International Journal of Cardiology 173 (2014) 46–54

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

The effect of timing of cardiac catheterization on acute kidney injury after cardiac surgery is influenced by the type of operation☆

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ARTICLE INFO

Article history:
Received 1 March 2013
Received in revised form 6 January 2014
Accepted 8 February 2014
Available online 20 February 2014

Keywords:
Cardiac surgery
Acute kidney injury
Cardiopulmonary bypass
CPB
Cardiac catheterization

ABSTRACT

Background: Acute kidney injury (AKI) is a vexing complication of cardiac surgery. Since exposure to contrast agents is a relevant contributing factor in the development of postoperative AKI, the optimal timing between cardiac catheterization and surgery is decisive.
Methods: A total of 2504 consecutive nonemergent patients undergoing isolated coronary artery bypass grafting (CABG), valve surgery (with or without concomitant CABG), and proximal aortic procedures were enrolled. AKI was defined by consensus RIFLE (Risk, Injury, Failure, Loss of function, End-stage renal disease) criteria. The association of postoperative AKI and time between cardiac catheterization and operation was evaluated using multivariable logistic regression modeling and propensity-matched analysis.
Results: Postoperative AKI occurred in 230 (9%) patients. The median number of days from cardiac catheterization to operation was 5 (25th to 75th percentile: 2 to 10). The incidence of AKI was significantly higher in patients operated on ≤1 day after cardiac catheterization compared to those operated on >1 day after (13% *vs.* 8%, $p = 0.004$). The time interval between cardiac catheterization and surgery (tested both as a continuous and a categorical variable) was not an independent AKI predictor in the propensity-matched population or the pre-matched one. Contrast exposure ≤1 day before surgery was independently associated with postoperative AKI in patients undergoing valve surgery with concomitant CABG only (post-matched: OR 3.68, 95%CI 1.30 to 10.39, $p = 0.014$).
Conclusions: Delaying cardiac surgery beyond 24 h of exposure to contrast agents seems to be justified only in patients undergoing valve surgery with concomitant CABG.

1. Introduction

Acute kidney injury (AKI) is a serious complication of cardiac surgery having significant adverse effects on patient recovery [1–3]. Postoperative AKI is associated with increased mortality and morbidity. It predisposes patients to longer hospitalization and requires additional treatments and expenditures [1–3]. Several studies suggest that postoperative AKI is a consequence of an interplay of different pathophysiologic mechanisms, with patient-related factors and cardiopulmonary bypass (CPB) being major causes [1]. Exposure to a contrast agent is a contributing factor in AKI development; as a consequence, the timing between cardiac catheterization and surgery is crucial [4–14]. However, the effect of cardiac catheterization timing on postoperative AKI has yielded conflicting results, and the specific influence of the type of operation on AKI development for patients undergoing cardiac surgery soon after coronary angiography has not been fully investigated [4–14]. Patients subjected to different types of operations normally exhibit different comorbidities with diverse responses to contrast exposure and CPB, with their unavoidable renal alterations [1–3]. As a matter of fact, patients undergoing isolated coronary artery bypass grafting (CABG) usually present the lowest incidence of postoperative AKI compared with those undergoing valve or aorta surgery

☆ Relationship with industry and financial disclosure: None.
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http://dx.doi.org/10.1016/j.ijcard.2014.02.010
0167-5273/

with or without concomitant CABG [1,2,4–14]. Therefore, the specific influence of the type of operation on AKI development is a relevant factor to be considered in the issue of the time interval between cardiac catheterization and operation.

The purpose of the present study was to analyze the impact of time interval between preoperative cardiac catheterization and different types of cardiac surgery in the development of postoperative AKI.

2. Material and methods

2.1. Study population

Between January 1, 2005, and December 31, 2011, all consecutive patients undergoing cardiac surgery at Varese University Hospital were screened for this observational cohort study. Enrolled patients underwent isolated CABG, valve surgery (with or without concomitant CABG), and proximal aortic procedures. Subjects with renal replacement therapy (RRT) before surgery, those without preoperative cardiac catheterization and those undergoing emergent operations were excluded from the analysis. Patients without CPB and those who died intraoperatively were also excluded. Accordingly, the final sample comprised a total of 2504 patients (80.9% — out of 3097). Data used in this analysis were retrieved from institutional databases, which remained consistent over the study period [15,16]. All data were prospectively collected, and information about demographics, comorbidities, medical and surgical history, operative details and postoperative events during the hospital stay were all registered.

The study protocol was in compliance with the local Institutional Review Board and received full approval; patient consent was waived.

2.2. Patient management

Preoperative management, anesthetic, and surgical techniques were standardized for all patients and have been previously reported [15,16]. Generally, the cardiac catheterization protocol included avoidance of preoperative potential nephrotoxic drugs and intravenous hydration with 0.9% saline solution at a rate of 1 mL/kg of body weight per hour for at least 6 h after the end of angiography or until the initiation of the cardiac operations. Preoperative intravenous hydration with 0.9% saline solution and reduced contrast volume were conversely adopted for patients with basal serum creatinine $\geq$1.8 mg/dL [17]. The enrolled patients usually underwent a standard preoperative cardiac catheterization with 4 views of the left coronary and 3 views of the right one. The volume of contrast administered during cardiac catheterization was not recorded. All surgical procedures were performed through a median sternotomy approach and CPB was of standardized fashion, with ascending aortic cannulation and right atrium or bicaval venous cannulation. After surgery, patients were transferred to a dedicated cardiovascular intensive care unit (ICU). Fluid intake, urinary output, acid–base and blood gases were monitored on an hourly basis throughout the ICU stay.

2.3. End-point and definitions

The primary end-point was the impact of timing between cardiac catheterization and surgery on AKI development. Postoperative AKI was defined by the consensus RIFLE criteria (Risk, Injury, Failure, Loss of function, and End-stage renal disease) using maximal change in serum creatinine (sCr) and estimated glomerular filtration rate (eGFR) during the first seven postoperative days compared with baseline values before surgery [18]. Therefore, in the present study the definition of AKI was a 50% increase in peak postoperative sCr over baseline. Generally, baseline sCr values were collected the day before surgery or immediately before surgery when cardiac catheterization was performed on the same operation day. Urinary output criteria in defining AKI were not considered. Patients who received RRT were considered to have met the criteria for class F irrespective of the stage they were in at the time of dialysis [19]. eGFR was calculated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [20]. Preoperative renal function was subdivided according to the National Kidney Foundation's Kidney Disease Outcome Quality Initiative guidelines [21]. Finally, additive European system for cardiac operative risk evaluation (EuroSCORE) was also considered [22].

2.4. Statistical analysis

Clinical data were prospectively recorded and tabulated with Microsoft Excel (Microsoft Corp, Redmond, Washington). Continuous variables were tested for normal distribution by the Kolmogorov–Smirnov test and compared between groups with unpaired Student t test for normally distributed values; otherwise, the Mann–Whitney U test was used. In the case of dichotomous variables, group differences were examined by Pearson chi-square or Fisher exact test as appropriate.

First, the temporal relationship between cardiac catheterization and cardiac surgery on AKI development was analyzed as a continuous variable (number of days) (Appendix 1). Subsequently, patients were stratified into six and seven groups on the basis of their interval between cardiac catheterization and surgery, with reference to preoperative renal function and type of operation (Appendix 2). Based on the obtained results, the final analysis was performed using $\leq$1 day as a cut-off, and in an attempt to control for selection bias related to this selected cut-off, a propensity score for the likelihood of receiving cardiac catheterization $\leq$1 day before the operation was developed and a hierarchic logistic regression model to calculate the propensity score was applied. The propensity score was based on the following variables: age (years), gender, body mass index, basal eGFR, hemoglobin, reoperation, preoperative left ventricular ejection fraction (LVEF), urgent operation, hypertension, diabetes, dyslipidemia, chronic obstructive pulmonary disease, peripheral vascular disease, history of cerebrovascular accident (CVA), preoperative beta-blocker agents, angiotensin receptor blockers, angiotensin-converting enzyme inhibitors, statins, type of operation, CPB time (min), and aortic cross-clamp time (min) (Table 1). This process generated a propensity score between 0 and 1 and patients receiving cardiac catheterization $\leq$1 day before the operation were matched 1:1 to patients receiving cardiac catheterization >1 day before, using the Rosenbaum optimal matching algorithm [23]. This approach minimizes the overall distance between observations and was conducted using the Mahalanobis distance within propensity score calipers (no matches outside the calipers) [23]. After the propensity score match was performed, we assessed differences between the two groups as above. Absolute standardized differences were estimated to evaluate the prematch imbalance and postmatch balance [23]. An absolute standardized difference of 0% indicates no residual bias and differences <10% are considered inconsequential [24].

Then, univariable analysis for postoperative AKI occurrence was carried out; the obtained predictors were subsequently tested in a multivariable model. The models were built using variables that demonstrated a p value <0.25 in univariable analysis (Table 2). A stepwise approach was used and confirmed by backward and forward methods. The significance within the models was evaluated with the Wald test, whereas the strength of the association of variables with AKI was estimated by calculating the odds ratio (OR) and 95% confidence intervals (CIs). The model was calibrated by the Hosmer–Lemeshow goodness-of-fit test, as well as residual diagnostics (deviance and dfBetas); model discrimination was evaluated by using the area under the receiver operating characteristic (ROC) curve. All tests were two-sided with the alpha level set at 0.05 for statistical significance. Separate analyses were then performed with reference to preoperative renal function classes and type of operation. Preoperative renal function was subdivided into three classes: normal (eGFR > 90 mL/min/1.73 m^2), reduced (eGFR = 60–90 mL/min/1.73 m^2), and impaired renal function (eGFR <60 mL/min/1.73 m^2). Type of considered operations was isolated CABG, valve surgery, valve surgery with concomitant CABG (combined procedures), and proximal aorta surgery.

Extracted database variables were tabulated using Microsoft Excel (Microsoft Corp, Redmond, WA) and statistical analysis was computed using SPSS, release 19.0 for Windows (SPSS Inc., Chicago, IL) and NCCS 2007, release 7.1 for Windows (Kaysville, UT).

3. Results

3.1. Population and AKI occurrence

The patient population had a mean age of 68.4 ± 10.2 years (range: 20 to 87) and contained 820 (32.7%) females. The overall AKI incidence was 9.2% (230 of 2504 patients), subdivided into 7.7% (n = 84), 9.5% (n = 72), 12.2% (n = 51), and 9.5% (n = 23) for isolated CABG, isolated valve surgery, combined procedures, and surgery of the proximal aorta, respectively. RIFLE class R accounted for 157 (6.3%) patients, RIFLE class I for 43 (1.7%), and finally RIFLE class F for 30 (1.2%). With regard to preoperative renal status, a normal eGFR (>90 mL/min/1.73 m^2) was present in 86 (37.4%) patients affected by postoperative AKI, a mild eGFR reduction (60–90 mL/min/1.73 m^2) in 32 (13.9%), while 112 (48.7%) subjects had a significant reduced basal eGFR (<60 mL/min/1.73 m^2).

The profile for patients affected by postoperative AKI was different with reference to several pre- and perioperative variables (Table 2). Patients affected by AKI were older than those unaffected (71.4 ± 8.9 *vs.* 68.1 ± 10.3 years, $p < 0.001$) and had a more severe profile of comorbidities (EuroSCORE: 6.9 ± 2.8 *vs.* 5.5 ± .8, $p < 0.001$). Intraoperatively, AKI patients required a longer CPB time (138.8 ± 63.1 *vs.* 114.4 ± 48.3 min, $p < 0.001$), had a higher rate of combined procedures (22.2 *vs.* 16.1%, $p = 0.061$), and of intra-aortic balloon pumps (10.4 *vs.* 2.9%, $p < 0.001$) compared with patients without AKI.

Patients affected by postoperative AKI experienced a longer hospital stay (both ICU and entire hospitalization; $p < 0.001$ for each variable)