

# Increased risk of acute kidney injury in patients undergoing tricuspid valve surgery

Lars Englberger<sup>a,b,\*</sup>, Rakesh M. Suri<sup>a</sup>, Heidi M. Connolly<sup>c</sup>, Zhuo Li<sup>d</sup>, Martin D. Abel<sup>e</sup>, Kevin L. Greason<sup>a</sup>, Joseph A. Dearani<sup>a</sup> and Hartzell V. Schaff<sup>a</sup>

- <sup>a</sup> Division of Cardiovascular Surgery, Mayo Clinic, Rochester, MN, USA  
<sup>b</sup> Clinic of Cardiovascular Surgery, University Hospital Berne (Inselspital), Berne, Switzerland  
<sup>c</sup> Division of Cardiovascular Diseases, Mayo Clinic, Rochester, MN, USA  
<sup>d</sup> Division of Biostatistics, Mayo Clinic, Rochester, MN, USA  
<sup>e</sup> Division of Cardiovascular and Thoracic Anesthesia, Mayo Clinic, Rochester, MN, USA

\* Corresponding author. Mayo Clinic, St Mary's Hospital, 200 First Street SW, Rochester, MN 55905, USA. Tel: +1-507-2557068; fax: +1-507-2557378; e-mail: lars.englberger@insel.ch (L. Englberger).

Received 9 April 2012; received in revised form 17 August 2012; accepted 17 August 2012

## Abstract

**OBJECTIVES:** We aimed to determine which patients undergoing tricuspid valve (TV) surgery are at increased risk for acute kidney injury (AKI).

**METHODS:** We reviewed 951 patients [mean age  $67 \pm 13$  years, 573 (60%) female] having TV surgery between 2000 and 2007. Analysis focused on clinical outcome; AKI was defined by the consensus RIFLE criteria (risk, injury, failure).

**RESULTS:** Surgical procedures included isolated TV surgery in 224 (24%) and TV surgery in conjunction with another cardiac operation in 727 (76%) patients. TV surgery involved redo surgery in 395 (42%). The incidence of postoperative AKI was 30% ( $n = 285$ ), and 75 (7.9%) of these patients required renal replacement therapy. AKI stratified by increased RIFLE class was associated with worse postoperative outcomes (prolonged intubation, length of hospital stay and mortality;  $P < 0.001$  for each variable). For patients with AKI, odds ratio for mortality was 4.2 [95% confidence interval (CI) 3.2–5.4,  $P < 0.001$ ; area under receiver operating curves 0.85 (95% CI 0.80–0.91)], and 2.3 (95% CI 1.9–2.9,  $P < 0.001$ ) for prolonged intubation for each increase in RIFLE class. Independent risk factors for AKI were older age, male gender, previous surgery, preoperative anaemia, length of cardiopulmonary bypass and TV replacement. Importantly, preoperative creatinine and pulmonary artery pressure were not independently associated with AKI.

**CONCLUSIONS:** TV surgery carries a high incidence of postoperative AKI that is associated with adverse outcome. The use of the RIFLE criteria allows comparison with prior studies and is an important predictor of early mortality. The estimation of patient risk for AKI should be based on multivariable prediction.

**Keywords:** Cardiac surgery • Cardio-renal syndrome • Right ventricular failure • Tricuspid valve replacement • Heart failure

## INTRODUCTION

Acute kidney injury (AKI) after cardiac surgery is a frequent complication and prognostically important. The correlation between tricuspid valve (TV) surgery and perioperative renal dysfunction has not been addressed in previous studies. In a recent investigation [1] focusing on different models to predict AKI after cardiac surgery, we found increased rates of severe postoperative AKI in the subset of patients undergoing TV surgery compared with other types of cardiac surgical procedures. Indeed, in patients with carcinoid heart disease undergoing right-sided valve replacement, the increased incidence of AKI contributes significantly to perioperative mortality and multiorgan failure [2]. In addition, among patients with different types of valvular surgery, TV procedures constitute one of the high-risk categories with poor outcome [3], but it is unclear whether high rates of postoperative AKI are the primary cause of mortality.

This retrospective study was undertaken to investigate the incidence, risk factors and clinical implication of AKI on patient outcomes in patients undergoing TV surgery.

## MATERIALS AND METHODS

### Study population

After institutional review board approval, we investigated all patients who underwent surgery for acquired TV disease at the Mayo Clinic, Rochester, Minnesota, between January 2000 and December 2007. Patient data were recorded in a prospective computerized database using definitions consistent with the Society of Thoracic Surgeons Adult Database definitions. Patients with renal replacement therapy (RRT) prior to surgery were excluded as were patients who underwent TV surgery because

of congenital cardiac anomalies. In accordance with Health Insurance Portability and Accountability Act guidelines, the few patients who denied access to their medical records for the purpose of research were not considered for analysis. In patients who had more than one TV procedure during the study period at our institution ( $n = 11$ ), only data related to the first operation were included. Patients who died intraoperatively or within 24 h postoperatively were excluded ( $n = 17$ ) because no meaningful definition of postoperative AKI could be made in these patients. Nine patients with baseline creatinine  $>3$  mg/dl were also excluded. In addition to the available data in the clinical database, all electronic patient records were reviewed to obtain preoperative haemoglobin, the latest preoperative serum creatinine (sCrea) and sCrea each day postoperatively up to Day 7, aprotinin use and temperature during CPB. If more than one sCrea was measured per day, the highest recorded value was used for study purposes.

## Data definitions

AKI was defined by the consensus RIFLE criteria using the maximal change in sCrea and glomerular filtration rate (GFR) during the first 7 postoperative days compared with baseline values before surgery. GFR was estimated with the simplified Modification of Diet in Renal Disease formula. The three thresholds for AKI severity according to RIFLE definitions are summarized in Table 1 [4]. We did not use urine output criteria in defining AKI. All patients who met the RIFLE criteria were classified as AKI. Patients with AKI were stratified according to the highest RIFLE class R (Risk), I (Injury) or F (Failure) attained using sCrea or GFR criteria within the first 7 days postoperatively. As a modification of RIFLE, any patient who required RRT (intermittent haemodialysis or continuous venovenous haemofiltration) during the first 7 postoperative days was staged in the failure class F [5]. Definitions of outcome variables were the following: RRT as outcome variable included the need for RRT during the entire postoperative hospital stay or within 30 days postoperatively. Operative mortality was defined as in-hospital mortality or 30-day mortality. Prolonged intubation included those requiring ventilation for  $>24$  h postoperatively. If the patient was

re-intubated, the additional time of mechanical ventilation was added to the initial postoperative ventilation period. Hours accrued during intensive care unit (ICU) readmission were added to the initial time in ICU after index surgery. Length of hospital stay was defined in days from index surgery to discharge.

## Statistical analysis

Descriptive statistics for categorical variables are reported as frequency and percentage while continuous variables are reported as mean (standard deviation) or median (range) as appropriate. Categorical variables were compared among RIFLE classes using the chi-squared test and continuous variables were compared using analysis of variance or Kruskal–Wallis tests where appropriate. Logistic regression models were used to find the univariate and multivariate predictors of AKI. The multivariable model considered univariately significant variables ( $P < 0.05$ ) with model selection through the stepwise method (backward and forward methods resulted in the same model). Regression models were used to predict prolonged intubation and mortality by increase of AKI severity. To determine predictive clinical accuracy, discriminative power was analysed by calculating the area under receiver operating curves (AUROC). All statistical tests were two-sided with the alpha level set at 0.05 for statistical significance. Data were analysed using SAS 9.1 software (SAS Inc., Cary, NC).

## RESULTS

After the exclusion criteria were applied, the total study cohort consisted of 951 consecutive patients, median age 69 years (range 24–92 years) and 573 (60%) were female. Comorbidities included hypertension (60%), diabetes (20%), chronic lung disease (19%), peripheral vascular disease (8%) and cerebrovascular disease (18%). Regarding functional TV pathology, 949 (99.8%) patients had TV regurgitation (trivial 1%, mild 2%, moderate 19% and severe 78%) and 34 (4%) had concomitant TV stenosis. TV repair/annuloplasty was performed in 642 (68%) patients, and the remaining (32%) had TV replacement with either biological or mechanical heart valve prosthesis. In 224 (24%) patients, surgery was isolated to the TV. Patients with combined tricuspid procedures are presented in Table 2. The majority of patients ( $n = 759$ , 80%) underwent elective surgery, 190 (20%) had urgent surgery and only 2 were operated on an

**Table 1:** Description of RIFLE definition criteria for acute kidney injury used in analysis

Definition criteria	Acute kidney injury		
	RIFLE class R	RIFLE class I	RIFLE class F
Creatinine	$\geq 1.5$ -fold increase compared with baseline	$\geq 2$ -fold increase compared with baseline	$\geq 3$ -fold increase compared with baseline or increase to $\geq 4$ mg/dl <sup>a</sup>
GFR	$>25\%$ decrease compared with baseline	$>50\%$ decrease compared with baseline	$>75\%$ decrease compared with baseline OR renal replacement therapy

<sup>a</sup>In setting of an increase of  $\geq 0.5$  mg/dl.

**Table 2:** Surgical procedures performed in study cohort

Type of surgery	Number of patients ( $n = 951$ )
Isolated TV surgery, $n$ (%)	224 (24%)
Combined procedures, $n$ (%)	727 (76%)
Mitral valve surgery, $n$ (%)	546 (57%)
Pulmonary valve surgery, $n$ (%)	68 (7%)
Aortic valve surgery, $n$ (%)	213 (22%)
CABG, $n$ (%)	189 (20%)
Other concomitant surgery, $n$ (%)	391 (41%)

TV: tricuspid valve; CABG: coronary artery bypass grafting.

emergent status. Three hundred and ninety-five patients (42%) had TV surgery as part of a reoperation.

Aprotinin was administered to 354 (37%) patients, and most others received tranexamic acid. Mean CPB time in the total study cohort was  $104 \pm 51$  min with an aortic cross-clamp time of  $65 \pm 39$  min. One hundred forty-seven (15%) patients were operated on without aortic cross-clamping on the beating or fibrillating heart.

Regarding the preoperative renal status, 396 (42%) patients had baseline sCrea  $>1.2$  mg/dl, and 47 (5%) had sCrea  $>2.0$  mg/dl. Moderate reduction of GFR (31–60 ml/min per  $1.73$  m<sup>2</sup>) at baseline was present in 538 (57%) patients, and 49 (5%) had severely decreased GFR ( $\leq 30$  ml/min per  $1.73$  m<sup>2</sup>).

Six hundred sixty-six (70.0%) patients were free of postoperative AKI and 285 (30.0%) were classified as AKI: 170 (17.9%) RIFLE class R, 58 (6.1%) class I and 57 (6.0%) class F. Demographic and operative variables of patients according to severity of RIFLE classification are presented in Table 3. Significant differences between patients with no-AKI and those patients who reached a RIFLE class for AKI were seen for the following variables: male sex, BMI, diabetes, hypertension, preoperative haemoglobin, previous cardiac surgery, TV replacement, CPB duration and cross-clamp time (Table 3).

Increased RIFLE class was associated with worse postoperative outcomes such as the need for prolonged intubation, length of hospital stay and operative mortality (Table 4,  $P < 0.001$  for each

variable). Odds ratio (OR) for mortality was 4.2 [95% confidence interval (CI) 3.2–5.4;  $P < 0.001$ ] for one class increase by RIFLE ( $P < 0.001$ ). Discrimination for the prediction of mortality was very good; the AUROC was 0.85 (95% CI 0.80–0.91). For each RIFLE class increase, patients had an OR of 2.3 (95% CI 1.9–2.9,  $P < 0.001$ ) for prolonged intubation (AUROC 0.65, 95% CI 0.61–0.69).

Seventy-five (7.9%) patients required RRT in the early postoperative period during hospital stay or within 30 days. Mortality in patients requiring postoperative RRT was 49.3% compared with 2.9% for patients without postoperative RRT ( $P < 0.001$ ; Table 5).

Several preoperative and operative variables were univariately predictive of postoperative AKI regardless of RIFLE class (Table 6). In the multivariate logistic regression model, older patient age, male gender, previous cardiac surgery, TV replacement (vs repair), lower preoperative haemoglobin and longer CPB duration were all identified as independent predictors of postoperative AKI (Table 7).

## DISCUSSION

AKI after cardiac surgery is an important complication that is associated with adverse outcome. Correlation between different types of cardiac surgery and the occurrence of postoperative AKI

**Table 3:** Patient characteristics by RIFLE classes

Variables	No AKI	RIFLE class R	RIFLE class I	RIFLE class F	P-value*
Number of patients, n (%)	666 (70)	170 (18)	58 (6)	57 (6)	
Demographics					
Age, years	$66 \pm 13$	$68 \pm 13$	$67 \pm 13$	$68 \pm 12$	0.13
Female sex, n (%)	425 (64)	85 (50)	35 (60)	28 (49)	0.003
Body mass index, kg/m <sup>2</sup>	$28 \pm 6$	$27 \pm 6$	$30 \pm 7$	$28 \pm 6$	0.048
Medical history					
Diabetes, n (%)	118 (18)	42 (25)	14 (24)	20 (35)	0.005
Hypertension, n (%)	384 (58)	109 (64)	44 (76)	35 (61)	0.03
Chronic lung disease, n (%)	121 (18)	36 (21)	15 (26)	14 (25)	0.32
Cerebrovascular disease, n (%)	105 (16)	38 (22)	14 (24)	12 (21)	0.10
Peripheral vascular disease, n (%)	49 (7)	13 (8)	3 (5)	7 (12)	0.51
Baseline renal function and haemoglobin					
Baseline sCrea level, mg/dl	$1.26 \pm 0.39$	$1.30 \pm 0.41$	$1.20 \pm 0.29$	$1.55 \pm 0.68$	0.25
Patients with baseline sCrea $>1.2$ mg/dl, n (%)	276 (41)	88 (46)	27 (39)	5 (50)	0.54
Patients with baseline sCrea $>2.0$ mg/dl, n (%)	36 (5)	10 (5)	0	1 (10)	0.23
Baseline GFR					0.56
Baseline GFR $>60$ ml, n (%)	258 (38)	76 (40)	27 (39)	3 (30)	–
Baseline GFR 31–60 ml, n (%)	384 (56)	106 (55)	42 (61)	6 (60)	–
Baseline GFR $\leq 30$ ml, n (%)	38 (6)	10 (5)	0	1 (10)	–
Preoperative haemoglobin, g/l	$12.6 \pm 1.8$	$11.7 \pm 1.7$	$11.9 \pm 1.8$	$12.6 \pm 1.7$	$<0.001$
Preoperative cardiac status					
Previous cardiac surgery, n (%)	249 (37)	105 (55)	35 (51)	6 (60)	0.001
Prior myocardial infarction, n (%)	81 (12)	29 (15)	7 (10)	1 (10)	0.61
LVEF (%)	$57 \pm 12$	$57 \pm 13$	$59 \pm 12$	$53 \pm 20$	0.39
Operative details					
Isolated TV surgery, n (%)	170 (25)	38 (20)	13 (19)	3 (30)	0.34
TV replacement, n (%)	202 (30)	79 (41)	24 (35)	4 (40)	0.03
CPB duration, minutes	$97 \pm 46$	$119 \pm 59$	$131 \pm 58$	$118 \pm 68$	$<0.001$
Cross-clamp time, minutes	$62 \pm 36$	$72 \pm 44$	$85 \pm 45$	$76 \pm 43$	$<0.0001$
Temperature, °C	$34.9 \pm 2.9$	$34.6 \pm 2.7$	$34.0 \pm 3.6$	$33.1 \pm 6.6$	0.17
Aprotinin, n (%)	244 (36)	72 (38)	34 (49)	4 (40)	0.18

AKI: acute kidney injury; BMI: body mass index; GFR: glomerular filtration rate; LVEF: left ventricular ejection fraction; CPB: cardiopulmonary bypass; LVEF: left ventricular ejection fraction. Data are mean  $\pm$  SD unless otherwise specified.

\*P-value regarding comparison over all three RIFLE classes.

**Table 4:** Outcomes by RIFLE classes (*n* = 951)

Variables	No AKI	RIFLE class R	RIFLE class I	RIFLE class F	P-value*
Number of patients, <i>n</i> (%)	666 (70)	170 (18)	58 (6)	57 (6)	
RRT, <i>n</i> (%)	6 (0.9)	9 (5.3)	6 (10.4)	54 (94.7)	<0.0001
Mortality, <i>n</i> (%)	10 (1.5)	11 (6.5)	10 (17.2)	31 (54.4)	<0.0001
Prolonged ventilation <sup>a</sup> , <i>n</i> (%)	98 (14.9)	47 (29.6)	25 (52.1)	17 (64.4)	<0.0001
Hospital length of stay <sup>a</sup> , days	9.8 ± 8.4 median 8	14.6 ± 17.5 median 10	18.6 ± 13.8 median 15	34.2 ± 24.6 median 28	<0.001

RRT: renal replacement therapy. Data are mean ± SD unless otherwise specified.

<sup>a</sup>Data only given for patients without mortality.

\*P-value regarding comparison over all three RIFLE classes.

**Table 5:** Outcomes in patients with postoperative RRT (*n* = 951)

Variables	No RRT	RRT	P-value
Number of patients, <i>n</i> (%)	876 (92.1)	75 (7.9)	–
Mortality, <i>n</i> (%)	25 (2.9)	37 (49.3)	<0.001
Prolonged ventilation <sup>a</sup> , <i>n</i> (%)	159 (18.7)	28 (73.7)	<0.001
Hospital length of stay <sup>a</sup> , days	10.5 ± 7.4 median 8	43.6 ± 37.0 median 35	<0.001

RRT: renal replacement therapy. Data are mean ± SD unless otherwise specified.

<sup>a</sup>Data only given for patients without mortality.

**Table 6:** Univariate analysis of risk factors for AKI within all RIFLE classes (*n* = 951)

Variable	OR	95% CI	P-value
Age	1.01	1.0–1.03	0.02
Male sex	1.63	1.23–2.16	<0.001
Body mass index	1.01	0.99–1.04	0.21
Diabetes	1.69	1.21–2.34	0.002
Hypertension	1.42	1.06–1.89	0.02
Chronic lung disease	1.33	0.95–1.87	0.10
Cerebrovascular disease	1.54	1.09–2.19	0.01
Peripheral vascular disease	1.11	0.66–1.85	0.70
Baseline sCrea level	1.83	1.29–2.58	<0.001
Patients with baseline sCrea >1.2 mg/dl	1.34	1.01–1.77	0.04
Patients with baseline sCrea >2.0 mg/dl	1.96	1.08–3.54	0.03
Preoperative haemoglobin	0.74	0.68–0.80	<0.001
Previous cardiac surgery	2.16	1.63–2.86	<0.001
Prior myocardial infarction	1.23	0.82–1.85	0.32
Left ventricular ejection fraction	1.0	0.99–1.01	0.81
PAP systolic	1.01	1.0–1.02	0.07
Isolated TV surgery	0.72	0.52–1.02	0.06
TV replacement	1.58	1.18–2.11	0.002
CPB duration	1.01	1.01–1.01	<0.001
Cross-clamp time	1.01	1.0–1.01	<0.001
Temperature	0.95	0.90–0.99	0.03
Aprotinin	1.24	0.93–1.65	0.14

AKI: acute kidney injury; TV: tricuspid valve; OR: odds ratio; CI: confidence interval; GFR: glomerular filtration rate; CPB: cardiopulmonary bypass.

has been described in various epidemiological studies [1, 6]. In a recent validation of different models to predict AKI after cardiac surgery, we found in a large non-selected cardiac surgical patient cohort (*n* = 12 096) significantly increased rates of postoperative RRT in the subset of patients undergoing TV surgery [1]. Although TV surgery was performed in only 8% of patients, 28% of the patients who required postoperative RRT had TV procedures (*P* < 0.001, TV vs other operations). These findings and the clinical experience of elevated rates of AKI in patients after TV surgery led us to the present detailed analysis.

Risk factors and incidence of renal dysfunction in patients undergoing TV surgery have not been studied in detail, and previous investigations are limited by small sample size. Furthermore, comparability of studies focusing on AKI is limited because of the variable definitions of AKI [4, 5, 7]. We aimed to investigate the incidence of and risk factors for AKI in patients undergoing TV surgery in a relatively large patient cohort. AKI was defined according to the consensus RIFLE criteria [4], which has been validated in a number of clinical studies and has been found to be of clinical relevance for the diagnosis of AKI and its classification in different stages of severity [5, 8, 9]. Consequently, we also aimed to determine the correlation between the occurrence of AKI and clinical outcomes in our patient population.

The main finding in our study cohort was a high incidence of postoperative AKI (30%) relative to the results given in the literature for other cardiac surgical cohorts. Much lower rates of postoperative AKI according to the RIFLE classification have been reported in non-selected consecutive patients undergoing various types of cardiac surgery [8]. In a consecutive cohort of all

**Table 7:** Multivariate analysis of risk factors for AKI within all RIFLE classes ( $n = 951$ )

Variable	OR	95% CI	P-value
Age (per 10 years)	1.16	1.02–1.31	0.02
Male sex	1.73	1.27–2.36	<0.001
Previous cardiac surgery	1.54	1.13–2.10	0.007
TV replacement	1.69	1.22–2.33	0.001
Higher preoperative haemoglobin (per 1 g/dl)	0.76	0.70–0.83	<0.001
CPB duration (per 10 min)	1.10	1.06–1.13	<0.001

AKI: acute kidney injury; OR: odds ratio; CI: confidence interval; TV: tricuspid valve; CPB: cardiopulmonary bypass.

patients ( $n = 4836$ ) operated on with CPB in our institution within a 3-year period, the incidence of AKI was 19.9% [5], and in a selected group of elective thoracic aortic surgery including patients operated on with or without deep hypothermic circulatory arrest, the incidence of postoperative AKI by all RIFLE classes was only 17.7% [10].

Among patients with different types of valvular heart surgery, TV procedures constitute one of the high-risk categories with poor outcome. A study from the STS database of valve procedures performed between 1994 and 2003 reported an unadjusted mortality of 10.7% for patients undergoing isolated TV surgery [3]. Several factors may contribute to this high surgical mortality and morbidity including multiple preoperative comorbidities, high incidence of reoperations, frequent concomitant cardiac procedures and the potential chronic sequelae of TV disease with progressive right ventricular (RV) and right atrial overload.

The pathophysiology of the development of AKI in cardiac surgical patients is complex and poorly understood. Impaired renal blood flow from left ventricular dysfunction (reduced cardiac output) is a principal mechanism. In recent investigations, however, right heart dysfunction was strongly associated with renal dysfunction. In patients with decompensated heart failure, venous congestion was more predictive of the development of AKI than left heart functional indices (cardiac index) [11]. The concept of venous congestion and renal dysfunction dates to studies performed in the 1930's, which documented the influence of venous pressure on kidney dysfunction in animal models [12]. In patients with TV regurgitation, both pathophysiological mechanisms may be causative, reduced cardiac output and elevated venous pressure. Volume overload leading to venous congestion and its impact in the pathophysiology of the various forms of cardiorenal syndromes are well described [13].

In our study, moderate (GFR 31–60 ml,  $n = 538$ ) or severe renal impairment (GFR  $\leq 30$  ml,  $n = 49$ ) was present preoperatively in 61.7% of all patients. This confirms the findings of Maeder *et al.* [14] that TV regurgitation, which was the predominant functional pathology in our series, contributes to renal dysfunction in patients with heart failure. Another investigation found postoperative central venous pressure greater than 14 cm H<sub>2</sub>O to be a significant independent risk factor for postoperative AKI [15].

Our results also demonstrate in this selected patient cohort undergoing TV surgery that the occurrence of postoperative AKI is strongly associated with an adverse outcome (prolonged ventilation, length of hospital stay and mortality). This is true for all three severity classes of the RIFLE definition as well as for the

most severe form of AKI requiring RRT. Half of the patients with postoperative RRT died, a finding supporting the hypothesis that RRT after cardiac surgery is independently associated with mortality [16]. This high mortality justifies our modification of the RIFLE classification in which all patients with postoperative RRT were placed in the highest stage of AKI (failure class).

The impact of AKI is predictive of mortality not only early after operation as we have documented, but also long-term as demonstrated recently by Hobson *et al.* [17]. In this respect, cardiac surgical patients show a similar pattern in which worsening renal function in the context of heart failure is associated with adverse outcome and prolonged hospitalization [18].

In the multivariate analysis, six variables were identified as risk factors for postoperative AKI. The independent association of AKI with increased age, previous cardiac surgery and length of CPB is not unexpected. Interestingly, male gender turned out to also be an independent risk factor for the development of postoperative AKI. In a larger series focusing on patients with TV surgery consistently more women were present, which is the case in our study cohort [19–21]. Some investigators have noted the poor survival of males undergoing TV repair or replacement for organic TV disease [19]. However, the reasons for this and the consistent predominance of women in TV surgical groups are unclear. In our clinical series, females had a lower risk of AKI in the postoperative period.

In accordance with other investigators, we identified preoperative low haemoglobin as an independent risk factor for AKI after cardiac surgery [9, 10, 22]. A recent large multicentre study of patients undergoing cardiac surgery with CPB found preoperative anaemia independently associated with AKI within the three thresholds of the RIFLE definition [9]. Previously, we confirmed these data in a selected patient group undergoing thoracic aortic surgery [10]. Interestingly, in a prospective evaluation of 61 patients undergoing surgery for severe TV regurgitation, only RV end-systolic area ( $<20$  cm<sup>2</sup>) and preoperative haemoglobin level ( $>11.3$  g/dl) were predictive of event-free survival [23]. It is unclear whether low preoperative haemoglobin is a potentially modifiable risk factor or only a surrogate marker of severity of illness.

TV replacement was independently associated with the occurrence of postoperative AKI. Previous investigators have reported high morbidity and mortality in patients undergoing TV replacement [21]. A very recent propensity analysis; however, demonstrated significant early and late mortality in patients undergoing TV surgery regardless of the operative approach [20]. Our finding of higher risk of AKI with valve replacement may be confounded



by other factors; patients who require TV replacement may simply be sicker and burdened with more severe valve pathology. Also, patients may be selected for valve replacement because they have more severe RV dysfunction than patients who undergo TV repair. Further, patients who underwent TV replacement in our series were significantly younger ( $65 \pm 12$  vs  $67 \pm 13$  years,  $P=0.002$ ), presented with higher preoperative sCrea values ( $1.33 \pm 0.41$  vs  $1.24 \pm 0.37$  mg/dl,  $P < 0.001$ ), more often had previous cardiac surgery (50 vs 38%,  $P < 0.001$ ), and more frequently underwent isolated TV surgery (41 vs 15%,  $P < 0.001$ ). In this respect, the need for TV replacement may be considered as a surrogate for poor outcome.

Preoperative elevated systolic pulmonary artery pressure was not an important predictor of postoperative AKI ( $P=0.07$ ), and this was true when patients were stratified into groups with moderate and severe pulmonary hypertension. In a recent study investigating preoperative factors associated with adverse outcomes after TV replacement, the presence of pulmonary hypertension ( $>50$  mmHg) alone was not associated with operative mortality [24]. It seems that more specific echocardiographic measurements of impaired RV function are predictive of adverse outcomes in this patient group.

Several variables associated with postoperative AKI in the univariate analysis were not identified as independent predictors in the multivariate regression model including elevated baseline preoperative sCrea. Interestingly, this is in accordance with previous findings [10] and may be explained by two factors: the RIFLE criteria are based on percentage changes in sCrea or GFR which results in a larger absolute change in patients who present with higher baseline values required for the definition of AKI. Secondly, and more important, is the well known finding of a wide overlapping range in baseline creatinine between patients who develop postoperative AKI and who do not [6]. This leads to the clear conclusion that risk estimation for postoperative AKI should be made with consideration of multiple variables rather than by baseline creatinine alone.

Several limitations in interpreting these results have to be discussed. The study is retrospective and we focused on pre- and intraoperative variables that may predict AKI. Both the association between postoperative AKI and the identified risk factors as well as the strong correlation between postoperative AKI and adverse outcome; however, may be confounded by postoperative complications other than AKI. For example, in our study cohort the risk of AKI increased 3-fold in patients who required re-exploration for bleeding (OR 3.1, 95% CI 1.8–5.2;  $P < 0.001$ , univariate analysis). As in all comparable study designs, a causal relation between AKI and outcome variables can only be hypothesized and not proven. There are complex interactions between different organ systems as illustrated by cardiorenal syndromes [25], and other interactions may be present. Our patients with prolonged postoperative ventilation showed a 5-fold increased risk of AKI (OR 4.9, 95% CI 3.6–6.7;  $P < 0.001$ , univariate analysis). An additional limitation is the lack of echocardiographic data on right heart (dys-)function in our database. Furthermore, reliable data on central venous pressure in the preoperative diagnostic evaluation in our patient group were not available.

In conclusion, TV surgery is associated with high rates of AKI relative to other types of cardiac surgery. Low cardiac output and especially right heart dysfunction associated with TV pathology and venous congestion are likely to be the principal mechanisms leading to AKI. The consensus RIFLE definition

system for AKI enables comparison between results and correlates well with adverse patient outcome within the 3-fold staging of AKI severity. Independent risk factors for AKI in patients undergoing TV surgery are older age, male gender, previous cardiac surgery, preoperative anaemia, prolonged CPB and TV replacement. Preoperative sCrea and pulmonary artery pressure are not independent risk factors for postoperative AKI, and the estimation of patients risk of AKI has to be based on multivariable prediction. Further studies are warranted to elucidate the correlation between right heart functional indices and AKI in patients with TV pathology prior to surgery and perioperatively.

## Acknowledgements

The authors wish to thank Judy Lenoch for her assistance with the cardiovascular database that forms the basis for our study.

## Funding

Lars Englberger received support from a grant of the Clinic for Cardiovascular Surgery (Chairman T.P. Carrel), University Hospital Berne (Inselspital), Switzerland.

**Conflict of interest:** none declared.

## REFERENCES

- [1] Englberger L, Suri RM, Li Z, Dearani JA, Park SJ, Sundt TM III *et al.* Validation of clinical scores predicting severe acute kidney injury after cardiac surgery. *Am J Kidney Dis* 2010;56:623–31.
- [2] Regner KR, Connolly HM, Schaff HV, Albright RC. Acute renal failure after cardiac surgery for carcinoid heart disease: incidence, risk factors, and prognosis. *Am J Kidney Dis* 2005;45:826–32.
- [3] Rankin JS, Hammill BG, Ferguson TB Jr, Glower DD, O'Brien SM, DeLong ER *et al.* Determinants of operative mortality in valvular heart surgery. *J Thorac Cardiovasc Surg* 2006;131:547–57.
- [4] Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute Dialysis Quality Initiative workgroup. Acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care* 2004;8:R204–12.
- [5] Englberger L, Suri RM, Li Z, Casey ET, Daly RC, Dearani JA *et al.* Clinical accuracy of RIFLE and Acute Kidney Injury Network (AKIN) criteria for acute kidney injury in patients undergoing cardiac surgery. *Crit Care* 2011;15:R16.
- [6] Mehta RH, Grab JD, O'Brien SM, Bridges CR, Gammie JS, Haan CK *et al.* Society of Thoracic Surgeons National Cardiac Surgery Database Investigators. Bedside tool for predicting the risk of postoperative dialysis in patients undergoing cardiac surgery. *Circulation* 2006;114:2208–16.
- [7] Noyez L. Influence of the definition of acute renal failure post-cardiac surgery on incidence, patient identification, and identification of risk factors. *Eur J Cardiothorac Surg* 2011;39:e8–12.
- [8] Kuitunen A, Vento A, Suojaranta-Ylinen R, Pettilä V. Acute renal failure after cardiac surgery: evaluation of the RIFLE classification. *Ann Thorac Surg* 2006;81:542–6.
- [9] Karkouti K, Wijeyesundera DN, Yau TM, Callum JL, Cheng DC, Crowther M *et al.* Acute kidney injury after cardiac surgery: focus on modifiable risk factors. *Circulation* 2009;119:495–502.
- [10] Englberger L, Suri RM, Greason KL, Burkhart HM, Sundt TM III, Daly RC *et al.* Deep hypothermic circulatory arrest is not a risk factor for acute kidney injury in thoracic aortic surgery. *J Thorac Cardiovasc Surg* 2011; 141:552–8.
- [11] Mullens W, Abrahams Z, Francis GS, Sokos G, Taylor DO, Starling RC *et al.* Importance of venous congestion for worsening of renal function in advanced decompensated heart failure. *J Am Coll Cardiol* 2009;53: 589–96.

- [12] Winton FR. The influence of venous pressure on the isolated mammalian kidney. *J Physiol* 1931;72:49–61.
- [13] Ronco C, Maisel A. Volume overload and cardiorenal syndromes. *Congest Heart Fail* 2010;16(Suppl 1):Si–iv.
- [14] Maeder MT, Holst DP, Kaye DM. Tricuspid regurgitation contributes to renal dysfunction in patients with heart failure. *J Card Fail* 2008;14: 824–30.
- [15] Palomba H, de Castro I, Neto AL, Lage S, Yu L. Acute kidney injury prediction following elective cardiac surgery: AKICS Score. *Kidney Int* 2007; 72:624–31.
- [16] Chertow GM, Levy EM, Hammermeister KE, Grover F, Daley J. Independent association between acute renal failure and mortality following cardiac surgery. *Am J Med* 1998;104:343–8.
- [17] Hobson CE, Yavas S, Segal MS, Schold JD, Tribble CG, Layon AJ *et al.* Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. *Circulation* 2009;119:2444–53.
- [18] Hillege HL, Nitsch D, Pfeffer MA, Swedberg K, McMurray JJ, Yusuf S *et al.* Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) Investigators. Renal function as a predictor of outcome in a broad spectrum of patients with heart failure. *Circulation* 2006;113:671–8.
- [19] Tang GH, David TE, Singh SK, Maganti MD, Armstrong S, Borger MA. Tricuspid valve repair with an annuloplasty ring results in improved long-term outcomes. *Circulation* 2006;114(1 Suppl):I577–81.
- [20] Moraca RJ, Moon MR, Lawton JS, Guthrie TJ, Aubuchon KA, Moazami N *et al.* Outcomes of tricuspid valve repair and replacement: a propensity analysis. *Ann Thorac Surg* 2009;87:83–8.
- [21] Guenther T, Noebauer C, Mazzitelli D, Busch R, Tassani-Prell P, Lange R. Tricuspid valve surgery: a thirty-year assessment of early and late outcome. *Eur J Cardiothorac Surg* 2008;34:402–9.
- [22] De Santo L, Romano G, Della Corte A, de Simone V, Grimaldi F, Cotrufo M *et al.* Preoperative anemia in patients undergoing coronary artery bypass grafting predicts acute kidney injury. *J Thorac Cardiovasc Surg* 2009;138:965–70.
- [23] Kim YJ, Kwon DA, Kim HK, Park JS, Hahn S, Kim KH *et al.* Determinants of surgical outcome in patients with isolated tricuspid regurgitation. *Circulation* 2009;120:1672–8.
- [24] Topilsky Y, Khanna AD, Oh JK, Nishimura RA, Enriquez-Sarano M, Jeon YB *et al.* Preoperative factors associated with adverse outcome after tricuspid valve replacement. *Circulation* 2011;123:1929–39.
- [25] Goh CY, Vizzi G, De Cal M, Ronco C. Cardiorenal syndrome: a complex series of combined heart/kidney disorders. *Contrib Nephrol* 2011;174:33–45.