

Factors associated with contrast-induced nephropathy in hospitalized patients who underwent computed tomography

Factores asociados a la nefropatía inducida por contraste en pacientes hospitalizados a quienes se les realizó tomografía axial computarizada

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Abstract

Introduction: Contrast-induced Nephropathy is the third most common cause of acute renal failure in patients. It has been observed in several studies that an important factor is the usage of a contrast given via IV and the angiograms. Our goal is to identify the factors associated to a Contrast-induced Nephropathy in patients who had a computerized axial tomography through an iodine contrast in a health institution of high complexity in Neiva, Colombia during 2016.

Material and methods: A case study and non-matched tests were applied in 108 patients (36 cases and 76 tests), who had a computerized axial diagnostic or therapeutic tomography through an iodine radiological contrast.

Results: The factors associated to contrast-induced Nephropathy, through a contrast dye, found in patients who had a CAT were the gender (male) (OR=3.22; CI=95 % 1.33 – 7.76; p=0.009) and the place where the procedure was made (hospitalization in general wards) (OR=0.26; CI=95 % 0.07 – 1.00; p=0.051).

Key words: Acute kidney injury, computed tomography, contrast media, risk factors.

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Resumen

Introducción: la nefropatía inducida por medio de contraste es la tercera causa de insuficiencia renal aguda en pacientes hospitalizados. En múltiples estudios se ha observado que un factor importante para su desarrollo es el uso de medio de contraste vía intraarterial y en las angiografías en general. Nuestro objetivo es identificar los factores asociados a nefropatía inducida por contraste en pacientes hospitalizados, a quienes se les realizó tomografía axial computarizada con medio de contraste yodado en una institución de salud de alta complejidad de Neiva, Colombia, durante el 2016.

Materiales y métodos: se desarrolló un estudio de casos y controles no pareado con 108 pacientes, 36 casos y 72 controles hospitalizados llevados a tomografía axial computarizada diagnóstica o terapéutica con medio de contraste radiológico yodado.

Resultados: los factores asociados con nefropatía inducida por medio de contraste encontrados en los pacientes hospitalizados llevados a TAC contrastada fueron, el sexo (hombre) (OR=3,22; IC=95 % 1,33 - 7,76; p=0,009), y el servicio de procedencia (hospitalización en sala general) (OR=0,26; IC=95 % 0,07 - 1,00; p=0,051).

Palabras clave: Insuficiencia renal aguda, tomografía computarizada, medio de contraste, factores de riesgo.

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Introduction

It is estimated that every year in the world, about two million people die from acute kidney failure and those who survive have a higher risk of developing chronic kidney disease. Studies on hospital acquired acute renal failure in developed countries show that this complication generates between 3.2 and 9.6 % of the hospitalizations, and it has a mortality rate of 20 %, and up to 50 % in the patients of the Intensive Care Unit.^{1,2,3}

Contrast-induced nephropathy¹ has been reported as the third leading cause of intrahospital acute renal failure.^{3,4,5,6,7} In some countries like the United States, the iodinated radiological contrast media are used annually in more than ten million procedures, and it is estimated that the probability of developing contrast-induced nephropathy (CIN) in a person who has one or more risk factors is 20.7%-23.3%.⁸ This risk is more than tenfold higher than that of a person without an underlying disease (1.5 %-2 %).³

In Latin America, Da Silva reported that the incidence of CIN after a computed tomography is 3.75 %-15.75 %.⁹ The studies have demonstrated an association between CIN and adverse clinical outcomes, such as cardiovascular complications, requirement for dialysis and death.^{4,6,8}

The guidelines for the prevention of CIN have been prepared with patients of interventional cardiology, a population that differs from the patients taken to tomography. For this reason, the risk factors should be identified and assessed in the group of patients who are going to undergo a diagnostic or therapeutic procedure with iodinated radiological contrast media.¹⁴ The identification of patients at risk of CIN will be useful at the time of making clinical decisions to reduce the incidence of the disease, for the optimization of resources and targeting of preventive actions.

Materials and methods

A non-matched case-control study was conducted in patients hospitalized in the observation, emergency and hospitalization (general and ICU)

services, who underwent diagnostic or therapeutic computerized axial tomography with iodinated radiological contrast medium. The study was developed in a healthcare institution of III/IV level of complexity of the private sector, a benchmark in the Southern Colombian region, which serves users of the healthcare system in Neiva, Colombia, during 2016.

We worked with the population census (Figure 1), by sampling exhaustion until finding cases (cumulative incidence sampling), and looked for a scenario of controls that would be plausible 1:2. According to the foregoing, with a confidence level of 90 %, the power calculated based on the normal approximation method was 80 %.

Type of contrast: according to the institutional protocol, the contrast media was administered intravenously and the dose was not variable.

Definition of case: hospitalized patient who underwent contrasted CAT scan and who 48, 72 or 120 hour after reported a relative increase in serum creatinine greater than 25 % or an absolute increase greater than or equal to 0.5 mg/dL with respect of its value prior to the tomography.

Definition of control: hospitalized patient taken to contrasted CAT scan who 48, 72 or 120 hours after did not develop the event of the study.

Inclusion criteria: patients taken to a CAT scan with iodinated radiologic contrast media, older than 18 years, hospitalized in general ward, ICU and emergency observation ward.

Exclusion criteria: patients who underwent an interventional cardiology procedure and/or who received another dose of contrast medium in less than 72 hours.

Measures of central tendency, dispersion, proportions and ratios were used for data analysis, according to the type of variable. The epidemiological association measure used was the Odds Ratio and the binary multivariate logistic regression model was used applying the method of introducing variables

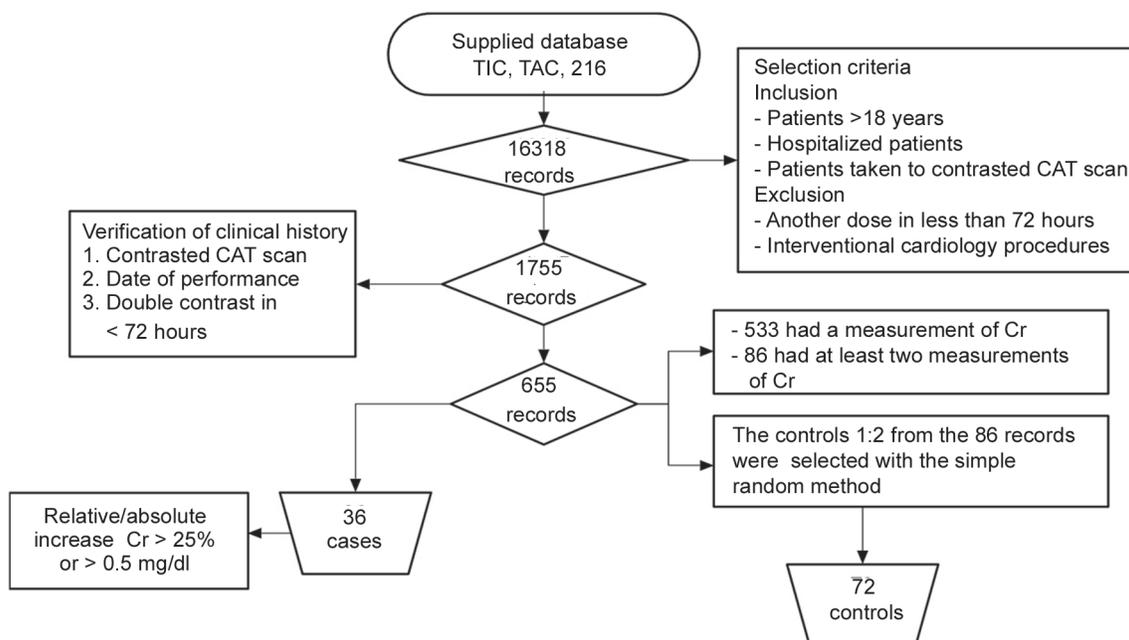


Figure 1. Selection of hospitalized patients taken to contrasted CAT scan, Neiva, Colombia, 2016.

(Enter) based on criteria of plausibility and previous evidence. The statistical package STATA 14.0 was used to carry out the analyses.

This research was classified as without risk according to resolution 8430 of 1993, the ethical principles established in the Belmont Report were taken into account and the informed consent of the custodian of the clinical history was obtained.

Results

During the year 2016, 655 patients hospitalized in a high complexity institution of Neiva, Colombia, were taken to contrasted tomography. Among them, 122 (18.6%) had at least two measurements of creatinine, one before the procedure and another at 48-72 hours, or until the fifth day. This allowed the configuration of the cases (36) and the selection of the controls (72). The most frequent type of CAT was the abdominal (72.2 %).

The demographic and clinical characteristics of the 108 patients are shown in Table 1. The incidence of CIN1 was 5.5 %. No differences between cases

and controls were found, except in the gender variable ($p=0.0140$).

When exploring the relationship between CIN and the demographic and clinical characteristics of interests reported in the literature (Table 2), the association with the gender variable was maintained (OR=2.8; CI=95% 1.12 – 7.11, $p=0.0143$). However, a non-significant association was also found between CIN and age, hematocrit, MPA, eGFR, diabetes, CHF and nephroprotection.

When adjusting the possible confounding factors (Table 3), CIN was found associated with the gender and the service of origin (hospitalization in general ward).

Discussion

Iodinated contrast media are commonly used in diagnostic or therapeutic studies, in order to visualize vessels, tissues and organs. Their use is usually safe, but the CIN¹ has been described as an adverse event that increases morbidity and mortality in those who develop it.²

Table 1. Demographic and clinical characteristics of the hospitalized patients taken to contrasted CAT scan, Neiva, Colombia, 2016.

Demographic characteristics					
	Positive CIN n=36 %	%	Negative CIN N=72%	%	P α value
Men	24	66.7	30	41.7	0.0140
Age > 65 years	15	41.7	26	36.1	0.5750
18-45	6	16.7	22	30.6	0.3600
46-59	7	19.4	16	22.2	
60-74	13	36.1	18	25.0	
>74	10	27.8	16	22.2	
Clinical characteristics					
	Positive CIN n=36 %	%	Negative CIN N=72%	%	P α value
Emergencies	21	58.3	31	43.1	0.2360
Hospitalization	4	11.1	16	22.2	
ICU*	25	34.7	11	30.6	
Abnormal Hb**	28	77.8	55	76.4	0.8720
Hematocrit < 34	18	50.0	28	38.9	0.2710
MAP*** < 70 mmHg	3	8.3	2	2.8	0.1950
eGFR+ <60ml/min/1.73 m ²	11	34.4	21	31.8	0.8
Cr_prec++ > 1.5	4	11.1	9	12.5	0.8340
Hb	11.2	± 1.71	11.56	± 2.38	0.4112
Hematocrit	34.54	± 5.40	35.37	± 7.33	0.5492
MAP	84.42	± 9.84	87.93	± 10.99	0.1082
eGFR	88.57	± 82.32	72.39	± 42.55	0.1801
Cr_pre	0.97	± 0.55	1.22	± 1.081	0.1798
Comorbidities					
	Positive CIN n=36 %	%	Negative CIN N=72%	%	P α value
Diabetes	7	19.4	7	9.7	0.156
Hypertension	9	25.0	17	23.6	0.874
CHF+++	3	8.3	3	4.2	0.373
Cancer	7	19.4	13	18.1	0.861
Pharmacological antecedents					
	Positive CIN n=36 %	%	Negative CIN N=72%	%	P α value
Nephrotoxic agents	6	16.7	18	25.0	0.326
Nephroprotection	23	63.9	50	69.4	0.561

α Chi square test, Pearson or t-student test for difference of means

* ICU: intensive care unit

** Hb: hemoglobin M: man < 13.5; W: woman < 12.6

*** MAP: mean arterial pressure

+ eGFR: estimated glomerular filtration rate (32 cases/66 controls)

++ Cre_prec: previous creatinine

+++ CHF: congestive heart failure

Table 2. Factors related to contrast-induced nephropathy in hospitalized patients taken to contrasted CAT, Neiva, Colombia, 2016.

Variables	Raw OR (CI=95%) n=108	p α value
Demographic characteristics		
Gender/Male	2.8 (1.12 – 7.11)	0.0143
Age > 65 years	1.2 (0.51 – 3.08)	0.5749
Clinical Characteristic		
Abnormal Hb*	1.0 (0.38 – 3.26)	0.8718
Hematocrit <34	1.5 (0.64 – 3.80)	0.2710
MAP** < 70 mmhg	3.1 (0.34 – 39.32)	0.1952
Cr+ > 1.5mg/dl	0.8 (0.18 – 3.44)	0.8344
eGFR++ <60 ml/min/1.73m ²	1.1 (0.40 – 2.97)	0.8002
Antecedents – Comorbidities		
Diabetes	2.2 (0.60 – 8.19)	0.1562
Hypertension	1.0 (0.37 – 2.96)	0.8736
CHF+++	2.0 (0.26 – 16.34)	0.3729
Cancer	1.0 (0.33 – 3.34)	0.8610
Nephrotoxic agents	0.6 (0.17 – 1.80)	0.3261
Nephroprotection	1.2 (0.50 – 3.22)	0.5609

α Chi square test, Pearson test

* Hb: Hemoglobin M: Men <13.5; W: Woman <12.6

** MAP: mean arterial pressure

+ Cr > 1.5: Previous creatinine ?1.5mg/dl

++ eGFR: Glomerular Filtration Rate estimated by Cockcroft and Gault (n=98)

+++ CHF: Congestive Heart Failure

Table 3. Factors associated with contrast-induced nephropathy in hospitalized patients taken to contrasted CAT, Neiva, Colombia, 2016.

Candidate covariable	Raw OR (CI=95 %)	Adjusted OR (CI=95 %)	p Value
Men	2.8 (1.12-7.11)	3.22 (1.33 – 7.76)	0.009
DM	2.2 (0.60 – 8.19)	3.48 (0.96 – 12.57)	0.057
Hospitalization++	0.36 (0.079-1.38)	0.26 (0.07 – 1.00)	0.051
ICU++	0.65 (0.24-1.74)	0.58 (0.22 – 1.49)	0.258

Probability: chi2=0.0104; Log likelihood=-62.155407; Pseudo R2=0.0958

++Reference category: emergencies

The literature reports a large number of studies^{1,3,4} on the development of this complication, its risk factors and its adverse outcomes after the intra-arterial administration of the contrast medium. However, few studies explore these relationships in hospitalized patients who receive intravenous contrast medium.

The procedure of data collection for the recruitment of the cases was carried out, in simultaneous verification, from the review of laboratory records (creatinine pre and post, according to criteria), the records of contrast tomography readings, the database with the codes of the CAT scans performed during the year 2016, the systematized clinical records and the nursing records. This allowed us to guarantee the quality of the data and control the possible information biases.

The incidence of CIN after a CAT scan with iodinated contrast medium was 5.5%, a result consistent with studies on CIN reported by other authors where the incidence varies between 3.4 and 13.9%, according to the definition of case used in this study.^{5,6,7,8}

The diabetes has been described as an independent factor for the development of this complication.¹³ The chronic tubulointerstitial changes make the kidney particularly susceptible to the intensification of the hypoxia and the oxidative stress subsequent to the administration of contrast medium. Although the association between CIN and diabetes was not statistically significant, this antecedent has been reported as one of the main risk factors for the development of CIN, as well as the advanced age (> 65 years) and previous renal failure.^{7,9,10,11}

It draws the attention the association of the gender (male) as a predictor of the development of CIN (OR=3.22; CI=95 % 1.33 – 7.76; p=0.009), a finding consistent with the study conducted by Inga Skarupskiene et al.¹⁴ In studies conducted in Central America, a higher prevalence of tubulointerstitial renal disease has been reported in males (78.3%) related to environmental factors such as agricultural work, exposure to agrochemicals and dehydration (excessive sweating).^{15,17} In Colombia, according to

the report of the high cost account 2015,¹⁶ the prevalence of renal replacement therapy in men is 89.2 per 100,000 inhabitants (in women it is 56.6 per 100,000 inhabitants). These data are consistent with the institutional experience, according to the statistics department, where the majority of treated patients with chronic renal failure are men (65%) coming from the South of the Department of Huila, where agricultural activities are the basis of the economy.

In relation to the service of origin, the hospital stay in the general ward behaved as a protective factor (OR=0.26; CI=95% 0.07–1.00; p=0.05) when compared with patients coming from the emergency department or the intensive care unit.¹¹ This result could be related with the risk assessment before and after the exposure to the contrasted computerized axial tomography, which would allow clinical decision making to prevent the CIN in this group of patients, because the patients in the general ward differ from the patients in the ICU and the emergency room in their clinical characteristics and pathological condition.

According to Valette et al.,¹⁷ the patients of the ICU report increased risk of CIN.¹⁸ However, these results should be interpreted carefully, because it is probable that the changes in creatinine could be attributable to factors other than the exposure to the contrast,^{10,19} such as the metabolic status, sepsis or exposure to nephrotoxic agents. Therefore, the incidence of CIN can be overestimated.

According to the presented findings, is important to insist on the risk assessment and follow-up of patients with a history of type 2 diabetes mellitus, patients hospitalized in the emergency observation room and in intensive care units, since the exposure to contrast medium is becoming increasingly common in clinical practice: it is used as a diagnostic aid for imaging and interventional cardiology or endovascular procedures. Therefore, the identification of patients at risk of developing CIN will be useful at the time of making clinical decisions to reduce the incidence of this disease, focus efforts on the implementation of preventive actions and optimize resources.

This study has some limitations. It was developed in a single hospital center, but the variability in clinical practice among the professionals within the institution could eventually be equated to the variability in clinical practice among institutions. In addition, the follow-up of the renal function through control tests post-exposure to the contrast medium was not performed routinely to the patients in the institution, so creatinine measurements were not found in all patients taken to contrasted CAT, which could underestimate the incidence of contrast associated nephropathy. Finally, the use of nephroprotection was not standardized, and for this reason it was not possible to measure the impact of this variable on the development of CIN.

Conclusions

During 2016, 655 patients were taken to contrasted CAT scan, of them, 18.6 % had post-exposure follow-up creatinine at 48, 72 or 120 hours.

Despite the fact that the follow-up of the renal function through control tests post-exposure to the contrast medium was not carried out routinely in the institution, the incidence of contrast induced nephropathy in the hospitalized patients taken to contrasted CAT during the year 2016 was 5.5 %.

The factors associated with contrast-induced nephropathy found in the hospitalized patients taken to contrasted CAT during the year 2016, were the gender (male) (OR=3.22; CI=95% 1.33 -7.76; p=0.009), and the service of origin (hospitalization in general ward) (OR=0.26; CI=95% 0.07-1.00; p=0.051).

Conflict of interest

The authors declare there is no conflict of interest.

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Ethical responsibilities

Protection of people and animals

The authors declare that no experiments were performed on human beings or animals for this research.

Data confidentiality

The authors declare that they have followed the protocols of their workplace on the publication of patient data.

Right to privacy and informed consent

The authors declare that patient data do not appear in this article

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