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Renal replacement therapy in patients with acute myocardial infarction: Rate of use, clinical predictors and relationship with in-hospital mortality☆

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ABSTRACT

Objectives: We evaluated the rate of use, clinical predictors, and in-hospital outcome of renal replacement therapy (RRT) in acute myocardial infarction (AMI) patients.
Methods: All consecutive AMI patients admitted to the Coronary Care Unit between January 1st, 2005 and December 31st, 2015 were identified through a search of our prospectively collected clinical database. Patients were grouped according to whether they required RRT or not.
Results: Two-thousand-eight-hundred-thirty-nine AMI patients were included. Eighty-three (3%) AMI patients underwent RRT. Variables confirmed at cross validation analysis to be associated with RRT were: admission creatinine >1.5 mg/dl (OR 16.9, 95% CI 10.4–27.3), cardiogenic shock (OR 23.0, 95% CI 14.4–36.8), atrial fibrillation (OR 8.6, 95% CI 5.5–13.4), mechanical ventilation (OR 22.6, 95% CI 14.2–36.0), diabetes mellitus (OR 4.8, 95% CI 3.1–7.4), and left ventricular ejection fraction <40% (OR 9.1, 95% CI 5.6–14.7). The AUC for RRT with the combination of these predictors was 0.96 (95% CI 0.94–0.97; P < 0.001). In-hospital mortality was significantly higher in RRT patients (41% vs. 2.1%, P < 0.001). Oligoanuria as indication for RRT (OR 5.1, 95% CI 1.7–15.4), atrial fibrillation (OR 4.3, 95% CI 1.6–11.5), mechanical ventilation (OR 20.8, 95% CI 6.1–70.4), and cardiogenic shock (OR 12.9, 95% CI 4.4–38.3) independently predicted mortality in RRT-treated patients. The AUC for in-hospital mortality prediction with the combination of these variables was 0.92 (95% CI 0.87–0.98; P < 0.001).
Conclusions: Patients with AMI undergoing RRT had strikingly high in-hospital mortality. Use of RRT and its associated mortality were accurately predicted by easily obtainable clinical variables.

1. Introduction

Renal replacement therapies (RRT) have become an established component of treatment in patients with severe acute kidney injury (AKI). Previous reports suggest that 3–4% of patients admitted to the Coronary Care Unit (CCU) with acute myocardial infarction (AMI) require hemodialysis or other forms of RRT during their index event [1–3]; this figure rises to 13% in those with AMI complicated by cardiogenic shock [4,5]. The need for RRT has been associated with a striking increase in in-hospital morbidity and mortality [1–6].

At present, there is limited information on the rate of use, clinical predictors and outcome of RRT in AMI. This is mainly because previous studies pooled them together with heterogeneous patient cohorts, including critically ill surgical and medical patients admitted to general Intensive Care Units [7–12]. Moreover, the main clinical features of RRT, such as correct indications, treatment modality, and timing of initiation and discontinuation remain poorly defined in this clinical setting. Indeed, guidelines on how to manage these patients are lacking due to the absence of significant clinical data on RRT and of randomized studies comparing different RRT modalities in AMI. Therefore, the current practice of RRT in AMI patients is often based on criteria set for other conditions, such as sepsis, trauma or cardiac surgery [13,14]. However, the

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

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main targets of RRT in AMI patients (circulatory volume control and renal function support during hemodynamic impairment) may differ from those in patients with other acute diseases (i.e. blood detoxification, prevention of uremic complications, metabolic homeostasis, and removal of inflammatory mediators). As a result, type of RRT and treatment protocol may critically affect AMI patients' outcome.

This study was set out to define the rate of use, clinical characteristics, and in-hospital outcome of RRT performed in AMI patients in a single center. Moreover, we aimed at evaluating clinical and procedural factors associated with in-hospital mortality.

2. Methods

2.1. Patient population

We included all consecutive AMI patients (both ST-elevation acute myocardial infarction [STEMI] and non ST-elevation myocardial infarction [NSTEMI]) admitted to the CCU of Centro Cardiologico Monzino, between January 1st, 2005 and December 31st, 2015. They were retrospectively identified through a search of our prospectively collected clinical database. Patients in chronic dialysis, undergoing emergency cardiac surgery, and those with AMI complicating elective percutaneous coronary intervention, were excluded. Patients were divided into two groups, one treated with RRT and the other not requiring the treatment. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki, the study was approved by the Ethics Committee of our Institute, and informed consent was obtained from all patients.

2.2. Study design

The decision to start RRT was based on the presence of ≥1 criterion used in critically ill patients [11,12]: AKI with prolonged (>24 h) oliguria, overt heart failure, increase in azotemia (≥200 mg/dl), severe hyperkalemia (>6.5 mEq/L, or less when associated with typical electrocardiographic abnormalities), and metabolic acidosis (pH <7.1). However, the final decision to initiate RRT, as well as the choice of RRT modality, was left to the discretion of the treating physician. In all patients, RRT was carried on until recovery of adequate urine output and correction of fluid unbalance, electrolyte abnormalities, and hemodynamic instability, or death. When RRT was started in the first 24 h the treatment was defined as very early, when it was started between 24 and 72 h it was defined as early, while it was defined as late when started afterwards.

In all cases RRT was performed with continuous veno-venous hemofiltration (CVVH) or continuous veno-venous hemodiafiltration (CVVHDF). The blood pump was set to deliver 100–150 ml/min, with an initial fluid replacement rate of 1000 ml/h and a fluid loss adapted to the clinical need. In case of CVVHDF, the dialysate rate was set at 2500 ml/h. Blood and fluid rates were adjusted during RRT in order to maintain the filtration fraction of the hemofilter below 20%.

Baseline renal insufficiency was defined as an estimated glomerular filtration rate (eGFR) ≤60 ml/min/1.73 m^2 [15,16]. We also assessed eGFR at the time of RRT initiation. In patients requiring RRT, AKI stage according to the AKIN criteria [17] was determined based on the maximum class reached before RRT initiation. An echocardiogram was performed in all patients within 24 h, and left ventricular ejection fraction (LVEF) was calculated [18].

The following clinical and procedural variables were evaluated in RRT-treated patients: 1) indication(s) to start RRT; 2) RRT characteristics (modality, time of initiation, renal and cardiac function at treatment start, duration, procedural complications, and reason for stopping treatment); 3) in-hospital clinical outcome (mortality and major adverse cardiac events [MACE]). The length of stay in the CCU was also recorded.

2.3. Statistical analysis

Continuous variables are presented as mean ± SD, and they were compared using the t-test for independent samples. Variables not normally distributed are presented as median and interquartile ranges, and compared with the Wilcoxon rank-sum test. Categorical data were compared using the chi-square test or the Fisher exact test, as appropriate. The identification of independent predictors of the RRT use in the whole population was assessed by a logistic regression analysis with stepwise selection of variables. All parameters representing clinical indications for RRT were excluded. The initial set of potential predictors undergoing selection included: age, diabetes, hypertension, smoking, serum creatinine concentration (sCr) >1.5 mg/dl, eGFR, CK-MB peak, LVEF <40%, previous AMI, previous coronary artery bypass graft, atrial fibrillation, AMI type (STEMI vs. NSTEMI), cardiogenic shock, mechanical ventilation, and ventricular fibrillation. To avoid spurious selection of predictors because the model was built and tested on the same sample, a cross-validation procedure was employed. The sample was randomly split in half 200 times, and the model, including the independent predictors, was selected in the first arm (training set) and subsequently tested in the second half (testing set). For each variable, we computed the number of times it was selected in the first step and the number of times it was confirmed (deemed as significant) in the second step. We considered a predictor validated when it was selected and confirmed at least 70% of times.

The identification of independent predictors of in-hospital mortality in patients requiring RRT was also assessed by performing a logistic regression analysis with stepwise selection of variables. The initial set of potential predictors undergoing selection included: age, dyslipidemia, CK-MB peak, LVEF <40%, AMI type, AMI treatment, cardiogenic shock, atrial fibrillation, mechanical ventilation, RRT indication, azotemia, serum potassium concentration, systolic and diastolic arterial pressure, and daily diuretic dose at the time of RRT start.

The results of the analyses were summarized as odds ratio (OR) with 95% confidence intervals (CI) and as area under the curve (AUC) at receiving operating characteristic analysis. In both models, ORs were adjusted for each other variable and collinearity was excluded by Variance Inflation Factor.

A p value <0.05 was considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina).

3. Results

A total of 2839 AMI patients (1581 STEMI and 1258 NSTEMI) were included. Of them, 83 (3%) were treated with RRT during their index hospitalization. Table 1 shows baseline clinical characteristics and MACE of patients who were treated with RRT and of those who did not require RRT. Patients treated with RRT were older and more likely to have co-morbidities and worse cardiac and renal function at admission. Moreover, they experienced a more complicated in-hospital clinical course, with a significantly higher in-hospital mortality rate (41% vs. 2.1%, P < 0.001).

The indications for and procedural characteristics of RRT in the 83 patients requiring this therapy are shown in Table 2. The most frequent clinical indications were acute fluid overload and prolonged oliguria, occurring individually or together. The median cumulative RRT duration was 44 (24–70) hours.

Among the variables that were found to be associated with RRT at univariate analysis, the following were confirmed at cross validation analysis with great reproducibility: cardiogenic shock (OR 23.0, 95% CI 14.4–36.8; P < 0.001), mechanical ventilation (OR 22.6, 95% CI 14.2–36.0; P < 0.001), admission sCr >1.5 mg/dl (OR 16.9, 95% CI 10.4–27.3; P < 0.001), LVEF <40% (OR 9.1, 95% CI 5.6–14.7; P < 0.001), atrial fibrillation (OR 8.6, 95% CI 5.5–13.4; P < 0.001), and diabetes mellitus (OR 4.8, 95% CI 3.1–7.4; P < 0.001) (Table 3). The corresponding adjusted ORs and the AUC of each variable are reported in Fig. 1 (Panel A). In the whole population, as the number of these variables raised, we observed a parallel increase in RRT use (Fig. 2). In ROC analysis, the AUC for RRT obtained with the combination of these six predictors was 0.96 (95% CI 0.94–0.97; P < 0.001) (Fig. 1, Panel B).

The characteristics of patients who underwent RRT according to whether they survived or not are reported in Table 4. Patients who did not survive were older and more likely to have STEMI, atrial fibrillation, lower LVEF, cardiogenic shock and oliguria at the time RRT was started. Conversely, no difference was observed in terms of RRT modality, time of its initiation, and year of hospitalization.

At multivariable analysis, the following variables were found to be independently associated with in-hospital mortality in this subset of patients: mechanical ventilation (OR 20.8, 95% CI 6.1–70.4; P < 0.001), cardiogenic shock (OR 12.9, 95% CI 4.4–38.3; P < 0.001), oliguria as indication for RRT (OR 5.1, 95% CI 1.7–15.4; P < 0.001), and atrial fibrillation (OR 4.3, 95% CI 1.6–11.5; P < 0.001). Fig. 3 (Panel A) shows their corresponding adjusted ORs with the AUC of each single variable. In ROC analysis, the AUC for in-hospital mortality prediction in patients requiring RRT, obtained combining these four predictors, was 0.92 (95% CI 0.87–0.98; P < 0.001) (Fig. 3, Panel B).

4. Discussion

Prognosis of AMI patients has improved substantially over the last years, thanks to remarkable advances in diagnosis, risk stratification, management strategies, and new therapies [19]. Patients with AMI requiring RRT are only a small minority that has been poorly studied and often neglected despite their very high risk [1–6]. Moreover, their management has been demanded to nephrologists or general intensive physicians, so that data on their outcome have been pooled with those