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Original article

Prediction of contrast-induced nephropathy by the serum creatinine level on the day following cardiac catheterization

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ABSTRACT

Background: The majority of patients who undergo coronary arteriography are discharged from the hospital on the day of the procedure or on the following day. The aim of this study is to investigate whether the change in serum creatinine (SCr) and estimated glomerular filtration rate (eGFR) on the day following cardiac catheterization can predict the development of contrast-induced nephropathy (CIN).

Methods: This is a multicenter prospective observational study, which consists of 860 patients who underwent cardiac catheterization. We measured SCr and eGFR before cardiac catheterization, on the following day, and 48–72 h post-procedure. Definition of CIN is changes in SCr ≥0.5 mg/dL or ≥25% from baseline 48–72 h after contrast exposure.

Results: CIN occurred in 40 patients. SCr levels significantly increased from a baseline of 1.55 ± 1.08 mg/dL to 1.79 ± 1.26 mg/dL on the following day in patients with CIN ($p < 0.0001$), but significantly decreased from a baseline of 1.21 ± 0.65 mg/dL to 1.18 ± 0.61 mg/dL on the following day in those without CIN ($p < 0.0001$). eGFR significantly decreased from a baseline of 47.3 ± 28.3 mL/min/1.73 m^2 to 40.6 ± 26.7 mL/min/1.73 m^2 on the following day in patients with CIN ($p < 0.0001$), but significantly increased from a baseline of 53.1 ± 22.0 mg/dL to 53.6 ± 21.2 mg/dL on the following day in those without CIN ($p = 0.0236$). Receiver operating characteristic curve analysis indicated that SCr change ≥0.1 mg/dL [area under the curve (AUC) = 0.852, sensitivity 72.5%, specificity 86.1%] and eGFR change ≤−1.1 mL/min/1.73 m^2 (AUC = 0.789, sensitivity 85.0%, specificity 64.9%) were the best cut-off values for predicting CIN. Multivariate logistic regression showed that a change in SCr ≥0.1 mg/dL [odds ratio (OR),

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29.3; 95% confidence interval (CI), 10.8–96.2] and change in eGFR ≤−1.1 mL/min/1.73 m^2 (OR, 69.7; 95% CI, 13.3–952) were powerful independent predictors of CIN.
Conclusions: Changes in SCr and eGFR on the day following cardiac catheterization predict the development of CIN.
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Introduction

Use of contrast media is necessary for diagnostic imaging, interventional radiology, and percutaneous coronary intervention in real-world clinical settings. However, contrast-induced nephropathy (CIN), a complication of contrast use, has been identified as the most frequent cause of hospital-acquired acute kidney injury, and is sometimes associated with poor prognosis [1–3]. Given that reduced renal function and an increased ratio of contrast volume to estimated glomerular filtration rate (eGFR) are risk factors for CIN [4,5], physiological saline or half saline are usually infused before and after contrast use and physicians try to minimize the volume of contrast used in patients with eGFR ≤60 mL/min/1.73 m^2 to prevent the development of CIN [6–9]. In spite of physicians' utmost efforts, however, CIN still accounts for a significant proportion of hospital-acquired acute kidney injury.

To improve the clinical course of CIN, early diagnosis and prompt, appropriate treatment of CIN are necessary. However, CIN is defined as an increase in serum creatinine (SCr) of ≥0.5 mg/dL or ≥25% from 48 to 72 h after exposure to contrast media [10,11]. Therefore, CIN cannot be diagnosed on the day of cardiac catheterization or on the following day, when the majority of patients who undergo elective cardiac catheterization are discharged from the hospital in the real-world setting. In this context, the aim of the present study is to investigate whether the change in SCr on the day following cardiac catheterization can predict the development of CIN before hospital discharge and allow for appropriate patient care, using the patient population of a study on CIN after cardiac catheterization in Japan (the CINC-J study).

Methods

Patient enrollment

The CINC-J study, a Japanese prospective, multicenter registry observational cohort study, was conducted to evaluate the incidence of CIN stratified by renal function, as described previously [12]. Briefly, we enrolled patients who underwent cardiac catheterization for diagnostic purposes or elective and emergent percutaneous coronary intervention treatment at 27 institutions from November 2011 to September 2013. Patients who were already on dialysis at the time of the procedure were excluded. We initially planned to enroll 40 patients at each hospital: 10 patients with eGFR ≥60 mL/min/1.73 m^2 (normal renal function group), 10 patients with eGFR between 45 and 59 mL/min/1.73 m^2 (mild renal dysfunction group), 10 patients with eGFR between 30 and 44 mL/min/1.73 m^2 (moderate renal dysfunction group), and 10 patients with eGFR <30 mL/min/1.73 m^2 (severe renal dysfunction group). For this set of 40 patients, 10 consecutive patients in the same renal function group were enrolled. After accruing the first set of 40 patients, investigators began to enroll subsequent sets of 40 patients. At the beginning of the study we planned to accrue a total of 1000 patients with equal numbers of patients in each subgroup.

However, since cardiac catheterization is less frequently performed in patients with severe renal dysfunction, there was an uneven distribution of study participants in terms of renal function; there were 339 patients with normal renal function, 271 patients with mild renal dysfunction, 254 patients with moderate renal dysfunction, and 129 patients with severe renal dysfunction. We enrolled a total of 993 patients. Among them, 133 patients were excluded because of unavailable SCr data on the day following catheterization and 48–72 h after contrast use; thus, ultimately 860 patients were studied in the present study as shown in Fig. 1.

This study was approved by the ethics committee of each hospital, and written informed consent was obtained from all patients, and observed the Declaration of Helsinki.

Clinical definitions and data collection

In the present study, CIN was defined as an increase in SCr of 0.5 mg/dL or 25% from 48 to 72 h after contrast medium exposure [11]. eGFR values were determined using the following equation: $194 \times \text{serum creatinine}^{-1.094} \times \text{age}^{-0.287}$ ($\times 0.739$ if female) [13]. Baseline data including clinical characteristics, laboratory data (blood and urine tests), and medications on admission as well as procedural variables were obtained for all patients. Blood samples were drawn from the median cubital vein early in the morning after an overnight fasting. SCr was measured on admission (baseline), on the day following cardiac catheterization, and 48–72 h after the procedure. Dipstick urinalysis with spontaneously voided fresh urine was performed on admission. The results of the urinalysis were recorded as (−), (±), (1+), (2+), (3+). We defined (−) and (±) to be proteinuria (−), and the rest were defined as proteinuria (+). The change in SCr (ΔSCr) was calculated as the difference between SCr on the day following cardiac catheterization and SCr on admission (SCr on the following day − SCr on admission). The change in eGFR (ΔeGFR) was calculated as the difference between eGFR on the day following cardiac catheterization and eGFR on admission (eGFR on the following day − eGFR on admission).

Statistical analysis

All analyses were carried out using JMP statistics version 11 (SAS Institute, Cary, NC, USA). All values are expressed as means ± SD or medians with interquartile range (IQR) for continuous variables, or counts and percentages for categorical variables. Continuous variables were compared using the *t*-test or Wilcoxon rank-sum test as appropriate on the basis of their distribution. Alterations in SCr and eGFR were compared using the Wilcoxon signed-rank test. Categorical data were evaluated using the Pearson χ^2-test. ROC curves were used to determine the best cut-off values for the change in SCr and eGFR on the following day for predicting CIN. The best cut-off value was defined as the value with the highest Youden's index (sensitivity + specificity − 1). For binary logistic regression analysis, we converted ΔSCr into $\Delta\text{SCr} < 0.1$ and $\Delta\text{SCr} \geq 0.1$, and ΔeGFR into $\Delta\text{eGFR} \leq -1.1$ and $\Delta\text{eGFR} > -1.1$. Multivariate logistic regression models for predicting CIN included variables that had a value of $p < 0.1$ or 0.05 in the univariate logistic regression analysis. A *p*-value less than 0.05 was considered statistically significant.

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