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• Original Article •

The Risk Factors for Developing Contrast-induced Nephropathy after the Evaluation of Trauma Patients at a Regional Trauma Center in Korea

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Purpose: Computed tomography (CT) with intravenous (IV) contrast is an important step in the evaluation of trauma patients; however, the risk factors for contrast-induced nephropathy (CIN) in these patients remain unclear. This study determined the rate of CIN in trauma patients at a regional trauma center in Korea and identified the risk factors for developing CIN.

Methods: We retrospectively reviewed the medical records of 138 patients for the patient demographics, creatinine levels, and vital signs. CIN was defined as an increase in creatinine by 0.5 mg/dL from admission after undergoing CT with IV contrast.

Results: Of the patients, 7.2% developed CIN during their admission after receiving IV contrast for CT. In the multivariate analysis, only the creatinine level at presentation (Adjusted odds ratio [aOR], 5.944; 95% confidence interval [CI], 1.486-23.733; p=0.012) and an injury severity score (ISS) greater than 22 (aOR, 1.096; 95% CI, 1.021-1.176; p=0.011) were independently associated with the risk of CIN.

Conclusion: CIN is uncommon in trauma patients following CT with IV contrast. The creatinine level at presentation and ISS were independent risk factors for developing CIN in trauma patients. [J Trauma Inj 2016; 29: 124-128]

Key Words: Contrast-induced nephropathy, Contrast medium

I. Introduction

Acute kidney injury (AKI) is the abrupt loss of kidney function, resulting in the retention of urea and other nitrogenous waste products and in dysregulation of the extracellular volume and electrolytes. The course of AKI is reversible in many cases; thus, it is important to determine its causes and to treat it early to restore normal kidney function. An estimated 3–5% of hospitalized patients develop acute renal failure (ARF).(1) Contrast-induced nephropathy (CIN) is a leading cause of hospital-acquired ARF (2) and is associated with increased mortality both during hospitalization and after discharge.(3-5)

Computed tomography (CT) is the gold standard for identifying injuries in trauma patients. CT enables the rapid, accurate diagnosis of injuries and leads to faster treatment. Frequently, iodinated intravascular contrast medium is used to obtain better CT images; however, it is associated with the development of CIN.

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(6,7) This problem has been studied most extensively in patients undergoing emergency cardiac catheterization.(8)

It is thought that contrast medium causes AKI via renal vasoconstriction and direct toxic effects on tubular epithelial cells via reactive oxygen species; however, the pathophysiology of CIN remains unclear. Several risk factors have been identified, including a low-effective circulatory volume, the use of nephrotoxic drugs, chronic kidney disease, diabetes mellitus, and congestive heart failure.(9)

We designed this study to investigate the incidence of and risk factors for CIN in a trauma population specifically.

II. Materials and Methods

1. Patients

We examined the medical records of trauma patients admitted to the regional trauma center in Busan, Korea from November 2015 to March 2016 who were more than 18 years old. A total of 360 trauma patients were identified from the trauma registry. Of these, 153 patients were excluded because the serum creatinine (sCr) level was not checked or the medical records were incomplete. In addition, 69 patients who lacked serial sCr level due to discharge on the day of admission or transfer to other hospitals were excluded. Ultimately, our study enrolled 138 patients (Fig. 1).

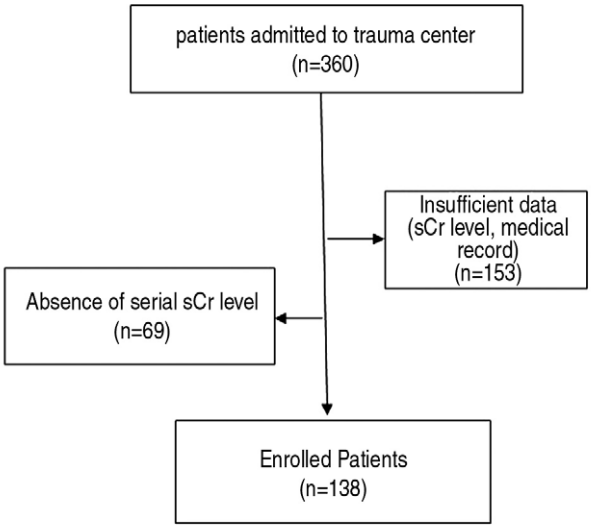

Fig. 1. Patient selection.

2. Methods

We performed a retrospective review of trauma patients admitted to a regional trauma center. The patient data, including demographic data, laboratory results, the amount of contrast agent injected, and injury severity score (ISS), were extracted from the trauma registry and medical records.

Rhabdomyolysis was defined as an increase in the serum creatine kinase (CK) level to five-fold greater than the upper-limit of normal, which was 217 U/L in our hospital. CIN was defined as an increase in the serum Cr level exceeding 0.5 mg/dL within 72 h of admission. We chose not to include an increase of 25% from baseline Cr level in our definition. The ISS is an established medical score used to assess trauma severity. It correlates with mortality, morbidity, and hospitalization time after trauma. The ISS is an anatomical scoring system that provides an overall score for patients with multiple injuries. Each injury is assigned an Abbreviated Injury Scale (AIS) score and is allocated to one of six body regions (Head, Face, Chest, Abdomen, Extremities (including Pelvis), External). Only the highest AIS score in each body region is used. The 3 most severely injured body regions have their score squared and added together to produce the ISS score. It is used to define the term major trauma, which is defined as an ISS greater than 15.

The patients in this study underwent CT with low-osmolar, nonionic iodinate (Xenetix 300, Guerbet, Roissy, France). The amount of contrast agent at the time of admission was calculated as the total amount of the contrast agent injected.

3. Statistical analysis

We divided the patients into two subgroups: those in which CIN occurred versus those in which CIN did not occur. Categorical variables were evaluated with the chi-square test. Continuous variables were reported as mean values with the standard deviation (SD) or median values with interquartile range (IQR). These variables were analyzed using Student's *t*-test or Mann-Whitney U-test. Variables were included in the multivariate logistic regression analysis if they were identified as risk factors associated with CIN in

univariate analyses. A p-value of less than 0.05 was considered significant. SPSS (ver. 20.0, IBM, Armonk, NY, USA) was used to perform the statistical analysis.

III. Results

1. Patient Characteristics (Table 1)

The mean age of the patients was 49.86± 17.25 years. The median contrast volume was 130.0 (120.0-140.0) mL, and the median ISS was 17.68 (2-50). The median sCr at admission and discharge was 0.87 (0.78-1.07) and 0.70 (0.61-0.83) mg/dL, respectively. The median systolic blood pressure at admission was 130.0 (100.0-140.0) mmHg, and the length of hospital stay averaged 21.0 (11.8-33.3) days.

2. Comparison of the groups with and without CIN (univariate analyses) (Table 2)

Overall, 7.2% of the trauma patients developed CIN during their admission after receiving IV contrast for CT (10 of 138). Compared with the patients who did not develop CIN, the patients who developed CIN had a higher ISS [31.5 (25.0-44.8) vs. 14.0 (9.0-22.0); p<0.001] and a greater total contrast volume [145 (130-243) mL vs. 130 (120-140) mL; p=0.01]. The patients who developed CIN were also more likely to have a higher sCr at admission [1.13 (0.86-1.61) mg/ dL vs. median 0.86 (0.78-1.04) mg/dL; p=0.021] and lower systolic blood pressure at admission [90 (75-123) mmHg vs. median 130 (105-140) mmHg; p=0.009]. There were no significant differences in age, sex, mechanism of trauma, history, sCr at discharge, or length of hospital stay.

Table 1. Characteristics of trauma patients who underwent CT with IV contrast

Alll patients	N=138
Age (y), mean (SD),	49.86 (17.3)
Sex (male/female), n (%)	115/23 (83.3/16.7)
ISS, median (IQR)	17.68 (2-50)
Admission sCr (mg/dL), median (IQR)	0.87 (0.78-1.07)
CRRT, n (%)	1 (0.7)
Discharge sCr (mg/dL), median (IQR)	0.70 (0.61-0.83)
Hospital length of stay (day), median (IQR)	21.0 (11.8-33.3)
Admission sBP (mmHg), median (IQR)	130.0 (100.0-140.0)
Contrast volume (ml), median (IQR)	130.0 (120.0-140.0)
Diabetes, n (%)	2 (1.4)
Hypertension, n (%)	13 (9.4)
Rhabdomyolysis, n (%)	11 (8.0)
CIN during admission, n (%)	10 (7.2)
CIN on discharge, n (%)	7 (5.1)

SD: standard deviation, IQR: interquartile range, CT: computed tomogaphy, ISS: Injury Severity Score, sCr: serum creatinine, sBP: systolic blood pressure, CRRT: continuous renal replacement therapy, CIN: contrast Induced nephropathy

Table 2. Univariate analysis of risk factors of development of CIN

	CIN (+), N=10	CIN (-), N=128	p
Age (y), mean (SD),	49.6 (18.7)	49.9 (17.2)	0.478
Male, n (%)	9 (90.0)	106 (82.8)	1.000
Contrast volume (ml), median (IQR)	145 (130-243)	130 (120-140)	0.010
ISS, median (IQR)	31.5 (25.0-44.8)	14.0 (9.0-22.0)	<0.001
Admission sCr (mg/dl), median (IQR)	1.13 (0.86-1.61)	0.86 (0.78-1.04)	0.021
Discharge sCr (mg/dl), median (IQR)	0.84 (0.65-1.68)	0.70 (0.62-0.81)	0.081
Hospital length of stay, median (IQR)	23.5 (12.3-40.0)	21 (12.5-34.5)	0.528
Admission sBP (mmHg), median (IQR)	90 (75-123)	130 (105-140)	0.009

CIN: contrast induced nephropathy, ISS: Injury Severity Score, sCr: serum creatinine, sBP: systolic blood pressure

Table 3. Multivariate analysis using a binary logistic regression of risk factors of development of CIN in trauma patients

Variable	Adjusted Odds ratio	95% CI	*p*
ISS	1.096	1.021-1.176	0.011
Admission sCr	5.944	1.486-23.733	0.012

CI: confidence interval, ISS: injury severity Score, sCr: serum creatinine

3. Risk factors for developing CIN (multivariate analysis) (Table 3)

In the multivariate analysis, only sCr at presentation (Adjusted odds ratio [aOR], 5.944; 95% confidence interval [CI], 1.486-23.733; p=0.012) and an ISS greater than 22 (aOR, 1.096; 95% CI, 1.021-1.176; p=0.011) were independently associated with the development of CIN.

IV. Discussion

The incidence of CIN is highly dependent on the clinical characteristics of the patient population, with an incidence of 50% or more in high-risk patients. (10-12) Procedures that use intravascular contrast medium such as coronary angiography and contrast-enhanced CT are being used more frequently for both diagnostic and therapeutic purposes. In addition, the major risk factors for CIN, *i.e.*, chronic kidney disease and diabetes mellitus, are also increasing in prevalence. (13,14) Both of these suggest that CIN will increase in incidence.

Various studies have identified risk factors for CIN following coronary angiography, including chronic kidney disease, hemodynamic instability, diabetes, and dehydration.(15,16) These risk factors are similar to those identified in our study of trauma patients, except diabetes. In addition, we identified the total contrast volume and ISS as risk factors.

We found that the overall incidence of CIN in trauma patients at a regional trauma center was 7.2%, with 5.1% of the patients having abnormal Cr level at discharge. This rate is slightly higher than in similar studies of trauma patients, which reported a range of CIN rates from 1.9% to 6.6%.(11-13) We found that contrast volume, sCr at presentation, hypotension at presentation, and ISS were all risk factors for CIN in univariate analyses. In the multivariate analysis, only sCr at presentation and ISS remained independently associated with the development of CIN. So, we recommend follow-up of renal function when initial sCr is elevated or ISS is high.

These risk factors are similar to those identified in other studies of trauma patients, as well as in patients receiving contrast for other reasons.(17-20,22-27) However, none of these studies agree about risk factors completely.

Hipp *et al.*(23) found a significantly increased risk of CIN in trauma patients older than 75 years, whereas others have found no association between increasing age and the risk of CIN.(19,28) Similarly, some studies have found that an elevated sCr level is associated with a risk for CIN,(22,23) while both Tremblay *et al.*(21) and Matsushima *et al.*(24) found no association in trauma patients admitted with elevated sCr level and the subsequent development of CIN.

In most studies, diabetes remains an independent risk factor for the development of CIN,(17,25) although diabetes was not a risk factor in our study. That our patients were substantially younger and healthier than most hospital and intensive care unit patients may be a contributing factor.

This study should be interpreted with certain limitations in mind. First, the study population comprised patients from a single regional trauma center, and the sample size was small. Second, this study was a retrospective, medical record review. Third, the difference in the definitions of CIN limits the comparisons that can be made with other studies. We used an increase in sCr level of 0.5 mg/dL from baseline as our definition, and our rates can be directly compared only with other studies that used this definition. Fourth, in our study, the ISS was an independent risk factor for developing CIN in trauma patients. We did not consider abdominal organ injuries as being similar to renal injury and we analyzed the ISS only. Fifth, the follow-up of CIN on discharge was not done exactly. Finally, we calculated the total volume of contrast agent without distinguishing between contrast-enhanced CT and angiography.

V. Conclusion

The rate of CIN in trauma patients following CT with IV contrast is low. The creatinine level at presentation and ISS were independent risk factors for developing CIN in trauma patients.

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