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ORIGINAL ARTICLE

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Acute kidney injury and aorta-related mortality during open surgery of the abdominal aorta with suprarenal clamping using different renal protection strategies

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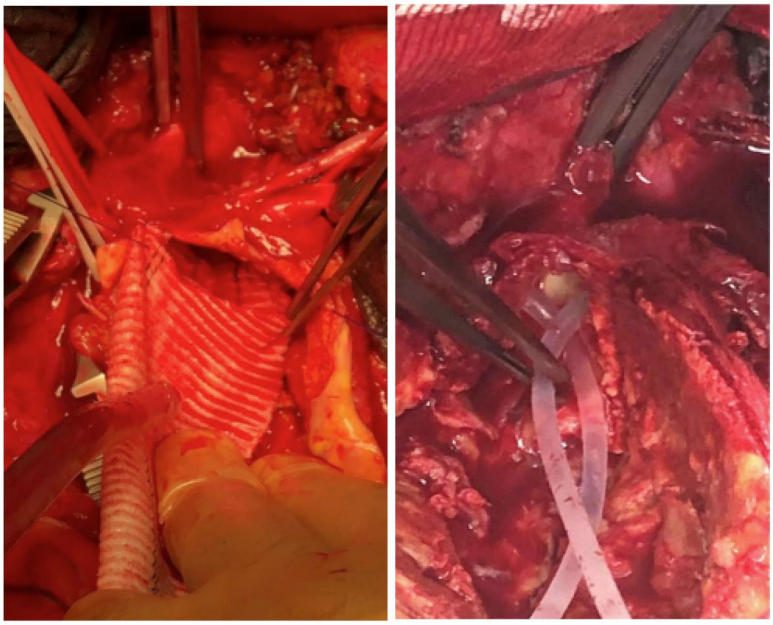
Acute kidney injury and aorta-related mortality during open surgery of the abdnominal aorta with suprarenal clamping using different renal perfusion solutions

Summary

Population
OSR for J/PAAA
Intervention
Is renal artery perfusion with HTK solution protective of postoperative AKI?
Comparison
No renal artery perfusion
Outcomes
At 30-day, AKI rate (37.6%) was not different between the two groups (P = 0.855), it did not impact mortality (OR: 3.4, P = 0.556), and freedom from HD was 100%.



OSR, open surgical repair; *J/PAAA*, juxtarenal/pararenal aortic aneurysm; *HTK*, histidine-tryptophan-ketoglutarate; *AKI*, acute kidney injury

Abstract

OBJECTIVES: The aim was to evaluate the incidence of acute kidney injury in patients treated with open surgical repair and suprarenal cross-clamp comparing no-perfusion strategy versus the renal perfusion with the histidine-tryptophan-ketoglutarate solution.

METHODS: It is a physician-initiated, multicentre, retrospective observational study including patients treated with open surgical repair for abdominal aortic aneurysm between 1 January 2015 and 31 December 2021. Patients already on dialysis were excluded from the final analysis. A coarsened exact match identified 2 cohorts: no-perfusion strategy versus renal perfusion with the histidine-tryptophan-ketoglutarate solution. Primary outcomes were acute kidney injury incidence and survival at 30 day. Secondary outcomes were freedom from haemodialysis and survival at 1 year.

RESULTS: We analysed 125 (28.7%) patients: 63 (14.5%) who did not receive renal perfusion and 62 (14.2%) who received the histidine-tryptophan-ketoglutarate perfusion. At 30 day, acute kidney injury rate (37.6%) was not different between the 2 groups [$n = 24$ (38.7%) vs 23 (36.5%); OR: 1.1, $P = 0.855$]. At 30 day, acute kidney injury development was associated with aneurysm extent (pararenal, OR: 2.28, 95% CI: 1.031–5.031, $P = 0.042$) and total time of intervention (threshold: 365 min, OR: 1.008, 95% CI: 1.003–1.012, $P = 0.001$). At 1 year, postoperative acute kidney injury did not impact mortality (OR: 3.4, $P = 0.556$), and freedom from haemodialysis was 100%.

CONCLUSIONS: Postoperative acute kidney injury remains high at nearly 38%, but it did not impact on freedom from haemodialysis at 1 year as well as on overall survival.

Keywords: Acute kidney injury • Suprarenal clamping • Open surgical repair • Juxtarenal aortic aneurysm • Pararenal aortic aneurysm • Histidine-tryptophan-ketoglutarate • Custodiol®

ABBREVIATIONS

AAA	Abdominal aortic aneurysm
AKI	Acute kidney injury
CEM	Coarsened exact matching
eGFR	Estimated glomerular filtration rate
HD	Haemodialysis
HTK	Histidine-tryptophan ketoglutarate
IQR	Interquartile range
JAA	Juxtarenal aortic aneurysm
OSR	Open surgical repair
PAA	Pararenal aortic aneurysm
RRT	Renal replacement therapy
SCr	Serum creatinine

INTRODUCTION

Even with the widespread adoption of the endovascular advanced technology, open surgical repair (OSR) of abdominal aortic aneurysms (AAA) continues to be used for patients who do not meet the anatomical requirements for endovascular

repair [1]. In case of a juxtarenal aortic aneurysm (JAA) or pararenal aortic aneurysm (PAA) extension, OSR remains a challenging intervention that necessarily requires suprarenal aortic cross-clamping [2, 3].

In this circumstance, one of the most significant risk factors for postoperative morbidity and mortality continues to be acute kidney injury (AKI) [4]. Currently, no convincing evidence exists regarding the superiority of a specific pharmacological protection protocol [5]. A recent randomized clinical trial showed that use of histidine-tryptophan ketoglutarate (HTK) solution was safe and provided improved perioperative renal function compared with Ringer's solution during thoraco-abdominal aortic surgery [6]. However, to date, no clinical experience has reported the use of this solution during suprarenal aortic cross-clamp for JAA or PAA repair [7].

The aim of this study was to compare, in a cohort of OSR with suprarenal cross-clamping for patients unfit for endovascular repair, the renal perfusion with the HTK solution against a no perfusion strategy, thereby evaluating the incidence of postoperative AKI, and the impact on overall survival and on kidney function at 1 year.

MATERIALS AND METHODS

Ethical statement

Helsinki Declaration and its later amendments were respected. The study was approved by the local Ethic Committee (Vascular Surgery—University of Insubria and ASST Settelaghi Circolo Universitary Hospital; Nr. 284/2021 on 22 November 2022) and registered as an observational study. Written informed consent was obtained from all participants.

Data availability

Data entry was managed by physicians involved into patient care, and merged into this single dataset by the corresponding author (G.P.). The data underlying this article will be shared on reasonable request to the corresponding author.

Study cohort

This is a multicentre, observational cohort study engaging 14 referral centres in Italy capable of offering either complex conventional or endovascular repair, led by vascular surgeon performing OSR for AAA repair with a yearly total caseload of >15 each by open and endovascular methods [4]. For this study, all interventions performed between 1 January 2015 and 31 December 2021 were identified. Specifically for the final analysis, the inclusion criteria for the overall cohort were as follows [4, 8, 9]:

- elective OSR for juxtarenal or pararenal AAA
- suprarenal bilateral aortic cross-clamping

Exclusion criteria were as follows:

- ruptured AAA
- single suprarenal aortic cross-clamping
- patient already on dialysis

Surgical technique

General principles shared by all centres included preoperative antibiotic prophylaxis that was performed with a second-generation cephalosporin and heparinization at a dose of 40–50 UI/kg, adjusted per estimated glomerular filtration rate (eGFR) in patient with chronic kidney disease (CKD). Surgical approach, whether transperitoneal or retroperitoneal, as well as left renal vein division and eventual reconstruction was left at surgeon's discretion. Renal artery preservation, whether through inclusion technique or Carrel's patch, or isolate bypass was left at surgeon's discretion based on local anatomy and expertise [2]. Throughout the entire experience, we used only Dacron knitted graft for the aortic reconstruction. Follow-up included the clinical visit and duplex ultrasound at 30 days, and annually thereafter.

Renal protection strategy

Whenever possible, renal protective measures included the discontinuation of all potentially nephrotoxic drugs, and dose adaptation of drugs excreted by the kidneys according to the patient's renal function. Because of the type of study, renal artery perfusion strategy was left at surgeon's discretion; in general, renal perfusion was performed primarily when prolonged renal ischaemia was anticipated, according to procedure complexity or it was the preferred method in some of the centres, in case of patients presenting with CKD. In particular, HTK usage began after the results of the Curitiba trial [6]. Accordingly, upon renal artery clamping, a balloon occlusion-perfusion catheter was inserted directly into the renal artery for continued infusion of a cold (4°C) HTK solution for a total of 1.5 ml of per gram of estimated kidney weight, thus implying an average of 400 ml of HTK solution for a 70 kg patient [5, 6]. Postoperatively, attention was given to the assessment of the circulating volume and fluid administration, the prevention and/or treatment of hyperkalaemia and metabolic acidosis, optimization (>10 g/dl) of hemoglobin level.

Definition and outcomes

Aortic disease extent was defined in agreement with the recent Society for Vascular Surgery classification system [7]. Preoperative and postoperative serum creatinine (SCr) levels and eGFR were evaluated. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used for reporting estimated eGFR [9]. Specifically for this study, CKD was defined in agreement with the position statement from Kidney Disease Improving Global Outcomes (KDIGO) guidelines [10]. AKI severity stage was classified according to the Acute Kidney Injury Network (AKIN) criteria. Specifically for this study, renal replacement therapy (RRT) included transitory or definitive haemodialysis (HD), continuous veno-venous hemofiltration (CVVH) and peritoneal dialysis [10]. Closing date of the study for the AKI-related analysis was 31 December 2022. Through June 2024, information on survival, date of death of individual patient, and aorta-related reintervention was validated by death certificates, electronic charts managed by the regional health care system, through general practitioner interview, or certified data from emergency department admission. For this specific study, primary outcomes of interest were AKI incidence at 30 day, and

overall survival. We also analysed the factors eventually associated with the development of AKI, postoperatively. Secondary outcome was freedom from HD at 1 year of follow-up.

Statistical analysis

Clinical data were collected in a prospective manner at each centre; thereafter, they were merged in a single database, recorded and tabulated in Microsoft Excel (Microsoft Corp, Redmond, Wash) and analysed retrospectively [11]. Statistical analysis was performed with SPSS, release 29.0 for Windows (IBM SPSS Inc.; Chicago, IL, USA). Interventions performed without renal perfusion (Group A) were matched to renal perfusion with the HTK solution (Group B) based on a 1:1 coarsened exact matching (CEM). For its calculation, all the significantly different baseline pretreatment demographic and clinical covariates in the 2 groups were used. A CEM-based matched control group was then generated and compared in terms of primary and secondary outcomes [12]. CEM was performed by IBM SPSS and software R (package CEM) for assessing the balance pre-post CEM application. Our software package provided the automatic CEM optimization. Continuous variables were tested for normality using the Shapiro–Wilk's test and compared between groups with unpaired Student's t-test for normally distributed values; otherwise, the Mann–Whitney *U*-test was used. Variables that were normally distributed are presented as mean and standard deviation (SD) and range; otherwise, they are presented as median and interquartile range (IQR). Categorical variables were presented using frequencies and percentages and analysed with the Pearson's χ^2 test or Fisher's exact test whether the expected cell frequencies were <5. Wilcoxon signed-rank test was used to evaluate the difference in creatinine and eGFR values before and after OSR. Multivariable analysis was used to adjust the relationship between preoperative and intraoperative covariate with AKI occurrence at 30 day. Associations that yielded a P value <0.20 on univariate screen were then included in a binary logistic regression analysis using the Wald's forward stepwise model. The strength of the association of variables with each outcome was estimated by calculating the OR and 95% CI (significance criteria 0.20 for entry, 0.05 for removal). The model was calibrated by the Hosmer–Lemeshow goodness-of-fit test, as well as residual diagnostics (deviance and df Betas); model discrimination was evaluated by using the area under the receiver operating characteristic (ROC) curve. Long-term survival was estimated according to Kaplan–Meier method and reported with standard error (SE; truncated when exceeding 10%) and associated 95% confidence intervals (95% CI). The Breslow test was used to compare the distribution of survival in the follow-up between different groups to have time points weighted by the number of cases at risk at each time point. All reported P values were 2-sided; P value <0.05 was considered significant.

RESULTS

Study population

Out of the 435 patients of the overall cohort, CEM identified 125 (28.7%) patients: 63 (14.5%) who did not receive renal perfusion, and 62 (14.2%) who received the HTK perfusion (Fig. 1). The significant differences between these 2 groups before matching reached adequate balancing post-CEM procedure, and the L1 distance was calculated to assess the balance between the groups before and after the application of CEM. The use of the HTK perfusion significantly changed across the quartiles of the study period (Supplementary Material, Fig. S1). The preoperative demographic data, comorbidities and risk factors are represented in Table 1, while preoperative blood tests are summarized in Table 2.

Surgical details

Most of the repairs ($n=101$, 80.8%) were performed using a transperitoneal route, while 24 (19.2%) through a retroperitoneal approach with no difference between the groups ($P=0.358$). There was no difference in terms of division (16.9% vs 26.2%) and reconstruction (53.8% vs 46.2%) of the left renal vein between the 2 groups ($P=0.270$, and $P=1.0$, respectively). There was a significantly higher number of renal artery transposition/bypass in the HTK group [$n=28$ (45.9%) vs 6 (9.5%); OR: 8.1, $P<0.001$]. The mean duration of suprarenal clamp time was 29.9 (11) min (range, 5–65) and was higher in the HTK group [31.9 (11.4) vs 24.9 (8), $P<0.001$]. Similarly, the HTK group was also associated with higher median total time of intervention [min, 340 (IQR, 252–400) vs 210 (IQR, 167–257); $P=0.016$], median amount of blood loss [ml, 1200 (IQR, 540–3000) vs 600 (IQR, 300–110); $P=0.022$] and median packed red blood cells transfusion [units, 2 (IQR, 1–9) vs 0 (IQR, 0–1); $P=0.002$].

AKI development ($\leq$ 30 days)

Overall, AKI occurred in 47 (37.6%) patients with no difference between the 2 groups [HTK, $n=24$ (38.7%) vs no-perfusion, 23 (36.5%); OR: 1.1, $P=0.855$]. The AKI distribution in HTK and no-perfusion group is represented in Fig. 2. RRT was needed in 8 (6.4%) patients. Overall, 7 (5.6%) patients required HD, but there was no significant difference between the HTK group and the no-perfusion group [$n=4$ (6.6%) vs 3 (4.8%); OR: 1.4, $P=0.715$]. Blood tests variations in the 2 cohorts are reported in Supplementary Material, Table S1: briefly, in the HTK group, there was a significant difference between preoperative and discharge values for eGFR ($P=0.029$), and only a trend for SCr ($P=0.058$) as depicted in Fig. 3. At binary logistic regression analysis, only aneurysm extent (PAA vs JAA, OR: 2.28, 95% CI: 1.031–5.031, $P=0.042$) and total time of intervention (OR: 1.008, 95% CI: 1.0031.012, $P=0.001$) were associated with AKI development at 30 day. The Hosmer–Lemeshow goodness-of-fit test (χ^2 [7 d.f.] $=6.3$, $P=0.505$) and ROC analysis (AUC of 0.69; 95% CI: 0.60–0.79) revealed adequate goodness of fit and discrimination for the obtained multivariable model. A prolonged operative time $\geq$356 min yielded a sensitivity of 95% and a specificity of 24%.

Early results ($\leq$ 30 days)

The median duration of intensive care unit stay was 1 day in each group. Postoperative complication developed in 43 (34.4%) patients with no difference between the 2 groups [$n=23$ (53.5%) vs 20 (46.5%); OR: 1.3, $P=0.575$, Supplementary Material, Table S2]. Thirty-day mortality occurred in 3 (2.4%) patients [HTK, $n=2$ (3.2%) vs no-perfusion, 1 (1.6%); OR: 2.1, $P=0.619$]. The development of AKI did not impact on 30-day mortality

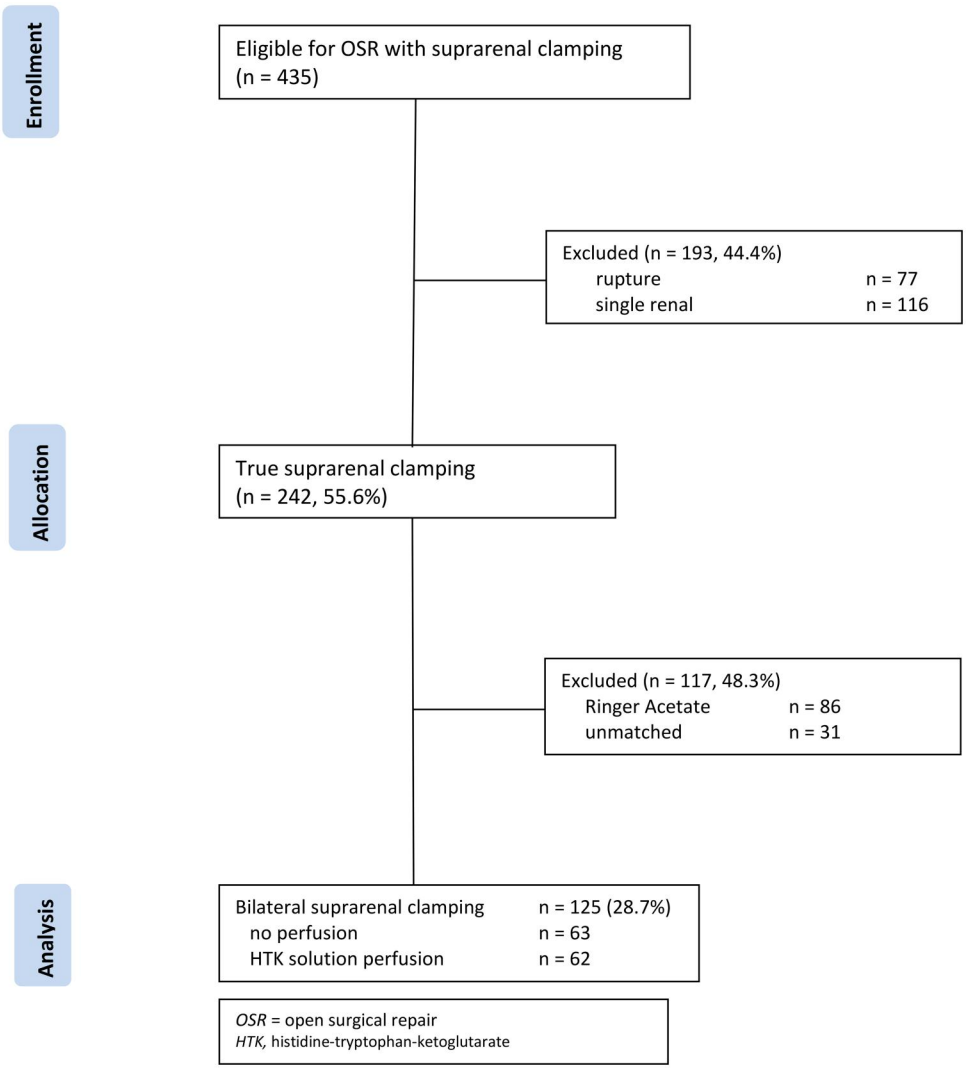


Figure 1: Consort diagram of open surgical aortic repair requiring suprarenal clamping for juxtarenal or pararenal aneurysm (2013–2023, $n = 435$). HTK: histidine-tryptophan ketoglutarate; OSR: open surgical repair.

[non-AKI, $n = 2$ (2.6%) vs AKI, $n = 1$ (2.1%); OR: 0.8, $P = 1.0$]. Causes of death were multiple organ failure ($n = 2$), and acute coronary syndrome ($n = 1$). There was not a difference between the groups considering the median length of hospitalization [days: HTK, 9.5 (IQR, 4.2–16) vs no-perfusion, 9 (IQR, 7–13), $P = 0.359$].

Follow-up results

The median of follow-up was 27.5 months (IQR, 8.5–42.5) for the no-perfusion group and 17 months (IQR, 4–33) for the HTK group ($P = 0.780$); the follow-up index was 0.72 (0.1) and 0.76 (0.1), respectively ($P = 0.779$). At the 1-year window, 3 (2.4%) additional patients died: all of them in the HTK group ($P = 0.116$): aorta-related mortality accounted for 3 (2.4%) deaths due to ruptured aortic arch ($n = 1$; 8 month), aortic graft infection ($n = 1$; 11 month) and multiple organ failure following thoracic endovascular aortic repair ($n = 1$; 12 month). Mortality was not affected by postoperative AKI development [AKI, $n = 2$ (4.3%) vs non-AKI, $n = 1$ (1.3%); OR: 3.4, $P = 0.556$]. At the 1-year window, freedom from HD was 100% in patients discharged and alive. Cumulative estimated survival was 98% ± 0.01 (94–99.5) at 1 year, 91% ± 0.04 (79.4–96.4) at 3 year and 70% ± 0.09 (51.5–84.2) at 5 year. The development of postoperative AKI did not impact on the distribution of follow-up survival (Breslow $\chi^2 = 0.1$; $P = 0.919$, Fig. 4), but there was a lower survival in the HTK group (Breslow $\chi^2 = 3.9$; $P = 0.074$, Fig. 5).

DISCUSSION

The main findings of our experience are 2-fold: first, AKI occurrence after OSR of JAA or PAA is still substantial at nearly 38% and was not directly correlated with the type of treatment strategy as far as kidney protection is concerned. Second, despite the high rate of postoperative AKI none of the patients was on HD at the 1-year follow-up, and AKI did not impact on follow-up survival.

In a literature review of papers reporting on OSR for AAA requiring suprarenal clamping, postoperative AKI has been reported in a wide range from 7.6% to 60%, and it has been demonstrated to be independent of the hospital volume as well as period of study [12–27] (Supplementary Material, Table S3).

Table 1: Demographic data, comorbidities, risk factors and aneurysm features

Covariates	Before matching			After matching		
	No perfusion ($n=292$)	HTK solution ($n=98$)	*P*	No perfusion ($n=63$)	HTK solution ($n=62$)	*P*
Demographics						
M: F (ratio)	252:40	91:7	0.090	58:5	57:5	1.0
Age, mean (± SD, range)	72 ± 7 (50–91)	71 ± 7 (49–85)	0.235	72 ± 7 (55–91)	71 ± 7 (49–85)	0.186
>80 years (%)	43 (14.7)	18 (18.4)	0.391	7 (11.1)	8 (12.9)	0.790
Comorbidities (%)						
Hypertension	236 (80.8)	80 (81.6)	0.859	51 (81.0)	52 (83.9)	0.815
Coronary artery disease	110 (37.7)	31 (31.6)	0.677	24 (38.1)	21 (33.9)	0.710
Chronic obstructive pulmonary disease	91 (31.2)	26 (26.5)	0.387	20 (31.7)	18 (29.0)	0.846
Chronic kidney disease	71 (24.3)	21 (21.6)	0.561	14 (22.2)	15 (24.6)	0.833
Diabetes	50 (17.1)	14 (14.3)	0.655	13 (20.6)	8 (12.9)	0.399
Risk factors						
SVS score, median (IQR)	3 (2–4)	3 (2–4)	0.599	3 (2–4)	3 (2–4)	0.794
ACS score, median (IQR)	4.2 (2.5–6.5)	3.5 (2–6.2)	0.348	4 (2.8–5.9)	3 (1.6–6.2)	0.205
JAA/PAA (ratio)	231:61	56:42	< 0.001	31:32	31:31	1.0
Diameter, median (mm, IQR)	60 (53–70)	58 (52–65)	0.254	60 (54–70)	58 (53–65)	0.273

ACS: American College of Surgeons; F: female; HTK: histidine-tryptophan-ketoglutarate; JAA: juxtarenal aortic aneurysm; M: male; n: number; PAA: pararenal aortic aneurysm; SD: standard deviation; SVS: Society for Vascular Surgery.

Table 2: Preoperative blood tests

Covariates	Before matching			After matching		
	No perfusion ($n=292$)	HTK solution ($n=98$)	*P*	No perfusion ($n=63$)	HTK solution ($n=62$)	*P*
Blood tests, median (IQR)						
Haemoglobin, (g/dl)	13.9 (12.3–14.8)	13.4 (11.8–14.4)	0.130	13.9 (12.4–14.8)	13.3 (12.2–14.3)	0.066
Haematocrit, (%)	41.7 (37.8–44.5)	39.8 (35.6–42.5)	0.009	42 (37.9–44.2)	40 (36.3–41.9)	0.097
Glucose, (mg/dl)	102 (90–118)	101 (93–121.5)	0.652	98 (84.5–107.5)	100 (92–113)	0.783
eGFR, (ml/min)	73.3 (54.1–89.9)	68.8 (48.5–89.5)	0.350	92.5 (65.5–99.2)	67 (56.2–88.5)	0.416
Creatinine, (mg/dl)	1.03 (0.86–1.30)	1.06 (0.86–1.37)	0.592	1 (0.9–1.2)	1.06 (0.9–1.3)	0.529
CPK, (U/l)	89 (58.2–122.7)	113 (60–213)	0.321	100 (60–248.7)	118 (62–246)	0.008
LDH, (U/l)	188.5 (141.2–243.7)	238.5 (174–338.7)	0.143	133 (81.2–227)	202 (170–287)	0.164
Lactates, (mmol/l)	0.9 (0.7–1.4)	1 (0.72–1.24)	0.001	0.9 (0.8–1.1)	1 (0.8–1.4)	0.578
Acid-base, (pH)	7.4 (7.36–7.42)	7.39 (7.34–7.43)	0.053	7.4 (7.36–7.42)	7.38 (7.33–7.42)	0.789

CPK: creatine phosphokinase; eGFR: estimated glomerular filtration rate; HTK: histidine-tryptophan-ketoglutarate; IQR: interquartile range; LDH: lactate dehydrogenase; n: number.

Our 'real-world' experience is in line with these data: hence, AKI is still a matter of concern during this type of surgery. Nevertheless, the 3.6% mortality rate at 30 day and the 2.9% need for postoperative RRT coupled with a high freedom from HD at 1 year confirm that OSR is still a safe option in those not suitable for advanced endovascular technologies [4, 20].

Apart from keeping the aortic cross-clamp as low as possible during OSR for AAA, currently there is low compelling evidence for the most beneficial renal protective strategy [4]. A randomized trial demonstrated that the use of the HTK solution during open thoraco-abdominal aortic repair was safe and resulted in significantly lower rates of postoperative AKI compared with the enriched Ringer's cold solution [28]. Our multicentre experience is the first to report on the use of the HTK solution for OSR of JAA and PAA. In this analysis, we recorded less optimal results compared to those reported in the Curitiba trial [28], despite adopted in different aortic disease extent. Overall, the incidence of postoperative AKI was not different from that reported abdominal aortic literature, and more disappointingly its incidence was not better in the HTK cohort [13–27]. Nevertheless, in our series, the HTK group presented significantly longer aortic cross-clamp time, as well as greater number of additional procedures on the renal arteries that led to increased operation time, blood loss and consequent need of transfusions. All these parameters have been identified, in various experiences, as predictors of postoperative AKI, and may have had important implications on the development of postoperative AKI in the HTK group [5, 13, 20, 21, 24]. In a large cohort of PAA, Chiesa *et al.* [2] observed worse renal outcomes in patients who underwent long clamping times, especially in case of additional renal artery procedures. West *et al.* [13] reported that patients who had worse renal outcomes required higher number of renal artery bypass, a situation that potentially reflected more complex interventions due to more complex lesions. Of note, an operation time requiring >365 min was a sensible threshold for the development of postoperative AKI; our data finds support in 2 previous studies that identified operation time as the strongest predictor of postoperative AKI with, interestingly, similar time threshold. Although our data showed that HTK solution did not improve the result in comparison with a standard 'clamp-and-go' strategy without

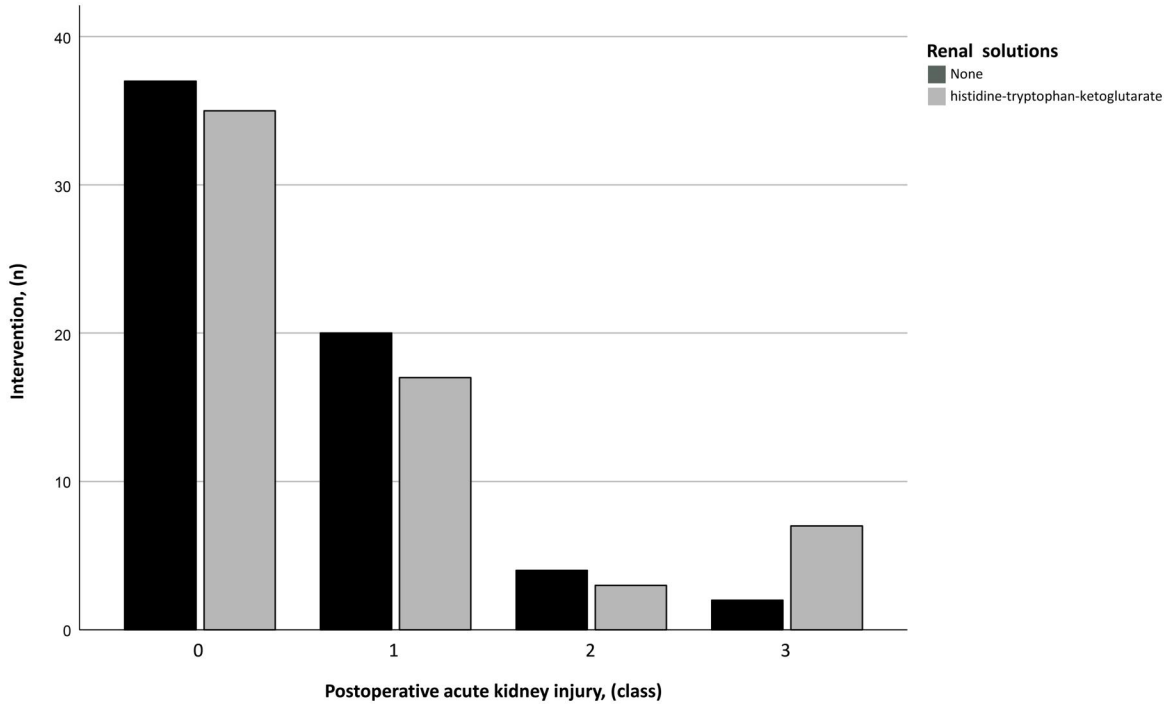


Figure 2: Postoperative acute kidney injury (AKI) distribution in histidine-tryptophan-ketoglutarate (HTK) solution and no-perfusion groups.

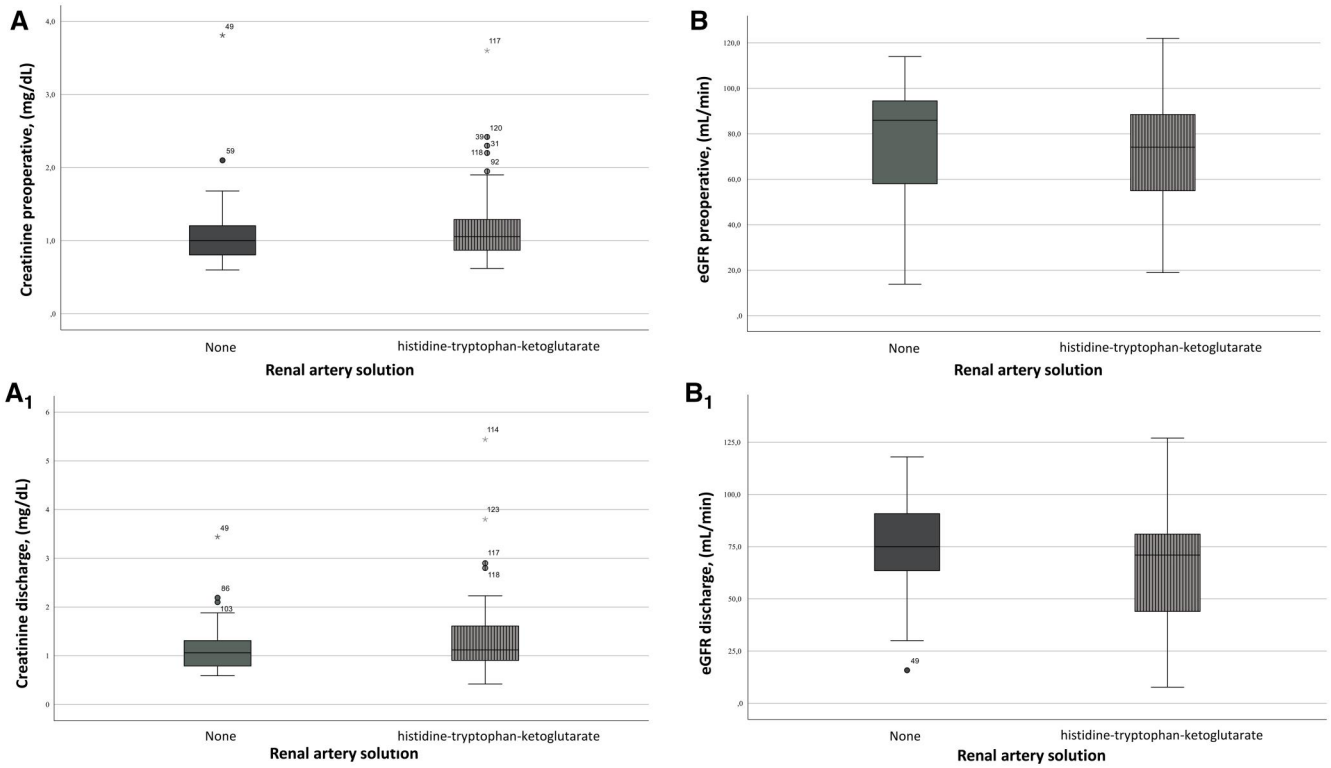
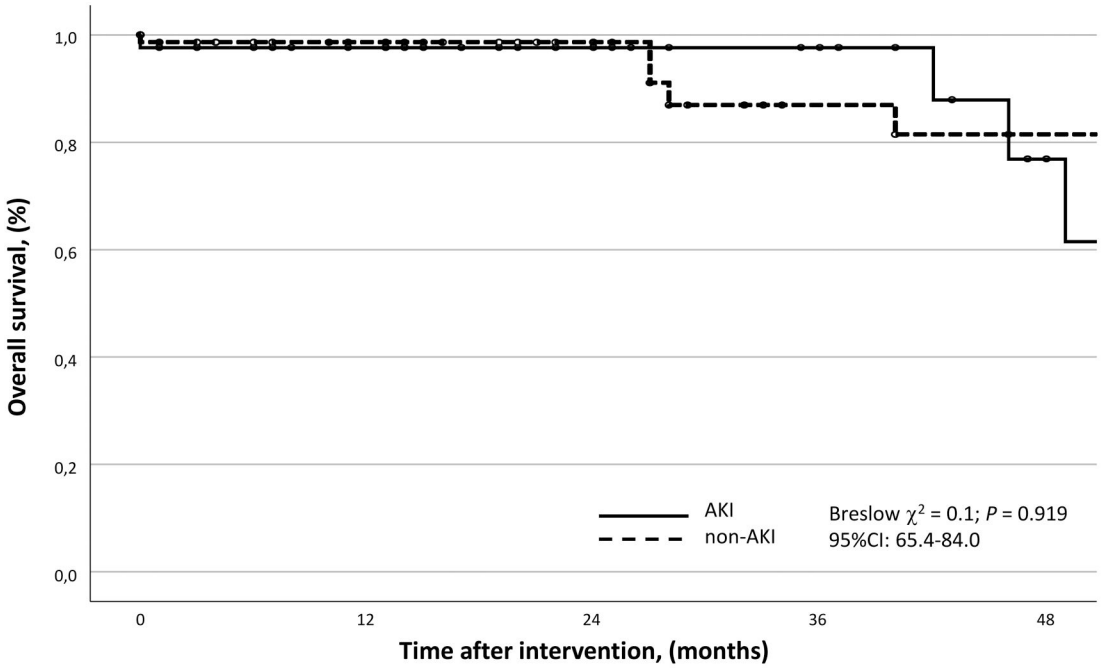


Figure 3: Variations of renal function from preoperative to postoperative period. Preoperative (A) and discharge (A1) value of creatinine level. Preoperative (B) and discharge (B1) value of estimated glomerular filtration rate (eGFR).

renal perfusion, the use of the HTK solution may have mitigated the incidence of postoperative AKI that could have been even worse considering the more complex interventions witnessed by the need of longer intervention time and increased number of renal artery bypass.

The impact of AKI on freedom from HD as well as on overall survival is underreported data in literature: in particular, the freedom from HD varied from 0% to 3.7% in our literature analysis [19–21, 23, 27]. A satisfactory finding in our cohorts was that, despite a significant decrease of postoperative eGFR and SCr, the



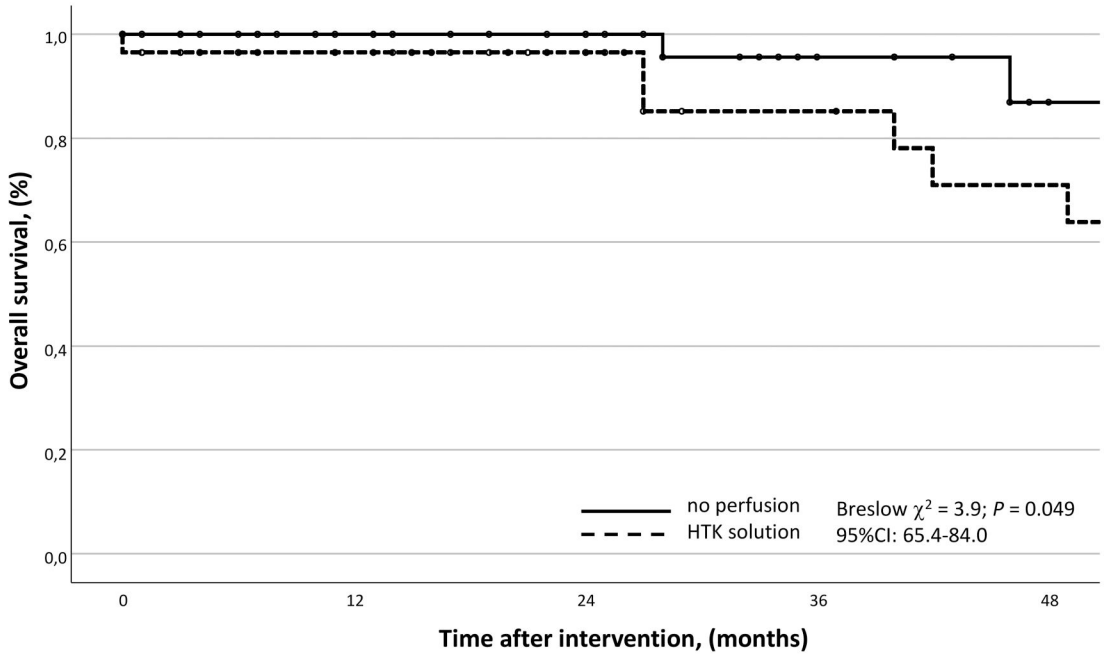
Time window	1m	12m	24m	36m	48m
Survival %					
AKI	97.7	97.7	97.7	97.7	87.9
non-AKI	98.6	98.6	98.6	86.9	81.5
SE					
AKI	0.02	0.02	0.02	0.02	0.09
non-AKI	0.01	0.01	0.01	0.06	0.08
95%CI					
AKI	87.9-99-6	87.9-99-6	87.9-99-6	87.9-99-6	59.9-97.2
non-AKI	93.1-99.7	93.1-99.7	93.1-99.7	69.5-95.1	63.9-94.8
@ risk					
AKI	35	28	17	12	9
non-AKI	60	41	60	21	15

Figure 4: Estimated overall survival stratified by postoperative development of acute kidney injury (AKI).

1-year freedom from HD was 100%. We opted to use this time window as primary outcome because it is later development of AKI can be multifactorial in aetiology. As far as long-term survival is concerned, not only postoperative AKI did not affect survival at 1 year, but it did not influence long-term survival [27]. Indeed, at this moment, it is impossible to give an unquestionable explanation for this kind of data; nevertheless, we consider them remarkable, especially if we ponder that these types of data are missing in most of the published, and an interesting starting point that needs to be explored in larger cohorts' studies.

Limitations

First, the retrospective nature of the analysis may have generated selection bias. Second, it is possible that investigators might have not identified all patients and all variables. However, missing data were not defaulted to negative, and denominators reflect only reported cases with $<$ 1% of missing data. Further, our results are not generalizable: we did not include patients with different demographic characteristics from different geographical regions, and different racial/ethnic origins. Despite the attempt to correct for potential confounding factors using exact matching and multivariable analyses, the small number of patients included in each cohort makes it underpowered. Also, we did not adjust for operative variables, which may have limited the effect of matching but, indeed, this would have significantly decreased the number of matched patients. Finally, the absence of statistically significant differences could reflect a type II error. Despite all these limitations, and the fact that CEM analysis included nearly 30% of the entire cohort, our data fit well with the available literature since it is the very first experience reporting on the effect of HTK in OSR for JAA/PAA, especially in a matched comparison with a no-perfusion strategy. Further, both the robust follow-up and the verification of data by official health records represent an acceptable attempt at the time of evaluating different renal protection strategies on the impact of



Time window	1m	12m	24m	36m	48m
Survival %					
no perfusion	100	100	100	95.7	87.0
HTK solution	96.6	96.6	96.6	85.2	78.1
SE					
no perfusion	0.00	0.00	0.00	0.04	0.09
HTK solution	0.02	0.02	0.02	0.08	0.09
95%CI					
no perfusion	100	100	100	78.7-99.3	61.2-96.6
HTK solution	88.2-99.1	88.2-99.1	88.2-99.1	64.6-94.8	54.7-91.3
@ risk					
no perfusion	47	35	26	15	7
HTK solution	48	34	20	13	10

Figure 5: Estimated overall survival stratified by renal perfusion strategy. HTK: histidine-tryptophan ketoglutarate.

postoperative AKI development. Further analysis on a larger dataset may be useful for assessing the predicted model performance by applying an adequate calibration method [29].

CONCLUSION

Our multicentre, contemporary, 'real-world' experience seems to demonstrate acceptable safety of OSR for JAA/PAA in selected patients, with low mortality rates in the immediate perioperative period. However, the incidence of postoperative AKI remains substantially high at nearly 38% but did not impact on freedom from HD at 1 year as well as on overall survival. Unexpectedly, the use of HTK for renal perfusion during suprarenal aortic cross-clamp did not decrease the rate of postoperative AKI; its use may have mitigated AKI occurrence in more complex interventions. Further high-quality prospective studies are warranted to confirm these findings and provide additional evidence on the topic.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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Bonardelli: Resources; Writing—review & editing. **Valerio Tolva:** Resources; Validation; Writing—review & editing. **Efrem Civilini:** Resources; Validation; Writing—original draft. **Giovanni Nano:** Resources; Writing—review & editing. **Raffaele Pulli:** Conceptualization; Software; Writing—review & editing. **Paolo Perini:** Resources; Writing—review & editing. **Sandro Lepidi:** Resources; Writing—review & editing. **Filippo Benedetto:** Resources; Writing—review & editing. **Fabio Verzini:** Resources; Writing—review & editing. **Gianfranco Veraldi:** Resources; Writing—review & editing. **Domenico Angiletta:** Resources; Writing—review & editing. **Raffaello Bellosta:** Resources; Writing—review & editing

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Appendix

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