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Original article

## Predictive value of acute kidney injury for major adverse cardiovascular events following tricuspid annuloplasty: A comparison of three consensus criteria

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### ABSTRACT

**Background:** Tricuspid annuloplasty (TA) is increasingly being performed, but the clinical outcome is unsatisfactory. Acute kidney injury (AKI) is a common complication following cardiac surgery and predicts outcome. Nonetheless the occurrence rate and prognostic value of AKI after TA are unclear.

**Methods:** This study reviewed 339 consecutive patients (age  $65 \pm 11$  years; male 42%) who underwent TA. The incidence of AKI was defined according to risk/injury/failure/loss/end stage (RIFLE), acute kidney injury network (AKIN), and kidney disease improving global outcomes (KDIGO) criteria, respectively. Major adverse cardiovascular events (MACE) was defined as death, heart failure, stroke, and myocardial infarction (MI). The influence of AKI on MACE was evaluated as a short-term outcome and outcome beyond 30 days.

**Results:** The incidence of AKI, defined according to RIFLE, AKIN, and KDIGO was 57%, 52%, and 53%, respectively. MACE occurred in 94 cases (21 deaths, 63 heart failure requiring hospitalization, 7 stroke, and 3 MI). For short-term outcome, AKI defined by all three scoring systems was independently associated with MACE and death ( $p < 0.01$  for both), but not heart failure, stroke, or MI. For outcome beyond 30 days, AKI by all three criteria was associated with MACE and heart failure. Only AKI by AKIN and KDIGO, but not RIFLE, was independently associated with death.

**Conclusion:** Our data suggest AKI affects over half of all patients who undergo TA, and has a major and long-lasting impact on survival, MACE, and heart failure. Use of AKIN and KDIGO is more useful than the RIFLE criteria when determining the prognostic value of AKI for mortality beyond 30 days.

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### Introduction

Acute kidney injury (AKI) is a serious complication following cardiac surgery and occurs in 5–40% of patients [1,2]. Even mildly

elevated creatinine level is independently associated with increased short-term and long-term adverse events [3–5]. Therefore, AKI is considered an important risk factor for adverse events following cardiac surgery [4].

Tricuspid regurgitation (TR) is not a benign condition and is associated with adverse events and decreased functional outcome [6,7]. In order to reduce TR and improve clinical outcome, interest in tricuspid annuloplasty (TA) has increased in recent years [8–10] and the number of tricuspid procedures has doubled over the past decade [11]. Although TA may improve the clinical outcome in

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patients with significant TR [12], postoperative mortality remains high [13]. Therefore, risk assessment following TA is important to identify high-risk patients. Although AKI is associated with mortality following cardiac surgery, its predictive value for other adverse events such as heart failure has not been determined. Further, prior study has used risk/injury/failure/loss/end stage (RIFLE) criteria for risk prediction in valve surgery [4]. In contrast, little is known regarding the prognostic value of AKI when determined by acute kidney injury network (AKIN) or kidney disease: improving global outcomes (KDIGO) criteria, the latter an evolution of RIFLE criteria that consider even a slight rise in creatinine. The aim of the present study was to determine the incidence of AKI and its impact on clinical outcomes in patients undergoing TA, and to compare the three commonly used AKI criteria with regard to prognostic value.

## Methods

### Study population

A total of 406 patients who underwent TA at Queen Mary Hospital between January 2011 and December 2015 were recruited. Exclusion criteria included congenital heart disease ( $n = 47$ ), presence of an implanted pacemaker ( $n = 13$ ), or requirement for renal replacement therapy ( $n = 6$ ). In addition, patients who died within 24 h after TA ( $n = 1$ ) were excluded. The remaining 339 patients (age,  $65 \pm 11$  years; male, 42%) were included for further analysis. Major adverse cardiovascular events (MACE) was defined as death, heart failure, stroke, or myocardial infarction (MI). Patients were censored at the first event and were not counted multiple times for MACE. All MACE events were collected from the inter-hospital electronic Clinical Management System. The influence of AKI on MACE was evaluated as a short-term outcome (within 30 days) and outcome beyond 30 days of follow-up. The study was part of the Chinese Valvular Heart Disease Study (CVATS) that evaluated Chinese patients with valvular heart disease to determine the pattern of disease, pathophysiology, and clinical outcome [14]. The study was approved by the ethics committee of the West Cluster Hospital Authority of Hong Kong, and all subjects gave written informed consent.

### Clinical parameters

Clinical data on preoperative variables were collected from patient records by one investigator. The etiology of valvular heart disease was recorded as chronic rheumatic heart disease (CRHD) or non-CRHD according to the predominant lesion of the valve. New York Heart Association (NYHA) classification was recorded as class I/II or class III/IV, and the status of valvular atrial fibrillation (AF) was also recorded for each subject. Conventional cardiovascular risk factors such as history of diabetes mellitus, hypercholesterolemia, hypertension, and smoking status were documented. Details of valvular surgery were also recorded for each subject. Detailed preoperative transthoracic echocardiography was performed in all subjects before cardiac surgery. Left ventricular (LV) ejection fraction, LV dimension, and right ventricular systolic pressure (RVSP) were measured according to the current recommendations [15,16].

### Definition of acute kidney injury

Serum creatinine (Scr) was measured before and within 7 days after surgery. Glomerular filtration rate (GFR) was calculated by the modification of diet in renal disease (MDRD) equation based on Scr [17]. In the presence of a change in Scr or GFR post-operatively, AKI was defined using the criteria of RIFLE [17], AKIN [18], and KDIGO

[19]. For RIFLE: AKI was diagnosed in the presence of a  $\geq 1.5$  increase in Scr from baseline or  $>25\%$  decrease in GFR within 7 days. For AKIN: an increase in Scr  $\geq 0.3$  mg/mL or  $\geq 1.5$  times from baseline within 48 h was considered AKI. For KDIGO: AKI was diagnosed when Scr increased by  $\geq 0.3$  mg/mL within 48 h or by a factor  $\geq 1.5$  from baseline within 7 days.

### Statistical analysis

Continuous variables are presented as mean  $\pm$  SD and the difference between two groups was compared using Student's *t* test. Categorical variables are expressed as frequencies and percentages. Pearson Chi-square test and Fisher's exact test were used appropriately to compare differences between two groups. Cumulative MACE rate beyond 30 days was estimated by Kaplan–Meier method, and survival differences between two groups were compared using log-rank test. Multivariable logistic regression and cox regression model adjusted for factors potentially associated with MACE were used to determine the independent predictors of short-term outcome and outcome beyond 30 days, respectively. All statistical analyses were performed using SPSS software (Version 22, IBM Corp, Armonk, NY, USA). A two-tailed *p*-value  $< 0.05$  was considered statistically significant for all tests.

## Results

### Clinical characteristics

Baseline clinical characteristics of the study patients are shown in Table 1. Over half of patients had underlying atrial fibrillation and CRHD as the cause of valve pathology. AKI developed in 194 (57%), 177 (52%), and 178 (53%) patients after TA surgery, defined according to the RIFLE, AKIN, and KDIGO, respectively.

Applying the RIFLE criteria, patients with AKI were likely to be older and have undergone isolated TA surgery compared with those without AKI. There were no significant differences in gender or cardiovascular risk factors between patients with and without AKI. Conversely, fewer patients developed AKI after TA combined with mitral valve repair surgery. According to AKIN and KDIGO criteria, patients with AKI were more likely to be older, male, have a history of hypertension and diabetes mellitus, and have undergone concomitant coronary artery bypass graft (CABG).

### Major adverse cardiovascular events

A total of 94 patients developed MACE; 21 deaths (15 cardiovascular death, 1 sudden death, and 5 refractory sepsis), 63 heart failure requiring hospitalization, 7 stroke, and 3 MI. Individual endpoints that occurred during the follow-up period were: 33 deaths (21 cardiovascular deaths, 1 sudden cardiac death, 11 refractory sepsis), 64 heart failure requiring hospitalization, 13 stroke, and 5 MI.

### Short-term MACE

At short-term (within 30 days) follow-up, 18 patients developed MACE: 13 death, 4 heart failure, 1 stroke. Comparison of MACE, mortality, and heart failure between patients with and without AKI defined by RIFLE, AKIN, and KDIGO criteria is shown in Fig. 1(A)–(C). Patients who developed AKI after TA had a higher incidence of short-term MACE (RIFLE: 4.7% vs. 0.6%; AKIN: 4.7% vs. 0.6%; KDIGO: 4.7% vs. 0.6%, all  $p < 0.01$ ) and higher mortality (RIFLE: 3.5% vs. 0.3%; AKIN: 3.5% vs. 0.3%; KDIGO: 3.5% vs. 0.3%, all  $p < 0.01$ ) than those without AKI. Nonetheless short-term incidence of heart failure did not differ significantly ( $p > 0.05$ ). Logistic regression analysis adjusted for age, gender, LVEF, NYHA class, and

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