Risk factors for contrast-induced nephropathy on computed tomography: an integrative review

Fatores de risco para nefropatia induzida por contraste na tomografia computadorizada: uma revisão integrativa

ABSTRACT

Objective: To identify the risk factors associated with contrast-induced nephropathy in patients undergoing computed tomography. Method: integrative review. The time frame was carried out in the period from 2019 to 2023, including publications in Portuguese and English. Search sites were MEDLINE/PubMed, LILACS, WOS, Scopus, and the SciELO library, using the PRISMA method for selecting articles. The descriptors used were: “Nursing”, “Nephrology Nursing”, “Risk Factors”, “Contrast Media” and “Nephropathy”, only 8 met the inclusion criteria. Results: Given the high prevalence of these injuries, the severity of their consequences, Results: Given the high prevalence of these diseases and the severity of their consequences, knowing the risk factors for their development will allow us to verify the incidence of induced nephropathy in the articles. The main risk factors were elderly, heart failure, female gender, hypertension, diabetes, non-steroidal anti-inflammatory drugs, glomerular filtration rate. Conclusion: Based on the review performed, the main risk factors identified were: advanced age, female gender, pre-existing comorbidities such as hypertension and diabetes mellitus, use of medications for such comorbidities and others such as non-steroidal anti-inflammatory drugs and antibiotics, a lower glomerular filtration rate, and increased serum creatinine rate. Descriptors: Nursing; Nursing in Nephrology; Risk Factors; Contrast Media; Kidney Diseases

RESUMO

INTRODUCTION

The use of Computed Tomography (CT) with the use of iodine contrast has increased gradually over the years, and one of the main complications of this procedure is the Contrast-induced nephropathy (CIN), also known as contrast-induced acute kidney injury (CI-AKI). This is a renal injury, secondary to iatrogenic caused by the intravascular administration of contrast media in patients who are more susceptible to this problem.\(^1,4\)

Despite all technological advances to minimize the aggravation caused by contrast media, CIN is the third cause of acute kidney injury in hospitalized patients, presenting a lower incidence only when compared to diseases causing renal hypoperfusion and the use of nephrotoxic drugs, respectively.\(^5-6\)

First described in 1950, CIN results from toxicity affecting the tubular epithelial cells, with subsequent changes in renal hemodynamics. It is believed that this disorder is divided into two phases, starting with a prolonged vasodilation, which promotes a decrease in renal blood flow, associated with the release of endogenous factors, which evolves to vasoconstriction and, consequently, hypoxia and tissue ischemia.\(^7,10\)

Several authors define CIN as a serum creatinine elevation above 0.5 ml/dL or more than 25% above baseline, between 48-72 hours after intravenous contrast administration, in the absence of other justification for the creatinine increase.\(^1,3, 10\)

Considering this context, the importance of nursing work arises, since within the care scenario, the professionals of this category are the main actors in health promotion. The main risk factors for the development of CIN are advanced age (>60 years), female gender, heart failure (HF), dehydration, Systemic Arterial Hypertension (SAH), Diabetes Mellitus (DM), use of nephrotoxic drugs, inflammatory process, anemia, type, and volume of contrast infused.\(^1,4\)

Thus, knowing the risk factors associated with contrast-induced nephropathy in patients undergoing computed tomography allows the development of protocols that facilitate its early recognition and minimize the risk of an unfavorable outcome.

OBJECTIVE

To identify the risk factors associated with contrast-induced nephropathy in patients, undergoing CT scanning.
METHOD

This is an integrative literature review, whose comprehensive, unbiased, and reproducible methodology locates and systematizes evidence from scientific studies to answer the research question: "What are the risk factors for contrast-induced nephropathy in patients undergoing computed tomography?"

The "Population, Intervention, Comparison, Outcome, Study design (PICo) research strategy was used: P: nephropathy patients; I: Identification of risk factors; Co: Improvement in care\textsuperscript{11,12} for the construction of the research question, to make the search directed toward clinical and scientific evidence.

Given the above, the following question arises and guides the study: what are the risk factors for contrast-induced nephropathy in patients undergoing computed tomography?

The searches were conducted between March and April 2023, in the Medical Literature Analysis and Retrieval System Online (MEDLINE)/National Library of Medicine (PubMed), Latin American and Caribbean Literature on Health Sciences (LILACS), Web of Science (WOS), Scopus, and the Scientific Electronic Library Online (SciELO) databases. The descriptors used were those in the Health Sciences Descriptors (DeCS): "Kidney Diseases", "Contrast Media", "Tomography", "Emission-Computed Tomography" and "Risk Factors" and in the MeSH (Medical Subject Headings): "Kidney Diseases", "Contrast Media", "Tomography", "Tomography, Emission-Computed" and "Risk Factors" and the Boolean operator "AND" and "OR" for the crossing between them.

Two cross-references were performed for the database searches, using the descriptors in the MeSH as follows: first: Kidney Diseases AND Contrast Media AND Tomography AND Risk factors, and second: Kidney Diseases AND Contrast Media AND Tomography, Emission-Computed AND Risk factors.

The eligibility criteria were full articles published from 2019 to 2023, available in the listed databases in Portuguese and English, as well as those addressing the risk factors for the occurrence of contrast-induced nephropathies in patients undergoing computed tomography. The choice of articles published within the last five years (2019 to 2023) aimed to search for recent evidence on the object of study. We excluded articles in the format of editorials, letters to the editor, abstracts, expert opinion, reviews, reviews, as well as books, book chapters, theses, dissertations, monographs, and other formats of course completion work not published in scientific article format.

Based on cross-referencing the descriptors in the databases, 845 articles were found, of which MEDLINE/PubMed $n = 10,694$, Scopus $n = 10$, SciELO $n = 19$, WOS $n =$
2 and LILACS n = 12. Subsequently, duplicate articles, literature reviews, and articles with full texts unavailable were excluded, leaving 102 articles selected for reading of the title and abstract, of which n = 29 articles were selected for the full reading stage. After reading the full text, n = 8 articles were excluded for not responding to the study objective, and n = 8 articles were selected for the analysis because they met the inclusion criteria and addressed the theme of this integrative review (figure 1).

Figure 1. Flowchart of the article selection steps on risk factors for contrast-induced nephropathy in patients undergoing computed tomography. Recife (PE) Brazil, 2023.

The selection of articles followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)\(^{13}\). In the first stage, two independent researchers read the titles, without knowing the authors and the journal in which they were published. The second stage took place after the repeated articles were excluded, and a thorough reading of the titles and abstracts was performed to determine which ones fit the determined criteria. Disagreements were resolved by consensus. In the third step, the selected studies were read in their entirety to select those to be included in this review. The electronic searches resulted in 845 studies, as shown in Figure 1.
For classification and analysis of the level of evidence of the articles, we used the GRADE\textsuperscript{14} system, a system developed by a collaborative group of researchers that aims to create a universal, transparent, and sensitive system to grade the quality of evidence and strength of recommendations. The quality of evidence is graded into four levels: high, moderate, low, and very low. These levels represent the confidence we have in the estimation of the effects presented.\textsuperscript{14}

The GRADE system is subdivided into four levels: High - characterized by strong confidence that the effect is close to the estimated one, sourced from well-designed clinical trials; Moderate - where confidence in the estimated effect is moderate, based on well-designed clinical trials, with the possibility that future work may modify the confidence; Low - confidence in the effect is limited, where future work is likely to have a major impact on the confidence of the findings, usually evidenced in moderately limited clinical trials and comparative observational cohort and control studies; Very Low - confidence is very limited, there is a major degree of uncertainty in the study findings, any estimate is of an uncertain nature.\textsuperscript{14} The quality of evidence is classified into four levels: high, moderate, low, and very low.

**RESULTS**

The eight selected articles were organized according to author/authors, year of publication, country of publication, type of study, sample number, time of execution and place of study, as described in Table 1. There was a predominance of articles in the retrospective study and cohort study modalities.

<table>
<thead>
<tr>
<th>Study</th>
<th>Author/Year</th>
<th>Country</th>
<th>Study Type</th>
<th>Sample</th>
<th>Execution Time</th>
<th>Study location</th>
</tr>
</thead>
<tbody>
<tr>
<td>E1</td>
<td>Ghelichi-</td>
<td>Iran</td>
<td>Case-control study</td>
<td>700</td>
<td>6 months</td>
<td>Hospital Base</td>
</tr>
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<td></td>
<td>Ghojogh et al.</td>
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</tr>
<tr>
<td></td>
<td>2022.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E2</td>
<td>Rowe et al.</td>
<td>United States</td>
<td>Case-control study</td>
<td>209</td>
<td>42 months</td>
<td>Emergency</td>
</tr>
<tr>
<td></td>
<td>2019.</td>
<td></td>
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</table>

Table 1. Characterization of the selected studies, regarding author, year, country, type of study, sample, time of execution and study site. Recife (PE) Brazil, 2023.
As for the level of evidence of the studies, two had high level of evidence, and two had moderate level of evidence, as presented in table 2 for better understanding and visualization of the information.

Table 2. Specification of the selected studies as to objective, level of evidence, results, and conclusion. Recife (PE) Brazil, 2023.

<table>
<thead>
<tr>
<th>Study</th>
<th>Objective</th>
<th>Level of Evidence (GRADE) (14)</th>
<th>Risk Factors</th>
<th>Results and Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>E1</td>
<td>Investigate the health-related risk factors of patients with chronic kidney disease.</td>
<td>High</td>
<td>Age (20 to 60 years), gender (male, due to greater genetic pre-disposition and exposure to influential factors), family history of kidney disease, primary kidney disease, urinary tract infections, cardiovascular disease, DM, and nephrotoxins.</td>
<td>The results pointed out that the average cases and control are approximately 59.6% and 12.2% for factors linked to chronic kidney disease.</td>
</tr>
<tr>
<td>E2</td>
<td>To investigate the prevalence of risk factors associated with contrast-</td>
<td>Low</td>
<td>Age, gender, race, first weight upon admission, vital signs, comorbidities (hypertension, heart failure, &quot;Patients with a history of DM or those who reported taking no</td>
<td></td>
</tr>
</tbody>
</table>

induced nephropathy in patients with ischemic stroke.

<table>
<thead>
<tr>
<th></th>
<th>To evaluate the frequency of diagnosis in intracranial aneurysms to describe autosomal dominant polycystic kidney disease in these patients.</th>
<th>Moderate</th>
<th>Age less than 50 years, sex, family history of intracranial aneurysms, previous history of hypertension.</th>
<th>The odds of prior diagnosis of intracranial aneurysms were n = 3.9% for patients aged 50 years, n = 6.2% for those aged 60 years, and n = 8.1% for those aged 70 years, respectively. Furthermore, these risks were similar for male and female subjects &lt;50 years, after that age, the risks increase brutally for female patients, reaching n = 10.8% and n = 5.4% at 70 years.</th>
</tr>
</thead>
<tbody>
<tr>
<td>E3</td>
<td>Evaluate hospitalized patients with acute kidney injury reduced by drug use.</td>
<td>Moderate</td>
<td>Female gender, chronic kidney disease, history of adverse drug reactions of any kind, and drug-induced acute kidney injury.</td>
<td>It was seen that out of 1,557 patients, n = 445 (20.6%) with acute kidney injury were drug induced (180 CA-AKIs (40.4%) and 265 HA-AKIs (59.6%)).</td>
</tr>
<tr>
<td>E4</td>
<td>To evaluate the incidence of post-contrast acute kidney injury in stroke patients receiving a contrast agent for CT</td>
<td>Moderate</td>
<td>Age, sex, secondary diagnosis, hypertension, DM, heart failure, ischemic cardiovascular disease, use medications at home were more likely to develop CIN. Incidence of CIN was 14.8%.</td>
<td></td>
</tr>
</tbody>
</table>
1089 consecutive ischemic stroke patients who had CT angiography, perfusion CT angiography, and mechanical thrombectomy, followed by a standardized hydration protocol with ringer's solution, at our large tertiary neurovascular center for a 3-year period.

| E6 | Examine the association of kidney disease and risk of future dementia. | Moderate | Kidney disease, future dementia, age, hypertension, and DM. The mortality rates in the 5 target years of the study were identified as 2.9% in patients with dementia and with kidney disease, 2.98% in the general population studied. |
| E7 | To evaluate the association of albuminuria and the risk of end-stage kidney disease. | Moderate | End-stage renal disease, associations between change in albuminuria and risk of end-stage renal disease, patient age, gender, race or ethnicity, DM, history of cardiovascular disease problems, smoking, systolic blood pressure, total cholesterol, creatinine measurements, hypertension status, use of antihypertensive medication, and estimated glomerular filtration rate, as well as mortality and end-stage renal disease events. The present study reports controversies between the association of serum creatinine and change in albuminuria and other 50 events in outcomes of interest. |
| E8 | To identify the risk factors for contrast-induced nephropathy in patients who underwent percutaneous trans luminal coronary angioplasty procedure. | Moderate | Gender, ethnicity, underlying disease, age (+18 years), cardiovascular risk factors, and education. The study analyzed a total of 87 medical records, with an age range of 58.6%. When questioned about the risk factors, cardiovascular and comorbidities found were hypertension, 77 (88.5%); dyslipidemia, 46 (52.9%); DM, 33 (37.9%) and... |
DISCUSSION

Iodine contrasts are widely indicated and used in the health practice, and their deleterious potential to the renal function is already widely recognized in the literature. The incidence of CIN may vary from 10% to 30%, depending on the definition used for its diagnosis and on the characteristics of the studied population.\(^{15}\)

Still, iodine contrast agents can be ionic and non-ionic, and there are studies\(^{7-10}\) which indicate that both have a high nephrotoxic potential. In a Brazilian study, it was shown that the use of an isosmolar non-ionic contrast medium was associated with a higher occurrence of CIN, when compared to a low osmolarity ionic contrast, with a 2.3-times increase in the chance of CIN occurrence, especially when associated with other risk factors and comorbidities.\(^{16,10}\)

In the presentation of results, studies show the main risk factors for CIN: age (especially the elderly, due to organic and immunological changes), gender (especially females), pre-existence of comorbidities of SAH and DM, use of medications (especially those with nephrotoxic potential, such as diuretics, hypoglycemic agents, and antibiotics), lower glomerular filtration rate (GFR) and increased serum creatinine.\(^{1,9,17-20}\)

Regarding gender, studies indicate that females are more prone to decreased GFR and, consequently, kidney injury.\(^{21-23}\) Hence, the study\(^{24}\) showed that the prevalence of chronic kidney disease is 67.71% for women, and the causes of this propensity are not clear, being established as a controversial issue in the literature.\(^{21}\)

Chronic non-communicable diseases, such as DM and SAH induce changes in specific organ groups, with emphasis on arterial stiffness, endothelial dysfunction, left ventricular hypertrophy and a microalbuminuria in kidney lesions, besides increasing glomerular injury. These factors are related to the association of chronic kidney disease and not only to demographic and non-communicable variants, age or even gender.\(^{25-26}\)

The kidney is exposed to several endogenous and exogenous substances due to its excretion function and hydro electrolytic concentration, and as many of them have nephrotoxic potential, they influence acute kidney injury. Among these substances, besides contrast media, there are antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), hypoglycemic agents, and diuretics, among others.\(^{27}\) Thus, when the kidney is exposed to these substances, concomitantly with the risk of acute kidney injury, the risk of CIN also increases, as shown in most studies.\(^{1,9,19-20}\)
However, it has been demonstrated that its normality is not necessarily synonymous with the absence of renal function impairment, and it can be a relatively late parameter for lesion detection. The other more reliable parameter to evaluate renal function is the determination of glomerular filtration, which was used in all studies of the sample.

Moreover, it can be obtained through creatinine clearance in 24-hour urine, the most used laboratory test because it precedes the onset of disease symptoms. When it cannot be performed, one can use formulas that predict the glomerular filtration rate from equations, such as the Cockroft-Gault equation and the one derived from the Modification of Diet in Renal Diseases study, also used by Porto et al. in their study.

Due to the existence of all the risk factors inherent to the process, a careful and stratified measurement of the renal function of these patients submitted to contrast-enhanced exams is necessary, based on the calculation of the GFR and the presence of associated pathologies, to enable the encouragement of the implementation of preventive measures and to elucidate issues concerning the kidney injury and, consequently, the minimization of the number of hospitalizations and injuries related to CIN.

The study limitations observed refer to the fact that, despite the synthesis of the knowledge of the selected studies being primary studies with predominant levels of evidence between moderate and high, there were variables in heterogeneous conditions such as sample, time, and place of study. It is also noteworthy the difficulty in finding studies that could answer to the objective and guiding question target of this study.

It is also evident the incipient research on the subject in populations with epidemiological contexts in which external causes occupy a prominent position among health problems and, therefore, are likely to influence the risk factors determining NIC.

**CONCLUSION**

Based on the review performed, the main risk factors associated with nephropathy are: advanced age; female gender; and pre-existence of comorbidities, such as arterial hypertension and DM, use of medications for such comorbidities and others such as nonsteroidal anti-inflammatory drugs and antibiotics, a lower glomerular filtration rate and increased serum creatinine rate.

The knowledge about such risk factors is relevant to support the development of protocols aimed at minimizing the damage caused by contrast agents, especially in the nursing context, since these are the professionals who deal directly and more closely with patients in diagnostic imaging services and health care, playing a key role in knowing
these characteristics and minimizing risks. Still, on this premise, the lack of further studies was observed, due to the scarcity of studies on the target theme, being seen the need for the advancement of knowledge.

CONTRIBUTIONS

All authors contributed equally to all phases of the study, namely: conception of the research project, search, analysis, interpretation, and discussion of the data, as well as writing and critical review of the content with intellectual contribution and approval of the final version of the scientific article.

CONFLICTS OF INTERESTS

Nothing to report.

REFERENCES


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