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Acute kidney injury and outcome following aortic valve replacement for aortic stenosis

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Abstract

OBJECTIVES: Most studies on acute kidney injury (AKI) following open-heart surgery have focused on short-term outcome following coronary artery bypass grafting. We reviewed the incidence, risk factors and outcome, including long-term survival, of AKI after aortic valve replacement (AVR) in a population-based cohort.

METHODS: A retrospective review of 365 patients who underwent AVR for aortic stenosis during 2002–2011 was made. AKI was defined according to the RIFLE criteria. All patients requiring dialysis were followed up in a centralized registry. Risk factors for AKI were analysed with univariable and multivariable analysis, and survival was graphically presented with the Kaplan–Meier method.

RESULTS: The rate of AKI was 82/365 (22.5%); 40, 28 and 14 patients belonging to the Risk, Injury and Failure groups, respectively. Preoperatively, 37 (45.1%) AKI patients had reduced kidney function. Transfusion of red blood cells, obesity and prolonged cardiopulmonary bypass time were independent risk factors for AKI. Acute postoperative dialysis was required in 15 patients (4.1%), and 1 patient developed dialysis-dependent end-stage renal disease. Major postoperative complications were more common in the AKI group (65 vs 22%, $P < 0.001$). The 30-day mortality rate in the AKI group was 18%, as opposed to 2% in the non-AKI group ($P < 0.001$), with a 5-year survival rate of 66 vs 87%, respectively ($P < 0.001$). In multivariable analysis AKI was an independent predictor of operative mortality [odds ratio = 5.89, 95% confidence interval (CI) = 1.99–18.91] but not of long-term survival (hazard ratio = 1.44, 95% CI = 0.86–2.42).

CONCLUSIONS: More than 1 in 5 patients (22.5%) who underwent AVR developed AKI postoperatively. AKI was associated with higher morbidity and was an independent predictor of operative mortality. However, AKI was not a determinant of long-term survival.

Keywords: Aortic valve replacement • Acute kidney injury • Risk factors • RIFLE • Survival

INTRODUCTION

Cardiac surgery-related acute kidney injury (AKI) (CS-AKI) is a common and serious complication of open-heart surgery, associated with increased morbidity as well as short- and long-term mortality [1, 2]. Until 2004, when the Acute Dialysis Quality Initiative published a consensus definition of AKI (the RIFLE criteria), comparison of studies on AKI was difficult because of widely differing definitions [3]. These criteria were later accepted by the Acute Kidney Injury Network with some modifications (the AKIN criteria) [4]. Ultimately, the Kidney Disease: Improving Global Outcomes (KDIGO) criteria that combines the RIFLE and the AKIN criteria was published in 2012 [5] and today most studies use one of these three classifications of AKI, thereby allowing better comparison of epidemiological research.

According to the RIFLE criteria, classification of AKI may be based on either a relative increase in serum creatinine (SCr) or an episode of oliguria. AKI is graded according to severity into three groups: Risk, Injury and Failure. The RIFLE criteria also define two outcome measures (Loss and End-stage kidney disease) depending on the duration of renal replacement therapy (RRT).

In recent years, several risk factors for CS-AKI have been identified, mostly in studies conducted on patients undergoing coronary artery bypass grafting (CABG). Risk factors can be divided into patient-related (e.g. advanced age, female sex, diabetes mellitus, pre-existing kidney disease and left ventricular impairment) or operation-related [such as perioperative hypotension and prolonged cardiopulmonary bypass (CPB) time] [6].

Valvular heart surgery is a proven risk factor for AKI [7]. Aortic valve replacement (AVR) is the second most common open-heart procedure, after CABG, in most Western countries [8]. AKI following AVR as well as the more recently developed technique of transcatheter aortic valve replacement was a topic of a recent review. However, none of the studies included in the review

focused solely on AKI following AVR, but rather on AKI after cardiac surgery in general [9]. In fact, there has been a lack of studies focusing solely on the incidence, risk factors and outcomes of AKI following conventional AVR. We therefore wanted to evaluate the incidence and risk factors for AKI following AVR for aortic stenosis (AS) in a population-based cohort. Furthermore, we also investigated short-term outcome and long-term survival in AKI patients.

MATERIALS AND METHODS

Patients

This was a retrospective whole-nation study of all patients who underwent AVR for AS at Landspitali–National University Hospital of Iceland between 1 January 2002 and 31 December 2011. The hospital is the only institution performing open-heart surgery in Iceland, and since 1986 over 7000 open-heart procedures have been performed. Patients were identified through two separate registries. Firstly, an electronic diagnosis and operation registry was searched for patients who had undergone AVR with either biological or mechanical prosthesis, with or without concomitant CABG. Subsequently, a centralized cardiac surgery database at our institution was used to identify patients, providing a 100% match with the subset identified in the aforementioned registry.

Of the 436 patients who underwent AVR with or without surgical coronary revascularization during the 10-year period, 71 patients were excluded, 31 because of a history of previous cardiac surgery, 27 because AS was not the indication for surgery and 13 because of missing data, since their patient charts were not found. None of these patients died during surgery. This left 365 patients for further analysis, of whom 298 (81.6%) received a biological prosthesis and 67 (18.4%) received a mechanical prosthesis.

Clinical parameters

Clinical information, obtained from patient charts and surgical reports, was registered on a standardized data sheet using Excel (Microsoft Corp., Redmond, WA, USA) and was reviewed by five of the authors (Dadi Helgason, Sindri A. Viktorsson, Solveig Helgadottir, Inga L. Ingvarsdottir and Tomas Gudbjartsson). Over 100 variables were registered, e.g. gender, age, cardiovascular risk factors and previous medical history. History of myocardial infarction (MI), diabetes mellitus, hypertension, dyslipidaemia and chronic heart failure was defined as a prior diagnosis of these conditions at any time. The modification of diet in renal disease (MDRD) study equation was used to calculate preoperative estimated glomerular filtration rate (eGFR) for each patient, and reduced preoperative renal function was defined as eGFR <60 ml/min/1.73 m^2. Information on left ventricular ejection fraction and medication was also collected, including antiarrhythmic drugs such as β-blockers, cholesterol-lowering statins and anticoagulation or antiplatelet drugs. Patients' symptoms were evaluated according to the New York Heart Association (NYHA) classification, and their EuroSCORE (European System for Cardiac Operative Risk Evaluation) was calculated [10]. In addition, information on preoperative haemoglobin, the severity of coronary artery disease (such as three-vessel disease, left main stem stenosis), acute versus elective surgery, CPB time, aortic cross-clamp time and skin-to-skin time was registered.

Hospital morbidity was assessed by means of intraoperative and postoperative complications (minor/major) and length of stay. Operative mortality was defined as the number of patients who died ≤30 days from surgery.

Definition of acute kidney injury and complications

AKI was defined according to the RIFLE criteria. The patient's highest postoperative SCr level in the first 7 days after surgery was compared with baseline levels (defined as the preoperative SCr level closest to surgery) and AKI patients classified into the Risk, Injury or Failure group according to the relative degree of SCr elevation (1.5-fold to 2-fold, >2-fold to 3-fold, and >3-fold, respectively). AKI patients were compared with patients with normal postoperative kidney function. The baseline SCr level was missing in 15 patients and, in these cases, the mean baseline SCr value of the study cohort was used instead.

Postoperative complications were categorized as either minor or major. Minor complications included leg wound infection, urinary tract infection, pleural effusion requiring drainage and pneumonia; major complications included stroke, mediastinitis, endocarditis, MI (defined as isolated ST-segment changes or a new left bundle branch block on electrocardiogram along with elevation of creatine kinase MB (CK-MB) of ≥70 μg/l), reoperation, sternum dehiscence and acute respiratory distress syndrome or multiple organ failure (MOF). We also recorded bleeding (defined as the 24-h postoperative chest tube output) and number of transfusions of packed red blood cells (PRBCs) during the hospitalization period. All patients were followed up regarding RRT and renal recovery after surgery by using a centralized dialysis database in Iceland.

Follow-up

Patients were assigned a date and a cause of death or were identified as still living on 1 June 2013, using data from the Icelandic National Population Registry. Overall survival (OS) was calculated using the Kaplan–Meier method. The mean follow-up time was 4.7 years (range: 0–11.2 years) and none of the patients were lost to follow-up.

Statistical methods

Continuous variables were compared between patients with and without AKI with a *t*-test or Mann–Whitney *U*-test, depending on whether or not the data were normally distributed. Categorical variables were compared by using the χ^2 test when the minimum expected number was >1, otherwise the Fisher's exact test was used. Survival was plotted on a Kaplan–Meier curve and the groups were compared with a log-rank test. A multivariable logistic regression model of independent risk factors for AKI and predictors of operative mortality was pursued by using variables from the univariable analysis with *P*-values less than 0.1 as predictor variables, and reducing the model using a stepwise backwards method and then adding factors with clinical reasoning until the best model was found. The goodness of fit of these models was tested with the Hosmer–Lemeshow test. Similarly, a Cox proportional hazards model was used to find predictors of survival. All factors known to have a possible effect on survival were used and the model was again modified with a stepwise backwards method and clinical reasoning. In the final model, all factors met the requirements of proportional hazards assumption according to the method of Grambsch and Therneau [11]. Odds ratios (ORs) in

the logistic models and hazard ratios (HRs) in the Cox model are reported, along with 95% confidence intervals (CIs).

The level of statistical significance was set at $P < 0.050$. All statistical analyses were performed with R software version 3.1.2 (the R Foundation, Austria) using the Survival, Epitools and Resource Selection add-on packages.

The study was approved by the Icelandic National Bioethics Committee and the Icelandic Data Protection Commission. As individual patients were not identified, obtaining individual consent for the study was waived.

RESULTS

Rate

Eighty-two patients (22.5%) developed postoperative AKI according to the RIFLE criteria. Of these patients, 40 (11.0%) had Risk-stage AKI, 28 (7.7%) had Injury-stage AKI and 14 (3.8%) were categorized as being at the Failure stage.

Demographic and perioperative data

Patient characteristics with and without AKI are presented in Table 1, including cardiovascular risk factors, logistic EuroSCORE and operative factors. The AKI group was 4 years older on average and had a higher proportion of females. A higher proportion of AKI patients had reduced preoperative renal function, lower haemoglobin and more often diabetes mellitus; these patients also had significantly higher body mass index (BMI), a significantly higher logistic EuroSCORE and more severe heart failure symptoms according to the NYHA classification. A previous history of MI and heart failure was more common in patients in the AKI group. During surgery, the aortic cross-clamp time was on average 24 min longer in the AKI group, the CPB time was 40 min longer and these patients more often required insertion of an intra-aortic balloon pump (IABP) perioperatively. The lowest intraoperative temperature was comparable in both groups. A stentless biological valve was the most commonly implanted valve type in both groups. Patients who received a stentless biological prosthesis compared to stented bioprosthesis had on average 23 min longer cross-clamp time, but the rate of AKI in the stentless versus stented prosthesis groups was not statistically different (56.1 vs 48.8%, $P = 0.30$). Although the operation time for AVR with concomitant CABG was longer (CPB time 181 vs 136 min, $P < 0.001$), there was no significant difference in the incidence of AKI between isolated AVR and concomitant AVR + CABG.

Postoperative outcomes

Short-term complications are listed in Table 2. Overall, complications were more common in the AKI group, both minor (including

Table 1: Comparison of patient characteristics and intraoperative data for patients with AKI and normal renal function (non-AKI) following AVR

Factor	AKI ($n = 82$)	Non-AKI ($n = 283$)	P-value
Male	42 (51.2)	188 (66.4)	0.017
Age (years)	74.2 ± 7.69	70.3 ± 10.03	<0.001
BMI (kg/m^2)	29.1 ± 5.92	27.2 ± 3.91	0.010
Diabetes mellitus[a]	20 (24.4)	34 (12.0)	0.010
Hypertension[a]	65 (79.2)	189 (66.8)	0.043
Dyslipidaemia[a]	38 (45.8)	117 (41.5)	0.51
History of smoking	44 (53.7)	189 (66.8)	0.041
History of MI[a]	19 (23.1)	29 (10.3)	0.005
Chronic heart failure[a]	29 (35.4)	49 (17.4)	0.001
Reduced preoperative renal function[b]	37 (45.1)	72 (25.4)	0.001
Preoperative serum creatinine	97.9 ± 27.33	93.4 ± 44.09	0.25
Preoperative Hb (g/l)	131.9 ± 15.13	138.6 ± 13.17	<0.001
Preoperative anaemia[c]	29 (35.4)	65 (23.8)	0.034
NYHA III/IV	61 (74.4)	159 (56.2)	0.005
Logistic EuroSCORE (%)	14.1 ± 15.37	8.3 ± 10.17	0.001
LVEF (%)	55.3 ± 9.37	57.0 ± 8.63	0.15
Acute surgery	1 (1.2)	4 (1.4)	0.86
Urgent surgery	17 (20.7)	23 (8.1)	0.003
IABP	15 (18.3)	8 (2.8)	<0.001
CABG	49 (59.8)	150 (53.0)	0.34
Cross-clamp time (min)	135.1 ± 40.21	110.7 ± 31.41	<0.001
CPB time (min)	191.4 ± 58.43	151.4 ± 45.62	<0.001
Stented biological valve	28 (34.1)	86 (30.4)	0.61
Stentless biological valve	46 (56.1)	138 (48.8)	0.30
Mechanical valve	8 (9.8)	59 (20.8)	0.034
Lowest intraoperative temperature (°C)	34.5 ± 1.01	34.6 ± 0.88	0.20

Data are number (%) or mean ± standard deviation.
[a]Defined as a prior diagnosis of these conditions at any time.
[b]Defined as eGFR <60 ml/min/1.73 m^2.
[c]Defined as Hg <120 g/l in females and <135 g/l in men.
AVR: aortic valve replacement; AKI: acute kidney injury; BMI: body mass index; NYHA: New York Heart Association; IABP: intra-aortic balloon pump; CPB: cardiopulmonary bypass; MI: myocardial infarction; LVEF: left ventricular ejection fraction; CABG: coronary artery bypass grafting.

Table 2: Short-term outcome after AVR, including short-term complications, length of hospital stay and operative mortality

Factor	AKI (n = 82)	Non-AKI (n = 283)	P-value
Minor	69 (84.1)	171 (60.4)	<0.001
Superficial wound infection	11 (13.4)	19 (6.7)	0.086
Atrial fibrillation	46 (78.0)	144 (65.2)	0.086
Pleural effusion	24 (29.3)	25 (8.8)	<0.001
Pneumonia	24 (29.3)	16 (5.7)	<0.001
Urinary tract infection	28 (34.1)	11 (3.9)	<0.001
TIA	2 (2.4)	5 (1.8)	0.66
Major	53 (64.6)	63 (22.3)	<0.001
Myocardial infarction	24 (29.3)	25 (8.8)	<0.001
Sternal dehiscence	4 (4.9)	3 (1.1)	0.048
Stroke	2 (2.4)	6 (2.1)	1.00
Deep sternal infection	1 (1.2)	3 (1.1)	1.00
Reoperation for bleeding	23 (28.0)	31 (11.0)	<0.001
Bleeding in the first 24 h (ml)	1320 ± 1063.6	1060 ± 770.6	0.041
Transfusions of PRBCs (units)	13.4 ± 11.09	5.5 ± 5.63	<0.001
ICU stay (days)	6 (1–80)	1 (0–15)	<0.001
Surgical ward (days)	13 (0–127)	9 (0–41)	<0.001
Operative mortality (≤30 days)	15 (18.3)	6 (2.1)	<0.001

Number (%), mean ± standard deviation or median (range).
AVR: aortic valve replacement; AKI: acute kidney injury; TIA: transient ischaemic attack; PRBC: packed red blood cell; ICU: intensive care unit.

Table 3: Analysis of risk factors for AKI after AVR (Hosmer–Lemeshow goodness-of-fit test; $\chi^2 = 6.17$, $P = 0.63$).

Factor	OR (95% CI)	P-value
PRBC transfusions (5 units, numerical variable)	1.64 (1.33–2.07)	<0.001
CPB time (10 min, numerical variable)	1.10 (1.04–1.16)	0.002
Obesity (BMI > 30): yes versus no	2.71 (1.41–5.22)	0.003
IABP: yes versus no	2.43 (0.81–7.53)	0.11
Anaemia[a]	1.11 (0.58–2.16)	0.76
Hypertension: yes versus no	1.74 (0.90–3.53)	0.11
Sex: female versus male	1.56 (0.85–2.87)	0.15
Reduced preoperative renal function: yes versus no[b]	1.30 (0.69–2.42)	0.42
Age (per year, cont. variable)	1.03 (0.995–1.078)	0.10

AVR: aortic valve replacement; AKI: acute kidney injury; OR: odds ratio; CI: confidence interval; PRBC: packed red blood cell; CBP: cardiopulmonary bypass; BMI: body mass index; IABP: intra-aortic balloon pump.
[a]Defined as Hg <120 g/l in females and <135 g/l in men.
[b]Defined as eGFR <60 ml/min/1.73 m^2

pneumonia, urinary tract infection and pleural effusion requiring drainage) and major (including MI, sternal dehiscence, reoperation for bleeding and MOF). Postoperative bleeding was on average increased by 260 ml in the AKI group and they received 8 more units of PRBCs. The median length of intensive care unit (ICU) stay was 5 days longer in patients with AKI, and they spent 4 days longer on the surgical ward.

Renal replacement therapy

Fifteen patients (4.1%) required acute RRT following the AVR procedure, but 1 patient who had been treated with chronic dialysis before surgery was excluded from this analysis. Fourteen of these patients received continuous renal replacement therapy (CRRT) in the ICU. Four patients died while on CRRT and 6 patients required intermittent dialysis after discharge from the ICU. Only 3 patients (0.8%) required RRT for more than 4 weeks after surgery, including 1 patient who required RRT for more than 3 months and developed end-stage renal disease (0.27%).

Risk factors of acute kidney injury

Multivariable analysis of risk factors for AKI showed that transfusions of PRBCs (OR = 1.64, 95% CI = 1.33–2.07, per 5 units), prolonged CPB time (OR = 1.10, 95% CI = 1.04–1.16, per 10 min) and obesity (BMI > 30 kg/m^2) (OR = 2.71, 95% CI = 1.41–5.22) were independent predictors of AKI (Table 3).

Survival

Operative mortality. Operative mortality was 9-fold higher in patients with AKI than in patients without AKI: 18% when compared with 2% (P < 0.001). The operative mortality was 10, 32 and 14% in the Risk, Injury and Failure groups, respectively, and was significantly higher in every one of the three groups compared with that in non-AKI patients (P < 0.050).

After adjustment for logistic EuroSCORE, CPB time and number of PRBC transfusions, AKI proved to be an independent predictor of operative mortality (OR = 5.89, 95% CI = 1.99–18.91) (Table 4).

Long-term survival. AKI patients had significantly lower 5-year survival than non-AKI patients: 65.7% as opposed to 87.1% (P < 0.001) (Fig. 1), where 5-year survival rate was 70.6, 60.5 and 63.5% in the Risk, Injury and Failure groups, respectively. However, AKI was not a predictor of long-term survival in the Cox proportional hazard analysis (HR = 1.44, 95% CI = 0.86–2.42) (Table 5). The effect remained insignificant when patients who

Table 4: Predictors of operative mortality (Hosmer–Lemeshow goodness-of-fit test; $\chi^2 = 239.65$, $P < 0.001$)

Factor	OR (95% CI)	*P*-value
AKI: yes versus no	5.89 (1.99–18.91)	0.002
Logistic EuroSCORE	1.04 (1.01–1.07)	0.002
PRBC transfusions (5 units, numerical variable)	1.38 (1.08–1.76)	0.009
CPB time (10 min, numerical variable)	0.97 (0.87–1.07)	0.63

AKI: acute kidney injury; OR: odds ratio; CI: confidence interval; PRBC: packed red blood cell; CBP: cardiopulmonary bypass.

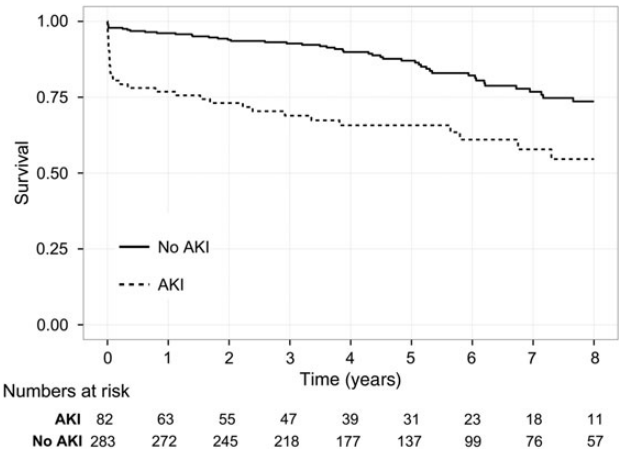

Figure 1: Overall survival in the AKI and non-AKI groups ($P < 0.001$, log-rank test). AKI: acute kidney injury.

died within 7 days from surgery were excluded from the analysis (HR = 1.72, 95% CI = 0.99–2.99). Nonetheless, when patients who lived longer than 7 days were categorized into two groups according to their type of surgery; AKI was an independent predictor of survival for patients who underwent AVR with concomitant CABG (HR = 3.01, 95% CI = 1.43–6.27), but not for isolated AVR patients (HR = 0.97, 95% CI = 0.36–2.67).

DISCUSSION

The results of this study show that the rate of AKI after AVR is high, with more than one in five patients affected following the procedure. This study also demonstrates that AKI is associated with increased risk of other postoperative complications and a predictor of operative mortality. However, we found that AKI following AVR is not an independent predictor of long-term survival.

AKI following open-heart surgery has been the subject of several studies in recent years. Most of these studies have investigated the incidence of AKI after CABG, with a rate ranging from 12 to 20% [1, 2]. To our knowledge only one prior study has focused on AKI following AVR [12]. That study reported an AKI rate of 17%, which is lower than in our cohort. The lower incidence might be partly explained by the fact that only patients who underwent isolated AVR were included. Our cohort, however, included both AVR and patients who underwent concomitant AVR and CABG.

Table 5: Predictors of long-term survival

Factor	HR (95% CI)	*P*-value
AKI: yes versus no	1.44 (0.86–2.42)	0.16
Logistic EuroSCORE	1.02 (1.002–1.031)	0.019
PRBC transfusions (5 units, numerical variable)	1.17 (1.06–1.31)	0.003
Age (per year, cont. variable)	1.08 (1.04–1.12)	<0.001
CPB time (10 min, numerical variable)	1.01 (0.96–1.06)	0.64
Sex: female versus male	0.99 (0.62–1.60)	0.96
Obesity (BMI >30): yes versus no	1.57 (0.95–2.59)	0.63

AKI: acute kidney injury; HR: hazard ratio; CI: confidence interval; PRBC: packed red blood cell; CBP: cardiopulmonary bypass; BMI: body mass index.

Although there was not a significant difference in the rate of AKI between these groups, there was a trend towards a lower rate in the isolated AVR group, or 19.9 vs 24.6% for patients who underwent AVR + CABG ($P = 0.34$). Studies focusing on AKI following open-heart procedures have reported AKI rates in their subanalysis on valve procedures ranging between 25 and 49%—which is a higher rate compared with the 22.5% found in the present study [13, 14].

The reason for a higher incidence of AKI following AVR compared with CABG is not fully understood. Patients who undergo AVR are often older than CABG patients, their preoperative kidney function is more often reduced and they generally undergo more complex operations with longer CPB times [15].

This study identified several risk factors for AKI including obesity, prolonged CPB time and transfusion with PRBCs, with ORs in the range of 1.10–2.71. Reduced preoperative renal function and history of diabetes are among well-defined risk factors for AKI in other studies [16] but did not reach statistical significance in the present study. Importantly, patient cohorts differ between studies; for instance diabetes is, for unknown reasons, less common in Iceland than in many other western countries [17]. Obesity is a risk factor for several postoperative complications, including AKI. The increased risk of postoperative AKI in obese patients can partly be explained by an increased risk of perioperative hypotension and insufficient volume resuscitation in this patient group [18].

Prolonged CPB time is a well-known and major risk factor for AKI [7, 14, 16]. The non-pulsatile flow of CPB causes vasoconstriction and hypoperfusion of the kidneys, and the haemodilution and inflammatory state caused by CPB are also thought to be contributory factors [19]. To increase the power of statistical analysis, we included patients who underwent isolated AVR as well as patients who underwent AVR with concomitant CABG. Even though the combined operations took on average 45 min longer, the rates of AKI and operative mortality were not statistically different following these procedures.

Overall, the transfusion rates in our study were high compared with transfusion rates following CABG in Iceland, where the rate has been comparable with those reported in neighbouring countries [20]. The reason for this higher rate could be that AVR, especially with concomitant CABG, is a more complex procedure than isolated CABG and carries an increased risk of bleeding. More restrictive guidelines have since the time of this study been implemented in Iceland with the aim of lowering perioperative transfusion rates.

According to our results, patients who received large numbers of PRBC transfusions are at an increased risk of developing AKI, as other studies have reported [14, 21]. In the present study the AKI patients received 8 more units of PRBCs compared with non-AKI patients; however, their 24-h postoperative chest tube output was increased by only 260 ml. The reason for this discordant use of PRBC transfusion in AKI patients is not fully known but can be partially explained by the fact that AKI patients more often had preoperative anaemia compared with non-AKI patients.

The effect of transfusion on AKI is not fully explained by preoperative anaemia, perioperative and postoperative bleeding, as transfusion remained a significant risk factor for AKI when reoperation for bleeding and 24-h postoperative chest tube output were included in the risk factor analysis. Some studies have suggested that when blood is stored, red blood cells undergo changes that cause impaired oxygen delivery, promote a proinflammatory state, and increase oxidative stress—resulting in injury to organs, including the kidneys [21, 22].

We experienced a relatively high rate (15%) of reoperation in patients. Possible explanations include a lower institutional threshold for bringing patients back for re-exploration. In addition, our study included both acute surgeries and AVR with concomitant CABG. In our patient cohort, combined surgery was associated with increased risk of postoperative bleeding compared with isolated AVR but other studies have shown a high reoperation rate following acute operations [23]. Despite the high reoperation rate, the rate of other complications and operative mortality were in line with other studies and we believe this high reoperation rate does not affect the generalizability of the main results of this study.

Of all patients in this study, 4.1% required RRT after surgery. Of these, 3 patients (0.8%) became dependent on haemodialysis for more than 4 weeks, with only 1 patient requiring dialysis for more than 3 months. Other studies on AKI after cardiac surgery have found rates of haemodialysis ranging between 1 and 5% [9], but when CRRT in the ICU is included, the rate is higher, or up to 8% [13, 24]. The overall RRT rate in our study is therefore comparable with that reported in other studies. The outcome of long-term dialysis must be regarded as excellent, since the only patient requiring dialysis for more than 3 months only needed dialysis treatment for 108 days and remained free of dialysis during the follow-up. Thus, none of the patients became permanently dependent on dialysis after surgery.

In the present study, AKI was associated with an increased risk of other complications and the operative mortality of the AKI group was nine times that of the non-AKI group. Overall long-term survival was also significantly lower in AKI patients. After correcting for preoperative and perioperative factors, AKI was found to be an independent predictor of operative mortality. We used a stepwise method with clinical reasoning to find the best model for predictors of operative mortality. Since only 21 patients died within 30 days, the stepwise method can lead to a selection bias of covariables. In addition, the predictability of the model was low according to the Hosmer–Lemeshow goodness-of-fit test. Therefore, although these results are suggestive, they should be interpreted with caution. Even so, AKI did not prove to be an independent predictor of long-term survival. According to the RIFLE criteria, patients can develop postoperative AKI during the first 7 postoperative days. However, some non-AKI patients could have died of other reasons before they developed AKI, which would skew the HR for AKI. Therefore, we performed a landmark analysis where all the patients who died within 7 days from surgery (the time frame for diagnosing AKI) were excluded. In that analysis, AKI did not prove to be an independent predictor of survival.

Our findings are different from those of most previous studies on this topic that show that AKI can have a profound effect on both short- and long-term patient survival. However, so far most studies have focused on AKI either following isolated CABG or cardiac surgery in general. To study the effect of AKI following AVR further, we performed a subanalysis where we categorized the patients into two groups according to their type of surgery (AVR or AVR + CABG). In the AVR + CABG group AKI was a significant predictor of long-term survival, but not in the isolated AVR group. A probable explanation for the difference of our results compared with other studies is the different patient cohort. Generally, patients undergoing AVR + CABG have different risk factors for atherosclerosis affecting the risk of AKI, kidney recovery, progression to chronic kidney disease and OS.

To our knowledge, our study is one of the first studies that focuses on the incidence and outcome of AKI following AVR surgery. Our findings not only are useful as a platform for other studies but also highlight the importance of AKI following cardiac surgery, especially valvular procedures. Furthermore, we think the identified risk factors of AKI should be taken into consideration in the pre-, peri- and postoperative periods of this group of patients.

We used the RIFLE criteria in their original form to evaluate AKI. Soon after the criteria were published in 2004, they were adopted and modified by the Acute Kidney Injury Network and republished (as the AKIN criteria) in an effort to enhance both sensitivity and specificity [4]. However, studies comparing the criteria have not shown any reliable superiority of the AKIN criteria [25]. In some of the most recent publications, new biomarkers for AKI have been used, such as neutrophil gelatinase-associated lipocalin (n-gal) and cystatin C. These studies show promising results for the markers in early detection of AKI. However, in our retrospective study we were not able to use these markers as they were not measured routinely.

The strengths of the study were that the patients were found using two separate registries and that the phenotype of AKI was well defined, with access to a centralized nationwide dialysis registry. All the patients were operated on and treated at a single centre, and they were therefore less likely to be affected by a selection bias. Furthermore, none of the patients were lost to follow-up. One of the limitations of this study was its retrospective observational nature, making it unable to demonstrate causal effects.

In summary, this study has shown that the incidence of AKI after AVR in Iceland is higher than that after CABG, but similar to that in other studies on valvular procedures. It identified risk factors for AKI that have been reported in other studies, including PRBC transfusions, obesity and prolonged CPB time. Development of AKI is associated with higher morbidity and is an independent predictor of operative mortality. In this study, however, AKI was not a determinant of long-term survival.

Further studies are needed on the long-term outcome—both survival and renal recovery—of AKI patients following AVR.

AUTHORS' CONTRIBUTIONS

Dadi Helgason, Sindri A. Viktorsson, Solveig Helgadottir and Tomas Gudbjartsson participated in the design of the study and collected the data together with Inga L. Ingvarsdottir, and Dadi Helgason, Solveig Helgadottir, Andri W. Orrason and Tomas Gudbjartsson performed the statistical analyses. Dadi Helgason,

Sindri A. Viktorsson, Solveig Helgadottir, and Tomas Gudbjartsson reviewed the literature and drafted the manuscript. Dadi Helgason wrote the article. All the authors read and approved the final manuscript.

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eComment. Obese aortic stenosis patients deserve special attention to prevent kidney injury

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Aortic stenosis and renal failure are mainly diseases of elderly population. Both of them consume a disproportionate share of healthcare resources worldwide. Each causes severe morbidity and mortality by itself, yet their coexistence alters upside down the clinical course. Helgason *et al.* published survival data of patients who develop acute kidney injury (AKI) after aortic valve replacement (AVR) for aortic stenosis. AKI is a frequent (22.5%) complication of AVR.

Authors defined transfusion of red blood cells, obesity and prolonged cardiopulmonary bypass time as independent risk factors for AKI [1]. According to recent studies obesity is a risk factor for renal failure even in healthy population. We want to underscore the possible contribution of obesity on renal failure in aortic stenosis patients. Even metabolically healthy overweight or obese individuals seem to be at higher risk for renal insufficiency. In a prospective cohort study, over 60 000 healthy individuals were stratified into underweight, normal weight, overweight and obese groups [2]. At baseline, all participants were free from renal insufficiency. Compared to those with normal weight, five-year cumulative incidence of renal insufficiency was higher among overweight or obese participants, with adjusted differences of 3.5 (95% CI 0.9-6.1) and 6.7 (95% CI 3.0-10.4) cases per 1000 respectively. The effect of obesity on eGFR increases with age, especially after age forty. According to another study even weight gain increases the risk for renal insufficiency if one remains within the "normal" category of body mass index [3]. In the light of present studies there is no doubt that obese aortic stenosis patients deserve special attention to prevent kidney injury especially after AVR. Chronic kidney disease may be under-recognized, which may contribute to the rising prevalence of end-stage renal disease. Screening of obese aortic stenosis patients even at early stages of the disease is crucial as renal insufficiency also increases the progression of stenosis. More than 1 in 5 AKI after AVR is a striking complication ratio. Physicians must be aware of kidney injury in obese AS patients. Risk modification with weight loss in early stages of aortic stenosis may prevent AKI after AVR and lengthen survival.

Conflict of interest: none declared.

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