International Journal of Cardiology 210 (2016) 4–9

Contents lists available at ScienceDirect

International Journal of Cardiology

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

A comparison between two different definitions of contrast-induced acute kidney injury in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention☆

Marco Centola [a,*], Stefano Lucreziotti [a], Diego Salerno-Uriarte [a], Carlo Sponzilli [a], Giulia Ferrante [a], Roberta Acquaviva [b], Diego Castini [a], Marianna Spina [a], Federico Lombardi [c], Mario Cozzolino [d], Stefano Carugo [a]

[a] Division of Cardiology, San Paolo Hospital, Department of Health Sciences, University of Milan, Italy
[b] Nextbit s.r.l., Italy
[c] Cardiovascular Disease Unit, Fondazione IRCCS, Ospedale Maggiore Policlinico, Department of Clinical Sciences and Community Health, University of Milan, Italy
[d] Renal Division, San Paolo Hospital, Department of Health Sciences, University of Milan, Italy

ARTICLE INFO

Article history:
Received 28 August 2015
Received in revised form 7 February 2016
Accepted 14 February 2016
Available online 17 February 2016

Keywords:
Contrast-induced acute kidney injury
Myocardial infarction
Primary angioplasty

ABSTRACT

Background: Contrast-induced acute kidney injury (CI-AKI) is associated with significantly increased mortality after primary percutaneous coronary intervention (pPCI) for ST-segment elevation myocardial infarction (STEMI). The prognostic value of CI-AKI depends on the definitions used to define it. We compare the predictive accuracy of long-term mortality of two definitions of CI-AKI on consecutive patients undergoing pPCI for STEMI.
Methods: Incidence, risk factors and long-term prognosis of CI-AKI were assessed according to two different definitions: the first as an increase in serum creatinine ≥25% or ≥0.5 mg/dl from baseline within 72 h after pPCI (contrast-induced nephropathy (CIN) criteria), the second one according to Acute Kidney Injury Network (AKIN) classification system.
Results: A total of 402 patients were enrolled. The median follow-up period was 12 ± 4 months. Long-term mortality rate was 9.5%. Independent predictors of long-term mortality were: older age, basal renal impairment, left ventricular ejection fraction <40%, in-hospital major bleedings and CI-AKI. A significant correlation was found between mortality and CI-AKI as assessed by both CIN (HR 4.84, 95% CI: 2.56–9.16, p = 0.000) and AKIN (HR 9.70, 95% CI: 5.12–18.37, p = 0.000) definitions. The area under the receiver operating curve was significantly larger for predicting mortality with AKIN classification than with CIN criteria (0.7984 versus 0.7759; p = 0.0331).
Conclusions: In patients with STEMI treated by pPCI, CI-AKI is a frequent complication irrespective of the criteria used for its definition. AKIN, however, seems to provide a better accuracy in predicting long-term mortality than CIN criteria.

1. Introduction

Contrast-induced acute kidney injury (CI-AKI) is a common complication in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI) [1]. CI-AKI is associated with high in-hospital and long-term morbidity and mortality rates [2]. Different definitions of CI-AKI have been used with mixed and conflicting results regarding the prevalence and the prognostic impact even in a selected population like that with STEMI [3–7]. The CI-AKI has commonly been referred to as contrast induced nephropathy (CIN) defined as an increase in serum creatinine ≥25% or ≥0.5 mg/dl from baseline within 48–72 h after contrast exposure. However, the CIN definition is not exhaustive. As matter of fact, it leads to a wide variation in its incidence and short- and long-term prognostic value [8–10]. Recently, the Acute Kidney Injury Network (AKIN) proposed a novel standardized definition of AKI that was validated in several clinical conditions [11–12]. However, debate still exists on a uniform and on a most appropriate definition in patients receiving contrast media [13]. To the best of our knowledge the predictive power of CIN and AKIN definitions has never been compared. Therefore, we compare the accuracy in predicting the long-term mortality of these two definitions of CI-AKI on consecutive patients undergoing pPCI for STEMI.

Abbreviations: CI-AKI, contrast-induced acute kidney injury; STEMI, ST-segment elevation myocardial infarction; pPCI, primary percutaneous coronary intervention; CIN, contrast-induced nephropathy; AKIN, acute kidney injury network; LVEF, left ventricular ejection fraction; ACS, acute coronary syndrome; eGFR, estimated glomerular filtration rate; TIMI, thrombolysis in myocardial infarction; RR, risk ratio; CI, confidence interval; OR, odds ratio; HR, hazard ratio.

☆ All the authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

* Corresponding author at: Division of Cardiology, San Paolo Hospital, Department of Health Sciences, University of Milan, Via A. di Rudinì 8, 20142 Milan, Italy.
E-mail address: marco.centola@ao-sanpaolo.it (M. Centola).

http://dx.doi.org/10.1016/j.ijcard.2016.02.086
0167-5273/

2. Methods

2.1. Study population

The present study enrolled 412 consecutive patients with STEMI undergoing pPCI from January 2009 to October 2012. All-comers design study was adopted with no restriction on age or on critically ill patients' inclusion. All patients' data were entered prospectively in the database of our center and retrospectively analyzed. Inclusion criteria were: chest pain persisting for more than 30 min with ST-segment elevation on the ECG of 0.1 mV or greater in 2 or more contiguous leads or left-bundle branch block; admission within 12 h of symptoms onset, as well as admission within 24 h for patients with cardiogenic shock or evidence of continuing ischemia. The exclusion criteria were: any dialysis treatment ($n = 3$); cardiac arrest requiring prolonged (>30 min) resuscitation ($n = 3$); death within 24 h of admission ($n = 4$); and inability to obtain an informed consent.

2.2. Protocol

All patients underwent a fast clinical examination with blood sampling and 12-leads ECG recording in the emergency room. Serum creatinine (sCr) measurements were recommended per protocol at baseline and daily after cardiac catheterization. pPCI was performed according to the current guidelines [14]. Briefly, before the procedure all patients received aspirin (300–500 mg) and clopidogrel (300 to 600 mg) or prasugrel (60 mg) or ticagrelor (180 mg). The anticoagulant (unfractionated heparin or bivalirudin) therapy or the use of glycoprotein IIb/IIIa inhibitors was left to the physician's judgment. The choice of the vascular approach was left to the discretion of the interventional cardiologist. An early removal of the arterial sheath was encouraged. Prophylaxis for CI-AKI was not routinely administered. All patients received iso-osmolar, non-ionic contrast agent iodixanol (Visipaque®, GE Healthcare, Princeton, New Jersey). Following pPCI, left ventricular ejection fraction (LVEF) was measured in all patients by means of echocardiography within 24 h of hospital admission. All of the surviving patients had follow-up data of 12 months; these data were obtained by regular visits in the out-patient clinics or by telephone interview. The study conforms to the principles outlined in the Declaration of Helsinki; the Research Ethics Board of the San Paolo Hospital and the University of Milan, Italy approved the study protocol. An informed consent was obtained from all patients.

2.3. Definitions

Estimated glomerular filtration rate (eGFR) was calculated by applying the recently validated CKD-EPI equation [15]. CI-AKI by CIN criteria was defined as an increase ≥25% or ≥0.5 mg/dl in sCr from baseline values within the first 72 h after contrast exposure [16]. CI-AKI by AKIN staging system was defined according to the maximum increase in sCr from baseline (within 48 h from hospital admission): stage 1 (AKI 1): increase of ≥0.3 mg/dl in sCr; stage 2 (AKI 2): increase of >2- to 3-fold in sCr; and stage 3 (AKI 3): increase of >3-fold or sCr ≥ 4.0 mg/dl with an acute increase of at least 0.5 mg/dl or need for renal replacement therapy [12]. The nephropathy risk score (Mehran risk score, MRS) was calculated as specified by Mehran et al. [17]. Reduced LVEF was defined as ejection fraction values < 40%. Cardiogenic shock was diagnosed in the presence of hypotension and signs of peripheral hypoperfusion that did not rapidly resolve after fluids and/or inotropic agents administration. Major and minor bleedings events were defined using the criteria defined by the TIMI trial group [18].

2.4. Statistical analysis

Baseline categorical variables were expressed as count (percentage) and compared with the X^2 test. Baseline continuous variables were presented as mean ± SD and compared using the t-test for independent samples (in the two cohorts, with and without CI-AKI observations). Independent predictors of CI-AKI (defined according to both CIN and AKIN definition) were explored by fitting a binary logistic regression model with CI-AKI as dependent variable. The first step was to analyze data with a univariate logistic model to identify significant predictors of CI-AKI. The results of the analysis were shown as odds ratio and 95% confidence intervals (CIs). Also a multivariate logistic regression was used. To add robustness to outcomes we sampled data with Bootstrap method: one hundred sub-samples of two hundred units were made and for each of them a multivariate logistic model through backward stepwise selection of variables was assessed, excluding all variables not statistical significant ($p > 0.1$). Variables observed in more than 40% of regressions were chosen for the final multivariate logistic model estimated on the whole dataset. The hazard ratios (HR) and 95% confidence interval (CI) of CI-AKI on clinical outcome were estimated by fitting a Cox proportional hazard regression model to identify predictors of long-term mortality. The association of CI-AKI on clinical outcome was adjusted for potential confounders and established risk factors. The following univariate predictors of all-cause death were included into the model: gender, aged 75 years or older, diabetes mellitus, smoking, body mass index (BMI), hypercholesterolemia, contrast volume, eGFR < 60 ml/min, LVEF < 40%, in-hospital major bleedings, anterior myocardial infarction, Mehran risk score > 6, Killip class > 2, and CI-AKI defined according to both CIN and AKIN criteria. Two multivariate Cox proportional hazard regression models were estimated with a forward stepwise selection of variables, by including all variables aforementioned: in the first one the variable CI-AKI by CIN definition was not included in the selection, vice versa in the second one CI-AKI by AKIN definition was not included. A two-sided probability value < 0.05 was considered significant. To compare the incremental prognostic value of using AKIN over CIN criteria, the area under the receiver operating characteristic (ROC) curves (AUC) was used as previously described [19]. The ROC curves were also used to compare the improved accuracy in predicting long-term mortality of both AKIN and CIN definition when added to in-hospital major bleedings and LVEF < 40%. Data were analyzed in STATA 11 for all analysis excluding the estimation of ROC curves and Cox regression, which were made using SAS 9.3.

3. Results

3.1. Patients characteristics

A total of 402 patients were enrolled. Clinical, angiographic and procedural characteristics of the patient population are reported in Table 1. Briefly, the mean age was 64.9 ± 13.1 years. Less than one-third of the total population was female (28%). Ninety-seven patients (24%) were older than 75 years. Diabetes mellitus was present in 65 (16%) patients. 188 (47%) had an anterior STEMI and only 52 (13%) were in Killip class ≥ 2. A small amount of patients (11%) presented with reduced LVEF. Fifty-nine percent of patients had multivessel coronary artery disease. The median time from symptom onset to PCI was 298 ± 335 min, whereas the median door-to-balloon time was 94 ± 79 min. The rate of major in-hospital bleedings was 4%. Baseline renal impairment was detected in 115 (29%) patients. The mean amount of administered contrast medium was 257 ± 105 ml. The median follow-up period was 365 ± 130 days.

3.2. Incidence and predictors of CI-AKI by AKIN and CIN criteria

CI-AKI assessed by CIN criteria was detected in 70 (17.4%) patients while CI-AKI according to AKIN classification system occurred in 43 (10.7%) patients. AKI 1 occurred in 35 patients (8.7%), AKI 2 in 2 patients (0.5%) and AKI 3 in 6 patients (1.5%). Among 43 patients with CI-AKI according to AKIN definition, 42 (97.7%) patients fulfilled the CIN criteria. On the other hand, among 70 patients with CI-AKI assessed by CIN