incidence risk of contrast-associated AKI following ICMA for CT scans.

Objectives

This study aimed to evaluate the correlation between AKI incidence and ICMA for CT scans in emergency patients.

Methods and Materials

Study design

This systematic review aimed to evaluate the incidence of AKI following ICMA for CT scans in emergency patients. The study protocol was conducted based on PRISMA (Preferred reporting items for systematic reviews and meta-analyses) checklist (8), and registered on the PROSPERO (CRD42023448461) and Research Registry (UIN: reviewregistry1690) website.

Search strategy

Search strategies were conducted using keywords across international databases such as Web of Science, PubMed, Scopus, Embase, and Cochrane, with no place and time limitation. Dimension, DOAJ, OpenGrey, WorldCat, and Google Scholar search engines were searched for a complete search. Additionally, manual searching was conducted using the references of related articles. The search strategy was upgraded until March 2023, using keywords, including acute kidney injury, acute renal insufficiencies, acute renal injury, acute kidney failures, acute renal failures, contrast media, intravenous computed tomography contrast media, radiocontrast agents, contrast agent, radiopaque media, contrast-associated nephropathy, contrast-induced nephropathy, emergencies, and emergency treatment.

Below is an example of a search strategy protocol in PubMed using OR and AND operators:

Search strategy protocol in PubMed as an example of the search strategy in databases using combination words of OR and AND: ((((((((((((Acute Kidney Injury[Title/Abstract]) OR (Acute Renal Insufficiencies[Title/Abstract])) OR (Acute Renal Injury[Title/Abstract])) OR (Acute Kidney Failures[Title/Abstract])) OR (Acute Renal Failures[Title/Abstract])) AND (Contrast Media[Title/Abstract])) OR (Intravenous CT Contrast Media[Title/Abstract])) OR (Radiocontrast Agents[Title/Abstract])) OR (Contrast Agent[Title/Abstract])) OR (Radiopaque Media[Title/Abstract])) OR (Contrast-associated nephropathy[Title/Abstract])) OR (Contrast-induced nephropathy[Title/Abstract])) AND (Emergencies[Title/Abstract])) OR (Emergency Treatment[Title/Abstract])

PICO components

- Population: Patients receiving intravenous CT-contrast media
- Intervention: Use of contrast media agent
- Comparison: Patients who underwent CT without contrast media
- Outcomes: Incidence of AKI following CT-contrast media

Inclusion criteria

Original studies that investigate the correlation between AKI incidence and intravenous contrast media CT in emergency patients.

Exclusion criteria

Exclusion criteria included studies with missing required data, no full-text available studies, low quality, and duplicates. Conference studies, case reports, systematic reviews, meta-analyses, and letter-to-editors' studies also were excluded. Additionally, studies that investigated contrast-associated nephropathy incidence in non-emergence and pediatric patients were excluded.

Quality assessment

For quality assessment, two reviewers separately assessed the articles based on the STROBE (strengthening the reporting of observational studies in epidemiology) checklist for the observational studies. This checklist includes 22 items; each item is worth 2 points, and these points are added together to give a total score. Values 1-15 mean low quality, 16-30 medium, and more than 30 high quality. We set the cutoff point at 15 (9). Any disagreement

was resolved by a third reviewer re-evaluating the article and reaching an agreement on a single option. All included studies were of good quality.

Data extraction

To prevent the risk of data collection bias, two researchers who were not the study searchers, separately derived the data using a checklist, including the first author's name, publication date, place, study design, mean age, sample size, population, AKI definition and incidence, study objective and final results. In case of disagreement, data were re-investigated by a third inspector.

Results

In this review study, studies investigating the correlation between AKI incidence and intravenous CT contrast media in emergency patients were assessed based on the PRISMA guideline. The initial search identified 1185 studies. After duplication, 652 were excluded. Following the abstract review, 417 of 533 remaining studies were removed due to meeting no inclusion criteria, and 116 studies were assessed for retrieval. After assessment for retrieval, 49 studies were excluded, and 67 were evaluated for eligibility. Eventually, 28 studies were included in the final review and 39 were excluded based on exclusion criteria (Figure 1).

Results showed that 28 studies from 10 countries were included in this systematic review. The total sample size was 48878 patients. The biggest study in terms of sample size was conducted by Su et al (10) in Taiwan with 10143 patients, and the smallest was conducted by Tremblay et al (11) in Canada with 56 patients. When it comes to study design, the majority of conducted studies were retrospective cohorts. The biggest AKI incidence rate was reported in the study by Lin et al at 15.9% (12), and the smallest incidence rate was reported by McGillicuddy et al at 1.9% (13). The most common definition for AKI in most of the studies was creatinine (Cr) increase >0.5 mg/dL or > 25% compared to baseline within the initial 48 to 72 hours after exposure to intravenous contrast media. Many studies have found no significant association between the AKI incidence and ICMA for CT scan (Table 1).

Discussion

In a review of 28 studies with a sample size of 48878 people, result demonstrated that the AKI incidence after ICMA for CT scans was reported at the range of 1.9% to 15.9% in different studies. Most studies reported no association between the AKI incidence and ICMA for CT scans, and this dose of contrast media could not cause AKI in septic patients, two studies by Hinson et al (4) and Hsu et al (30) showed that using CECT is not associated with the incidence of AKI. In stroke patients, five studies evaluated the correlation between CECT and AKI incidence, and all

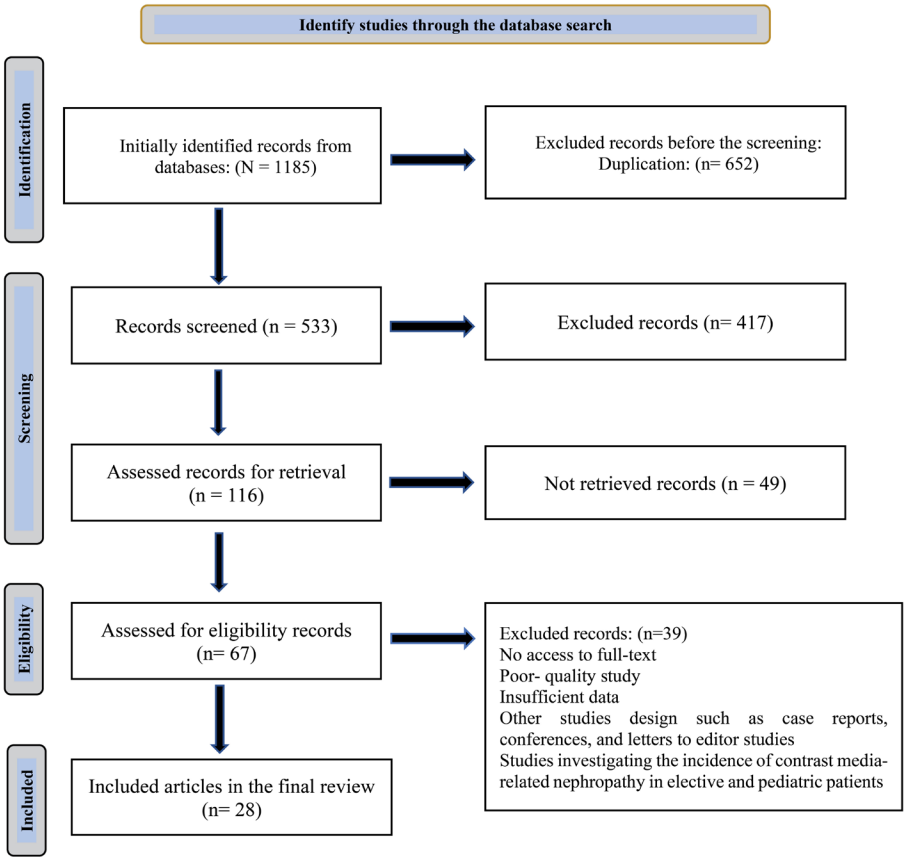

Figure 1. Four phase PRISMA diagram.

Table 1. Baseline information of included studies in the systematic review

First author	Publication years	Country	Study design	Sample size	Population	AKI Incidence (%)	Mean age (y)	Objective	AKI Definition	Results
Hinson (4)	2019	USA	Retrospective cohort	1464	Septic patients	7.2	51	To assess the risk of AKI following ICMA in septic patients	Cr increase >0.3 mg/dL or 1.5 fold increase compared to baseline	There is no correlation between ICM and AKI incidence
Tremblay (11)	2005	Canada	Retrospective	56	Trauma patient	3	48.2	Evaluate contrast nephropathy in trauma patients	Cr increase > 0.5 mg/dL or >25% compared to baseline within the initial 48 hours	In terms of AKI incidence, the benefits of utilizing ICM outweigh its disadvantage
Hopyan (14)	2008	Canada	Cohort study	198	Acute stroke	2.9	65.4	Evaluate the incidence of acute CIN and CKD after Contrast CTA	Cr increase ≥ 25% compared to the baseline within the initial 72 hours	Occurrence of acute and chronic nephropathy following contrast CTA in stroke patients is almost little
Lima (2)	2010	USA	Cohort study	575	Acute ischemic stroke	5	68	Assessment of the acute nephropathy following CECT	Cr increase ≥25% compared to baseline at the time of less than 72 hours	CECT does not increase the risk of CIN
STARSurg Collaborative (15)	2020	UK	Cohort study	1249	Gastrointestinal surgery	NA	63.8	Evaluation of the AKI incidence influenced by preoperative intravenous contrast media	Based on KDIGO definition	There was no risk of CIN after undergoing a contrast-enhanced CT
Mitchell (5)	2010	USA	Cohort study	633	Initial diagnosis in ED patient	11	50	Examining the correlation between CIN and CECT	Cr increase ≥ 0.5 mg/dL or ≥ 25% compared to the baseline in the initial 2 to 7 days	CECT is correlated with the occurrence of CIN and renal failure
Hsieh (16)	2016	Taiwan	Cross-sectional study	326	Blunt splenic injury patients	10	36.3	Assessment the risk of AKI incidence following CECT	Cr increase > 0.5 mg/dL or > 25% compared to baseline within 48 h	CECT with or without angiography is not correlated with CIN
Ferrer Puchol (17)	2019	Spain	Cohort study	6642	Initial diagnosis in ED patient	7.72	65.71	Assessment of the correlation of IV contrast CT with AKI incidence	Increase of 0.3-0.5 mg/dL or a 25-50% increase of Cr compared to baseline	CECT was not associated with increased AKI
Burgess (18)	2022	USA	Retrospective study	67	Burn Patients	9.1	42.6	Investigation of the incidence of AKI in burn patients following IV contrast CT	2-fold increase in Cr level compared to baseline	There was no meaningful difference in the occurrence of AKI with IV contrast in comparison to without
Heller (19)	2016	USA	Retrospective study	6954	Initial diagnostic CT for ED patient	8.6	54	To assess the correlation between IV contrast and CIN	Cr increase > 0.5 mg/dL or > 25% compared to baseline	There is no significant correlation between IV contrast CT and CIN
Demel SL, (20)	2017	USA	Population-based study	204	Stroke Patients	1.5	58.2	Evaluation of the correlation between AKI and IV contrast CT scan	NA	We found no correlation between AKI and IV contrast for CT in stroke patients

Table 1. Continued

First author	Publication years	Country	Study design	Sample size	Population	AKI Incidence (%)	Mean age (y)	Objective	AKI Definition	Results
Su TH, (10)	2021	Taiwan	Retrospective study	10143	Diagnostic CT in ED patient	10.9	66	Evaluation of the correlation between AKI incidence and ICMA	Cr increase > 0.3 mg/dL or > 50% compared to the baseline during 48-72 h from admission	There was no correlation between AKI and CECT except in the presence of eGFR less than 30 mL/min
Ehrlich (21)	2016	USA	Retrospective study	157	Acute Stroke Patients	3.18	66.7	Investigating the incidence rate of AKI after CTA in stroke patients	Cr increase > 25% compared to baseline	There was no correlation between the occurrence of AKI and CTA in stroke patient
Huang (22)	2013	Taiwan	Retrospective study	594	Diagnostic CT in elderly ED patient	8.6	79.8	Assessment of the occurrence of CIN in elderly patients following IV-CM for CT	Cr increase >0.5 mg/dL compared to baseline	We found no correlation between AKI occurrence and IV contrast unless in the presence of risk factors such as hypotension, diabetes, and pre-contrast Cr >1.5 mg/dL
Lin KY, (12)	2018	China	Prospective study	558	Patients with ACS undergoing emergent PCI	15.9	64.3	Evaluating the correlation between the occurrence of CI-AKI and hyperglycemia as a risk factor	Cr increase > 0.3 mg/dL or > 50% compared to baseline	The increased risk of CI-AKI was found only in the presence of hyperglycemia as a risk factor for ACS patients who underwent PCI
Dagar (23)	2022	China	Retrospective study	631	Initial diagnostic CT in ED patients	4.9	52	To assess the risk of CI-AKI following IV-CM in the ED patients	Cr increase > 0.5 mg/dL or > 25% compared to baseline within 48-72 hours after administration	There was no correlation between the occurrence of AKI and IV-CM except in the presence of the risk factors such as older age, hypotension, anemia, and hypoalbuminemia
Lee MJ, (24)	2019	South Korea	Cohort study	327	Initial diagnostic CT in ED patients	9.79	63.84	Evaluate the correlation between AKI incidence and diastolic dysfunction	Cr increase >0.5 mg/dL or >25% compared to baseline	There is a significant correlation between the incidence of AKI and CECT in the patients with diastolic dysfunction
Cho A, (25)	2019	South Korea	Retrospective study	632	Pulmonary embolism patients	6.49	NA	Investigate the occurrence of AKI in pulmonary embolism patients undergoing CTPA	Cr increase > 0.3 mg/dL or 1.5-1.9 fold compared to baseline	There was no significant association between the incidence of AKI and CTPA
Petek BJ, (26)	2016	USA	Cohort study	94	Survivors of sudden cardiac arrest patients	12.8	58	Assessment of the AKI incidence following IV contrast within the initial 24 hours	A 0 to 3 ordinal scale according to the change (baseline to peak) in Cr levels within the initial 48 hours	There was no significant association between the incidence of AKI and IV contrast in survivors of sudden cardiac arrest patients
Yoshizawa J, (27)	2023	Japan	Retrospective observational	262	Initial diagnostic CT in the hypotension patients at the ED	11.8	64	Evaluation of the AKI incidence in the transient hypotension patients	Cr increase ≥ 0.5 mg/dL or ≥ 25% compared to baseline within 72 hours after CT	Incidence of AKI is associated with IV-CM at the presence of transient hypotension

Table 1. Continued

First author	Publication years	Country	Study design	Sample size	Population	AKI Incidence (%)	Mean age (y)	Objective	AKI Definition	Results
Bashir (28)	2019	South Africa	Prospective study	755	Trauma patient	5.4	31	Investigate the incidence of CIN in trauma patients undergoing CECT	Based on KDIGO definition	CIN is a serious risk in trauma patients undergoing CECT
Sorimachi (29)	2019	Japan	Retrospective study	1082	Initial diagnostic CT in ICH patients at the ED	9	66.4	Assessment of the benefits of CTA in terms of AKI incidence	Cr increase > 0.5 mg/dL or > 25% compared to baseline within 72 hours after CTA	The incidence of AKI is not associated with CTA
Hsu (30)	2019	Taiwan	Cohort study	105	Sepsis patient	12.4	64.3	Evaluating the association between the use of CECT and AKI incidence in patients with sepsis	Cr increase > 0.5 mg/dL or > 50% compared to baseline within 48 to 72 hours after CECT	The use of CECT is not correlated with the incidence of AKI
McGillicuddy EA, (13)	2010	USA	Cohort study	760	Elderly trauma patients	1.9	71.6	Evaluation of the AKI rate in elderly patients undergoing IV contrast CT	Chloride increase > 0.5 mg/dL or > 50% increase compared to baseline within initial 72 hours	ICM in elderly patients cannot increase the risk of AKI
Kene (31)	2021	USA	Cohort study	5980	Initial diagnostic CT in CKD patients at the ED	13.2	NA	Assessment of the AKI incidence among ED patients with pre-existing CKD undergoing CECT	Cr increase > 0.3 mg/dL or 1.5-Fold compared to baseline within 72 hours after exposure	In pre-existing CKD patients, CECT is associated with increased risk of AKI
Sonhaye (32)	2015	Togo	Prospective study	1068	Initial diagnostic CT in ED patients	4.77	51	Evaluation of AKI following CT-ICMA	Cr increase > 0.5 mg/dL compared to the baseline	No correlation was found between AKI incidence and CT-ICMA unless in the diabetes patients
Hinson (33)	2017	USA	Retrospective study	7201	Initial diagnostic CT	10.2	53	Investigating the relationship between IV contrast CT and AKI incidence	Cr increase > 0.5 mg/dL or > 25% compared to baseline	ICM was not associated with AKI incidence
Brito (34)	2020	Spain	Cohort study	161	Acute Ischemic Stroke	6.2	73.07	The assessment of the incidence of AKI after IV-ICM exposure in Ischemic Stroke patients	Cr increase > 0.3 mg/dL within initial 48 or > 50% increase within initial 72 hours compared to baseline	There was no significant association between the occurrence of AKI and IV-ICM

eGFR, Estimated glomerular filtration rate; PCI, Percutaneous coronary intervention; CTA, Computed tomography angiography; ED, Emergency department; IV-CM, Intravenous contrast media; CTPA, Computed tomographic pulmonary angiogram; ICH, Intracerebral hemorrhage; KDIGO, Kidney Disease: Improving Global Outcomes; ICM, Iodinated contrast media; CI-AKI, Contrast-induced acute kidney injury; ACS, Acute coronary syndrome; CKD, Chronic kidney disease; NA, Not available.

found no significant correlation (2,14,20,21,34).

In trauma patients, two studies by Tremblay et al (11) and McGillicuddy et al (13) reported that ICM in trauma patients cannot increase the risk of AKI; however, Bashir et al (28) stated that CIN is a serious risk following CECT. A study by Mitchell et al (5) also stated that CECT is associated with CIN incidence and renal failure.

Some studies on initial diagnostic CT in ED patients demonstrated no significant correlation between the incidence of AKI and ICMA for CT scans (4,17,19,29). The other studies on burn patients (18), gastrointestinal surgery (15), blunt splenic injury (16), pulmonary embolism (25), and survivors of cardiac arrest patients (26) reported that ICMA does not increase the risk of AKI after CT scans in emergency patients.

On the other hand, some studies reported that specific situations can increase the risk of AKI incidence after the ICMA for CT scans; Su et al stated that ICMA in the presence of eGFR less than 30mL/min increases the risk of AKI incidence (10). Huang et al reported that the correlation between AKI occurrence and IV contrast cannot be significant unless in the presence of risk factors such as hypotension, diabetes, and pre-contrast Cr >1.5 mg/dL (22). In a study by Dagar et al, older age, hypotension, anemia, and hypoalbuminemia were reported as the most common risk factors for the incidence of AKI following contrast media administration (23). Hyperglycemia (12), diastolic dysfunction (24), transient hypotension (27), pre-existing CKD factors (31), and diabetes mellitus (32) were the other reported risk factors for AKI incidence after contrast media administration in reviewed studies.

Conclusion

The review of the literature showed that intravenous contrast media with a dose of CT scans doesn't cause AKI except in the presence of a specific situation such as older age, diabetes mellitus, anemia, hypoalbuminemia, hypotension, eGFR < 30 mL/min, and pre-contrast Cr >1.5 mg/dL. The results of our study can be a valuable resource for doctors who may be worried about the impact of CECT on kidney function.

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Authors' contribution

Conceptualization: Hamidreza Khodabandeh and Hussein Soleimantabar.
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Writing–reviewing and editing: Negar Jafari, Hanie Fooladi, Ali Zolfi gol, and Reza Faramarzzadeh.

Conflicts of interest

There are no competing interests.

Ethical issues

This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (International Prospective Register of Systematic Reviews) website with (ID: CRD42023448461) and Research Registry website with (UIN: reviewregistry1690). Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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