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# Protective Effects of Cold Ringer's Solution Perfusion in Abdominal Aortic Surgery Requiring Renal Artery Clamp

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**Abstract.** *Background/Aim: Treating abdominal aortic aneurysms (AAA) of the juxtarenal artery with renal artery clamps burdens the kidneys. We investigated the outcomes of intra-operative renal artery perfusion using the cold Ringer's solution method for renal protection. Patients and Methods: We enrolled 290 AAA patients who underwent open aortic repair. Surgical outcomes were investigated based on renal protection. Results: We evaluated 231 patients requiring infrarenal artery clamp (Group I), and 59 patients requiring perfusion in addition to the clamp (Group J). Patient demographics, acute kidney injury (AKI) incidence (Group I: 11.7% and Group J: 20.3%), hospital mortality (Group I: 1.3% and Group J: 1.7%), and 30-day mortality (Group I: 0.4% and Group J: 0%) were not different between the groups. The AKI incidence was low (13%) in cases requiring a renal artery clamp for ≥45 min (n=40). Conclusion: Perfusion with cold Ringer's solution offers renal protection and may improve surgical outcomes.*

Juxtarenal artery abdominal aortic aneurysms (AAA) reportedly account for 8-20% of AAA (1, 2). Because of the short neck length associated with these aneurysms (<10 mm), endovascular surgery alone is not indicated because of an increased risk of complications, such as endo-leak and stent migration (3). Therefore, other techniques, such as the chimney method or the fenestration method, are employed. In particular, open aortic repair is the first choice of treatment for juxtarenal AAA; however, mortality and morbidity rates are higher when this procedure is performed for juxtarenal AAA compared to the infrarenal AAA (2, 4-6).

Due to the need for renal artery clamps, acute kidney injury (AKI) is the most serious complication that affects the outcomes of the AAA surgery, especially in cases of juxtarenal AAA (7). In this study, we assessed the treatment outcomes of surgery using a renal artery clamp and the renal protective effects of cold Ringer's solution in patients with juxtarenal AAA.

## Patients and Methods

*Patient characteristics*. Open aortic repair was performed in 331 AAA patients between January 2008 and December 2018 at Nara Medical University Hospital in Japan. Forty-one patients were excluded from the study for the following reasons: i) the surgery was emergency surgery, ii) the patient was undergoing dialysis, iii) the patient had an infectious aneurysm, and iv) the patient had a pseudoaneurysm. Among the remaining 290 patients, 231 required an infrarenal artery clamp (Group I), while 59 required a renal artery clamp due to juxtarenal AAA associated with renal perfusion (Group J). In all patients, drug-loaded myocardial scintigraphy or cardiac computed tomography (CT) was performed as a screening method for pre-operative ischemic heart disease.

*Surgical procedure*. In all cases, we approached the abdominal median incision under general anaesthesia. In Group J, there was no need to disconnect the left renal vein. The bilateral renal arteries were taped, and the abdominal aorta was detached from surrounding tissue for suprarenal aortic-cross clamping. After detachment of the abdominal aorta at the distal side, heparin sodium was administered at a dose of 80-unit/Kg. After confirming that the activated coagulation time (ACT) exceeded 200 seconds, the bilateral renal artery was clamped, followed by clamping of the aortic aneurysm. After incision, the aortic sclerosis was promptly removed and bleeding from the lumbar artery was controlled using 3-0 polypropylene suture (Ethicon, Somerville, NJ, USA) thread. For renal artery perfusion, an 8Fr Atom Tube® (Atom MEDICAL, Tokyo, Japan) was inserted into the renal artery. The temperature of the perfusion solution was at 4˚C, and was comprised of 1,000 ml of 0.9% Ringer's solution, 125 mg of methylprednisolone, and 63 ml of mannitol. Perfusion was carried out for 10 min at a rate of 20 ml/min per kidney, before being sustained at a rate of 10 ml/min.



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*Key Words:* Juxtarenal abdominal aortic aneurysm, cold Ringer's solution perfusion, renal artery clamp, renal artery perfusion, renal protection.

Table I. *Kidney disease improving global outcomes (KDIGO) criteria.*

| Stage Definition | I. Increase in SCr to ≥0.3 mg/dl (within 48 h)<br>II. Increase in SCr to 1.5 times baseline (within 7 days)<br>III. Urine output less than 0.5 ml/kg/h for 6 h | |
|---|---|---|
| | SCr criteria | Urine output criteria |
| Stage I | ≥0.3 mg/dl increase<br>or<br>1.5-1.9 times baseline | <0.5 ml/Kg/h for 6 h |
| Stage II | 2.0-2.9 times baseline | <0.5 ml/Kg/h for 12 h |
| Stage III | 3.0 times baseline<br>or<br>Increase in SCr to ≥4 mg/dl<br>or<br>Initiation of renal replacement therapy | <0.3 ml/Kg/h for 24 h<br>or<br>Anuria for ≥12 h |

SCr: Serum creatinine.

*Endpoints*. The primary endpoint of this study was 30-day mortality, while the secondary endpoint was post-operative AKI. AKI was evaluated according to the Kidney Disease Improving Global Outcomes (KDIGO) (8) guidelines (Table I), excluding the diagnostic criteria with respect to the urine volume.

*Statistical analyses*. The measured values are expressed as mean±standard deviation. The *t*-test, chi-squared test, Mann-Whitney *U*-test, and Kaplan Meier methods were used for analyses, as appropriate. Statistical significance was defined by a $p<0.05$. All statistical analyses were performed using IBM SPSS Statistics® (IBM Tokyo, Tokyo, Japan).

*Ethical considerations*. This study was approved by the institutional review board of the Nara Medical University Hospital on August 26, 2019 (No. 2304). Designated consent was obtained using the "opt-out" method.

## Results

The average age of patients was 71.6±7.5 years in Group I and 71.7±6.8 years in Group J ($p=0.65$). There was no significant difference in age, sex, maximum aneurysm diameter, comorbidities, or pre-operative renal function between the two groups (Table II). Although there were 12 cases (20.3%) of renal artery reconstruction in Group J, the operative time and bleeding volume did not differ significantly between the two groups (Table III).

Table II. *Patient characteristics*.

| | Group I (n=231) | Group J (n=59) | *p*-Value |
|---|---|---|---|
| Age (years) | 71.6±7.5 | 71.7±6.8 | 0.65 |
| Male gender (%) | 198 (86) | 56 (95) | 0.07 |
| Maximum diameter of aneurysm (cm) | 5.2±1.1 | 5.4±1.0 | 0.18 |
| Current smoker (%) | 195 (84) | 51 (86) | 0.84 |
| Hypertension (%) | 192 (83) | 51 (86) | 0.69 |
| Diabetes mellitus (%) | 28 (12) | 10 (17) | 0.39 |
| Dyslipidemia (%) | 99 (43) | 30 (51) | 0.31 |
| COPD (%) | 68 (29) | 19 (32) | 0.75 |
| Ischemic heart disease (%) | 37 (16) | 13 (22) | 0.33 |
| Preoperative SCr (mg/dl) | 1.02±0.47 | 1.09±0.41 | 0.20 |
| Preoperative eGFR (ml/min/1.73m$^2$) | 60.7±17.7 | 56.7±15.4 | 0.05 |
| Preoperative CKD stage | | | |
| I | 11 | 0 | 0.25 |
| II | 114 | 27 | |
| III | 89 | 29 | |
| IV | 15 | 3 | |
| V | 2 | 0 | |

COPD: Chronic obstructive pulmonary disease; SCr: serum creatinine; eGFR: estimated glomerular filtration rate; CKD: chronic kidney disease.

The 30-day mortality rate in Group I was 0.4% (one case of gastrointestinal bleeding) and 0% in Group J ($p=0.32$). The rate of hospitalization death was 1.3% (3 cases: i) one case of multiple organ failure, ii) one case of gastrointestinal bleeding, and iii) one case of interstitial pneumonia) in Group I, and 1.7% (one case of ischemic heart disease) in Group J; no significant differences were observed ($p=1.00$) (Table III). Post-operative AKI occurred in 27 cases (11.7%) in Group I and in 12 cases (20.3%) in Group J ($p=0.09$). The KDIGO classification was: i) stage I in 21 cases (77.8%), ii) Stage II in 3 cases (11.1%), and iii) Stage III in 3 cases (11,1%) in Group I. In Group J, the classification was: i) Stage I in 9 cases (75.0%) and ii) Stage II in 3 cases (25.0%) ($p=0.49$). Interestingly, at the time of discharge, 17 cases in Group I (63.0%), and 9 cases in Group J (75.0%) showed improved serum creatinine (SCr) levels compared to pre-operative levels (Figures 1A and B).

The three cases of KDIGO stage III in Group I are described below. The first case was a patient with pre-operative chronic kidney disease (CKD) Stage IV [SCr 2.29

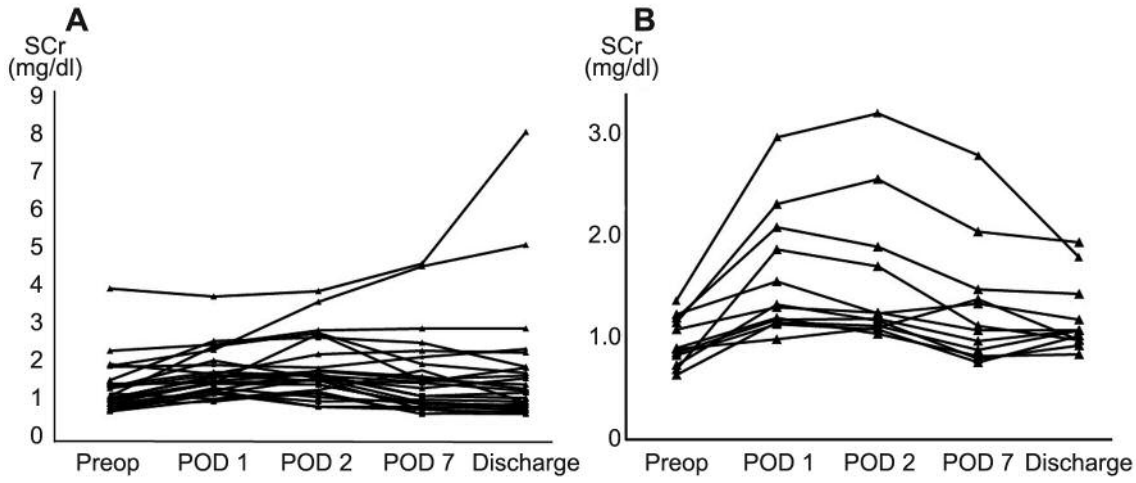


Figure 1. *Changes in SCr levels for cases of AKI in (A) group I and (B) group J. SCr: Serum creatinine; AKI: acute kidney injury; POD: post-operative day.*

mg/dl and estimated glomerular filtration rate (eGFR) 22.7 ml/min/1.73 $m^2$] whose post-operative SCr was elevated to 4.67 mg/dl. Thankfully, this level returned to the pre-operative level at the time of discharge because of continuous hemodiafiltration (CHDF). The second case was a patient with pre-operative CKD Stage V (SCr 3.92 mg/dl and eGFR 12.3 ml/min/1.73 $m^2$) who was scheduled to restart dialysis after temporary cessation for CHDF; however, the patient died on post-operative day 66 due to interstitial pneumonia. The third case was a patient with pre-operative CKD Stage IV (SCr 1.9 mg/dl and eGFR 27.9 ml/min/1.73 $m^2$) who started dialysis after CHDF; however, the patient died from multiple organ failure as a result of cardiac failure on post-operative day 115.

For further analysis, Group J patients were divided into two groups: i) patients requiring a renal artery clamp for ≥45 min (Group L, n=40) and ii) patients requiring a renal artery clamp for <45 min (Group S, n=19) (Table IV). There were no significant differences between the two groups with regard to the duration of intensive care unit (ICU) stay or length of post-operative hospitalization. The 30-day mortality rates were assessed because no patient died within 30 days from either group, although one patient in Group L died on post-operative day 604 (2.5%). Although the pre-operative SCr was lower in Group L compared to Group S (1.15±0.06 mg/dl in Group L *vs*. 0.96±0.15 mg/dl in Group S, $p<0.05$), the rate of post-operative AKI was significantly smaller in Group L (13%) compared to Group S (37%) ($p<0.05$). With respect to the KDIGO classification, there were four Stage I cases (80.0%) and one Stage II case (20.0%) in Group L, and five Stage I cases (71.4%) and two Stage II cases (28.6%) in Group S, but there were no Stage III cases in either group.

## Discussion

AKI is a very common complication of AAA because it affects the surgical outcome and thus, the patients' survival. In general, the main risk factors for post-operative AKI associated with AAA are i) the pre-operative renal dysfunction and ii) the intra-operative renal ischemic time (9-11). During surgery for infrarenal AAA, infrarenal arterial vessel clamping causes a reduction of renal blood flow by 38% (12) and changes the blood flow distribution inside the kidney (13-17). Therefore, the use of a renal protection method is important for near-renal artery aortic aneurysms that require renal artery clamping.

Several methods, such as implementation of a shorter cut-off time, use of infusion load and diuretics to ensure urine volume, treatment of renal blood flow with continuous dopamine administration, the renal cooling method, and the renal artery perfusion method using oxygenated blood have been used to protect the kidney (9, 18, 19). In our institution, for cases of juxtarenal AAA we perform renal protection using the cold Ringer's solution perfusion method, which has evolved mainly in the field of renal transplantation (7). In one study, the renal oxygen demand was reduced to 40%, 15%, and less than 5% by cooling the renal substance to 30, 20, and 10˚C (20), respectively. Although the efficacy of the cold Ringer's solution perfusion method of renal protection was reported in 1992 by Svensson *et al*. (21), there is some scepticism regarding the use of this method for all cases requiring interception of the renal artery. There are studies that report no use of renal perfusion (18), while others indicate prolonged renal ischemia duration in patients with renal dysfunction before surgery (7). However, we routinely perform renal protection

Table III. *Intra- and postoperative factors.*

| | Group I (n=231) | Group J (n=59) | *p*-Value |
|---|---|---|---|
| Intraoperative variables | | | |
| Renal artery clamp (bilateral: unilateral) | – | 23:36 | – |
| Renal artery reconstruction (%) | – | 12 (20) | – |
| Renal artery clamp time (minutes) | – | 53±18 | – |
| Total perfusate volume (ml) | – | 525±339 | – |
| Graft type (bifurcated: tube) | 168:64 | 28:31 | <0.05 |
| IMA reconstruction (%) | 154 (67) | 34 (58) | 0.22 |
| Operative time (min) | 277±60 | 286±71 | 0.37 |
| Blood loss (ml) | 1365±980 | 1330±1092 | 0.56 |
| Postoperative variables | | | |
| In-hospital mortality (%) | 3 (1.3) (1:pneumonia, 1:gastrointestinal haemorrhage, 1: MOF) | 1 (1.7) (1: ACS) | 1.00 |
| 30-day mortality (%) | 1 (0.4) (1: gastrointestinal haemorrhage) | 0 (0) | 0.32 |
| ICU stay (days); median (range) | 1 (1-115) | 1 (1-26) | 0.66 |
| Postoperative hospital stay (days); median (range) | 15 (10-219) | 16 (10-600) | 0.44 |
| ACS (%) | 0 (0) | 1 (1.7) | 0.20 |
| Pneumonia (%) | 7 (3.0) | 2 (3.3) | 0.82 |
| Stroke (%) | 1 (0.4) | 1(1.7) | 0.46 |
| Paraplegia (%) | 0 (0) | 1 (1.7) | 0.20 |
| Lower limb reperfusion injury (%) | 0 (0) | 1 (1.7) | 0.20 |
| Chylous ascites (%) | 0 (0) | 1 (1.7) | 0.20 |
| Gastrointestinal haemorrhage (%) | 1 (0.4) | 1 (1.7) | 0.37 |
| Ileus (%) | 4 (1.7) | 0 (0) | 0.59 |
| Graft infection (%) | 1 (0.4) | 0 (0) | 1.00 |
| AKI (%) | 27 (11.7) | 12 (20.3) | 0.09 |
| KDIGO Criteria | | | |
| Stage I | 21 | 9 | |
| Stage II | 3 | 3 | |
| Stage III | 3 | 0 | 0.49 |

IMA: Inferior mesenchymal artery; ICU: intensive care unit; AKI: acute kidney injury; KDIGO: kidney disease improving global outcomes; ACS: acute coronary syndrome; MOF: multiple organ failure.

with the cold Ringer's solution perfusion method in all cases of juxtarenal AAA to achieve stable renal protection and effective surgery in cases where prolonged renal artery clamping time cannot be predicted.

There are various reports regarding the composition, volume, and method of administration of fluid perfusion (21-23). Using our method, we found no differences in the post-operative course, the incidence of AKI, hospital mortality, or the 30-day mortality between patients who underwent infrarenal artery interception (Group I) and patients who underwent renal artery interception due to juxtarenal type and renal perfusion (Group J). In addition, even in cases that required a long renal artery clamping duration (≥45 min), the incidence of AKI was no higher compared to that of patients with shorter renal artery clamping duration. This observation indicated that surgery can be performed safely using the cold Ringer's solution method for renal protection, even in cases requiring prolonged renal artery clamping.

There were some limitations to this study, such as its retrospective nature, the single-centre design, and the limited number of patients. Despite this, our method prevented severe AKI in all cases, and a renal protective effect was observed, even in cases requiring long-term renal artery clamping. Prospective studies with a larger number of patients from multiple centres should be conducted for a better evaluation of the cold Ringer's perfusion solution towards the surgical outcome and survival of AAA patients.

In conclusion, our surgical outcomes were good, and our findings suggest that renal perfusion with cold Ringer's solution for juxtarenal AAA that requires suprarenal aortic-cross clamp is effective for renal protection.

Table IV. *Extracted analyses of juxtarenal type abdominal aortic aneurysm according to clamp time.*

| | Group L (n=40) | Group S (n=19) | *p*-Value |
|---|---|---|---|
| Age (years) | 70.7±5.7 | 73.9±6.2 | 0.08 |
| Male sex (%) | 38 (95) | 18 (95) | 1.00 |
| Maximum diameter of aneurysm (cm) | 5.3±0.4 | 5.6±0.8 | 0.28 |
| Preoperative SCr (mg/dl) | 1.15±0.06 | 0.96±0.15 | <0.05 |
| Preoperative eGFR (ml/min/1.73m$^2$) | 54.9±2.3 | 60.3±11.5 | 0.16 |
| Preoperative CKD stage | | | |
| 1 | 0 | 0 | 0.44 |
| 2 | 16 | 11 | |
| 3 | 21 | 8 | |
| 4 | 3 | 0 | |
| 5 | 0 | 0 | |
| Renal artery clamp (bilateral: unilateral) | 26:14 | 10:9 | 0.26 |
| Renal artery reconstruction (%) | 12 (30) | 0 (0) | <0.05 |
| Renal artery clamp time (min) | 61 (45-109) | 38 (29-44) | <0.05 |
| Total perfusate volume (ml) | 570 (200-1800) | 385 (50-888) | <0.05 |
| Operative time (min) | 303±28 | 249±47 | <0.05 |
| Blood loss (ml) | 1051 (340-5830) | 677 (160-1955) | <0.05 |
| ICU stay (median) | 1 day (1-26) | 1 day (1-6) | 0.12 |
| Postoperative hospital stay (median) (range) | 17 days (17-433) | 15 days (10-36) | 0.17 |
| In-hospital mortality (%) | 1 (2.5) | 0 (0) | 1.00 |
| 30-day mortality (%) | 0 (0) | 0 (0) | 1.00 |
| AKI (%) | 5 (13) | 7 (37) | <0.05 |
| KDIGO criteria | | | |
| Stage I | 4 | 5 | 0.66 |
| Stage II | 1 | 2 | |
| Stage III | 0 | 0 | |

SCr: Serum creatinine; eGFR: estimated glomerular filtration rate; CKD: chronic kidney disease; ICU: intensive care unit; AKI: acute kidney injury; KDIGO: kidney disease improving global outcomes.

## Conflicts of Interest

The Authors have no conflicts of interest directly relevant to the content of this article.

## Authors' Contributions

TH, TA, YH, SH, HN performed the operations. TH collected and analysed the data and wrote the manuscript. NS wrote and reviewed the manuscript. ST supervised the study.

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