

Long-term Renal Outcomes of Consecutive Patients Undergoing Open Type IV Thoracoabdominal Aneurysm Repair

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WHAT THIS PAPER ADDS

We report contemporary long-term renal outcomes following open type IV thoracoabdominal aneurysm (TAAA) repair within a centralised, high-volume UK centre. This study describes the trends in renal function following open TAAA surgery, which, following an early and significant postoperative creatinine rise, returns to baseline level on discharge and at follow up (>1 year postoperatively). Renal function improved in a similar proportion to those in whom renal function declined, and remained stable in approximately half of patients. In the era of endovascular repair, with its incumbent concerns regarding a gradual decline in renal function, we report durable outcomes following open surgery.

Objective: To evaluate long-term renal outcomes after open type IV thoracoabdominal aneurysm (TAAA) repair.

Design: Retrospective analysis of a prospectively collected database of consecutive operated non-ruptured type IV TAAAs (2007–2011).

Methods: Renal function was analysed by serum creatinine concentration, estimated glomerular filtration rate (eGFR) and Kidney Disease Outcomes Quality Initiative (KDOQI) stage. The primary outcome was the change in creatinine concentration from before surgery to defined time points after surgery: peak postoperative; discharge; at follow-up (>1 year postoperatively). Secondary outcomes were change in eGFR, change in KDOQI stage, dialysis requirement, and 30-day mortality.

Results: Between 2007 and 2011, 53 open type IV TAAA repairs were performed. Median creatinine levels significantly increased in the immediate postoperative period, but returned to baseline by discharge. Thirteen patients (28.2%) had an improvement in follow-up eGFR of at least 20% compared with pre-operative eGFR or improved by one KDOQI stage. Twelve patients (26.1%) had a decline in eGFR of at least 20% or one KDOQI stage at follow-up. Three patients (7.5%) required temporary dialysis and one patient (1.9%) required permanent dialysis. The 30-day mortality was 1.9%.

Conclusions: This study demonstrates acceptable renal outcomes following open type IV TAAA repair. Open type IV repair remains the standard against which newer techniques should be compared.

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INTRODUCTION

The Crawford classification of thoracoabdominal aneurysm (TAAA) defines type IV as aneurysmal change extending distally from the diaphragm and involving the origins of the coeliac, mesenteric, and renal arteries.¹ We have previously presented the outcome data for type IV thoracoabdominal repair over a 10-year period with a 1-year mortality of 6%.² Open type IV TAAA repair involves supra-coeliac aortic cross-clamping, and the consequent renal ischaemia can

often lead to postoperative renal dysfunction.³ However, increasingly advanced peri-operative anaesthetic, medical, and surgical management may help to minimise the impact of extensive surgery and supra-renal cross clamping.

The endovascular repair of TAAAs is becoming increasingly prevalent; however, it requires the administration of nephrotoxic contrast during the procedure and instrumentation of the visceral vessel ostia with an associated risk of microembolisation.⁴ Furthermore, endovascular stent grafts require regular follow-up imaging, and are associated with late complications such as endoleak and renal artery branch stenosis or occlusion.^{4,5}

The aim of this study was to assess contemporary renal outcomes following open type IV repair in order to provide a benchmark against which newer techniques can be compared.

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METHODS

Consecutive patients undergoing type IV TAAA repair were entered into a prospectively collected database between 1 January 2007 and 31 December 2011 at the Royal Infirmary of Edinburgh, UK, which is the national centre for the treatment of thoracoabdominal aneurysms in Scotland. Patients were included if they had undergone non-ruptured (including urgent/symptomatic) open Crawford type IV TAAA repair. Patients were excluded if they had undergone any operation other than open Crawford type IV repair, so that hybrid or endovascular repairs were excluded.

Patient demographics, pre-operative co-morbidities, intra-operative parameters, and peri-operative complications were recorded.

Patient selection

Open type IV TAAA repair is offered to patients with >5.5 cm diameter, rapidly expanding, or symptomatic aneurysms. Patients are pre-assessed by a consultant surgeon and anaesthetist, with pre-operative tests usually including electrocardiogram, chest radiograph, and stress echocardiogram. Patients included towards the end of the study period were also assessed using cardiopulmonary exercise testing, and computed tomography (CT) coronary angiography. There is no renal function threshold below which surgery is not offered.

Operative methodology

All operations were performed in a similar manner with one of the two senior authors (P.J.B or R.T.A.C) as primary operator. All patients had epidural and general anaesthesia with one of the anaesthetists (A.F.N or C.M) as the primary anaesthetist. A cerebrospinal fluid (CSF) drain for spinal cord protection was sited only in patients who had undergone previous thoracic aortic aneurysm repair. All operations were undertaken through an abdominal approach. Medial visceral rotation was used for aortic exposure. Before aortic clamping the patient was cooled to 32–33 °C by a combination of lowering the operating room temperature, passing cold water through under-body blankets, and blowing ambient temperature air over the upper body. Intravenous mannitol was administered before aortic clamping.⁶ Following systemic heparinisation (5000 Units or 70 Units/kg), a supra-coeliac aortic cross clamp was applied and a bevelled Crawford type IV repair was performed incorporating the renal and visceral ostia into the repair. A Dacron graft (Maquet, Rastatt, Germany) was used for repair. Renal and visceral ischaemic time was kept to a minimum. No local cooling of the kidneys or infusion of drugs or fluids into the renal arteries was employed. Depending upon the distance between the visceral ostia, some patients required a renal artery jump-graft (the longer of the ischaemic times presented).

Red cell salvage, and frequent point-of-care testing of arterial blood gases, electrolytes, glucose, lactate, and coagulation (ROTEM thromboelastometry; TEM International, Munich, Germany) were undertaken during surgery.

After reperfusion of the kidneys and other abdominal viscera, rewarming of the patient was commenced. In most cases the tracheal tube was removed in the operating theatre when the patient was normothermic (≥ 36 °C). The patient was subsequently transferred to the High Dependency Unit (HDU) or Intensive Care Unit (ICU) for postoperative care.

Serum creatinine was measured the day before surgery, after surgery in the recovery room, or on admission to the HDU and ICU at least once daily while the patient was in HDU or ICU, and at less frequent intervals once the patient was transferred back to the vascular surgery ward. Three subgroups were identified for analysis: (1) standard repair (no jump graft); (2) those requiring a renal jump graft; and (3) those with a pre-operative estimated glomerular filtration rate of <60 mL/min.

Outcome measures of renal function

Within the literature there are multiple methods of measuring renal function.⁷ Many studies primarily use serum creatinine changes,⁸ whereas others support the use of glomerular filtration rate (GFR) and Kidney Disease Outcomes Quality Initiative (KDOQI) stage⁹ as a more sensitive determinant of early renal dysfunction.⁷ To present our data in a transparent fashion and to allow comparison with published data from other centres, we have analysed the data using all three methods.

1. Creatinine concentration

Creatinine ($\mu\text{mol/L}$) was recorded from patient notes, and electronic and general practice (GP) records pre-operatively, peak postoperatively, at discharge, and at follow up (>1 year postoperatively).

The primary outcome was a change in baseline creatinine levels between before surgery and the postoperative time points mentioned above. In order to compare our results with other published data, we analysed data using the following definitions of renal dysfunction: creatinine >1.5 mg/dL (=133 $\mu\text{mol/L}$) and increase in baseline creatinine of at least 50%.¹⁰

2. Estimated GFR and KDOQI stage

The GFR has been described by some authors as a more sensitive measure of chronic renal impairment than serum creatinine concentration, and pre-operative GFR has been shown to correlate with mortality after TAAA repair.^{7,11,12} Estimated GFR (eGFR; mL/min) was calculated according to the Cockcroft-Gault formula ($[(140 - \text{age}) \times \text{weight (kg)} \times \text{constant} / \text{creatinine } (\mu\text{mol/L})]$ [constant = 1.23 men and 1.04 women]).¹³ Patients were then stratified according to the KDOQI stages of chronic kidney disease using this calculated eGFR ("Normal" or "Stage 1": eGFR ≥ 90 mL/min; "Stage 2": eGFR 60–89 mL/min; "Stage 3": eGFR 30–59 mL/min; "Stage 4": eGFR 15–29 mL/min).⁹ We defined deterioration in renal function as a decline from pre-operative to follow up eGFR by 20% or moving down a

Table 1. Patient demographics and peri-operative variables in operated and non-operated type IV thoracoabdominal aneurysms (TAAAs). All type IV repairs and non-operatively managed TAAAs are compared using Mann–Whitney^a or Fisher's exact test^b.

	Operated open type IV TAAA		Pre-operative eGFR <60 mL/min	Non-operatively managed	<i>p</i> (All type IV repairs versus non-operative management)
	All type IV repairs	Renal jump graft			
Number	53	7	21	21	—
Age (y; median)	70	66	70	74	.003 ^a
Sex (M/F)	41/12	6/1	11/10	17/4	1.0 ^b
Mean weight (kg)	76.0	75.4	70.6	—	—
Median aneurysm diameter (cm)	6.8	7.7	7.0	6.2	.03 ^a
Ischaemic heart disease	19	2	8	13	.06 ^b
Positive stress echocardiogram	7	1	4	9	.01 ^b
Median preoperative creatinine (μmol/l)	99	140	135	105	.3 ^a
Median estimated glomerular filtration rate (mL/min)	66.3	50.8	44	—	—
Pre-operative renal artery stenosis on CT	6	3	4	—	—
Previous aortic surgery	7	0	1	1	.4 ^b
Median renal ischaemic time in mins (range)	46 (30–104)	75 (60–104)	46 (32–104)	—	—
30-day mortality	1	0	1	—	—

stage in KDOQI scale in line with other reports.⁷ Freedom from deterioration in renal function was calculated using the Kaplan–Meier method allowing for variable follow-up lengths. A comparison between the subgroups (eGFR ≥60 mL/min, eGFR <60 mL/min, and renal jump grafts) was performed using the logrank test.

3. Other variables

The temporary or permanent dialysis requirement and 30-day mortality were also recorded.

Statistical analysis

Variables were entered into a Microsoft Excel version 14.2.3 worksheet and analysis was performed using R environment for statistical computing (reference index version 3.0.1; R Foundation for Statistical Computing, Vienna, Austria). Fisher's exact test was used to compare categorical data due to small counts. Where given creatinine was deemed unlikely to be normally distributed, non-parametric tests were used. The Mann–Whitney *U* test was used to compare continuous variables. To compare creatinine results for the same individuals at different time periods a Wilcoxon rank signed test was used. The Kaplan–Meier method was used to analyse freedom from deterioration renal function. A logrank test was performed to compare survival curves between subgroups. A *p*-value <.05 was considered significant.

RESULTS

Between 2007 and 2011, 73 patients were referred to the Royal Infirmary of Edinburgh for consideration for type IV

TAAA repair. Fifty-three patients underwent type IV TAAA repair by one of the two senior authors (P.J.B/R.T.A.C) as primary operator. Twenty patients were managed non-operatively for the following reasons: cardiac disease (nine), cardiac and renal disease (three), malignant disease (two), respiratory disease (three), renal and respiratory disease (one), and patient choice (two). Patient demographics and operative parameters, and comparison between patients managed operatively and non-operatively, are presented in Table 1. Seven patients had undergone previous aortoiliac surgery (four infra-renal open abdominal aortic aneurysm [AAA] repair, one thoracic endovascular aortic aneurysm repair [TEVAR], one endovascular AAA repair, one common iliac artery endarterectomy). One patient who had previously undergone TEVAR had a CSF drain inserted pre-operatively. One patient within the cohort died within 30 days of operation as a result of a cerebral infarction and was excluded from further analysis.

Four patients required dialysis postoperatively (7.5%). Three of these patients (all renal jump graft patients) required temporary dialysis postoperatively, and successfully recovered from dialysis dependence. One patient (1.9%) went on to require lifelong dialysis and was excluded from further discharge and follow-up creatinine analyses. This patient was at high pre-operative risk of developing renal failure (pre-operative CT showed bilateral renal atrophy and pre-operative creatinine >200 μmol/l). Full data on all patients were available for pre-operative and peak creatinine. Discharge creatinine was available for all patients, apart from the patient who died. Follow-up creatinine (mean time from surgery = 2.5 years, range 52–265 weeks) was obtained from GP records and was missing from

Table 2. Median difference in pre-operative creatinine and at various peri-operative stages in (1) all type IV repairs; (2) renal jump graft repairs; and (3) patients with a pre-operative estimated glomerular filtration rate (eGFR) <60 mL/min.

	Median creatinine (µmol/L)	IQR	Difference in medians from pre-operation [IQR]	p
(1) All type IV repairs (n = 46)				
Pre-operative	98	79–116	–	–
Peak postoperative	150	106–233	45 (12–122)	<.001
Discharge	92	68–118	–10 (–23 to 10)	.2
Follow up	92	80–118	–8 (–17 to 10)	.1
(2) Renal jump graft (n = 7)				
Pre-operative	140	116–144	–	–
Peak postoperative	273	210–440	133 (100–284)	.02
Discharge	166	126–172	13 (–2 to 29)	.2
Follow up	113	90–144	–1 (–22 to +1)	.4
(3) eGFR <60 mL/min (n = 20)				
Pre-operative	135	105–145	–	–
Peak postoperative	176	140–256	47 (1–133)	.002
Discharge	114	90–142	–23 (–37 to 9)	.2
Follow up	117	100–141	–10 (–25 to –1)	.1

the records of six patients (11.5%; four patients died during follow-up period, one patient failed to return for follow up, one patient moved GP practice).

Creatinine concentration

Table 2 shows the median creatinine levels (µmol/l) at the various stages postoperatively. Median creatinine was significantly elevated immediately postoperatively (difference in medians +45, interquartile range 12–122, p <.001); however, the median creatinine returned towards the baseline level at discharge and at follow up. The median creatinine at follow up in all subgroups was lower than the pre-operative creatinine; however, this result failed to reach statistical significance. Several studies¹⁰ define renal failure as creatinine >1.5 mg/dl (=133 µmol/l); when using this arbitrary cut-off, 10 (21.7%) patients had a pre-operative creatinine >133 µmol/l compared with six (13.3%) at follow up (p = .4). Some studies define renal failure as increase in baseline creatinine by 50%;¹⁰ by this definition no patients had renal failure on follow up.

eGFR and KDOQI stage

Table 3 summarises changes in eGFR and KDOQI between before surgery and follow up after surgery. Eleven patients

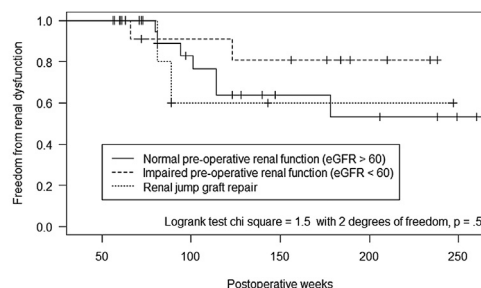
Table 3. Changes in estimated glomerular filtration rate (eGFR) and Kidney Disease Outcome Quality Initiative (KDOQI) stages between pre-operative levels and follow up (>1 year postoperatively) after open type IV thoracoabdominal aneurysm (TAAA) repair.

	Open type IV TAAA repairs n = 46 (%)
eGFR decline >20%	8 (17.4)
KDOQI stage decline	6 (13.0)
eGFR decline >20% and/or KDOQI stage decline	11 (23.9)
eGFR improvement >20%	13 (28.2)
KDOQI stage improvement	4 (8.7)
eGFR improvement >20% and/or KDOQI stage improvement	13 (28.2)

had a decline in eGFR by 20% or one KDOQI stage at follow-up. The eGFR was <60 mL/min in 19 patients pre-operatively compared with 19 patients at follow up, which was not significant (p = 1.0). Fig. 1 demonstrates the Kaplan–Meier deterioration in renal function-free survival of TAAA patients with pre-operative eGFR >60, eGFR <60, and renal jump graft patients. There were no significant differences in deterioration in renal function survival between subgroups (p = .5).

DISCUSSION

Our results demonstrate that, after open type IV TAAA repair, renal function is preserved or improved in the majority, and declines in just under a quarter of patients. This echoes the findings of a contemporary series analysing long-term renal outcomes in open type IV repair.¹⁴ Nathan et al.¹⁴ reported that the renal function of 25.3% of patients declined by one KDOQI stage and that the renal function of 19% of patients improved by one KDOQI stage. This is similar to the results reported in our study (Table 3). It can be difficult to directly compare renal outcomes between



	Postoperative weeks				
Normal renal function (eGFR > 60)	26	13	6	5	2
Impaired renal function (eGFR < 60)	13	9	8	3	0
Renal jump graft repair	7	2	1	1	0

Figure 1. Kaplan–Meier freedom from deterioration in renal function over time (renal function deterioration defined as decline in pre-operative estimated glomerular filtration rate [eGFR] by 20% or moving down a stage in the Kidney Disease Outcomes Quality Initiative scale).

studies because of differences in the definition of renal dysfunction, as well as a lack of published medium-to-long-term renal data following type IV repair.³ When considering infra-renal AAA, Mills et al.⁷ reported a long-term $\geq 20\%$ decline in eGFR in 21% of patients undergoing open and endovascular repair, which is, again, comparable with our result of a $\geq 20\%$ decline in eGFR in 17.4% of patients 1 year after open type IV repair. The outcomes of dialysis requirement and 30-day mortality appear to be the most universally reported and easily compared variables. Our reported rates of dialysis and 30-day mortality rate compare favourably with other type IV open case series, although we did not include ruptures in our analysis (Table 4).^{14–20} One patient (1.9%) in a 5-year period required permanent dialysis and was known pre-operatively to be at high risk of developing permanent renal failure (pre-operative bilateral renal atrophy pre-operative creatinine $>200 \mu\text{mol/L}$). Three patients (5.8%), all of whom had undergone renal jump graft, required temporary dialysis. Patients requiring renal jump graft repair are recognised as having a higher risk for acute renal failure and dialysis postoperatively.²¹

The satisfactory renal outcomes presented follow open type IV TAAA with no specific renal perfusion techniques. The operative technique for type IV at our centre focuses on minimising aortic clamping times and induced systemic hypothermia to reduce metabolic demand. In an effort to prevent end-organ ischaemic injury, various renal protective techniques have been described. Cold crystalloid renal perfusion was described more than 30 years ago, and in randomised trials demonstrated reduced renal dysfunction compared with isothermic, but not cold, blood perfusion.^{22,23} The authors of these studies postulate that cold renal perfusion protects against renal dysfunction, and the substrate (blood, crystalloid, mannitol) used is less important.²⁴ Additional measures, such as left heart bypass, balloon perfusion catheters, and shunts, have been used for selective visceral perfusion.^{25,26} While these measures are undoubtedly useful for extent types I and II, the role in type IV repair is less clear. Similarly, at our centre, endarterectomy or stenting is not routinely performed in the case of renal artery stenosis.

This study demonstrates the common clinical scenario of an acute creatinine rise immediately after surgery followed by a gradual improvement towards baseline by discharge.³ An important finding from this study is that renal function typically remains stable following discharge. Indeed, there was a trend towards lower median creatinine concentration at follow-up compared with pre-operative levels in all subgroups; however, this was not statistically significant. Possible reasons for this may not be exclusively surgical, and may involve the addressing of cardiovascular risk factors, for example blood pressure control. When considering infra-renal AAA, there have been reports of a late decline in renal function in those undergoing endovascular stent grafting, perhaps as a result of repeated doses of nephrotoxic contrast administered for surveillance CT scans.^{7,8} Endovascular repair of TAAAs may be associated with late renal artery branch occlusion^{4,5} occasionally causing deterioration in renal function or dialysis requirement.^{4,27} Endovascular repair can also be associated with a high re-intervention rate (10%).^{5,27} A study of fenestrated endorepair of supra-renal ($n = 13$), juxtarenal ($n = 63$), and four type IV TAAAs has shown good results with a worsening in renal function in 11%, improvement in 19%, a temporary dialysis rate of 3%, and long-term dialysis rate of 1%.⁵ A study of 119 juxtarenal aneurysms repaired by fenestrated endovascular grafts reported a worsening of renal function in 25%.⁴ The authors postulated that the reason for renal impairment in this context could be nephrotoxic contrast or micro-embolisation from manipulation of the device within the aorta. A total of 22 renal stenoses and occlusions occurred in the course of follow-up in that study (12 renal artery stenoses and 10 renal artery occlusions). Five patients required dialysis (two permanently); this included four patients with renal artery occlusions. The largest UK series of total endovascular repairs of type I–IV TAAAs reported a median 3.4% deterioration in eGFR at discharge, a temporary dialysis rate of 6.5%, and a permanent dialysis rate of 3.2%.²⁸ Although renal outcomes published following open type IV surgery may suggest superiority over endovascular repair, the aforementioned endovascular studies consist of an older cohort of patients with more co-

Table 4. Comparison of clinical outcomes of type IV thoracoabdominal aneurysm repair with other published data.

Author (year)	Number of patients	Mean age (y)	Short-term 30-d renal dysfunction Doubling of creatinine or creatinine $>3.0 \text{ g/dL}$ (%)	Long-term renal dysfunction Decrease in KDOQI stage (%)	Dialysis Temporary dialysis (%)	Permanent dialysis (%)	Operative mortality or 30-d mortality
This study	53	68.6	13 (24.5)	6 (13)	3 (5.7)	1 (1.9)	1 (1.9)
Nathan et al. (2011) ¹⁴	108	72.9	—	25 (25.3)	—	6 (6.1)	6 (5.6)
Patel et al. (2011) ¹⁸	179	73	8 (4.5)	—	5 (2.8)	—	5 (2.8)
Coselli (2007) ²⁴	427	66.1 ^a	—	—	—	23 (5.4)	13 (3)
Bicknell (2003) ¹⁵	130	68	—	—	20 (15)	—	22 (19.9)
Cinà et al. (2002) ¹⁶	42	69 ^a	17 (40.4)	—	4 (9.5)	2 (1.8)	2 (4.8)
LeMaire et al. (2001) ¹⁹	207	—	—	—	—	11 (5.4)	8 (3.9)
Schwartz et al. (1996) ²⁰	58	70	16 (28)	—	5 (8.8)	1 (1.9)	2 (5.3)

Note. KDOQI = kidney disease outcome quality initiative.

^a Mean age for all types of aneurysm; mean age of type IV not detailed.

morbidity. The role of hybrid open and endovascular repair for TAAAs is slightly less clear. A recent meta-analysis for hybrid repairs (types I–V) demonstrated a dialysis requirement of 8.8%.²⁹

Limitations

The main limitation of this study is the retrospective design. Results are available only from operated patients, potentially introducing selection bias of those patients fit enough to undergo a major operation. Renal function was assessed using serum creatinine derived from blood tests taken postoperatively, at clinic visits, and GP practice records. As a consequence, the interval between operation and creatinine measurement was variable between patients. Measures of renal function, such as inulin clearance, may be more accurate in the prospective setting. Another limitation of the retrospective study design was the inability to obtain >1 year renal function results in six patients, mainly as a result of mortality within the follow-up period (four patients).

We feel that a centralised, high-volume centre with specialised anaesthetic and surgical techniques and peri-operative management, as well as rigorous patient assessment and selection, is key in obtaining these positive renal outcomes. Given the mixed long-term renal outcomes following hybrid and totally endovascular repair of type IV TAAAs, we advocate that open repair remains the standard to which these newer methods are compared.

FUNDING

None.

CONFLICT OF INTEREST

None.

Note. M/F = male/female; CT = computed tomography; eGFR = estimated glomerular filtration rate.

Note. Comparison using Wilcoxon rank signed test. IQR = interquartile range.

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