ORIGINAL ARTICLE

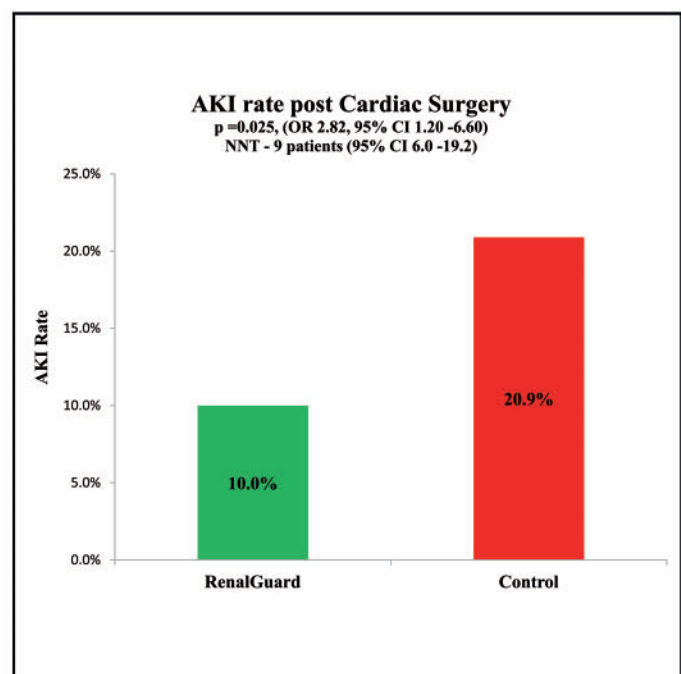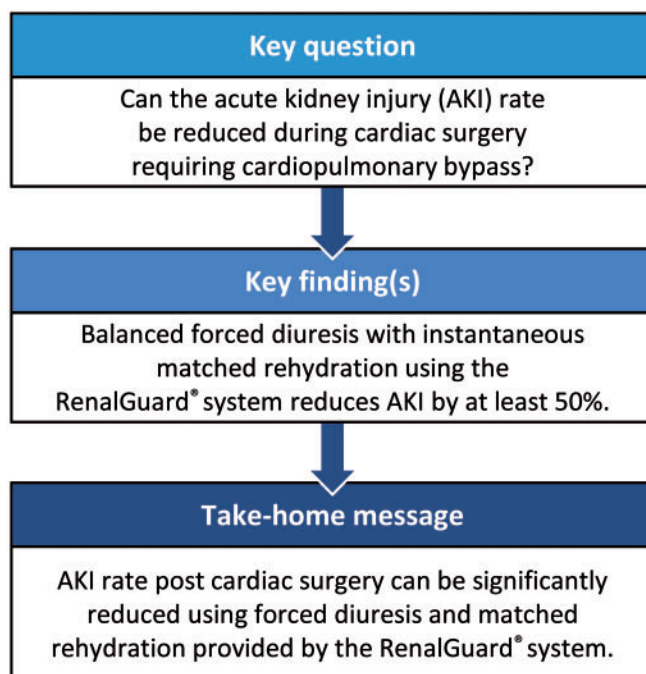# Reduction in acute kidney injury post cardiac surgery using balanced forced diuresis: a randomized, controlled trial

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Key question

Can the acute kidney injury (AKI) rate be reduced during cardiac surgery requiring cardiopulmonary bypass?

Key finding(s)

Balanced forced diuresis with instantaneous matched rehydration using the RenalGuard® system reduces AKI by at least 50%.

Take-home message

AKI rate post cardiac surgery can be significantly reduced using forced diuresis and matched rehydration provided by the RenalGuard® system.

AKI rate post Cardiac Surgery
p =0.025, (OR 2.82, 95% CI 1.20 -6.60)
NNT - 9 patients (95% CI 6.0 -19.2)

Abstract

OBJECTIVES: Our goal was to investigate the efficacy of balanced forced diuresis in reducing the rate of acute kidney injury (AKI) in cardiac surgical patients requiring cardiopulmonary bypass (CPB), using the RenalGuard® (RG) system.

METHODS: Patients at risk of developing AKI (history of diabetes and/or anaemia; estimated glomerular filtration rate 20–60 ml/min/1.73 m^2; anticipated CPB time >120 min; log EuroSCORE > 5) were randomized to the RG system group ($n = 110$) or managed according to

current practice (control = 110). The primary end point was the development of AKI within the first 3 postoperative days as defined by the RIFLE (Risk, Injury, Failure, Loss of kidney function, End-stage renal disease) criteria.

RESULTS: There were no significant differences in preoperative and intraoperative characteristics between the 2 groups. Postoperative AKI rates were significantly lower in the RG system group compared to the control group [10% (11/110) vs 20.9% (23/110); *P* = 0.025]. This effect persisted even after controlling for a number of potential confounders (odds ratio 2.82, 95% confidence interval 1.20–6.60; *P* = 0.017) when assessed by binary logistic regression analysis. The mean volumes of urine produced during surgery and within the first 24 h postoperatively were significantly higher in the RG system group (*P* < 0.001). There were no significant differences in the incidence of blood transfusions, atrial fibrillation and infections and in the median duration of intensive care unit stays between the groups. The number needed to treat with the RG system to prevent AKI was 9 patients (95% confidence interval 6.0–19.2).

CONCLUSIONS: In patients at risk for AKI who had cardiac surgery with CPB, the RS RG system significantly reduced the incidence of AKI and can be used safely and reproducibly. Larger studies are required to confirm cost benefits.

Clinical trial registration number: NCT02974946

Keywords: Acute kidney injury • Cardiac surgery • RenalGuard® • system

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ABBREVIATIONS

AKI	Acute kidney injury
CICU	Cardiac intensive care unit
CPB	Cardiopulmonary bypass
i.v	Intravenous
KDIGO	Kidney Disease: Improving Global Outcomes
MAP	Mean arterial pressure
OR	Operating room
RG	RenalGuard®

INTRODUCTION

Acute kidney injury (AKI) after cardiac surgery is well documented [1]. Over the last decade, standardization of the definition of AKI has been achieved with a view to improving diagnosis, treatment and prevention [2]. Although several strategies have been trialled to reduce AKI [3], it continues to account for significant morbidity and mortality in patients undergoing cardiac surgery [1, 4, 5].

The 'Kidney Disease: Improving Global Outcomes' (KDIGO) guidelines for AKI recommended initiation of various supportive measures (volume management, maintenance of adequate blood pressure and judicious avoidance of nephrotoxins) in patients at risk for AKI [6]. Using such strategies in high-risk patients has been reported to reduce the rate of AKI from 71.1% to 55.1% [7].

The RenalGuard® (RG) system (RenalGuard Solutions Inc., Milford, MA, USA) has been reported to reduce AKI in patients at risk of contrast-induced nephropathy in percutaneous coronary intervention and transcatheter aortic valve implantation [8–10]. These studies showed that the RG system reduced the incidence of AKI by 60–75%. The RG system uses forced diuresis with low-dose (0.25–0.5 mg/kg) furosemide along with administration of intravenous (i.v.) fluids at a rate that is matched in real time to the urine output to prevent inadvertent volume depletion. Forced diuresis with matched rehydration as a protection against contrast-induced nephropathy has been endorsed in the European Society of Cardiology guidelines [11].

The various aspects of the RG system have previously been described [12]. It includes a closed-loop fluid management system, high-volume fluid pump, high-accuracy dual weight measuring system, a single-use i.v. set and a urine collection system that interface with a standard Foley catheter. There are (i) real-time displays of urine and replacement fluid volumes, (ii) alerts to drain the urine bag or to replace the hydration fluid bag and (iii) safety features such as automatic air and occlusion detection. The console measures the volume of urine in the collection set (also calculates urine flow rate) and infuses a preset volume of hydration fluid to match the urine output, as required. The console allows the user to set the parameters for achieving a net fluid gain above or loss below the matched hydration. The console also allows infusion of a bolus of fluid at the user's request. The first-in-man assessment of the use of the RG system in patients having cardiac surgery was described in 2017 [12].

This randomized control trial [the KIDNEY (Kidney protection using the RenalGuard system in cardiac surgery) study] assessed if the RenalGuard system reduces the rate of AKI by using balanced forced diuresis in cardiac surgical patients requiring cardiopulmonary bypass (CPB).

PATIENTS AND METHODS

Ethical approval

The KIDNEY (Kidney protection using the RenalGuard system in cardiac surgery) study was reviewed and approved by the institutional research committee (16CARD13) prior to seeking ethical committee approval (16/NI/0246, 2 December 2016) and was registered on the ClinicalTrials.gov website (NCT02974946). The study was also supported by the National Institute of Healthcare Research, Clinical Research Network, UK (NIHR ID: 32769). All recruited patients gave written informed consent to partake in the study. Trial patients were treated according to the Declaration of Helsinki 2013.

Power calculations

Because there were no studies using the RG system in cardiac surgery, power calculations were carried out with some assumptions. Data from our cardiac surgery database (from 2005 to 2015, around 10 000 patients) and our previous publications [5] had shown that the rate of AKI in all patients undergoing cardiac surgery in our institution was around 10% and that the rate of AKI was just over 40% in patients with (i) diabetes, (ii) an estimated glomerular filtration rate of 20–60 ml/min/1.73 m^2, (iii)

cardiac procedures when CPB time exceeded 120 min, (iv) a haemoglobin level of 12.5 g/dl or below and (v) a logistic EuroSCORE of 5 or above. Previous publications describing patients undergoing percutaneous coronary intervention or transcatheter aortic valve implantation [8–10] reported an average reduction in the rate of AKI of 66% when the RG system was used. Moreover, none of the patients managed with the RG system developed AKI after cardiac surgery in a pilot study assessing safety and feasibility [12]. Thus, for this study, the reduction in the rate of AKI was estimated at 60%. Allowing for some patients to be lost to follow-up during the study, 110 patients per group were deemed adequate to achieve the primary end point with a power of 0.8 and an alpha of 0.05.

Recruitment and follow-up were completed as suggested in the Consolidated Standards of Reporting Trials flow diagram (Fig. 1) from 1 March 2017 to 4 September 2019.

Aims and objectives

The primary aim of the study was to assess the impact of the RG system on the reduction of AKI (RIFLE—Risk, Injury, Failure, Loss of kidney function, End-stage renal disease—criteria definition—50% increase in preoperative 'baseline' serum creatinine levels within the first 3 days after surgery) in patients undergoing cardiac surgery. The baseline creatinine level was defined as the latest creatinine level available prior to surgery. Secondary objectives included evaluation of any additional benefits of the use of the RG system in terms of postoperative complications, cardiac intensive care unit (CICU) length of stay and early postoperative creatinine surgical follow-up.

Inclusion criteria

Inclusion criteria included 1 (or more) of the following: (i) diabetes (insulin or non-insulin-dependent diabetes mellitus), (ii) estimated glomerular filtration rate of 20–60 ml/min/1.73 m^2, (iii) cardiac procedures when CPB time was likely to exceed 120 min, (iv) haemoglobin level of 12.5 g/dl or below and (v) logistic EuroSCORE of 5 or above (Table 1).

Randomization

Consenting patients were randomized, on the evening prior to surgery, using a sealed opaque envelope system (devised and managed by an independent researcher based in the research and development department). Patients in the RG system group had the RG system started in the anaesthetic room once the peripheral line and arterial lines were inserted and the patient was intubated. The RG system ran throughout the cardiac procedure in the operating room (OR) and for up to 6 h after transfer to the CICU. Patients were managed at a 0 balance, i.e. volume of urine output was matched to volume of Hartmann's fluid replacement infusion given through the RG system. Forced diuresis was initiated on induction of anaesthesia with a 20-mg i.v. bolus of furosemide aiming for a urine output of at least 200 ml/h, if possible. If required, the urine output rate was maintained by furosemide infusion that was titrated up to 10 mg/h during the operation The infusion was stopped in the OR at the end of procedure. In the CICU, the RG system was continued for 6 h (matching Hartmann's i.v. infusion rate to the urine output rate).

If the urine output fell below 200 ml/h within the first 6 h after the patient was admitted to the CICU, an additional bolus of furosemide (20 mg i.v.) was administered. Patients in the control group were managed according to current medical practice, which did not include any forced diuresis with i.v. furosemide in the OR. Otherwise, the management of the patients was similar, including the anaesthetic technique and the CPB run, including the need for inotropic support to maintain a mean arterial pressure (MAP) >65 mmHg. The CPB flow was calculated and maintained at a cardiac index of 2.4 l/min/m^2. Bypass was performed with mild to moderate (32–34°C) hypothermia. The patients were warmed to a nasopharyngeal temperature of 36.5–37°C and a bladder temperature of >35°C prior to discontinuation of CPB. Both groups of patients were transferred to the CICU postoperatively.

Statistical analyses

Continuous variables are expressed as mean (standard deviation) or median (minimum–maximum) for Gaussian and skewed distributed data, respectively. Group comparisons were carried out using a two-tailed *t*-test or the Mann–Whitney *U*-test accordingly. Categorical data are expressed as percentages; differences between the 2 groups were assessed using the χ^2 test of independence. The tests were considered significant at *P*-value <0.05. The presence (or absence) of AKI was compared using binary logistic regression (backward elimination) controlled for the effects of age, gender, ethnicity, study group (RG system or control), urgency and type of surgery, diabetes, left ventricular function category, history of renal impairment, preoperative creatinine level, preoperative estimated glomerular filtration rate, preoperative haemoglobin level, log EuroSCORE, CPB time, cross-clamp time, atrial fibrillation postoperatively and blood transfusions. SPSS version 23.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analyses.

Two patients who were randomized to the RG system group could not be catheterized per the urethra at the start of the operation and needed suprapubic catheter insertion at the end of procedure and hence were not connected to the RG system. Additionally, 2 patients in the RG system group and 1 patient from control group had their surgery cancelled and therefore did not have postoperative data. All patient data were analysed on an intention-to-treat basis.

RESULTS

Two hundred and twenty patients were recruited to the study (110 patients per group). There were no significant differences in the preoperative and intraoperative patient characteristics (age, gender, left ventricular function, surgery urgency and type, log EuroSCORE, creatinine level, e-GFR, haemoglobin level and history of diabetes, cerebrovascular disease and renal impairment) between the 2 groups (Table 2). Isolated coronary artery bypass grafting was performed in 48% of the RG system group and 54% of the control group. The mean number of grafts was 3.04 and 3.08, respectively (*P* = 0.79). Isolated valve surgery (aortic valve replacement, mitral valve replacement, mitral valve repair) was performed in 14% and 17% of the patients, respectively. Finally, combined procedures were performed in 38% of the RG system group and in 29% of the control group. The combined
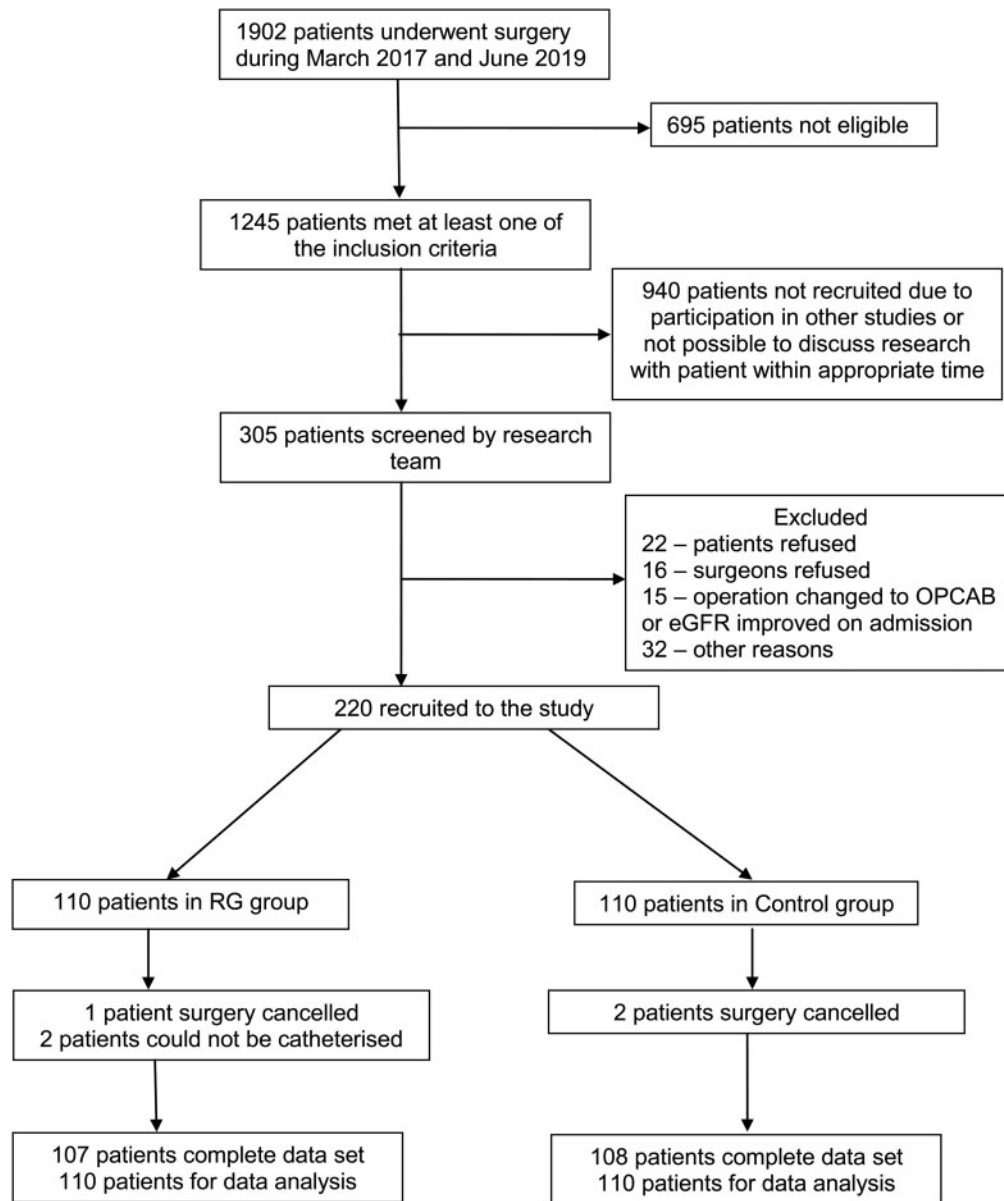
Figure 1: CONSORT flow diagram for recruitment. eGFR: estimated glomerular filtration rate; OPCAB: off-pump coronary artery bypass; RG: RenalGuard®.

Table 1: Inclusion criteria factors for the 2 groups

	RG group (n = 110)	Control group (n = 110)	P-value
Diabetes, n (%)	70 (63.6)	73 (66.4)	0.67
e-GFR <60, n (%)	44 (40)	45 (40.9)	0.89
Anaemia, n (%)	32 (29.1)	34 (30.9)	0.77
Log EuroSCORE >5, n (%)	48 (43.6)	39 (35.5)	0.22
CPB time >120 min, n (%)	41 (38)	44 (40.4)	0.71

CPB: cardiopulmonary bypass; e-GFR: estimated glomerular filtration rate; RG: RenalGuard®.

procedures included coronary artery bypass grafting, aortic valve replacement, mitral valve replacement, mitral valve repair, tricuspid valve repair, Cox-maze IV atrial fibrillation ablation, aortic root surgery, ascending aorta replacement, myxoma surgery and left ventricular aneurysmectomy, in various combinations.

Postoperative AKI rates were significantly lower in the RG system group compared to those in the control group [10% (11/110) vs 20.9% (23/110); $P = 0.025$]. This effect persisted even after controlling for potential confounders (odds ratio 2.82, 95% confidence interval 1.20–6.60; $P = 0.017$) when assessed by binary logistic regression analysis. Mean volumes of urine produced during the operation (2366 ± 877 vs 765 ± 549 ml) and within the first 24 h postoperatively in the CICU (3310 ± 1303 vs 2052 ± 804 ml) were significantly higher in the RG system group ($P < 0.001$).

There were no significant differences in the incidence of blood transfusions (including intraoperative), re-exploration rates for bleeding, atrial fibrillation rate, infections (chest, surgical site infection, sepsis) and median durations of CICU stays between the

Table 2: Preoperative characteristics of the patients in the 2 groups

	RG group (n = 110)	Control group (n = 110)	P-value
Age[a] (years)	67.8 (9.3)	67.0 (9.2)	0.33
BMI[a] (kg/m^2)	29.8 (5.1)	30.7 (5.5)	0.25
Preop haemoglobin[a] (g/l)	135 (16)	134 (18)	0.72
Preop creatinine[a] (µmol/l)	99.0 (28.2)	98.3 (34.7)	0.29
Preop eGFR[a] (ml/min/1.73 m^2)	66.5 (17.2)	68.2 (20.3)	0.47
Logistic EuroSCORE[b]	3.8 (0.9–67.4)	3.2 (0.9–32.5)	0.3
Male gender, n (%)	87 (79)	84 (76)	0.63
Elective, n (%)	76 (69)	86 (78)	0.13
Non-diabetic, n (%)	30 (27)	30 (27)	0.66
Impaired LVEF, n (%)	51 (46)	38 (34)	0.14
History of CVA, n (%)	11 (10)	8 (7)	0.47
CKD stage >2, n (%)	44 (40)	42 (38)	0.94
Isolated CABG, n (%)	53 (48)	59 (54)	0.41

[a]Denotes mean (SD).
[b]Denotes median (minimum–maximum).
BMI: body mass index; CABG: coronary artery bypass surgery; CKD: chronic kidney disease; CVA: cerebrovascular accident; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; preop: preoperative; RG: RenalGuard®; SD: standard deviation.

2 groups (Table 3). One patient in the control group required renal replacement therapy. The MAP and central venous pressure during surgery and within the first 12-h of CICU admission were not significantly different (Figs 2 and 3). Inotropic support (Supplementary Material, Table S1) was used to maintain a MAP >65 mmHg in 70% of patients in the RG system group and in 77% patients in the control group (P = 0.53). Although only patients in the study group received i.v. furosemide in the OR [median dose 28 (0–92) mg], 61% of the study group and 53% of the control group received i.v. furosemide in the CICU. The median dose of furosemide used in the CICU was 20 (0–160) mg for the RG system group and 20 (0–180) mg for the control group (P = 0.99), within the first 24 h in the CICU. The median in-hospital stay for both groups was 6 days. The creatinine levels at various periods are depicted in Fig. 4.

One patient in the RG system group and 2 patients in control group died prior to hospital discharge. Causes of death were not related to the use of the device and included cardiogenic shock, cardiac failure and sepsis (pneumonia), respectively. The number needed to treat with the RG system to prevent AKI was 9 patients (95% confidence interval 6.0–19.2). At a median postoperative follow-up of 8 weeks, most patients had recovered from their AKI (Table 3).

DISCUSSION

This study confirmed that, in a selected group of patients at risk for developing AKI post cardiac surgery, the rate of AKI was reduced when the RG system was used perioperatively.

Given the morbidity and mortality associated with AKI post cardiac surgery [4, 5, 13], investigative research has ranged from identifying at-risk patients [14, 15] to using urinary and plasma biomarkers [7] and goal-directed therapies [16].

This study assessed the potential benefit of the RG system, which provides both continuous diuresis and balanced

rehydration. The importance of appropriate intravascular volume management in the prevention of AKI has already been highlighted by the KDIGO group [6]. However, the use of furosemide after cardiac surgery to prevent AKI has been contentious. Interestingly, as reported by Penk *et al.* [17], the renal response to i.v. furosemide can be an indicator of the development of AKI. They showed that a low urine flow rate after furosemide administration was independently associated with AKI. Fakhari *et al.* [18] found that continuous infusion of low-dose furosemide in the perioperative period was beneficial to the kidneys compared to infusion of 0.9% saline. However, that study was conducted in a low-risk group (for AKI), and there was no description of the fluid volume status of the patients. Mahesh *et al.* [19] confirmed that the perioperative use of furosemide increased postoperative diuresis significantly but did not have an impact on AKI in a high-risk group (for AKI) of patients. Kunt *et al.* [20] found that furosemide was beneficial in low-risk (for AKI) patients, whereas Lassnigg *et al.* [21] reported that furosemide infusion was detrimental. However, patients who received furosemide infusions had the same volume of i.v. fluid as the placebo group, begging the question of whether these patients were adequately rehydrated.

Furosemide may also be beneficial in preventing renal hypoxia at the level of the loop of Henle whereas forced diuresis prohibits the buildup of casts within the renal tubules—a process well known to occur in acute tubular necrosis. Some vasodilatory effects on renal cortical vessels have also been attributed to furosemide, causing an improvement in renal blood flow [22].

Appropriate fluid management after cardiac surgery is extremely complex, especially in patients in whom the CPB machine is used because there are significant volume shifts, and fluid can be 'sequestered' in the extravascular, extracellular space. This situation leads to a confusing clinical picture of a fluid overloaded but an intravascularly volume-depleted patient. Using diuretics in these patients leads to further intravascular dehydration, which in turn causes poor organ perfusion and, for the kidneys, acute injury. Hence appropriate intravascular rehydration is vital despite a clinical picture of 'fluid overload'. There has also long been a debate regarding the type of fluid used for intravascular rehydration [23, 24]. In this study, Hartmann's solution (a mixture of sodium chloride, sodium lactate, potassium and calcium chloride in water) was used for fluid replacement by the RG system. Although the volumes of urine were significantly higher in RG system group, this forced diuresis coupled with large volume rehydration with Hartmann's solution did not seem to have impacted the postoperative recovery of the patients because both groups had similar blood transfusion rates, atrial fibrillation incidence and infection rates, denoting that the use of the RG system is safe.

Maintenance of adequate renal perfusion is also important because the kidneys receive 25% of the cardiac output and produce 180 l of filtrate daily. In its guidelines, the KDIGO AKI working group suggested the maintenance of adequate arterial perfusion pressure: 65–90 mmHg [3, 6]. In this study, the organ perfusion pressure (difference between MAP and central venous pressure) was maintained throughout the operation and during the stay in the CICU with inotropic support as required (Figs 2 and 3). There were no significant differences in the MAP and central venous pressure between the 2 groups during the period that they were recorded, namely in the anaesthetic room, prior to initiation of CPB, 15 min post initiation of CPB, prior to CPB termination,

Table 3: Postoperative data

Intraoperative and postoperative data	RG group	Control group	*P*-value
CPB time[a] (min)	120 (56)	114 (46)	0.64
Total urine output in OR[a] (ml)	2366 (877)	765 (549)	**<0.001**
Urine volume at 6 h in CICU[a] (ml)	1911 (904)	911 (407)	**<0.001**
Urine volume at 24 h in CICU[a] (ml)	3310 (1303)	2052 (804)	**<0.001**
Intubation time[b] (h)	6 (2–74)	5.5 (2–486)	0.39
CICU stay[b] (h)	27 (16–410)	28 (8–486)	0.92
Atrial fibrillation, *n*/total (%)	12/108 (11)	10/108 (9)	0.62
Reexploration, *n*/total (%)	4/108 (3.6)	1/108 (0.9)	0.4
Blood transfusion, *n*/total (%)	29/108 (27)	21/109 (19)	0.16
Infection, *n*/total (%)	10/108 (9)	8/108 (7)	0.59
In-hospital mortality, *n*/total (%)	1/110 (1)	2/110 (2)	0.56
Primary end point, *n*/total (%)			
AKI rate (RIFLE)	11/110 (10)	23/110 (20.9)	**0.025**
Follow-up, *n*/total (%)			
AKI at follow-up	1/100 (1)	2/105 (2)	1
Alive at follow-up	104/105 (99)	104/108 (96)	0.37

[a]Denotes mean (SD).

[b]Denotes median (minimum–maximum).

Boldface data reflects statistically significant difference between the two groups.

AKI: acute kidney injury; CICU: cardiac intensive care unit; CPB: cardiopulmonary bypass; RIFLE: Risk, Injury, Failure, Loss, End stages of kidney damage; OR: operating room; RG: RenalGuard®; SD: standard deviation.
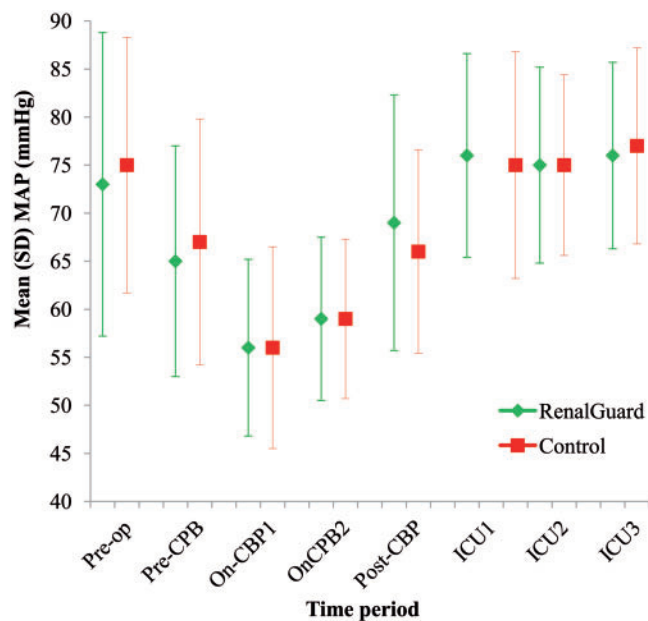

Figure 2: MAP (mmHg) at various time intervals for RenalGuard® and control groups. CPB: cardiopulmonary bypass; ICU: intensive care unit; ICU1: arrival in ICU; ICU2: in ICU for 6 h; ICU3: in ICU for 12 h; MAP: mean arterial pressure; On CPB1: on cardiopulmonary bypass for 15 min; On CPB2: prior to stopping cardiopulmonary bypass; Preop: preoperative; Preop: in anaesthetic room; Pre-CBP: prior to initiation of cardiopulmonary bypass; Post-CPB: after stopping cardiopulmonary bypass for 15 min; SD: standard deviation.

Figure 3: Central venous pressure (cm H_2O) at various time intervals for the RenalGuard® system and control groups. CPB: cardiopulmonary bypass; CVP: central venous pressure; ICU: intensive care unit; ICU1: arrival in ICU; ICU2: in ICU for 6 h; ICU3: in ICU for 12 h; MAP: mean arterial pressure; On CPB1: on cardiopulmonary bypass for 15 min; On CPB2: prior to stopping cardiopulmonary bypass; Preop: preoperative; Preop: in anaesthetic room; Pre-CBP: prior to initiation of cardiopulmonary bypass; Post-CPB: after stopping cardiopulmonary bypass for 15 min; SD: standard deviation.

prior to transfer from the OR and within 1, 6 and 12 h of admission to the CICU (Figs 2 and 3).

There was no significant difference in the median duration of CICU stays between the 2 groups, it being around 1.2 days for both groups (27 h for the RG system group and 28 h for the control group). This result is probably due to the fact that the study was powered to assess rate of AKI rather than CICU stay. A larger study would be required to assess this aspect. Other authors of a
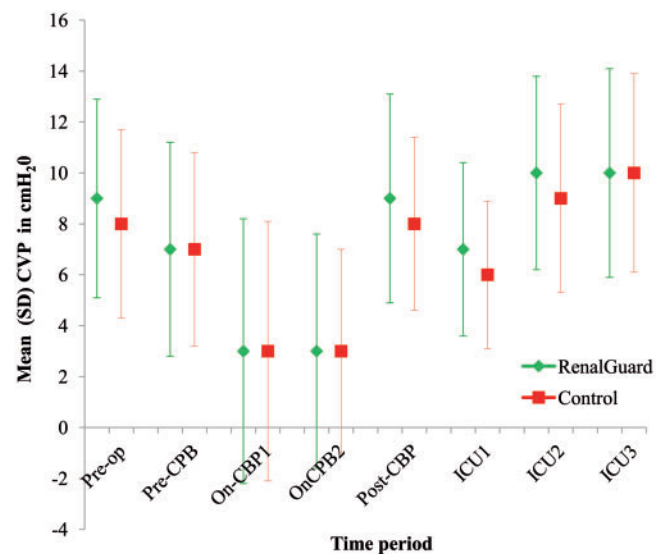
large meta-analysis (>300 000 patients) reported a significantly longer CICU stay when AKI occurred: an average CICU stay of 2.2 days for non-AKI patients compared to 5.4 days for those in the AKI group [25]. This finding would impact not only the morbidity of the patient but also the cost of treatment when AKI develops after cardiac surgery. The cost of managing AKI post cardiac surgery relates not only to the immediate postoperative phase but also to the long term and to changes in quality of life.
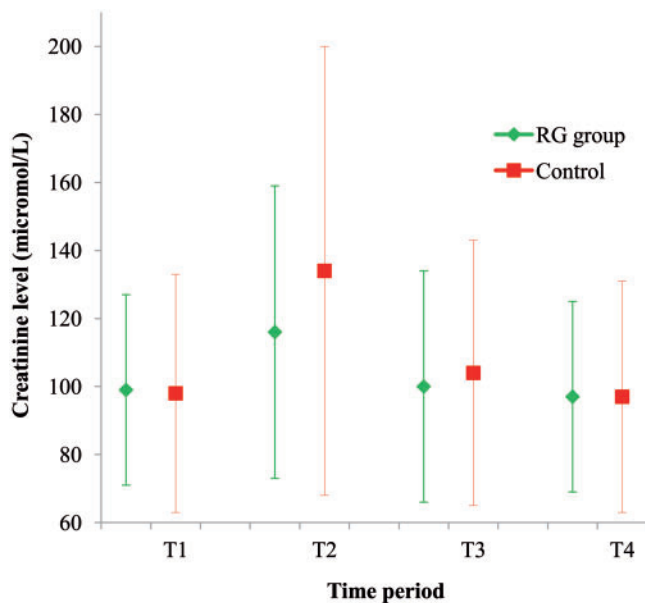
Figure 4: Creatinine levels at various time periods for the 2 groups. T1: baseline; T2: peak postoperatively; T3: predischarge; T4: follow-up.

Lastly, early postoperative follow-up data suggested that most patients in this study recovered from their AKI episodes. However, other reports with longer term follow-up data have shown that around 20% of patients with AKI after cardiac surgery may require long-term renal follow-up [5, 26]. Importantly, these patients also had a poorer quality of life [5, 26, 27].

This study was powered to assess if the use of the RG system would reduce AKI rates as defined by the RIFLE (Risk, Injury, Failure, Loss of kidney function, End-stage renal disease) criteria. It confirmed that the RG system does reduce the rate of AKI and is safe to use in cardiac surgery in patients at high risk of developing AKI. A larger, adequately powered randomized control trial is needed to demonstrate the clinical benefit, such as a reduction in the ICU stay. Additionally, a cost-benefit analysis needs to be carried out to justify the use of the device, because the RG system costs £450 per patient in the UK.

Limitations

The main limitation of this study is that it is a single-centre study. However, given that the number of patients recruited was determined by power calculations, the primary outcome was achieved as per statistical recommendations. Also, because this study was not blinded, the control group could have been influenced by some aspects of the Hawthorne effect.

CONCLUSION

In patients at risk for AKI who had cardiac surgery with CPB, the RG system significantly reduced the incidence of AKI and can be used safely and reproducibly. Larger studies are required to assess cost benefits.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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Author contributions

Heyman Luckraz: Conceptualization; Data curation; Funding acquisition; Methodology; Project administration; Supervision; Validation; Visualization; Writing—original draft; Writing—review & editing. **Ramesh Giri:** Conceptualization; Data curation; Funding acquisition; Investigation; Methodology; Project administration; Supervision; Validation; Visualization; Writing—original draft; Writing—review & editing. **Benjamin Wrigley:** Conceptualization; Data curation; Funding acquisition; Investigation; Methodology; Project administration; Supervision; Validation; Visualization; Writing—original draft; Writing—review & editing. **Kumaresan Nagarajan:** Investigation; Visualization; Writing—original draft; Writing—review & editing. **Eshan Senanayake:** Investigation; Visualization; Writing—original draft; Writing—review & editing .**Emma Sharman:** Investigation; Project administration; Visualization; Writing—original draft; Writing—review & editing. **Lawrence Beare:** Conceptualization; Investigation; Visualization; Writing—original draft; Writing—review & editing. **Alan Nevill:** Conceptualization; Data curation; Formal analysis; Methodology; Visualization; Writing—original draft; Writing—review & editing.

Reviewer information

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