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CONTRAST - INDUCED NEPHROPATHY, OLD STORY - NEW TWISTS

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Abstract

Aim: Radiological procedures utilizing intravascular iodinated contrast media are being widely applied for both diagnostic and therapeutic purposes and represent one of the main causes of contrast-induced nephropathy (CIN). In this hospital-based study we tried to assess predictors for development of CIN in patients undergoing cardiac catheterization. A total of 5604 patients undergoing coronary angiogram/PCI from 2007-2017 were enrolled in the study. Multivariate predictors of CIN were identified by logistic regression using stepwise selection with entry and exit criteria of $p < 0.1$. A two-sided 95% confidence interval (CI) was constructed around the point estimate of the odds (OR). A p value <0.05 was considered significant. CIN occurred in 6 (1‰) patients. The mean age of patients suffering from CIN was higher than in the whole population (66.5± 31.15 *vs*. 58.66± 28.57, p=0.03). Characteristics of patients who developed CIN were: older age, diabetes, higher creatinine and lower EF. The incidence of CIN in patients with diabetes was higher and statistically significant (84% *vs*. 16%, p=0.01). Emergency cases were at higher risk of developing CIN than elective patients (85% *vs.* 15%, p=0.001), respectively. Diabetes, CKD and EF < 50% were independent predictors of CIN (RR 2.4, 95% CI: 1.88 - 7.132, p=0.008; RR 3.1, 95% CI: 2.17 - 6.682, p=0.003; RR 1.6, 95% CI: 2.88 - 7.132, p=0.01, respectively). The development of contrast-induced nephropathy in patients who underwent angiography and PCI was mainly related to older age, diabetes, lower GFR and heart failure, but not contrast material exposure.

Key words: contrast, nephropathy, PCI, AKI, GFR, CKD

Introduction

Radiological procedures utilizing intravascular iodinated contrast media are being widely applied for both diagnostic and therapeutic purposes and represent one of the main causes of contrast-induced nephropathy (CIN) and hospital-acquired renal failure [1]. Despite technological advances, CIN remains responsible for a third of all hospital-acquired acute kidney injury (AKI) [2, 3] and affects between 1% and 2% of the general population and up to 50% of high-risk subgroups following coronary angiography (CA) or percutaneous coronary intervention (PCI) [4]. The estimated risk of an individual developing CIN can be calculated using known pre-existent clinical and periprocedural factors, which are consistent with the proposed pathological mechanisms of CIN. Pre-existent stage III chronic kidney disease (CKD), defined as an estimated glomerular filtration rate (eGFR)<60 mL/min/1.73 m^2 for greater than 3 months, is the most commonly identified risk factor for CIN; however, CIN can occur in the absence of underlying CKD if a number of other risk factors are also present [5]. In hospital mortality it is approximately five times higher in patients who suffer from CIN [6].

In Kosovo, prevalence of cardiovascular disease and its risk factors are high [7]. Since there is increasing need and performance of cardiac interventions, patients are exposed to contrast media. Seeking for patients at risk for CIN in our population undergoing PCI will help risk stratification and undertaking preventive measures for CIN. In this hospital-based study we tried to assess risk factors (predictors) for development of CIN in patients undergoing cardiac catheterization.

Methods

In this retrospective study we enrolled 5604 patients undergoing coronary angiogram/PCI from 2007-2017. Percutaneous radial approach was the most widely used technique (in 95%), and femoral arterial catheterization in the rest of the patients. All patients received evidence- based

standard pre- and post-procedural care as per guideline directed medical management. The absolute amount of contrast media was recorded for each patient. All patients received Ultravist contrast. If a patient developed CIN, appropriate treatment either conservatively or by dialysis support was done. Decision was made in consultation with nephrologists. CIN was defined as an increase of >25% or 0.5mg/dl in pre-PCI serum creatinine or after 48 h after PCI. Hypertension, hypotension, cardiogenic shocks, diabetes mellitus (DM), hypercholesteremia, chronic kidney disease (CKD), unstable angina, were defined as per standard definitions.

Statistical analysis

Statistical software SPSS, version 17 was used for statistical analysis. Continuous variables are expressed as mean, standard deviation (SD); categorical data were presented as absolute values and percentages. T-test and ANOVA were used for parametric comparison. Mann-Whitney U and Kruskal-Wallis test were used for nonparametric comparison. Chi-square or Fisher-exact tests were used for comparison of categorical variables as required. Multivariate predictors of CIN were identified by logistic regression using stepwise selection with entry and exit criteria of $p<0.1$. A two-sided 95% confidence interval (CI) was constructed around the point estimate of the odds (OR). A p value <0.05 was considered significant.

Results

Baseline characteristics

In ten years, 5604 patients underwent cardiac catheterization and 3684 (66%) needed PCI (Table 1). The mean age of all patients was 58.66± 28.57 years and 23% of patients were diabetic. More than 40% were hypertensive and 17% had hypercholesteremia. CKD was present in 36 (6.4%) patients and 2 were already on hemodialysis.

Table1. The baseline clinical characteristics of study population (N=5604)

All patients N = 5604	n	%
Cardiac catheterization	3684	66
PCI	1920	35
DM	128	23
HTA	224	40
Hypercholesteremia	95	17
CKD	86	16
CKD -5D	2	0.4
EF <50%	56	10

PCI – Percutaneous Coronary Intervention, DM - Diabetes Mellitus, HTA – hypertension, CKD - Chronic Kidney Disease, CKD – 5D - Chronic Kidney Disease on hemodialysis, EF – Ejection Fraction

Subgroup analysis of CIN occurrence

CIN occurred in 6 (1‰) patients. The mean age of patients suffering from CIN was higher than in the whole population (66.5± 31.15 *vs.* 58.66± 28.57, p=0.03). Both genders were equally represented in patients suffering from CIN (three men and women). Five were diabetics and hypertensive, two with hypercholesteremia. EF less than 50% was observed in four of the patients. CKD was already present in most of the patients – five of them had elevated level of creatinine before catheterization. The mean amount of contrast medium administrated in the CIN group was 232 ml (range 100-550 ml) and it was not significantly different from the whole population (178 ml (range 80-500 ml)), p= 0.137) (Figure 1). In two of the CIN patients PCI was performed twice in two days. Dialysis treatment was inevitable in four of the patients and two of them died after the first dialysis.

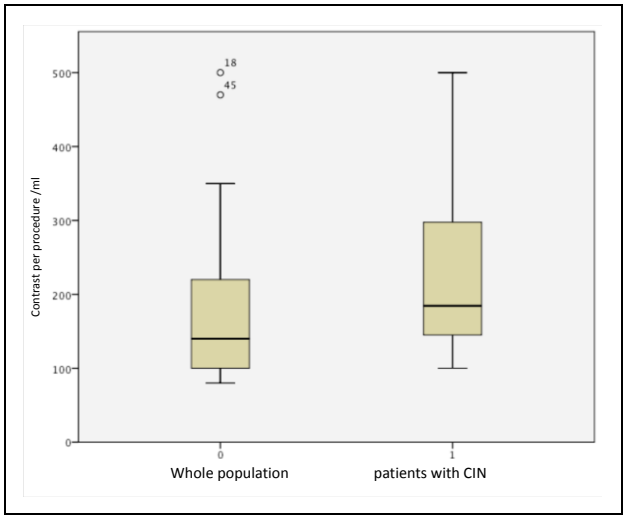

Figure 1. Comparative analysis of CIN occurrence according to amount of contrast media exposure per procedure

The characteristics of the patients who developed CIN were: older age, diabetes, higher creatinine and lower EF. The incidence of CIN in elderly (>65 years) was equal to younger patients (50% *vs*. 50%, p=1). The incidence of CIN in patients with diabetes was higher and statistically significant (84% *vs*. 16%, p=0.01). Emergency cases were at higher risk of developing CIN than elective patients (85% *vs*. 15%, p=0.001), respectively.

Multivariate logistic regression analysis

In the first step of multivariate analysis age, sex, presence of diabetes, hypertension, hypercholesteremia, CKD, amount of administrated contrast agent, PCI/angiogram, EF<50%, and presence of multivessel disease, were included. The last significant model is shown in Table 2. Diabetes, CKD and EF < 50% were independent predictors of CIN (RR 2.4, 95% CI: 1.88 - 7.132, p=0.008; RR 3.1, 95% CI: 2.17 - 6.682, p=0.003; RR 1.6, 95% CI: 2.88 - 7.132, p=0.01, respectively).

Table 2. Multivariate logistic analysis of CIN predictors

Variable	RR	95% CI	p
Diabetes	2.4	1.88 - 7.132	P=0.008
CKD	3.1	2.17 - 6.681	P=0.003
EF<50%	1.6	1.01 - 4.815	P=0.01

RR – relative Risk, CI – Confidential Interval, CKD Chronic Kidney Disease, EF – Ejection Fraction

Discussion

Contrast-induced nephropathy is the third leading course of acute renal failure and a recognized complication of cardiac catheterization. Identifying prevention strategy of CIN is a challenge for many investigations [8]. Among cardiac patients CIN ranges from 1% to 50% and the incidence varies depending on the clinical setting of the procedure, population evaluated and the definition of CIN [9]. In our 10-year report, only 1‰ of patients developed CIN after cardiac catheterization or PCI. The coronary unit was the unique center that covered whole country population and performed angiography and PCI. Another study from the region observed the lack of information on mortality and other risk factors [10]. In our analysis 23% of whole study population had diabetes, 40% HTA and 16% CKD, which is comparable to other regions studies [5]. CIN is found to be an iatrogenic disorder with high incidence in elderly, diabetics and patient with preexisting renal failure [11, 12]. Generally, our CIN patients were older but, in the group above and under 65 years, the incidence of CIN was equal. Diabetics were at higher risk of renal impairment, as were the patients with preexisting CKD. There are still controversies about the role

of contrast media in CIN occurrence [5]. Exploring the causal association of contrast material exposure and the incidence of AKI showed different results. Caspi et al. found that risk for acute renal failure is similar among ST segment – elevation myocardial infarction patients with or without contrast material exposure [12]. In our study CIN patients were exposed to similar quantity of contrast media as the whole study population, but it must be considered that all measurements for prevention were taken before and after procedure. Previous renal impairment strongly affected development of CIN in our patients, and this factor was already recognized by many studies [2, 5, 13, 14]. Heart failure in PCI patients was found to be contributing to renal ischemia and development of CIN [11], which was confirmed in most of the affected patients in our study, as well. Multivariate logistic regression analysis confirmed diabetes as an independent risk factor for CIN in the study population. Patients with diabetes had 2.4 folds higher risk to develop this complication. Patients with lower ejection fraction were 1.6 times more at risk for CIN. Still, the highest risk of 3.1 times was observed in patients with previous renal impairment. These results are in line with recently published studies and confirmed the interaction of many factors contributing to development of CIN, in spite of contrast media as a cofounder. Our study had some limitations. The follow-up of treated patients lasted for few days in well recovering patients; therefore we might have missed a late CIN occurrence. This might have resulted in slight underestimation of CIN.

Conclusions

The development of contrast-induced nephropathy in patients who underwent angiography and PCI was mainly related to older age, diabetes, lower GFR and heart failure, but not contrast material exposure.

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