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## Routine Continuous Cold Perfusion of the Kidneys during Elective Juxtarenal Aortic Aneurysm Repair

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**Objectives.** Surgical treatment of JAAs (juxtarenal aortic aneurysms) requires suprarenal aortic cross-clamping, causing temporary renal artery occlusion. We implemented a standardized protocol of hypothermic renal perfusion for all elective JAA operations.

**Design.** Retrospective study.

**Materials and methods.** Over a period of 6 years, 23 consecutive patients received a 300 ml bolus followed by an infusion (20 ml/minute) of cold (4 °C) saline to each kidney during suprarenal aortic clamping. We assessed outcome in terms of rise in serum creatinine, new onset of dialysis and mortality.

**Results.** None of the patients suffered from postoperative acute renal failure and in-hospital mortality was zero. Five patients did not show any rise in serum creatinine level, whereas in the others rises were <25% in comparison with the admission level, except for one patient (38%). Postoperative rise in serum creatinine level was not related to renal ischemia time (Spearman rank correlation = 0.24,  $p = 0.27$ ), preoperative renal function, total aortic clamping time or renal re-implantation. There were no renal complications at 6 months.

**Conclusions.** Our results suggest that a standardized strategy to apply renal hypothermia during the ischemic period of elective JAA surgery may reduce postoperative renal failure.

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**Keywords:** Aortic surgery; Suprarenal aortic clamping; Renal hypothermia; Acute renal failure.

### Introduction

Juxtarenal aortic aneurysms (JAAs) account for approximately 15% of all abdominal aortic aneurysms.<sup>1</sup> Surgical treatment of JAAs requires suprarenal aortic cross-clamping, causing temporary renal artery occlusion. Suprarenal clamping is associated with frequent renal impairment (dialysis is required in up to 13%) and a mortality of up to 18%.<sup>2–5</sup> The risk of postoperative renal failure increases at longer durations of suprarenal clamping, especially when the ischemic period exceeds 50 minutes.<sup>6</sup> Another risk factor for postoperative renal failure is preoperative renal insufficiency.

Kidney hypothermia may help to improve surgical outcome of suprarenal aortic clamping, especially when the patient has preoperative renal impairment or clamp time is excessive.<sup>7–10</sup> However, renal ischemia time can be difficult to predict beforehand. The purpose of this study was to apply routine renal preservation for all elective JAA surgery, and to examine postoperative renal function.

### Materials and Methods

Between January 2000 and January 2006, a total of 258 elective abdominal aortic aneurysm repairs (AAA) were performed, of which 23 consecutive patients underwent elective JAA repair with aortic clamping just above the renal arteries. The latter all received routine continuous renal hypothermic perfusion during the entire period of renal ischemia, and were included in the present study. Excluded from this study were

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type IV thoracoabdominal aneurysms and ruptured aneurysms.

The mean age of the 5 women and 18 men was  $70 \pm 11$  years. Eight patients (35%) presented with back pain or abdominal pain, fifteen patients (65%) were asymptomatic (Table 1). The mean diameter of the aneurysms was  $6.7 \pm 1.3$  cm. One woman had a symptomatic AAA of 4.5 cm diameter. A smoking history was common (74%). Fifty-seven percent of the patients had undergone prior abdominal surgery and two of them had undergone previous aortic grafting. Preoperative workup included cardiac assessment, abdominal ultrasound and angiography or CT scanning to determine the size and extent of the aneurysm. Two patients had multiple renal arteries.

Mean preoperative serum creatinine was  $1.66 \pm 1.00$  mg/dL ( $147 \mu\text{mol/L}$ ). Preoperative serum creatinine  $\geq 1.25$  mg/dL ( $111 \mu\text{mol/L}$ ) was defined as preoperative impaired renal function. Twelve patients (52%) had preoperative renal insufficiency (Table 1). In four of the latter the preoperative serum creatinine level was  $>1.8$  mg/dL ( $159 \mu\text{mol/L}$ ), while in two of them it was  $>3.0$  mg/dL ( $265 \mu\text{mol/L}$ ), of which one required chronic hemodialysis preoperatively. In four patients one of the kidneys was found to be atrophic (two of them had preoperative creatinine  $\geq 1.25$  mg/dL, but  $< 1.80$  mg/dL).

#### Surgical technique

All patients received Sufentanil and Bupivacaine epidurally, general anaesthesia with Isofluran (0.9%) and

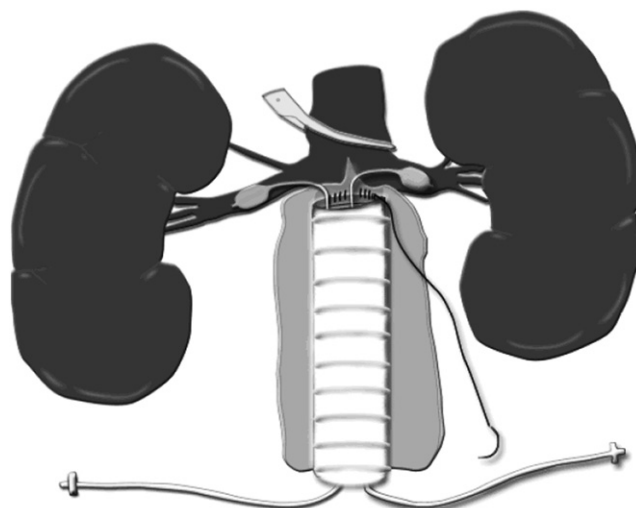
**Table 1. Characteristics of 23 patients who underwent elective surgery for juxtarenal abdominal aortic aneurysm during a six years period in our hospital**

|  | n*    | %     |
|--|-------|-------|
| Gender                                       |       |       |
| Male/Female                                  | 18/5  | 78/22 |
| Age  |       |       |
| Mean   | 70    |       |
| Range  | 39–83 |       |
| Associated disease                           |       |       |
| Chronic Obstructive Pulmonary Disease        | 4     | 17    |
| Coronary heart disease                       | 5     | 22    |
| Hypertension                                 | 13    | 57    |
| Diabetes Mellitus                            | 1     | 4     |
| Hypercholesterolaemia                        | 10    | 43    |
| Smoking                                      | 17    | 74    |
| Previous surgery                             |       |       |
| Abdominal surgery                            | 13    | 57    |
| Aortic stentgrafting                         | 2     | 9     |
| Preoperative serum creatinine level (mg/dL)* |       |       |
| <1.25  | 11    | 48    |
| 1.25–1.80                                    | 8     | 35    |
| >1.80  | 4     | 17    |

\* n = number of patients; mg = milligram; dL = deciliter.

a standard transperitoneal approach to the aorta. Before placing the aortic cross-clamp 5000 units of heparin were administered intravenously. The upper aortic clamp was placed proximal to both renal arteries ( $n = 16$ ) or proximal to only the left ( $n = 3$ ) or right renal artery ( $n = 2$ ). Perfusion of the kidneys with cold NaCl solution was then started and continued for the duration of the renal ischemia (see below). After completion of the proximal anastomosis, the suprarenal aortic clamp was replaced on the aortic graft in order to restore blood flow to the kidneys. Renal blood flow was examined intraoperatively using Doppler in order to confirm restoration of renal blood flow. Twelve patients received an aortic tube graft and eleven a bifurcated aortoiliac graft. Reimplantation of the renal arteries was performed in four patients. In one patient an endarterectomy of the renal artery was performed.

Cold perfusion of the kidneys was applied in all patients during the whole period of renal ischemia. One litre of 0.9% NaCl solution with an initial temperature of  $4^\circ\text{C}$  was placed one meter above each kidney. A 9 French gauge balloon-tipped Pruitt irrigation catheters (LeMaitre Vascular Inc, Burlington USA) were inserted in the orifice of the renal arteries from within the opened aneurysm (see Fig. 1). First, a 300 mL bolus of this solution was quickly infused to instantly induce renal hypothermia. Then renal perfusion was continued at a rate of approximately 20 mL/minute. Measurement of the temperature of this solution at the point of entrance into a kidney revealed a rise from  $4^\circ\text{C}$  in the beginning to  $16^\circ\text{C}$  at the



**Fig. 1.** Insertion of the 9 F Balloon-tipped Pruitt irrigation catheters (LeMaitre Vascular Inc, Burlington USA) from the opened juxtarenal aneurysm in the renal orifices to provide renal hypothermia with cold NaCl-solution during aortic graft placement.

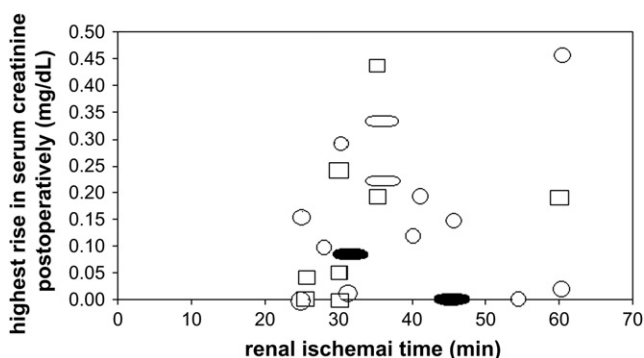
end of the perfusion. The catheters in the renal arteries were removed after completion of the proximal aortic anastomosis.

### Statistical analysis

Statistical programme SPSS 14.0 was used for analysis of data. We employed the non-parametric Spearman rank correlation, Mann–Whitney *U* and Kruskal Wallis tests to perform univariate statistical comparisons of preoperative and postoperative serum creatinine concentrations as well as duration of intraoperative renal ischemia times. Data are expressed as median, or mean  $\pm$  SD (standard deviation), and all tests were considered significant at  $p < 0.05$ .

### Results

None of the patients suffered from postoperative acute renal failure and mortality within 30 days was zero. The duration of renal ischemia ranged from 25 to 60 minutes, with a mean of  $37.2 \pm 11.7$  minutes. In 4 patients renal ischemic time exceeded 50 minutes (Fig. 2). Mean total operation time was  $215.2 \pm 56.7$  minutes, with a mean total aortic clamping time of  $58.4 \pm 24.4$  minutes. Patients were divided in three groups based on their preoperative serum creatinine level. Group one had normal preoperative renal function ( $<1.25$  mg/dL), group 2 had preoperative impaired renal function ( $1.25$ – $1.80$  mg/dL) and group 3 had preoperative renal insufficiency ( $>1.80$  mg/dL). None of the patients in the three groups showed a rise in serum creatinine exceeding  $0.50$  mg/dL ( $44 \mu\text{mol/L}$ ) above the admission level, defined as transient azotemia.<sup>10,11</sup> Only one patient experienced



**Fig. 2.** Renal ischemia time (x-axis) versus highest rise in serum creatinine level (y-axis). Three groups were made based on the preoperative serum creatinine level: circles =  $<1.25$  mg/dL ( $n = 11$ ); squares =  $1.25$ – $1.80$  mg/dL ( $n = 8$ ) and ellipsoids =  $>1.8$  mg/dL ( $n = 4$ ), with the two solid ellipsoids  $>3.0$  mg/dL.

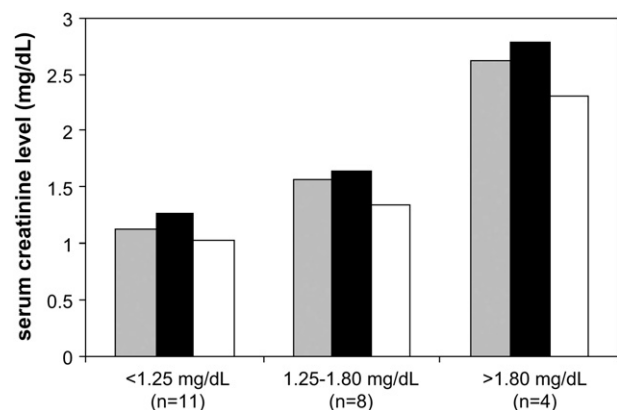
**Table 2.** Renal ischemia time and the highest rise of serum creatinine in the three groups based on the preoperative serum creatinine level

|                                       | Preoperative serum creatinine level (mg/dL)* |                                |                        | P value    |
|---------------------------------------|--|--------------------------------|------------------------|------------|
|                                       | $<1.25$<br>( $n = 11$ )*                     | $1.25$ – $1.80$<br>( $n = 8$ ) | $>1.80$<br>( $n = 4$ ) |            |
| Mean renal ischemic time (minutes)    | $40.0 \pm 13.5$                              | $30.0 \pm 11.3$                | $35.0 \pm 6.3$         | $p = 0.50$ |
| Mean rise in serum creatinine (mg/dL) | $0.14 \pm 0.14$                              | $0.15 \pm 0.15$                | $0.16 \pm 0.15$        | $p = 0.94$ |

\* mg = milligram; dL = deciliter;  $n$  = number of patients.

a rise of serum creatinine  $>25\%$ . Five patients did not show any rise in serum creatinine level (Fig. 2; note that the two patients with the highest preoperative levels (solid ellipsoids) had no deterioration of renal function). Renal artery reimplantation ( $n = 4$ , ischemia time:  $30$ – $45$  min) had no clear influence on rise in serum creatinine level (mean  $0.21 \pm 0.19$  mg/dL).

Postoperative rise in serum creatinine level was not related to renal ischemia time (Spearman rank correlation =  $0.24$ ,  $p = 0.27$ ; Fig. 2), total aortic clamping time, presentation with symptomatic AAA, tube or aortoiliac grafts, clamping above two or one renal artery, one or two functioning kidneys, surgery with or without renal implantation or preoperative renal function (Table 2). The peak in serum creatinine level occurred on average at postoperative day  $3 \pm 0.8$ . In most of the patients ( $56\%$ ) the postoperative serum creatinine level had returned to baseline the day after its peak. In all three groups the serum creatinine levels on discharge from the hospital were equal to or somewhat lower than preoperatively (Fig. 3). The



**Fig. 3.** Serum creatinine levels preoperatively (grey), at their peak postoperatively (black) and at the last day in hospital (white). Three groups were made based on the preoperative creatinine level:  $<1.25$  mg/dL ( $n = 11$ ),  $1.25$ – $1.80$  mg/dL ( $n = 8$ ) and  $>1.8$  mg/dL ( $n = 4$ ). Presented are the medians.

mean hospital stay was  $12 \pm 5$  days. Patient records at 6 months showed no renal complications.

The occurrence of larger renal atheroembolism was unlikely based on total restoration of renal blood flow as assessed intraoperatively by ultrasound Doppler. Non-renal postoperative complications were observed in 7 patients (26%), including respiratory failure ( $n=3$ ), cardiac failure ( $n=1$ ) and haemorrhage ( $n=3$ ). During relaparotomy blood from the splenic hilus, a duodenal ulcer, and diffuse retroperitoneal haemorrhage were found. Average blood loss was  $2237 \pm 1608$  mL. A temporary drop of body core temperature of mean  $0.5 \pm 0.3$  °C during cooling of the kidneys was observed.

## Discussion

The present single-center study suggests that continuous hypothermic perfusion of the kidneys after an initial cold bolus may reduce deterioration of renal function after ischemia and reperfusion during elective repair of juxtarenal aortic aneurysms. This also holds for patients with increased preoperative levels of serum creatinine and/or duration of renal ischemia between 50–60 minutes. However, a limitation of this study is the absence of a comparative group due to an ethical constraint in our hospital, which prescribed routine renal cooling for all elective JAA repairs.

Rates of mortality and renal morbidity are the main issues concerning the safety and feasibility of juxtarenal and suprarenal aortic aneurysm surgery.<sup>12</sup> Transient azotemia is reported in 14–50% of the patients, while a new onset of dialysis was seen in 0–13%.<sup>2–23</sup> In our study none of the patients died within 30 days, no dialysis was required postoperatively, and the highest rise in serum creatinine level did not exceed the critical value of 0.50 mg/dL. Acute renal insufficiency post AAA repair is associated with a mortality of 25% to 50%.<sup>24</sup> Postoperative renal insufficiency is usually secondary to acute tubular necrosis, while atheroemboli due to the suprarenal aortic clamping may be another cause.<sup>14</sup>

Several studies have shown that the risk for postoperative renal failure after suprarenal aortic cross clamping for elective AAA repair is low in case of renal ischemia times below 20 minutes, but that it increases 10 times if the clamping time lasts more than 50 minutes. However, the critical renal ischemic time remains controversial.<sup>3,6,11</sup> Longer ischemia times, even up to 100 minutes, do occur and aren't always predictable.<sup>6,9</sup> In our series, the renal ischemia time exceeded 50 minutes in four patients. None of these patients showed a significant rise in serum creatinine

postoperatively or developed transient renal failure or dialysis in the postoperative course. However, this should still be interpreted with care given the lack of a control group in this study.

One of the major determinants of postoperative renal failure is preoperative renal insufficiency. In our series, preoperative renal insufficiency was present in twelve patients (52%). Also in these patients we observed no significant rise in serum creatinine level postoperatively, which seems to corroborate the efficacy of our cooling strategy to prevent the occurrence of renal dysfunction postoperatively.

Peroperative measures to preserve renal function are still a matter of debate during juxtarenal aortic aneurysm repair. Critics of preservation techniques state that renal perfusion does not protect against renal ischemic damage and that total ischemia times are elongated by these extra proceedings, thereby increasing the risk of harming postoperative renal function.<sup>25</sup> The continuous cooled perfusion technique as described in this article is swift and doesn't interfere with the juxtarenal aortic anastomosis. Another criticism is that dissection of the renal arteries could occur during insertion of the balloon-tipped Pruitt irrigation catheters. However, in all of our patients, restoration of renal artery blood flow was confirmed with intraoperative Doppler examination. Although in our series the use of renal hypothermia resulted in a drop of body core temperature of  $0.5 \pm 0.3$  °C, this was not associated with complications and seemed to be well tolerated, as has also been reported.<sup>26</sup>

Experimental studies have demonstrated that renal hypothermia preserves renal function by reducing its oxygen consumption. Renal oxygen consumption is reduced to 40% when the renal parenchyma is cooled to 30 °C, to 15% at 20 °C, and to less than 5% at 10 °C.<sup>27–31</sup> More recent studies have, on the other hand, concentrated on additives to the perfusion solution of the kidney or agents (e.g. PGE, L-arginine) to protect the kidney from ischemia/reperfusion injury, rather than on cooling.<sup>32–35</sup> Also in kidney transplantation surgery additives are being examined to improve cold preservation of the kidney.<sup>36,37</sup> In humans, organ perfusion for preservation is more often used and studied during thoracoabdominal aortic aneurysm repair (ThAAA).<sup>38–43</sup> Köksoy *et al.* have indicated that selective cold crystalloid perfusion offers superior renal protection when compared with normothermic blood during extensive ThAAA repair.<sup>44</sup> PGE1 addition to the perfusion fluid during ThAAA surgery was of no advantage over 4 °C Ringer's lactate plus 1000 IU of heparin/l alone.<sup>45</sup>

At present endovascular treatment for aortic aneurysms is becoming more and more widespread and

versatile.<sup>46</sup> However, the neck of a juxtarenal aneurysm is often too short for stable stent-graft implantation. Fenestrations in the stent-graft permit implantation at a more favorable level by providing a means for flow to the renal arteries, although suprarenal fixation could have effect on the renal function.<sup>47</sup> Several studies have examined postoperative renal function after endovascular aneurysm repair.<sup>48</sup> Alsac *et al.* have found a decline in renal function over time after endovascular aortic repair. This is probably due to multiple factors and not the suprarenal fixation.<sup>49</sup> In most cases, juxta and suprarenal aneurysms still require open surgery, while future endovascular branch graft repairs ultimately will require comparison with open repair.

In conclusion, a standardized strategy to routinely apply renal hypothermia during the ischemic period of elective JAA surgery may protect renal function, even in patients with preoperative renal failure.

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