

PREVALENCE OF CONTRAST-INDUCED NEPHROPATHY IN CARDIAC PATIENTS IN A HEMODYNAMIC SECTOR

Prevalência de nefropatia induzida por contraste em pacientes cardíacos de um setor de hemodinâmica

Prevalencia de nefropatía inducida por contraste en pacientes cardíacos de un sector de hemodinámica

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ABSTRACT

Objective: To determine the prevalence of contrast-induced nephropathy in cardiac patients undergoing diagnostic and / or treatment angiographic procedures. **Method:** A prospective, quantitative study in the hemodynamics sector of a large hospital, located in the northern region of Rio Grande do Sul, Brazil. The sample consisted of 79 participants through the calculation of sample size. **Results:** The sample consisted of 52 (65.8%) men and 27 (34.2%) women. The mean age was 65.9 ± 9.52 years. The incidence of contrast-induced nephropathy was 30,38%, totaling 24 patients. **Conclusion:** A high prevalence of contrast nephropathy was evidenced, despite the fact that patients presented few risk factors, which highlights the need for preventive measures and reduction of contrast volume.

Keywords: Nephropathy; Means of contrast; Acute kidney injury; Coronary disease; Hemodynamics

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RESUMO

Objetivo: Determinar a prevalência da nefropatia induzida por contraste em pacientes cardiopatas submetidos a procedimentos angiográficos de diagnóstico e/ou tratamento. **Método:** Estudo prospectivo, quantitativo, realizado no setor de hemodinâmica de um hospital de grande porte, situado na região norte do Rio Grande do Sul, Brasil. A amostra foi constituída por 79 participantes através do cálculo de tamanho amostral.

Resultados: A amostra foi formada por 52 (65,8%) homens e 27 (34,2%) mulheres. A idade média foi de $65,9 \pm 9,52$ anos. A incidência de nefropatia induzida por contraste foi de 30,38%, totalizando 24 pacientes.

Conclusão: Foi evidenciada uma alta prevalência de nefropatia por contraste, apesar dos pacientes apresentarem poucos fatores de risco, o que ressalta a necessidade de medidas preventivas e redução do volume de contraste.

Descritores: Nefropatia; Meios de contraste; Lesão renal aguda; Doença das coronárias; Hemodinâmica.

RESUMÉN

Objetivo: Determinar la prevalencia de la nefropatía inducida por contraste en pacientes cardiopatas sometidos a procedimientos angiográficos de diagnóstico y / o tratamiento. **Método:** Estudio prospectivo, cuantitativo, realizado en el sector de hemodinámica de un hospital de gran porte, situado en la región norte de Rio Grande do Sul, Brasil. La muestra fue constituída por 79 participantes a través del cálculo de tamaño muestral.

Resultados: La muestra fue formada por 52 (65,8%) hombres y 27 (34,2%) mujeres. La edad media fue de $65,9 \pm 9,52$ años. La incidencia de nefropatía inducida por contraste fue del 30,38%, totalizando 24 pacientes. **Conclusión:** Se evidenció una alta prevalencia de nefropatía por contraste, a pesar de que los pacientes presentaban pocos factores de riesgo, lo que resalta la necesidad de medidas preventivas y reducción del volumen de contraste.

Descriptores: Nefropatía; Medios de contraste; Lesión renal aguda; Enfermedad de las coronarias; Hemodinámica.

INTRODUCTION

Contrast-induced nephropathy (CIN) is a form of acute kidney injury that occurs in patients undergoing diagnostic and therapeutic medical procedures using iodinated contrast¹.

During last decade, CIN has been identified as the third leading cause of acute renal failure (ARF) in hospitalized patients and may reach 12% of cases. This complication increases mortality, morbidity, length of hospitalization and associated costs²⁻³.

CIN is defined as an absolute increase in serum creatinine ≥ 0.5 mg / dL or an increase of 25% relative to basal creatinine within 24 to 72 hours after exposure to the contrast agent and in the absence of another alternative cause⁴.

The volume and type of contrast used add to the pre-existing risk factors to determine the severity of side effects. High osmolarity contrasts are more nephrotoxic when compared to low osmolarity contrasts⁵.

Models that seek to elucidate the mechanism of CIN development are complex but point to tubular

injury caused by direct toxicity or associated with oxygen free radical generation and renal arteriolar vasoconstriction. This decrease in vascular lumen causes medullary hypoxia through the release of nitric acid, endothelin and adenosine producing a contrast-induced cytotoxic effect⁶.

Considering the potential harmfulness of contrast agent-induced nephropathy, the implementation of effective prevention measures for this complication is justified, based on the profile of specific risk factors of patients treated at the hemodynamic sector. Given the above, this study aimed to determine the prevalence of CIN in heart disease patients undergoing angiographic diagnostic and / or treatment procedures.

METHODOLOGY

This is a prospective, quantitative study conducted in the hemodynamics sector of a large hospital located in the northern region of Rio Grande do Sul, Brazil, from May 1 to September 28, 2018.

Eligibility criteria included adult patients of both genders with heart disease who underwent angiographic procedures for diagnosis and / or treatment in the hemodynamics department who were hospitalized for at least 72 hours after the procedures. Patients who had incomplete data and/or died before the end of the period of 72 hours after the use of contrast were excluded.

To determine the sample size of this research, a sample size calculation was performed, with an error of 5%; 90% confidence level; population of 253 patients, maximum percentage of CIN 12%, totaling a sample of 79 individuals.

The primary outcome of the study was the development of CIN, verified by creatinine variation 24 to 72 hours after the use of contrast. The secondary outcome was the proportion of risk factors through the stratification score.

Data were collected from interviews with patients, analysis of medical records and laboratory tests. The variables evaluated were: age, blood pressure, creatinine, hematocrit, hemoglobin, glomerular filtration rate (GFR), weight, height, body mass index (BMI), comorbidities, smoking, procedure performed, contrast volume, use of measurements, preventive measures, creatinine at 24, 48 and 72 hours after administering contrast, post-procedural complications and patient discomfort with contrast administration.

The risk of developing CIN and the need for dialysis was performed using the Mehran Stratification Score⁷. Secondary data (medical records) were used to confirm the following: age, sex, hematocrit, presence of intra-aortic balloon, contrast volume, diabetes mellitus (DM), hypotension, congestive heart failure (CHF) and GFR. The score was assessed within the first 24 hours after the contrast procedure.

The type of contrast used was the same for all patients, Ultravist® (iopromide) 300, Bayer laboratory, with osmolarity equal to 0.64 Osm / kgH₂O at 37°C used intravascularly⁸.

The diagnoses of systemic arterial hypertension (SAH), stroke, DM and CHF were included according to data contained in the medical records. GFR was determined based on serum creatinine using the Chronic kidney Disease Collaborative Epidemiology (CKD-EPI) equation. Hypotension was considered to be systolic blood pressure below 80mmHg. Anemia, hematocrit <39% if male and <36% if female. Renal insufficiency (RI) was defined as creatinine prior to examination greater than or equal to 1.4 mg / dL.

For data analysis, the SPSS (Statistical Package for Social Sciences) version 25.0 for Windows, Brazil was used. The significance level adopted was p≤0.05. Data were exported and tabulated in a spreadsheet using Excel, version 15.0 for Windows, Brazil, twice by same typist, later the data were compared. The discrepancies were verified and corrected based on the collection instrument and medical records.

Continuous variables were described as mean and standard deviation (SD); categorical variables such as frequency and percentage. To compare a continuous variable between two groups, Student's t-test and Mann-Whitney test were used.

The study was approved by the institution of the collection and later by the Research Ethics Committee (CEP) of the University of Passo Fundo (UPF), under protocol

No. 2,572,548 and CAAE No. 84987518.0.0000.5342, in compliance with ethical and legal principles in line with the Resolution No. 466/2012 of the National Health Council⁹. Study participants signed the Informed Consent Form (ICF) shared before data collection.

RESULTS

We studied 79 patients who underwent diagnostic and / or contrast treatment in the hemodynamic sector, 52 (65.8%) males and 27 (34.2%) females. The average age of the participants was 65.9 ± 9.52 years. No patient in the study underwent dialysis therapy at least 72 hours after contrast use. The prevalence of CIN was 30.38%, totaling 24 patients.

During the research, we found that 51 (64.6%) patients who underwent contrast procedures did not receive prophylactic measures related to CIN prevention, while 28 (35.4%) received saline hydration (SF) 0.9 % intravenously.

There was no significant difference between basal creatinine values in patients with and without CIN. Serum creatinine values after the procedure were higher among patients who developed CIN within 48 to 72 hours of contrast use, as shown in Table 1.

When comparing patients with and without CIN, patients who developed nephropathy were more hypertensive, had a higher percentage of reduced left ventricular ejection fraction (EF), and a higher incidence of CHF. Interestingly, patients with prior IR developed less CIN. The other comparisons of clinical and demographic variables did not differ and are presented in table 1.

Table 1 - Comparison between patients with and without Contrast-induced nephropathy (CIN). Passo Fundo, RS, Brazil, 2018

Variables	Without CIN n=55 (69,62%)	With CIN n=24 (30,38%)	P
Age (years)	65,34 ± 9,57	67,25 ± 9,47	0,68*
Men	36 (65,5%)	16 (66,7%)	0,83*
Body Mass Index (Kg / m ²)	27,09 ± 3,81	27,24 ± 4,03	0,61*
Risk factors for CIN			
HAS	42 (74,5%)	20 (83,2%)	0,030*
Hypotension	9 (16,4%)	3 (12,%)	0,37*
DM	16 (29,1%)	7 (29,2%)	0,98*
Dyslipidemia	17 (30,9%)	3 (12,5%)	< 0,001*
DAC	16 (29,1%)	7 (29,2%)	0,75*
Arrhythmias	3 (5,5%)	5 (20,8%)	0,10*
Previous stroke	11 (20%)	2 (8,3%)	0,34*
EF <50%	13 (23,6%)	9 (37,5%)	0,006*
Smoking	17 (30,9%)	4 (16,7%)	0,15*
Former smoker	6 (10,9%)	8 (33,3%)	0,68*
ICC	1 (1,8%)	7 (29,2%)	< 0,001*

Variables	Without CIN n=55 (69,62%)	With CIN n=24 (30,38%)	P
GO	9 (16,4%)	1 (4,2%)	0,001*
Anemia	20 (36,4%)	14 (58,3%)	0,43*
PAS	120,09 ± 21,56	130,92 ± 31,04	0,054*
Preventive Measures and Creatinine Levels	70,16 ± 12,22	76,42 ± 17,28	0,033*
Contrast Volume (ml)			
Pre procedure hydration	154,11 ± 81,53	212,92 ± 100,67	0,007**
TFG	21 (38,2%)	7 (29,2%)	0,098*
Cr Basal	61,33 ± 19,73	71,01 ± 24,39	0,23*
Cr 24	1,30 ± 0,57	1,01 ± 0,38	0,26*
Cr 48	1,26 ± 0,54	1,21 ± 0,50	0,67*
Cr 72	1,20 ± 0,49	1,37 ± 0,56	0,12*
Cr 72	1,18 ± 0,49	1,30 ± 0,44	0,53*

Result in mean ± standard deviation and percentages in parentheses. * Student t test, ** Mann - Whitney test.

The contrast volume used ranged from 50 to 500mL, with a mean volume of 171.97 ± 91.27mL. Patients undergoing catheterization (CAT) followed by percutaneous transluminal coronary angioplasty (ACTP) received a higher contrast volume, as shown in table 2.

Table 2 - Type of procedure and contrast volume. Passo Fundo, RS, Brazil, 2018

Procedure	Frequency	Volume (mL)
CAT	29 (36,7%)	110,86 ± 56,30
ACTP	8 (10,1%)	225 ± 132,23
CAT + ACTP	27 (34,2%)	232,96 ± 62,80
CAT + AORTO	15 (19%)	152,06 ± 84,08

CAT: catheterization; PTCA: percutaneous transluminal coronary angioplasty; AORT: Aortography.

Of the total patient sample, 46.6% (n = 36) mentioned some type of discomfort after contrast administration. The most cited were heat 29.1% (n = 23), nausea 5.1% (n = 4) and 11.4% (n = 9) reported feeling both symptoms.

The CIN risk stratification score was performed for patients undergoing angiographic procedures that were part of the study. The group of patients who developed CIN had higher score, respectively, 8.17 ± 4.67 versus 6.60 ± 5.08 (p = 0.12).

Patients who developed CIN had more complications after the procedures, corresponding respectively to 25% (n = 6) versus 3.6% (n = 2); (p = ≤ 0.001). Among the complications, the most frequent was cardiopulmonary arrest (CRP) 5.1% (n = 4), followed by arrhythmias 3.8% (n = 3) and hypotension 1.3% (n = 1).

DISCUSSION

Constant evolution of science and technologies in health, through modern, complex and sophisticated equipment, allow high quality imaging for early diagnosis and treatment of diseases⁹. Diagnostic and imaging procedures, such as arteriography and coronary angiography, may cause adverse events such as CIN¹⁰.

CIN, often underdiagnosed, is considered the third cause of ARF in a hospital setting, and may correspond to 12% of cases, remaining behind only prerenal and drug-induced ARF²⁻³. In this study, a higher prevalence was observed, corresponding to 30.38% (n = 24) of the patients.

Regarding the prevalence and clinical relevance of CIN, prevention would be the ideal approach. However, due to ineffective prophylactic measures and difficulty in establishing specific biomarkers, early diagnosis is the best alternative for treatment efficacy¹¹.

The prevalence of CIN depends on the factors related to the technique (type of contrast, volume and osmolarity) and is associated with pre-existing risk factors: decreased renal function, age over 75 years, DM, hypotension, CHF, intra-aortic balloon implantation (IAB), anemia and dehydration¹². The most significant risk factors for CIN observed in our study were CHF and reduced EF. The association between CHF and CIN may be due to the characteristic aspects of these patients: low cardiac output and high catecholamine levels, which result in reduced renal perfusion¹³.

In the present study, we observed that the institution where the research was conducted presents weaknesses in compliance with measures standardizing the prevention of acute kidney injury after the use of contrast media.

Only 35.4% (n = 28) of the patients received intravenous hydration with 0.9% SF prior to contrast use. There is also no standardization of the records of contrast volume used.

Annotations regarding the type and volume of contrast used are of utmost importance, as contrast use has been cited as one of the most common causes of acute renal dysfunction, and the lack of this information may negatively interfere with possible management of CIN prevention. The volume and type of contrast used add to the pre-existing risk factors to determine the severity of side effects⁵.

According to the literature, the cut-offs at risk for infused contrast volume is <200ml¹⁴⁻¹⁵. In the present study, the mean volume infused in patients who developed CIN was 212.92 ± 100.67mL, above the recommended cut-off point.

There is evidence of the benefit of using low osmolarity or nonionic isosmolar contrasts in the prevention of CIN in higher risk patients. Prophylactic use of N-acetylcysteine is still controversial in the literature. A proven effective measure is hydration with 0.9% SF 1mL / kg / hour 12 hours before and after the procedure¹⁶.

Although most often reversible, CIN is associated with increased morbidity, prolonged stay at the medical facility, high hospital costs, and higher chances of death even without hemodialysis. CIN is known to increase by 14.4% the 30-day death rate and by 17.4% after the three-year period¹⁷. In this study, a high complication rate was observed after the contrast procedures, corresponding to 25%.

In this context, the previous intervention of nurses and the performance of a multiprofessional team in interventional cardiology seek to promote excellence in care, favor rapid recovery and minimize negative impacts on the individual's quality of life. Such conduct contributes to the reduction of hospital costs, contributes to effective and comprehensive care¹⁸.

As limitations of the study, the first is short patient follow-up period, which made it impossible to identify the adverse outcome, whether death or complications, in the medium and long term. Second limitation is the lack of compliance with the CIN protocol as well as data recording routines related to the contrast exams.

Further prospective studies are considered extremely important in the institution so that the existing protocol can be implemented, thus avoiding the risk of evolution to chronic condition or even CIN.

CONCLUSION

The results of this study demonstrated a high prevalence of CIN in patients undergoing contrast procedures and, in most cases, they exhibited few risk factors. CHF and reduced EF were statistically significant risk

factors for the development of nephropathy. A high dose of contrast volume has been observed in the procedures, especially the therapeutic ones.

The high prevalence of CIN indicates the need reduce contrast volumes and to use protocols of prevention before and after contrast-enhanced examinations, thus increasing patient safety.

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