The Incidence of Contrast Induced Nephropathy in Trauma Patients

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Abstract

PURPOSE: Contrast-induced nephropathy (CIN) has been recognized as a potential adverse outcome in patients receiving contrast dye for CT evaluation for over 50 years. Despite the time and resources dedicated to better identifying at-risk patients and implementing preventative measures, contrast induced nephropathy continues to be a significant cause of hospital acquired renal insufficiency. This study was aimed to evaluate the incidence and factors associated with contrast-induced nephropathy in the trauma patient population.

MATERIALS AND METHODS: A retrospective institutional review of 563 patients admitted to the trauma service at St. Joseph's Hospital and Medical Center were evaluated. Data were recorded for each patient including demographics, injury severity score (ISS), clinical prediction score (CPS), laboratory values on admission, 24, 48 and 72 hours including hematocrit, blood urea nitrogen, creatinine and eGFR, IV fluid volume given, contrast volume given, systolic blood pressure (SBP), urine output (UOP), intensive care unit length of stay (ICU LoS) and total hospital length of stay (tot LoS). Contrast induced nephropathy was considered to be present if the patient received contrast material for CT scan and 24-48 hour creatinine increased by an absolute value of 0.5mg/dl or if there was a 25% increase in 24-48 hour creatinine when compared to admission creatinine. Contrast volumes given to each patient before CT scan were determined by the Department of Radiology.

RESULTS: As seen in *table 1* results of univariate analysis demonstrate the following significant data: CIN vs age (p 0.004), CIN vs ISS (p <0.000), CIN vs CPS (p <0.000), CIN vs ICU length of stay (p 0.006), CIN vs total length of stay (p 0.002), CIN vs SBP (p <0.000), CIN vs IVF volume given in the 2nd 24 hours (p <0.000) and CIN vs IVF volume given in the first 48hrs (p <0.000). Data from multivariate analysis demonstrate the following significant data: CIN vs CPS (p <0.000, CI $1.92E^{-2}$ – $3.93E^{-2}$), CIN vs SBP (p 0.003 CI $8.61E^{-4}$ – $4.41E^{-3}$) and CIN vs IVF vol 2nd 24 hours (p 0.001, CI $1.47E^{-5}$ – $5.91E^{-5}$). The mean data for patients who did and did not develop CIN respectively were CPS: 9.09 and 3.12, SBP 84mmHg and 99mmHg, and IVF vol 2nd 24 hrs 2504ml and 5931ml

CONCLUSION: Contrast induced nephropathy continues to be a significant problem in many hospital populations including trauma patients. Certain patient groups including those with

higher CPS, hypotension or receiving decreased IV fluids may benefit from aggressive mindfulness of the risk of contrast induced kidney injury and continued investigation is needed to better identify trauma patients at increased risk.

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Introduction/Significance

Background

Contrast-induced nephropathy has long been identified as a potential adverse outcome in patients receiving intravenous contrast infusion. Though this was first recognized some 50 years ago, contrast induced nephropathy is still the third largest cause of hospital-acquired renal insufficiency in the United States, accounting for over 11% of cases and more than 180 million dollars in potentially preventable healthcare costs per year[1,8]. Many risk factors have been identified as having a significant association with contrast-induced nephropathy. These include; age>70, preexisting renal insufficiency, diabetes mellitus, hypertension, congestive heart failure, anatomical kidney disease, volume depletion, large contrast volume/use of ionic contrast and concomitant use of nephrotoxic drugs[1,5,7,8,9]. For many patients, the effects of some of these risk factors may be mitigated with preventative measures before intravenous contrast administration. Previous studies have demonstrated the effects of multiple contrast doses on patients, outcomes associated with acute kidney injury up to 72 hours after contrast administration and the limitations of using creatinine as a marker for acute kidney injury. It has also been postulated that some radiological studies such as cardiac catheterization are associated with increased incidence of contrast-induced nephropathy perhaps because of a greater urgency inherent in the imaging[8]. Trauma patients provide a novel view into the effects of contrast agents on kidney function because diagnostic radiological examinations, requiring contrast, are often vital. For this reason these patients may not undergo many of these preventative measures and will receive contrast infusion for diagnostic radiologic scans regardless of other risk factors or comorbidities. This study will retrospectively examine the incidence of contrast-induced nephropathy in trauma patients who received contrast infusion for a CT scan upon admission to the trauma service at St. Josephs Hospital and Medical Center in Phoenix, Arizona.

In the past there has been much research done looking at the incidence of hospital acquired nephropathy in the setting of contrast administration, however, trauma patients provide a novel population because of the acute need for radiologic evaluation, most often in

the form of CT scans, with contrast. Multiple mechanisms for how contrast agents damage and can ultimately shut down normal kidney function have been postulated. An article published in the *Clinical Journal of the American Society of Nephrology* in 2008 by Heyman et al details the recent studies examining the possible causes of contrast induced nephropathy[5]. They report that it is thought to be contrast mediated medullary hypoxia possibly from both a decrease in microcirculation and increased oxygen demand. This leads to the development of reactive oxygen species, which then lead to increased tubular transport, and subsequent increased oxygen demand, endothelial damage and interference with the protective response to hypoxia (nitric oxide and other vasoactive compounds). These events result in a cycle of increasing hypoxia in the medulla ultimately resulting in nephropathy[5]. Many of the risk factors for contrast-induced nephropathy are thought to play a role in either increasing this hypoxia and free radical damage or decreasing the body's ability to combat hypoxia with vasoactive compounds. Not surprisingly, a study published by Trivedi et al found that repeated contrast administration, within 3 days of initial infusion, for the purpose of CT evaluation, even in patients with preserved glomerular filtration rates significantly increased their risk of contrast induced nephropathy[6]. Another study published in the *Journal of TRAUMA Injury, Infection and Critical Care* in 2010 by McGillicuddy et al found that development of acute kidney injury within 72 hours of admission to a trauma service was an independent risk factor for in-hospital mortality and prolonged length of stay[3].

Because of the morbidity and mortality associated with contrast-induced nephropathy many strategies have been developed attempting to prevent this negative outcome in patients who require a less urgent scan turnaround time. Unfortunately we have yet to develop a definitive preventative strategy to combat contrast-induced nephropathy. While the use of bicarbonate and N-acetylcysteine were initially found to be efficacious, multicenter trials have shown mixed results including their effect on long-term morbidity and mortality regardless of how well these agents prevent contrast induced nephropathy[2]. For now hydration has been shown to be the most consistently efficacious treatment[5], however, protocols commonly include hydration as well as use of nonionic contrast agents, limiting contrast volume, spacing

multiple doses >10 days apart, N-acetylcystine administration before and after contrast infusion and discontinuing nephrotoxic drugs for at least 24 hours as the preventative strategies[1,7].

Impact

As the body of evidence regarding contrast induced nephropathy continues to grow, this study hopes to build on previous findings with a retrospective study investigating the incidence of contrast-induced nephropathy as well as associated morbidity in this trauma patient population. Past studies have looked at contrast-induced nephropathy in patients undergoing CT examination, however, after reviewing the literature, there has been very few studies looking at the relationship between the volume of contrast dose during emergency CT scans and the subsequent development of contrast induced nephropathy as was done in this study.

Aims/Goals/Hypothesis

Identify all patients admitted to the St. Joseph's Hospital and Medical Center trauma service and collect data related to incidence of contrast induced nephropathy, demographics, contrast doses, age, sex, comorbidities, number of CT's or CTA's received, number of follow up scans received during hospital stay, renal function tests and IV fluid bolus administration. The study will help identify the incidence of contrast induced nephropathy as well as associated factors contributing to increased morbidity in trauma patients receiving contrast infusions with the end goal of using data from this retrospective study to create a prospective trial to find interventions that decrease morbidity and provide better outcomes to trauma patients.

The hypothesis is that contrast induced nephropathy will be present in patients who are elderly, if there is the presence of shock, if less IV fluids are given and if more contrast is administered.

Materials and Methods

A single institution, retrospective chart review of trauma patients undergoing contrast enhanced CT scans upon admission from 2005 to 2010 was conducted. This study was done in conjunction with the Department of Radiology, who provided all contrast dosages for each individual scan. Inclusion criteria consisted of all trauma patients age 18 years of age and older undergoing radiologic evaluation requiring intravenous contrast. Exclusion criteria included age younger than 18 years and/or not receiving intravenous contrast for radiologic evaluation. 815 patients were initially identified to participate in the study, 252 met the exclusion criteria leaving 563 patients eligible for the study. Medical records were examined and the following data were recorded for each study participant: age, sex, race, injury severity score (ISS), contrast-induced nephropathy grade (CIN grade), clinical prediction score (CPS), disposition location, intensive care unit length of stay (ICU LOS), total length of stay (total LOS), admission, 24hour, 48hour and 72hour laboratories including hematocrit (hct), blood urea nitrogen (BUN), creatinine, estimated glomerular filtration rate (eGFR), 24hour, 48hour and 72hour urine output, intravenous fluid volume given at 24hours, 48hours and 72hours, lowest systolic blood pressure (SBP) in 72 hours, number of CT scans, contrast volume administered and contrast type. In this study, each patient was considered to have contrast-induced nephropathy if they received contrast material for a CT scan and 24-72 hour creatinine increased from admission creatinine by an absolute value of greater than or equal to 0.5 mg/dl or 24-72 hour creatinine increased from admission creatinine by greater than or equal to 25%. A CIN grade was assigned to each patient based on admission and 24-72hr creatinine. A "2" was assigned to any patient whose admission creatinine increased by an absolute value of greater than or equal to 0.50 in the 24-72 hours following admission. A "1" was assigned to any patient whose admission creatinine increased by greater than or equal to 25% in the 24-72 hours following admission. A "0" was assigned to any patient whose creatinine did not meet criteria for a "1" or "2" and these patients were considered to have no evidence of acute kidney injury. ISS was calculated

for each patient using the method described by Baker et al[10]. CPS was calculated for each subject retrospectively[11]. Subjects were given points for the presence of the following conditions; 5 points for hypotension, 4 points for age >75 years, 3 points for anemia, 1 point for every 100cc of contrast media, 4 points for creatinine >1.5mg/dl or 2 points for an eGFR of 40-60, 4 points for eGFR of 20-40, 6 points for eGFR <20. Anemia was defined as hct <39 for males and <36 for females. Hypotension was defined as systolic blood pressure <80mmHg. Descriptive statistics were performed and expressed as mean and standard deviation unless otherwise specified. Categorical data was expressed as counts and proportions. Analysis was done using univariate and multivariate regression.

Results

Retrospective review of patients admitted to St. Joseph's Hospital and Medical Center from 2005 to 2010 yielded 812 patients meeting the inclusion criteria. After excluding patients without admission laboratories or 24hour laboratories and patients with no recorded contrast doses, a total of 562 patients were eligible for review. Regression analysis was used to evaluate the significance of several factors as they relate to the incidence of contrast-induced nephropathy. Demographic data for the subjects included in the study can be found in *table* 1 with the majority of subjects being Caucasian (55%). Results of univariate analysis can be seen in *table 2* and demonstrate the following significant data: CIN vs age (p value: 0.004), CIN vs ISS (p value <0.000), CIN vs CPS (p value <0.000), CIN vs ICU length of stay (p value 0.006), CIN vs total length of stay (p value 0.002), CIN vs IVF volume given in the 2nd 24 hours (p value <0.000) and CIN vs IVF volume given in the first 48hrs (p value <0.000). Also of note CIN vs contrast volume given acutely upon admission came close, however did not reach significance with a p value of 0.067. Data from multivariate regression analysis are shown in *table 2.* The relationship between CIN and Clinical Prediction Score remains significant (p value <0.000, CI $1.92E^{-2}$ – $3.93E^{-2}$), as did the relationship between CIN and SBP (p value 0.003 CI $8.61E^{-4}$ – $4.41E^{-3}$) and CIN vs IVF volume given in the 2nd 24 hours (p value 0.001, CI $1.47E^{-5}$ – $5.91E^{-5}$). Age, ISS, ICU length of stay, total length of stay and IVF volume given in the first 48 hours did not continue to have a statistically significant relationship with development of contrast induced nephropathy after multivariate analysis. The means of each factor relating to CIN can also be found in *table 1* and *figure 2*. The mean clinical prediction score of a patient who developed contrast-induced nephropathy was 9.09 compared to 3.12 for a patient who did not develop CIN. The mean lowest systolic blood pressure of a patient who went on to develop CIN was 84mmHg while the mean SBP of a patient who did not develop CIN was 99mmHg. The IV fluid volume given to a patient in the 2nd 24 hrs who went on to develop contrast induced nephropathy was 2504ml compared with 5931ml given to a patient who did not develop CIN. Patients who developed contrast-induced nephropathy got on average more contrast than patients who did not develop CIN (115ml vs 102ml) but this difference was not statistically significant.

Table 1. Patient demographic information, number of patients, percent of total, mean age of

patients enrolled in the study and incidence of contrast induced nephropathy.

Demographic	Total	%
Men	393	69.9
Women	170	30.1
Hispanic	170	30.3
African American	40	7.1
Caucasian	309	55.0
Asian	3	0.5
Native American	14	2.5
Other	27	4.8
Mean Age	43yrs	
CIN Incidence	6.40%	

Table 2. Univariate and Multivariate p values, confidence intervals for multivariate analysis and the mean data for subjects who developed contrast induced nephropathy vs those who did not develop contrast-induced nephropathy.

	Univariate	Multivariate	95% Conf. Interval		Mean	
	p value	p value			(+) CIN	(-) CIN
CIN vs Age	0.004	0.914	-0.0013361	0.0015060	54	41
CIN vs ISS	<0.000	0.541	-0.0032229	0.0017886	23	13
CIN vs CPS	<0.000	<0.000	0.0192418	0.0393293	9.09	3.12
CIN vs ICU LoS	0.006	0.709	-0.0101594	0.0069159	7	3
CIN vs Total LoS	0.002	0.709	-0.0053490	0.0078563	12	6
CIN vs SBP	<0.000	0.003	0.0008613	0.0044137	84	99
CIN vs IVF Vol 2nd 24hr	<0.000	0.001	0.0000147	0.0000591	2504	5931
CIN vs IVF Vol 48h	<0.000	0.654	-0.0000125	0.0000208	3470	7033
CIN vs Contrast Vol 24h	0.235	-	-0.0002575	0.0010471	118	108
CIN vs Conrast Vol Acute	0.067	0.111	-0.0014413	0.0001685	115	102

Figure 1. Mean data for variables of patients who developed contrast induced nephropathy compared to the mean data for variables of patients who did not develop contrast induced nephropathy.
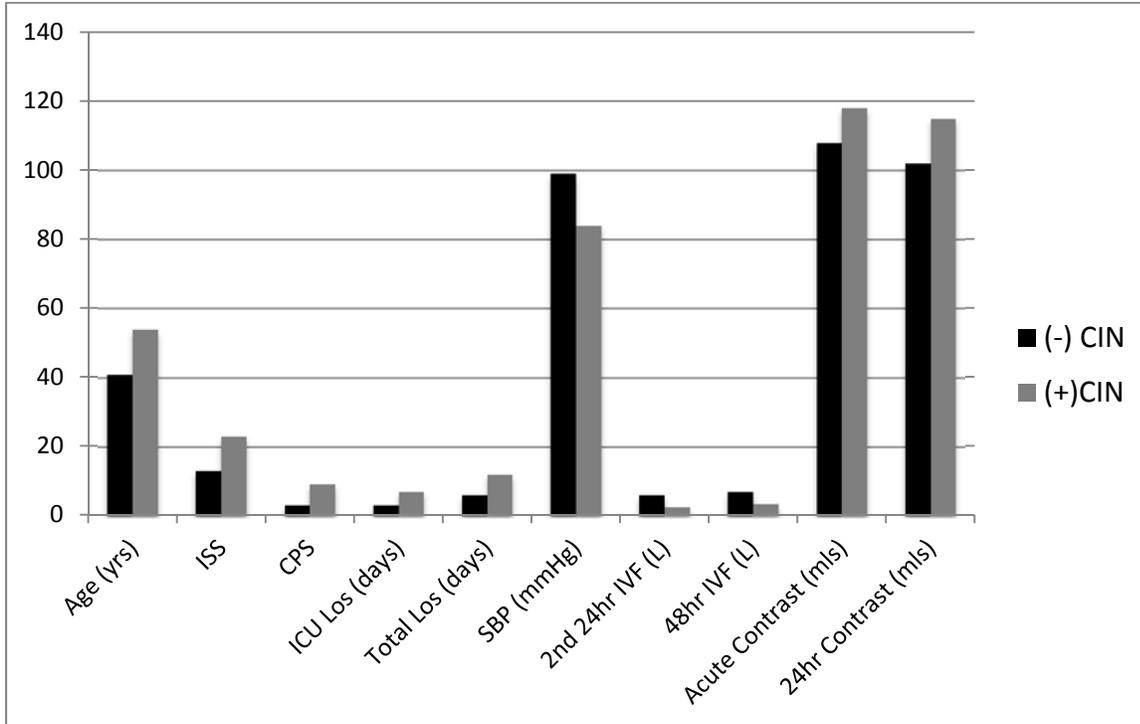
Discussion

This study will help further delineate the risk of contrast-induced nephropathy in trauma patients. A higher clinical prediction score, lower systolic blood pressure and fewer IV fluids administered in the second 24 hours seem to be significantly associated with increased risk of developing contrast induced nephropathy. This may not be surprising given that CPS looks at factors that can affect kidney function (ie. hypotension, contrast volume, creatinine) and IV fluids have been shown in other populations to be protective against the development of CIN. Hypotension may be somewhat of a confounder in this analysis as it can, independently of contrast administration, lead to kidney damage. ISS was shown in this analysis to not be significantly associated with CIN, most likely because it is focuses more broadly on the anatomic severity of injury only (ie. laceration to kidney parenchyma and/or injury to vascular structures). Past studies have looked at contrast-induced nephropathy in patients undergoing CT examination, however, after reviewing the literature, there has been very few studies looking at the relationship between the volume of contrast dose during emergency CT scan and the subsequent development of contrast induced nephropathy as was done in this study. We hypothesized that the amount of contrast administered would be associated with the development of contrast-induced nephropathy. However, these data demonstrate no significant correlation between volume of contrast given and the development of CIN. We believe that these negative findings probably reflect the insufficient power of this study rather than truly no correlation between these variables. In the future, certain patient groups including those presenting with higher clinical prediction scores, lower SBP and those receiving less IV fluids may benefit from aggressive mindfulness of the risk of contrast-induced kidney injury before contrast administration. Continued investigation is needed to identify risk factors and characterize methods to better identify trauma patients at increased risk for contrast induced nephropathy.

Limitations

As mentioned above, one limitation of this study was that we believe it was underpowered. We believe this is the reason this study was unable to demonstrate some correlations that have been well documented in previous studies looking at contrast-induced nephropathy in other populations. These correlations include CIN grade and volume of contrast administered as well as day-2 GFR. One more limitation of this study is the presence of potential confounders such as hypotension.

Future Directions

There are a multiple future directions that can be taken using this study as a starting point. The first would be to continue to evaluate this trauma patient population in order to increase the power of the study to better evaluate the relationships between the variables investigated here. This may allow future investigators to more properly characterize the relationships between variables that showed no statistical significance in this investigation. This study clearly demonstrated a relationship between acute kidney injury and CPS, the presence of hypotension as well as decreased IV fluid administration. In future prospective investigations these would clearly be a place to start when evaluating which patients to target for more aggressive strategies to prevent and combat contrast induced nephropathy.

Conclusion

Contrast induced nephropathy continues to be a significant problem in many hospital populations including trauma patients. Certain patient groups including those presenting with higher clinical predication scores, those who become hypotensive, and those who receive fewer IV fluids may benefit from aggressive mindfulness of the risk of contrast induced kidney injury. Continued investigation is needed to characterize methods to better identify trauma patients at increased risk for contrast induced nephropathy so that these patients can receive aggressive prophylactic treatments.

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