ORIGINAL ARTICLE

A Retrospective Comparison of Creatinine Changes Among Patients Receiving, Not Receiving, and Not Yet Receiving Contrast Administration

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Abstract

Objective: We sought to compare variability in serum creatinine among inpatients in our institution receiving contrast imaging studies and among inpatients not receiving such studies.

Materials and Methods: This retrospective, single-site, multiple-cohort study in a 550-bed academic medical center in October 2016 used the electronic medical record data to analyze the greatest absolute and relative changes in serum creatinine over periods no longer than 48 hours (1) during the admission for 1,134 patients who did not receive a contrast imaging study, (2) before the earliest contrast study for 155 patients who had not yet had a scheduled contrast examination, and (3) straddling the time when 266 patients received their earliest contrast study. We compared creatinine changes in the first cohort with those in the second and the third using histograms and *t* tests.

Results: Among those who did not receive contrast, 18.3% had a creatinine increase of greater than 0.3 mg/dL, and before contrast, 14.2% had such increases ($P = .22$). After contrast, 6.4% had increases at least this great ($P < .001$). Patients with increases in creatinine before contrast tended to have such increases after as well (Pearson's 0.48, $P < .001$).

Conclusions: Physiological variability may explain the similar increases among patients who did not receive contrast versus patients who had not yet received contrast. Hydration therapy may explain the milder and fewer increases after contrast. Only a randomized clinical trial can determine whether acute kidney injuries are caused by contrast; these results support equipoise for such a trial.

Key Words: Creatinine, contrast media, acute kidney injury, quality, safety

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INTRODUCTION

The prevention of sudden renal injury after the administration of iodinated contrast material has long been a key objective for both radiologists and referring physicians when determining the risk-benefit ratio in establishing an imaging diagnosis [1]. Contrast-induced nephrotoxicity is a well-defined and well-documented effect associated with contrast media [2], although recently, authors have questioned the causal relationship [3].

Yet investigation of postcontrast acute kidney injury (PC-AKI) has often not considered control patients [4-7]. Because creatinine varies physiologically without exposure to contrast media [8], and because such increases in creatinine are of magnitudes similar to the PC-AKI criteria [9], doubt has risen to the extent to which contrast administration causes observed creatinine increases [1,10].

The relatively few studies that do use control groups show mixed results. One recent, large, and well-controlled study among emergency department patients found no difference in acute kidney injury (AKI) attributable to contrast administration regardless of pre-existing kidney function [11]. Another found higher risk of AKI among those with compromised kidney function [12]. A third found no higher risk, regardless of kidney function [3].

These questions are important both for quality of care among patients receiving contrast during a study, but also

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for selection criteria into a diagnostic pathway including a contrast study.

We sought to compare variability in serum creatinine among inpatients in our institution receiving contrast imaging studies, among control inpatients not receiving such studies, and among those who had such a study scheduled at a future date in the current admission.

We hypothesized that creatinine varies naturally both among inpatients who did not have a contrast study and inpatients who were selected and scheduled for a contrast study but had not had such a study yet. We further hypothesized that such "natural" increases would be similar to increases seen among patients who had had a contrast study.

This latter group forms a key control group: it represents patients selected into a diagnostic pathway involving contrast administration but not yet exposed to the contrast media. As such, they differ both from patients never receiving a contrast study (eg, perhaps selected as having better kidney function) and from patients who have already received their contrast study (because the exposure is still missing).

The goal of this investigation was to contribute to the small volume of literature that supports the notion of clinical equipoise between contrast administration and unenhanced imaging and thus enables a randomized clinical trial to be ethically conducted.

MATERIALS AND METHODS

Research Plan

This retrospective, single-site, controlled-cohort study was approved by the Institutional Review Board of the College of Medicine at the study institution, which waived the requirements of informed consent and deemed this study HIPAA-compliant. We queried our electronic medical record system (Cerner Millennium, Cerner Corporation, Kansas City, Missouri, USA) for all adult patients admitted during October 2016 with at least two serum creatinine laboratory test values, a routine metabolic panel laboratory test ordered at least once on inpatients.

Subject Cohorts

Our institution admits approximately 2,000 new inpatients a month; the total of 1,280 unique patients, each with two draws, in the three cohorts described herein represents more than 60% of typical monthly admissions.

We constructed three cohorts of inpatients as follows. The first cohort had no contrast imaging study during their admission and consisted of all 1,134 inpatients with at least two serum creatinine test values recorded in any period no longer than 48 hours during the admission. These patients are referred to hereafter as the "no-contrast" cohort. Some of these patients may have been considered for a contrast study but were rejected based on our institutional guidelines or due to physician discretion. The great majority are unlikely to ever have been considered for a contrast study, making selection effects possible but likely to be of small magnitude. For this reason, we consider this cohort a control group.

The second cohort ultimately had one or more contrast studies during the admission, but we consider only creatinine draws *before* a contrast study. We refer to these hereafter as the "before-contrast" cohort. This cohort consisted of all 155 inpatients with at least two serum creatinine test values recorded in any period no longer than 48 hours before the earliest of one or more contrast imaging studies. These patients have been subject to a selection bias because only patients meeting our institutional guidelines for contrast studies and whom the referring physician and radiology technologist have approved for contrast studies are actually imaged with contrast.

Yet these patients *also* represent an important control group for two reasons. Their earliest contrast study is in the future and so cannot directly affect the blood draws before. Moreover, pretreatment such as hydration immediately before the study has usually not happened yet, so observed creatinine variability is unlikely to be attenuated due to such interventions. They are thus similar to the first cohort of control patients in not having the exposure but different in that they have been selected into a pathway for an eventual contrast examination.

These patients therefore provide some understanding of the impact of unobserved selection criteria into the contrast study pathway. For example, if patients who tended to have higher or lower creatinine variability also had conditions that made a contrast study more likely, then this could confound the results of assessing changes in creatinine around the time of a contrast study.

The third cohort is the "active" cohort, consisting of all 266 inpatients with at least two serum creatinine test values recorded in a period no longer than 48 hours *straddling* the earliest of one or more contrast imaging studies obtained during the admission. To make this concrete, the first draw had to be before the contrast study, the second after the contrast study, and these could be no longer than 48 hours apart.

The second and third cohorts differ in number because not every patient subsequently obtaining a contrast study had two or more creatinine values beforehand or two creatinine values straddling their study. As a result, only 146 patients are common to both cohorts.