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Investigation of the relationship between contrast nephropathy development and body mass index in patients receiving contrast media in the emergency department

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ABSTRACT

Objectives: This study aims to investigate the risk factors in patients presenting to the emergency department, undergoing contrast-enhanced computed tomography (CT), and developing contrast-induced nephropathy (CIN) and whether there is a relationship between CIN and body mass index (BMI).

Methods: A total of 336 patients presenting to the emergency department between 15.3.2019 -31.12.2019 and underwent CT by administering intravenous (IV) contrast agent (CA) were prospectively analyzed. Patients' age, gender, chronic diseases, height, weight, BMI, and hospitalization or discharge information were recorded. Control creatinine was measured at 72nd and 120th hours. Patients who developed CIN were recorded.

Results: The mean age of the patients was 57 years (min: 18-max: 96) and 56.5% were male. CIN developed in 6.5% of the patients. Congestive heart failure (CHF) was associated with the increased risk of CIN (p = 0.045). There was a significant increase in CIN risk in patients aged 40-70 years (p = 0.008). The risk of CIN development was increased with advanced age (p = 0.002). Dialysis was required in 13% of patients who developed CIN. There was no significant relationship between BMI and CIN development (p = 0.740).

Conclusions: We did not find a significant relationship between BMI and CIN. However, the risk of CIN development was higher in patients over 40 and especially in patients with CHF.

Keywords: Contrast-induced nephropathy, body mass index, emergency medicine, contrast-enhanced computed tomography.

Globally, contrast agent (CA) is used to monitor approximately 60 million patients per year [1]. All water-soluble, nephrotropic iodinated CAs have a direct toxic effect on renal epithelial cells and may cause contrast-induced renal medullary ischemia [2]. With the spread of diagnostic and therapeutic imaging methods and the effectiveness of contrast agents, the use of imaging methods is increasing, which causes an increase in side effects related to CA. Early and late side effects or even death can be seen due to CA use. The most important side effect is contrast-induced nephropathy (CIN) [3]. CIN is a 25% increase in basal serum creatinine value or at least 0.5 mg/dl increase in absolute serum creatinine value within the first 48 hours after radiographic contrast agent use [4]. The incidence of CIN has been calculated as 2% in the gen-

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eral population, but its incidence reaches 20-30% in high-risk groups such as elderly patients and patients with diabetes, congestive heart failure, and chronic kidney disease [5].

The use of contrast media for diagnostic purposes is increasing day by day in emergency departments. However, the number of studies on the frequency of CIN in the emergency department is very limited in the current literature. CIN is a potentially preventable clinical condition. The first step to prevent CIN is to identify risk factors. Mortality and morbidity associated with CIN will be reduced by identifying high-risk patients, taking necessary precautions, and applying appropriate treatments. Therefore, we aimed to evaluate the frequency of CIN occurring after contrast-enhanced tomography, to contribute to predict CIN risk, and to investigate whether there is a relationship between body mass index (BMI) and CIN. Our study is the first study conducted in an emergency service in terms of determining whether there is a relationship between CIN and BMI.

METHODS

Six thousand two hundred patients patients who presented to the Emergency Service of the University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital between 15.03.2019-31.12.2019 and underwent contrast-enhanced computed tomography were prospectively included in the study. Five thousand eight hundred and sixty-four patients were excluded because they did not meet the criteria. A total of 336 patients were included in the study. Ethics committee approval was obtained with the date and number of 2011-KAEK-25 2019/03-16 prior to the study.

Patients with a history of chronic renal failure (CRF), who were pregnant, who were under the age of 18, who refused to give consent, who received contrast media in the last two weeks, whose creatinine value could not be measured before or after contrast agent application at 72nd and 120th hours, who were discharged from the emergency department and were not followed up, who were in shock, and who had a diagnosis of sepsis were excluded.

The Patient Information and Consent Forms prepared according to the Declaration of Helsinki were read to the patients and their signed consents were obtained. PHILIPS 128 Multislays computed tomography device was used in the emergency radiology unit. Nonionic contrast agent (iopromide, Ultravist™; 370 mg I/ml -100 mL vial Bayer Schering Pharma and Iohexol, Omnipaque GE Healthcare 350mg I/ml-100ml) was used as intravenous contrast agent. Saline was intravenously infused to the patients before and after tomography scanning. Age, gender, chronic disease history, height, weight, BMI, creatinine value before tomography, creatinine values at 72nd and 120th hours after contrast-enhanced tomography were recorded.

Statistical Analysis

Data were analyzed with SPSS (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.), and type I error level was accepted as $\alpha = 0.05$ in statistical analysis. The conformity of height, weight, and body mass index measurements to normal distribution was examined with the Shapiro Wilk test. Descriptive statistics were expressed as median (minimum: maximum) and mean ± standard deviation, while the Mann Whitney U test was used for comparisons between groups with and without contrast nephropathy. Categorical variables were expressed as n (%), and Pearson chi-square, Fisher's exact chi-square and Fisher Freeman-Halton tests were used for comparisons between groups. As other causes that could cause acut renal failure (ARF) were used as exclusion criteria, in contrast-enhanced CT group, those with a 25% increase in serum creatinine values measured before the contrast agent administration (0 hour) and at 72nd and 120th hours after administration were accepted as having contrast agent nephropathy. In the study, the body mass index was calculated as kg/m^2 in all patients.

RESULTS

A total of 336 patients were included in the study. 56.52% (n = 190) of the patients were male while 43.5% (n = 146) were female. There was no statistically significant difference in the development of CIN in patients in terms of gender ($p = 0.255$).

The mean age was 57 years (min: 18-max: 96). Patients were divided into three as young (18-40 years), middle aged (41-70 years) and old (71 years and over) and risk analyses were performed. There

Table 1. Age groups and comorbidities

Age group	n	%
18-40	68	20.2
40-70	183	54.5
71 and over	85	25.3
Total	336	100
Comorbidities	**n**	**%**
DM	87	25.8
HT	144	42
CHF	12	3.5
CVD	65	19.3
CAD	27	8
Other	57	16.9

DM = diabetes mellitus, HT = hypertension, CHF = congestive heart failure, CVD = cerebrovascular disease, CAD = coronary artery disease

was no statistically significant difference in the development of CIN in young patients ($p = 0.255$) while a statistically significant increase in terms of the CIN development risk was found in middle-aged patients ($p = 0.008$). In addition, the risk of developing CIN in elderly patients increased even more ($p = 0.002$). 110 (32.7%) of 336 patients did not have any comorbidities. The distribution of comorbidities and age groups of the cases are shown in Table 1.

It was seen that 100 (30%) of 336 patients were discharged from the emergency department, while 236 (70%) were hospitalized. 22 (6.5%) of the patients developed CIN. The mean age of the patients with CIN was 64. 68.2% (n = 15) of the patients were males. 14 (4.1%) of the hospitalized patients developed CIN.

When the relationship between CIN and comorbidities (diabetes mellitus [DM], hypertension [HT], congestive heart failure [CHF], cerebrovascular disease [CVD], coronary artery disease [CAD]) in 22 patients who developed CIN was examined, a significant statistical relationship was found between CHF and CIN development ($p = 0.037$). The mean height of the group with CIN was found to be 167.09 cm. The mean height was 161 cm for females and 172 cm for males. No statistically significant difference was found between the CIN development and height ($p = 0.991$). The mean weight in the group with CIN was 77 kg. The mean weight was 76 kg for females and 78 kg for males. No statistically significant relationship was found between the development of CIN and weight ($p = 0.835$).

The mean BMI of the patients with CIN was found to be 26.05 kg/m^2. The mean BMI was found to be 29.3 kg/m2 for females and 26.4 kg/m^2 for males. The relationship between CIN and BMI was examined and no statistically significant relationship was found ($p = 0.740$). Table 2 shows the relationship between CIN with comorbidities in addition to the height, weight, and BMI of patients. Using BMI, the patients were divided into four as underweight, normal weight, overweight and obese and their CIN development risk was evaluated. No statistically significant relationship was found ($p = 0.886$). Table 3 shows the results of the statistical analysis between BMI and CIN. The basal creatinine and glomerular filtration rate (GFR) values of the patients and the control creatinine and GFR values are shown in Table 4.

Table 2. Data regarding CIN, comorbidities, height, weight, and BMI

Comorbidities	With CIN	Without CIN	*P* value
DM	9	78	0.096
HT	13	131	0.111
CHF	3	9	0.037
CVD	2	63	0.272
CAD	3	24	0.404
BMI	26.05	26.85	0.74
Height	167.50	167	0.991
Weight	77	75	0.835

DM = diabetes mellitus, HT = hypertension, CHF = congestive heart failure, CVD = cerebrovascular disease, CAD = coronary artery disease, BMI = body mass index, CIN = contrast-induced nephropathy

Table 3. Data regarding the relationship between CIN and weight

Weight	With CIN	Without CIN	*p* value
≤ 18 (underweight)	0	8	0.886
19-25 (normal weight)	7	97	
25-30 (overweight)	9	118	
31 ≤ (obese)	6	91	

CIN = contrast-induced nephropathy

Tablo 4. Creatinine and GFR values

	Basal	Control
Creatinine (mean ± SD)	0.94 ± 0.39	0.90 ± 0.51
GFR (mean ± SD)	86.01 ± 26.14	89.91 ± 27.18

GFR = Glomerular filtration rate

DISCUSSION

In this study, we aimed to investigate the risk factors and the relationship between CIN and BMI in patients who presented to the emergency department and developed CIN after contrast-enhanced tomography.

CIN is defined as an increase in serum creatinine greater than 25% or ≥ 0.5 mg/dL occurring within 3 days of intravenous contrast agent administration without an alternative cause and is defined as the third cause of hospital-acquired ARF [6]. It is associated with hospitalization, increased length of hospital stay, and high mortality rates [7].

The mechanism of formation of CIN is not known precisely and in detail. However, hemodynamic changes in the kidney (contrast-induced biphasic response in renal blood flow, shunt of medullary blood flow to the cortex, tubulo-glomerular feedback), free radicals and reperfusion damage (the formation of free oxygen radicals as a result of hypoxia, resulting in oxidative stress and apoptosis), tubule direct toxicity and immunological damage to cells, hematological factors (increase in blood viscosity as a result of decrease in erythrocyte flexibility and development of medullary hypoxia as a result) are blamed in the physiopathogenesis of CIN [8].

Although renal functions usually return to their former state with appropriate treatment, CIN development is clinically associated with long and short-term survival, the need for hemodialysis, prolonged hospitalization, increased cost, mortality, and morbidity [9].

Volume expansion and the use of low osmolar contrast media are the most effective methods to prevent CIN development [10]. However, in our study, despite intravenous saline infusion and the use of low osmolar contrast media before the procedure, CIN developed in some patients, which makes the data even more valuable. Nash *et al*. [11] determined that the third most common cause of ARF in hospitalized patients was CIN. The number of studies investigating the relationship between the development of CIN and the use of contrast media in the emergency department is very limited. Most studies have been conducted on patients undergoing percutaneous coronary intervention. Mitchell *et al*. [12] reported the incidence of CIN due to contrast-enhanced CT scan as 11% in outpatients in the emergency department. In their study in which the frequency of CIN related to the use of contrast agent for abdominal CT in the emergency department was investigated, Kim *et al*. [13] reported the frequency of CIN as 4.5%. In our study, we found the frequency of CIN to be 6.5%, which is consistent with the literature.

The incidence of contrast media nephropathy increases with age. Although there is no certain age limit, it has been shown in the literature that the risk increases in patients aged 60-75 years [14]. Being 75 and over is accepted as a risk factor in many scoring system. In our study, the incidence of CIN was seen to increase with age ($p = 0.004$). Studies have reported that the rate of CIN development is higher in women [15]. Kiski *et al*. [16] found a higher rate of CIN development in women in their study, and stated that increase might be due to the fact that female patients included in the study were older, had lower eGFR, had a higher DM diagnosis, and most of the female patients were using loop diuretics. In the study of Isler *et al*. [17], on the other hand, the risk of CIN was found to be higher in men. In our study, no significant

relationship was found between the development of CIN and gender ($p = 0.225$).

In the study of Marenzi *et al*. [18], which included 208 patients who underwent percutaneous coronary intervention, DM was not defined as a risk factor. In Koruk's thesis study [19], which included 342 patients in the emergency room, DM was not found to be a risk factor. Similarly, in our study, when diabetic patients were compared with non-diabetic patients, no risk was found in terms of CIN development in patients with diabetes ($p = 0.096$).

Rihal *et al*. [9] reported that HT is a risk factor for the development of CIN [9]. Additionally, Mehran *et al*. [20] expressed that HT is a risk factor for the development of CIN. In the study of Marenzi *et al*. [21], on the other hand, hypertension was not defined as a risk factor for the development of CIN. In our study, no CIN development risk was found in patients with HT ($p = 0.111$).

In literature, heart failure has been reported as an increased risk factor for the development of CIN [14]. There are some studies reporting a left ventricular ejection fraction (LVEF) < 40% as a risk factor for CIN [22]. Those studies were performed on patients undergoing percutaneous coronary intervention. In our study, an increased risk was found for the development of CIN in patients with CHF ($p = 0.037$).

In a retrospective study on 7586 patients who underwent percutaneous coronary intervention Rihal *et al*. [9] reported that patients with a history of CVDs or transient ischemic attack were at increased risk for the development of CIN. In their study including 8357 patients who underwent percutaneous coronary intervention, Mehran *et al*. [23] did not define previous CVDs as a risk factor for the development of CIN. In our study, there was no statistical significance in terms of CIN development risk in patients with a history of CVDs ($p = 0.272$).

We did not find any studies investigating the relationship between CIN and CAD in the literature, and no relationship was found between CIN and CAD in our study ($p = 0.404$).

BMI is a good indicator of intravascular volume. Considering the data showing that the risk of developing CIN increase in patients with intravascular volume deficiency, it may be a guide in identifying risky patients [24].

When the publications comparing kidney size and body parameters were examined, it was found that there was a linear relationship between kidney size and BMI [25]. Accordingly, it is reported that in the evaluation of kidney dimensions, the values measured by ultrasonography should be examined by considering BMI. In the study of Weisenbach *et al*. [26], in which they evaluated 330 normal children, kidney size was found to be associated with body weight and height. Schmidt *et al*. [27], examined 717 infants aged between 0 and 18 months, and kidney sizes were found to be associated with age, gender and BMI in this study. In the study of Cohen *et al*. [25], in which kidney volume was measured by magnetic resonans, a statistically significant correlation was found between kidney volume and height, weight and BMI. While a strong relationship was found between kidney volume and body weight, a moderate relationship was found with height and a weak relationship with BMI [25]. In their study, Şengül *et al*. [28] showed a significant relationship between BMI with serum uric acid level, glucose, and HbA1c in patients with chronic renal failure. In another study, Güngören *et al*. [29], demonstrated that BMI was an independent predictor of CIN development in patients undergoing cardiac catheterization. In our study, however, BMI was not found to be as an independent predictor of CIN.

In the study of Kandemir *et al*. [30], on the prevalence of contrast nephropathy in patients who underwent percutaneous coronary intervention in acute coronary syndrome, a significant correlation was found between CIN and BMI ($p = 0.044$). In our study, however, no significant relationship was found between the development of CIN and BMI ($p = 0.740$). We think that the application of hydration in all patients in our clinic may have played a role.

In the study of Nikolsky *et al*. [31], 3.1% of patients who developed CIN required dialysis. In the study of Marenzi *et al*. [32], hemofiltration was started four to six hours before the procedure and continued for 18-24 hours in the patients in the intensive care unit for angiography. Hemofiltration was stopped during angiography. As a result, a 45% reduction in the development of CIN, a 22% decrease in the need for renal replacement therapy, and a 20% lower mortality rate were reported [32]. In the study of Gruberg *et al*. [33], it was reported that the need for dialysis was up to 35%. In our study, dialysis need developed in 3 of the patients who developed CIN. One of these patients

died on the 45th day of intensive care follow-up, and one required permanent dialysis (operated with aortic dissection).

It has been reported that ARF developing after surgical intervention is most commonly seen in patients undergoing cardiovascular surgery. Major surgery has been identified as a risk factor for the development of postoperative renal failure and the most common cause is hemodynamic instability observed during the operation [34]. During our study, one of the patients who underwent cardiac surgery needed permanent hemodialysis. We think that the majority of the previous studies were on patients who underwent percutaneous coronary intervention and the frequent use of cardiac surgery after the procedure in these patients may have been the cause.

Limitations

The fact that our study was single-centered and some patients who were discharged from the emergency department did not come for follow-up and thus were excluded may have affected the results. In addition, since our hospital is a regional trauma and stroke center, the inability to give preventive treatment to patients because of an urgent need for imaging before CT angiography may have had an impact on the results.

CONCLUSION

CIN is a condition that can lead to mortality and morbidity. However, it is preventable on condition that causes are known and precautions are taken. Therefore, identifying the causes is of the utmost importance. In our study, we found that the risk starts in patients over 40 years old and especially in those with CHF. In addition, patients over 70 have more risks compared to the other age groups. However, we did not find a significant relationship between BMI and CIN. Considering the results, mortality and morbidity associated with CIN can be reduced by measures to be taken before and after contrast-enhanced CT scan in elderly patients with a history of CHF. This should also be considered, since there is no significant relationship between BMI and CIN.

Authors' Contribution

Study Conception: MSŞD, HK; Study Design: Yİ, HK; Supervision: MSŞD, MY; Funding: MSŞD, Yİ; Materials: HK, MY; Data Collection and/or Processing: Yİ, HK; Statistical Analysis and/or Data Interpretation: Yİ, HK, MY; Literature Review: MSŞD, MY; Manuscript Preparation: MSŞD, Yİ, HK, MY and Critical Review: MSŞD, Yİ, HK, MY.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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