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Original scientific paper

The Incidence of Contrast Induced Nephropathy in Major Trauma Patients in the University Clinical Center of the Republic of Srpska

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ABSTRACT: Contrast-induced nephropathy (CIN) is characterized as an acute renal injury after the administration of intravascular iodinated radio-contrast medium in the absence of any other etiology. There is a small number of studies that analyze the occurrence and impact of CIN in traumatized patients who require whole-body CT according to the polytrauma protocol. In the period from January 2021 to May 2022, patients in the University Clinical Center of the Republic of Srpska who underwent CT according to the protocol for polytrauma were retrospectively analyzed. The study included 51 patients. CIN was defined as a 25% rise from baseline creatinine, or an absolute increase in creatinine of ≥ 44 μmol/l 24–48 h after administration of contrast. Of the total number of patients, 12% (n = 6) met the criteria for CIN. Age, sex, comorbidity, severity of injury based on ISS (injury severity score) were analyzed. Hemoglobin and fibrinogen levels, length of hospitalization, stay in the intensive care unit, mortality were monitored. A value of $p < 0.01$ was considered statistically significant. CIN is common in traumatized patients, but it is not an independent risk factor for length of hospitalization or mortality.

Keywords: Contrast Induced Nephropathy, Trauma, Computed Tomography.

INTRODUCTION

The intravascular administration of iodinated radiocontrast media can lead to acute renal dysfunction, which in the absence of other causes is defined as contrast-induced nephropathy (Weisbord & Palevsky, 2005).

The proposed pathophysiologic mechanisms of CIN are complex including intrarenal vasoconstriction with resultant medullary hypoxia, generation of reactive oxygen species, and direct renal tubular toxicity.

The pathophysiological mechanism of contrast-mediated nephropathy (CIN) is not completely clear. It is most likely due to vasoconstriction of intrarenal blood vessels with consequent medullary hypoxia, release of oxidative factors and direct renal tubular toxicity (Hossain et al., 2018).

It is a reversible impairment of renal function with an increase creatinine levels at 2-3 days and returning to baseline within 7-10 days after the administration of contrast medium.

There is no specific therapy for CIN, so risk assessment and the implementation of certain prophylactic measures are extremely important to reduce morbidity and mortality. CIN risk assessment is performed based on eGFRs (estimated glomerular filtration rates). Patients with eGFRs ≥ 45mL/min/1.73m2 have a minimal risk of CIN, patients with eGFRs < 30mL/min/1.73m2 are at high risk of CIN, while patients with eGFRs between 30 and 44mL/min/1.73m2 have a medium risk of development of CIN which is particularly increasing in diabetic patient (Rudnick et al., 2020; Tao et al., 2016). CIN is commonly diagnosed as an increase in creatinine value of 25% compared to normal values or an increase in initial creatinine value by ≥ 44 μmol/l 24–48 h after iodine contrast agent administration (Feldkamp & Kribben, 2008).

The incidence of CIN varies from 0.6 to 2.3% in patients who have not previously had impaired renal function, while in patients with increased risk factors it is up to 30% (Feldkamp & Kribben, 2008). Older age, diabetes, previous kidney disease, volume depletion, heart failure, and the use of nephrotoxic drugs are risk factors for developing CIN (McCullough, Wolyn, Rocher, Levin, & O'Neill, 1997; Owen, Hiremath, Myers, Fraser-Hill, & Barrett, 2014).

Contrast enhanced whole-body CT is more and more routinely performed for the initial evaluation of severely injured patients (Gordic et al., 2015). Although there is an increased risk, there are few studies that analyze the incidence and clinical significance of CIN in polytraumatized patients (Kelemen et al., 2022).

MATERIAL AND METHODS

This is a retrospective research, for the implementation consent of the Ethics Committee of the University Clinical Centre of the Republic of Srpska was obtained. Patients with a referral diagnosis of polytrauma, admitted to the Emergency Department of the University Clinical Centre of the Republic of Srpska between January 2021 and May 2022, were retrospectively analyzed. The study included patients older than 18 years who had CT performed according to the polytrauma protocol immediately upon admission. The study did not include patients who died in the first 24 hours after admission and patients who did not have recurrent creatinine levels 24 and 48 hours after iodine contrast agent administration. Patients with repeated CT diagnostics with contrast in the first 48 h were also excluded from the study. The study included a total of 51 (n = 51) patients.

CT according to the protocol for polytrauma in University Clinical Centre of the Republic of Srpska means native CT of the head and neck followed by contrast application of 1 ml/kg TT of isosmolar, non-ionized contrast containing 300 mg of iodide per milliliter (Ultravist®; Bayer Healthcare, Leverkusen, Germany) with saline lavage at a dose of 30 ml for chest and abdominal imaging.

Patients selected according protocols from the Emergency Department of the University Clinical Centre of the Republic of Srpska in the mentioned period, and the data were obtained from the clinical information system. Demographic data were collected: age, sex, comorbidity, severity of injury based on ISS (Injury Severity Score) (Elgin, Appel, Grisham, & Dunlap, 2019), length of hospitalization, hospitalization in the intensive care unit and mortality. The values of hemoglobin and fibrinogen (g/L) at admission, creatinine level at admission, creatinine level 24 and 48 h after CT imaging according to the polytrauma protocol were monitored. The need for transfusions of blood derivatives in the first 24 hours after admission was analyzed. The aim of this study was to analyze the incidence of CIN in polytraumatized patients, to identify risk factors for CIN in this group of patients, and to indicate the impact of CIN on treatment outcome. CIN was defined as a 25% increase in creatinine from normal or an increase in baseline creatinine of ≥ 44 μmol/l 24–48 h after iodine contrast agent administration (Feldkamp & Kribben, 2008).

The incidence of CIN in polytraumatized patients was expressed at 95% confidant interval (CI).

Categorical data are presented as frequency and numerically as mean ± standard deviation (SD). The Chi - square test was used to compare categorical variables and the Mann–Whitney U-test for numerical data.

All statistical analyses were performed by IBM SPSS. A p value of <0.01 was considered statistically significant.

RESULTS AND DISCUSSION

There are a small number of studies on the occurrence of CIN in major trauma patients. Most of the research about CIN have been performed in patients undergoing percutaneous coronary interventions (PCI) (McCullough et al., 1997). Cause of creatinine increase in severely injured patients can be multifactorial e.g., hemorrhagic shock, blood transfusions, injury mechanism, rhabdomyolysis advanced age (Kelemen et al., 2022).

Our study included a sample of 51 patients. Of the total number of patients, 6 or 12% met the criteria for CIN. Table 1 shows the differences between patients with CIN and those who did not develop renal impairment 8 (non-CIN) in terms of age, sex, comorbidity, ISS, hemoglobin and fibrinogen levels, need for transfusion, length of hospital stay (LOS) and length of stay in the intensive care unit (ICU).

In a retrospective cohort study conducted in Zurich, 14% of patients had CIN (Kelemen et al., 2022). This study was conducted over a long period of time, included 284 patients, was performed in the trauma center of the first degree and referred to polytraumatized patients who were intubated at admission and with a significantly high ISS. Other similar studies showed a significantly lower prevalence of 2.1 to 5.1% (Colling et al., 2014).

Our study included 8 (15.68%) women and 43 (84.32%) men. All patients who had CIN were male, but due to the small number of patients who had CIN, the influence of gender on the occurrence of CIN cannot be proven.

The age analysis showed that the mean value of years in the CIN group was 49 ± 18 and in the second group it was 48 ± 19 ($p = 0.0001$). Age is considered to be a significant risk factor for CIN (Colling et al., 2014) , which has been confirmed in our study.

A significant factor for the development of CIN is comorbidity. This has been proven by results of similar studies (Toprak et al., 2007). We analyzed the presence of cardiovascular disease, diabetes mellitus and previous kidney disease. However, possibly due to the small sample group of our study and the large variety of preexisting conditions, we haven not proven that the presence of comorbidities significantly influenced the occurrence of CIN ($p = 0.8471$).

The ISS (Injury Severity Score) has been used to estimate the severity of trauma since 1974, the value can be from 0-75. The ISS score in our patients in the CIN group was 22 ± 11, and in the non-CIN group 14 ± 7. We have not ben able to prove a significant statistical difference between these two groups ($p = 0.4718$). In a retrospective cohort study (Kelemen et al., 2022) in the CIN group the ISS was 30 ± 16 and in the non-CIN group 28 ± 17 ($p = 0.296$). In this study, patients admitted to the trauma center was endotracheal intubated. Our study included patients who had a referral diagnosis of polytrauma, while data on how many patients were intubated prior to hospitalization were not available.

The mean hemoglobin level (g/L) in the CIN group was 12.9 ± 1.7. In the non-CIN group it was 13.6 ± 1.8 ($p = 0.001$). The value of fibrinogen (g/L) in the CIN group was 2.7 ± 0.9 and in non-CIN 2.6 ± 0.5 ($p = 0.4443$). Low hemoglobin levels at admission have been reported as a risk factor for nephropathy in patients undergoing coronary angioplasty (Spahn, Spahn, & Stein, 2015). In major trauma patients, anemia was not assessed as a significant risk factor for CIN, but CIN in combination with low hemoglobin levels doubled the mortality in their population (Banda et al., 2016).

In our study, 67% of patients in the CIN group and 40% of patients in the non-CIN group required a transfusion in the first 24 hours. Erythrocyte transfusion is a significant risk factor for renal impairment, studies have shown that each unit of erythrocyte increases the risk of nephropathy by 10 to 20% in cardiac surgery patients (Karkouti, 2012).

No patient in our study required hemodialysis in the first 48 h after trauma. Similar studies have not shown that CIN significantly increases the risk of hemodialysis in trauma patients (McDonald et al., 2014).

The mean length of hospital stay in the CIN group was 16.8 ± 9.6 days, while in the non-CIN group it was 11,4 ± 10,7 days. Possibly due to the large variety in length of stay in both groups, we have not been able to prove a significant statistical difference between these two groups (p = 0.4408) which showed that in our study the occurrence of CIN did not certainly affect the length of hospital stay. The mean number of hospitalization days in the intensive care unit (ICU) in the CIN group was 7 ± 7 days and in the non-CIN group 5 ± 8 days. All patients in our CIN group stayed in intensive care for at least 1 and at most 19 days. Not all patients in our non-CIN group stayed in intensive care. That might indicate that patients in CIN group dealt with more serious injuries than those in non-CIN group, but for making any further correlation larger sample group is needed.

No patient died in CIN group in our study. Furthermore, in the study (Kelemen et al., 2022), CIN did not affect mortality and duration of treatment.

There are some limitations to this study. This study was conducted on a small sample, conducted retrospectively in a short period of time. The study included patients who underwent contrast-enhanced CT according to the polytrauma protocol. There are no clearly defined criteria for whole body CT for major trauma patients. Medical records are often incomplete, a large number of patients could not be included due to lack of individual data. Lactate levels were not analyzed, as a factor that would indicate hypovolemia and the presence of shock. No data were available on the amount and application of crystalloid solution in the first 24 or 48 hours after trauma.

Table 1. Summary of patient characteristics between the CIN and non-CIN group

	Non-CIN n = 45 (88%)	CIN n = 6 (12%)	p value
Age (years)	48 ± 19	49 ± 18	0.0001
Gender (male)	37 (82%)	6 (100%)	0.5628
Comorbidities	12 (27%)	4 (67%)	0.8471
Injury severity score	14 ± 7	22 ± 11	0.4718
Hemoglobin (g/l)	13.6 ± 1.8	12.9 ± 1.7	0.0001
Fibrinogen	2.6 ± 0.5	2.7 ± 0.9	0.4453
Transfusion	18 (40%)	4 (67%)	0.7805
Length of stay (days)	11,4 ± 10,7	16.8 ± 9.6	0.4408
Stay in the intensive care unit (days)	5 ± 8	7 ± 7	0.3652

CONCLUSION

Based on the obtained data, we have concluded that the use of iodine contrast agent in the diagnostic treatment of major trauma patients does not lead to additional damage in these patients. The development of CIN does not certainly lead to prolonged hospitalization or increased mortality. Polytraumatized patients, especially those with high ISS, require contrast-enhanced CT, regardless of the risk of CIN. There are other risk factors for kidney damage in these patients. Additional research is needed to examine the effect of fluid and blood transfusion, the mechanism of injury, the injured part of the body on the development, as well as the consequences of CIN in these patients.

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