The Mid-term Effect of Bare Metal Suprarenal Fixation on Renal Function Following Endovascular Abdominal Aortic Aneurysm Repair

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Objective. The aim of this study was to assess the mid term effect of proximal bare metal fixation design on renal function in patients undergoing endovascular repair (EVR) of abdominal aortic aneurysm (AAA).

Methods. Consecutive EVR patients for AAA from December 1995-2001 were included and grouped to either infrarenal (Group 1) or uncovered suprarenal (Group 2) fixation. Peri-operative renal function and at 6, 12 and 24 months was determined by serum creatinine (sCr mmoll⁻¹) and Cockroft-Gault creatinine clearance (CrC mlmin⁻¹). Changes in renal function were compared using non-parametric analysis.

Results. Of the 179 EVR procedures during this six-year period, paired renal data was available for 135 patients at a minimal follow-up of 6 months (Gp1, n = 63; Gp2, n = 72). Median pre-EVR sCr and CrC were 113, 57 in Group 1 and 108, 58 in Group 2, p = NS. There was no significant deterioration in renal function within or between either group at 2 years post-EVR; median sCr, CrC values were 118, 56 (Group 1) and 111, 56 (Group 2), all p = NS.

Conclusion. This study suggests mid-term renal function remains unaffected following EVR of AAA, irrespective of proximal fixation type. Designs to improve stent durability and EVR applicability do not appear to compromise renal function.

Keywords: AAA repair; Endovascular repair; Renal function; Suprarenal fixation; Transrenal fixation; Stenting.

Introduction

A specific adaptation designed to improve the suspect long-term durability of early endografts¹,² for AAA repair has been the addition of an uncovered bare metal stent to allow supra-renal fixation.³–⁵ There are a few potential advantages of this EVR device scheme. Firstly, an enhanced seal may be achieved in native non-aneurysmal supra-renal aortic tissue, reducing the chance of late failure due to device migration and proximal endoleak.⁶,⁷ This is of particular importance in view of published concern regarding continued infra-renal neck dilatation post-EVR.⁸–¹⁰ Secondly, these endografts may in fact improve patient eligibility for EVR in cases of adverse neck morphology, since less infra-renal neck is required to generate an adequate seal.¹¹,¹²

The deployment of bare metal stents across the renal artery ostia raises concern regarding subsequent kidney function. Review of the current literature would suggest that this practice is safe at least in the short-term,⁶,¹²⁻²⁴ but little data exists to confirm this safety in the longer term. The aim of this study was to examine our own EVR experience and assess the consequence of SR-fixation on delayed renal function.

Patients and Methods

One hundred and seventy-nine consecutive patients undergoing EVR for AAA at a single centre over a six-year period (December 1995-December 2001) were identified from a prospectively maintained endovascular database. All case-notes were reviewed and patients alive between 6 months and 2 years post-EVR were recalled.

Patients’ sex, age, weight, AAA size (maximal antero-posterior CT projection) and renal function were recorded both pre- and post-operatively (peak value) and at each subsequent follow-up interval of 6, 12 and 24 months. Procedural variables included device type and radiological contrast load. In order to assess any renal effect of fixation-type, the series was divided into two groups depending upon whether they had received infra-renal (IR, Group 1) or suprarenal fixed devices (SR, Group 2). Supra-renal fixation was defined as the presence of a bare-metal stent segment across both renal artery ostia with a proximal seal generated in the native supra-renal
aorta. The initial decision as to which device to use, was based primarily on endograft availability at the
time of AAA repair, with the IR devices tending to
be implanted prior to the availability of the SR de-
vices. In other words, the two study groups were vir-
tually consecutive in chronology with the earlier EVR
cases almost exclusively Group 1 (IR) and the latter
patients receiving Group 2 devices (SR).

Assessment of renal function was based on the clin-
cally used biochemical marker of serum creatinine (sCr/\mu\text{mol}^{-1}). Paired renal data was available for 135
patients from the entire series at a minimal follow-up
time of 6 months. Serum creatinine samples were ana-
ysed on an Olympus 2700 multi-channel analyser
(Jaffé reaction-based) using the manufacturers sup-
plied reagents (Olympus Instruments, London), pro-
viding a between-batch imprecision of less than 2%
for each analyte. Creatinine clearance (CrC/mlmin^{-1})
values were then derived using the well validated
Cockroft-Gault formula^{25} with a gender correction fac-
tor (multiplication by 0.85) applied for female patients.

Data Analysis

All study information was anonymised and stored
within a Microsoft Excel (Microsoft Ltd., Reading,
UK) spreadsheet. Relevant data was exported to Mini-
tab Version-13 for Windows (Minitab Inc., PA, USA)
software package for statistical and graphical analy-
sis. Unless indicated, median values are quoted for
continuous variables. Presentation of renal data is by
means of serial box-and-whisker plots.

Observational comparisons with non-continuous
data were made using the chi-square test ($\chi^2$). The
one-sample Wilcoxon test was used to compare
paired non-parametric continuous variables (i.e.
within group) and Mann-Whitney U-test for 2-sample
(i.e. between group) non-parametric analysis. A Bon-
ferroni correction factor was applied in both tests for
repeated observations. Results were considered statis-
tically significant if $p < 0.05$. The term ‘NS’ denotes not
statistically significant.

Results

One hundred and seventy-nine patients underwent
EVR for AAA within the six-year study period. Eighty-
seven cases were IR-fixed stents (Group 1) and the
remaining 92 patients had SR-fixed devices (Group 2).

Pre-operative status

Group-specific patient demographics, aneurysm size
and pre-operative renal function (sCr and CrC) for
the entire series are shown in Table 1. The age range
and sex distribution of the study limbs were analo-
gous. The aneurysms of Group 2 were significantly
larger than those repaired with infra-renal fixed devices ($p = 0.001$).

Thirty-eight patients (Group 1, $n = 23$; Group 2,
$n = 15$, $p = \text{NS}$) were noted to have occult renal impair-
ment indexed by a serum creatinine $> 130$ $\mu\text{mol}^{-1}$
pre-operatively. No patients were receiving renal
replacement therapy (RRT) pre-EVR.

Early outcome & Renal function

Stent deployment was technically successful in all
cases with no intra-operative deaths. Endograft type
for both groups is summarized in Table 2. Contrast
load during EVR was significantly higher in Group
1 (median 300 ml, range 100–900 ml) as opposed to
the later Group 2 cases (median 230 ml, range 110–
800 ml, $p = 0.01$). The procedural mortality (both in-
hospital and 30-day) for the entire series was 4.5%
(8 of 179 cases). Fixation-specific EVR mortality
was not significantly different: 5.7% for Group 1
(5/87; 3 Vanguard & 2 Talent devices) and 3.3% for
Group 2 (3/92). Apart from one fatal CVA in a pa-
tient receiving a Vanguard device, the documented
cause of death in all other cases was myocardial
infarction.

No significant difference in sCr was detected post-
EVR to either corresponding pre-operative values or
between the two groups. Using the Cockroft-Gault
formula, group specific CrC values were calculated
as a surrogate estimate for GFR in the peri-operative
phase. Again, there was no significant difference in
CrC either within, or between the groups pre and
post-operatively (see Fig. 1).

Table 1. Pre-EVR demographic factors & renal function

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (IR)</th>
<th>Group 2 (SR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>73</td>
<td>74</td>
</tr>
<tr>
<td>Range</td>
<td>56–87</td>
<td>56–90</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>78:9</td>
<td>82:10</td>
</tr>
<tr>
<td>AAA diameter (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>60</td>
<td>65*</td>
</tr>
<tr>
<td>IQR</td>
<td>55–70</td>
<td>58–78</td>
</tr>
<tr>
<td>Range</td>
<td>45–145</td>
<td>41–100</td>
</tr>
<tr>
<td>sCr ($\mu\text{mol}^{-1}$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>113</td>
<td>108</td>
</tr>
<tr>
<td>Range</td>
<td>72–243</td>
<td>75–307</td>
</tr>
<tr>
<td>CrC (mlmin^{-1})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>57</td>
<td>58</td>
</tr>
<tr>
<td>Range</td>
<td>22–102</td>
<td>22–139</td>
</tr>
</tbody>
</table>

*($p < 0.05$)
Renal replacement therapy (namely CVVH) in the early post-operative period was required by 2 patients, one from each group. In Group 1, a patient with a functionally impaired single kidney (pre-operative sCr $243 \text{ mmol/L}$) became anuric post-EVR with established renal failure reflected by a peak sCr of $461 \text{ mmol/L}$. After temporary CVVH in the initial post-operative period, he returned to his pre-operative renal state with 12-month sCr value of $264 \text{ mmol/L}$.

In Group 2, a patient with pre-existing diabetic nephropathy required RRT post-operatively following the development of acute-on-chronic renal failure (pre-operative sCr $206 \text{ mmol/L}$; post-operative sCr $630 \text{ mmol/L}$). This was precipitated by a peri-operative myocardial infarction with subsequent cardiogenic shock and multi-organ failure. The patient died six days post-EVR.

Inadvertent single renal artery occlusion occurred during stent deployment in two EVR procedures (both Group 2). This insult was reflected in higher post-EVR peak sCr measurements of 125 and $142 \text{ mmol/L}$ (pre-operative sCr: 91 and $96 \text{ mmol/L}$ respectively). Nevertheless at 24-month follow-up, no RRT had been necessary in either patient.

Of the 179 cases included in the study, paired renal data was available for 135 patients at a minimal follow-up time of 6 months (Group 1, $n = 63$; Group 2, $n = 72$). Omitted patients had either died within 6 months of EVR ($n = 16$), lost to follow-up ($n = 11$) or were not reviewed nor blood sampled at a correct time interval post-EVR ($n = 17$).

At 6, 12 and 24-month review, patients of both Groups had no significant elevation in sCr compared to their pre-operative status (see Fig. 2). Similarly, there was no difference between the IR and SR groups at each follow-up time interval. Group specific mid-term creatinine clearance following EVR is illustrated in Fig. 3. CrC remained remarkably constant over the 2-year study, regardless of fixation type. Comparison of these GFR estimates between both study limbs at each defined time-point confirmed no significant differences in delayed CrC post-EVR.

There were 3 cases of evolving chronic renal failure post-operatively in the series. The Group 1 case concerned a patient who received a Vanguard device and was noted to have an increasing sCr over the first year’s follow-up (pre-op sCr 129 $\text{ mmol/L}$, 12-month sCr 212 $\text{ mmol/L}$) in the absence of other renal disease processes. A renal biopsy was performed which revealed evidence of cholesterol embolization, most likely as a complication of EVR. At last review the patient was clinically well and not requiring RRT. In Group 2, one patient with recognized diabetic nephropathy (pre-EVR sCr 235 $\text{ mmol/L}$) was found at first annual follow-up to have a sCr of 318 $\text{ mmol/L}$.

### Table 2. Group-specific EVR devices

<table>
<thead>
<tr>
<th>Device Type</th>
<th>Group 1 (IR)</th>
<th>Group 2 (SR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vanguard (Boston Scientific)</td>
<td>49</td>
<td>–</td>
</tr>
<tr>
<td>Talent (WMC/Medtronic)</td>
<td>13</td>
<td>–</td>
</tr>
<tr>
<td>Excluder (Gore)</td>
<td>8</td>
<td>–</td>
</tr>
<tr>
<td>Endologix (Powerlink)</td>
<td>5</td>
<td>–</td>
</tr>
<tr>
<td>Other (AneuRx, EVT, Mintec)</td>
<td>12</td>
<td>–</td>
</tr>
<tr>
<td>Zenith (Cook)</td>
<td>–</td>
<td>92</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>87</strong></td>
<td><strong>92</strong></td>
</tr>
</tbody>
</table>

**Mid-term renal function**

Fig. 1. Peri-EVR Creatinine Clearance (all $p = \text{NS}$). Boxes represent the inter-quartile range and connect bar indicates median value. Whiskers define the 90% range. Statistical analysis by the 1-sample Wilcoxon (within group) and Mann Whitney (between group) tests with Bonferroni correction.

Fig. 2. Fixation Specific Late Serum Creatinine (all $p = \text{NS}$). Boxes represent the inter-quartile range and connect bar indicates median value. Whiskers define the 90% range. Statistical analysis by the 1-sample Wilcoxon (within group) and Mann Whitney (between group) tests with Bonferroni correction.
An angiogram was obtained for further investigation, but no evidence of renal artery stenosis was found. The patient is currently under close review by the nephrologists with no RRT. The other patient with a SR device was commenced on haemo-dialysis 3 months post-EVR for progressive renal dysfunction attributed to known polycystic kidneys.

**Discussion**

The incidence of renal dysfunction post-EVR is reported at approximately 6% and this is notably higher in those patients with pre-operative renal impairment.\(^{26}\) Although the exact cause of this complication is unclear, implicated factors include radiological contrast-associated nephropathy, renal artery trauma, stent-induced stenosis and aortic neck thromboembolism following vessel instrumentation and manipulation.\(^{12,20}\) All of these features are generic to EVR, irrespective of graft configuration.

Since the concept of uncovered supra-renal fixation was first proposed, concern has naturally persisted with respect to its potential additive adverse effect on renal function. Preliminary laboratory studies with animal models suggested that the placement of bare metal stent struts across the renal artery ostia was indeed safe at least in the short-term,\(^{27,28}\) and introduction of the practice to man soon followed.

The Lund Group published the earliest report of renal outcome following SR-fixed EVR in humans in 1997. In this study, 18 patients underwent EVR of AAA with deliberate Gianturco Z-stent deployment across one or both renal artery ostia to improve graft durability. At median follow-up of 6 months, all of the 25 stent-covered renal arteries remained patent (imaged by spiral CT and angiography) and no elevation in the cohorts’ sCr was observed.\(^{13}\)

Since this seminal paper, several independent groups have addressed the issue of renal function following EVR with uncovered bare metal supra-renal fixation (see Table 3).\(^{6,12,14--24,29}\) Despite varying biochemical and radiological methods for analysis, there is currently no evidence suggesting that these endografts are associated with any clinically significant renal compromise.

In this retrospective study we compared the renal outcome in patients undergoing EVR with devices utilizing either IR or SR fixation by serial measurement of the biochemical markers sCr and Cockroft-Gault formulated CrC. We acknowledge the physiological and analytical limitations of sCr methods,\(^{30,31}\) but their measurement permits an appraisal of renal excretory function, which is generally accepted as the best clinical estimate of functional renal mass.\(^{32,33}\) Furthermore, it is these indices of kidney function that tend to be routinely used in daily clinical practice.

The two study limbs were comparable in terms of age, sex distribution and pre-operative renal function. No patient in either group required renal replacement therapy pre-operatively. The significantly larger aneurysms of Group 2 reflected both the non-randomized nature of the study and the chronological fact that the first SR device at our institution was not deployed until September 1998, nearly 3 years (and 60 IR devices) after our EVR program had commenced. As a result, Group 2 patients had the benefits of clearer AAA management guidelines,\(^{34}\) latest device technology and finally the considerable accrued procedural experience of the EVR team i.e. a completed learning curve. The decision regarding the nature of device used (i.e. infrarenal or suprarenal) was dependant on both the aneurysms’ morphological suitability determined by contrast-enhanced CT scanning and the commercial availability of specific suitable devices at the time of implantation. Patients were not randomized in this study to one specific treatment limb, rather to the most clinically appropriate, cost-effective stent available to them at that particular time.

Although the recently published UK EVAR and Dutch DREAM trials reported a more favourable early survival,\(^{35,36}\) this particular series included those patients pre-dating EVAR trial recruitment (commencing early 1999) and also higher-risk individuals who may with hindsight have been better managed conservatively. In spite of this, no deaths were documented as directly due to an acute renal cause.
Analysis of sCr and CrC values suggest preserved peri-operative and mid-term renal function, regardless of the presence or absence of uncovered bare metal graft struts across the renal artery ostia. Despite no formalized renal protection policy within the unit, all those patients with ‘renal impairment’ (abnormally elevated sCr in the absence of RRT) underwent careful intravenous fluid optimization with routine urinary catheterisation and central venous monitoring where appropriate. If possible, the administration of any contrast agent prior to EVR (within 2 weeks) was avoided and the volume used during EVR was restricted to the minimum required. Although it was not the policy of this unit to routinely prescribe putative ‘reno-protective’ agents such as dopexamine or mannitol, a peri-operative intravenous infusion was commenced if clinically indicated. An additional intra-operative measure taken to minimize renal injury is the angiographic imaging of the renal arteries following partial stent deployment. This permits confirmation of correct device positioning prior to complete release in order to reduce the incidence of renal artery occlusion by the covered segment of the stent. The technique is not completely failsafe and we observed two cases of deployment error in the series (both Zenith devices) with cranial slip after imaging and subsequent single renal artery occlusion. Fortunately, apart from an observed elevation in the sCr of both cases there have been no other clinically significant renal sequelae to this point.

In their series of 315 patients with a mean follow-up of 30.1 months, the Nottingham group report renal outcome following EVR for both ruptured and elective AAA. Pre-EVR renal impairment was defined as sCr $> 130 \mu\text{moll}^{-1}$ and/or long-term dialysis. Significant post-operative renal dysfunction was referred to as a 20% increase in sCr from baseline in patients with a ‘normal’ sCr pre-EVR and additional deterioration in sCr in those with pre-operative renal impairment ($n = 69, 21.9\%$). They concluded that it was only the presence of pre-operative renal failure and not the use of SR fixation that was associated with the permanent post-operative renal dysfunction detected in 9.2% of EVR patients. Although not a formal sub-group analysis, application of the Nottingham renal criteria to our study reveals a comparable rate of pre-operative renal impairment of 21.2% (38 of 179 cases with sCr $> 130 \mu\text{moll}^{-1}$ and none receiving long-term dialysis). Group specific renal failure is not significantly different (Fisher exact test): 2.3% for Group 1 (2/87) and 6.5% (6/92) for Group 2. These results are only slightly inferior to the 5% permanent renal dysfunction rate reported by Izzedine et al. following SR-EVR.

Table 3. Summary of Renal studies post Supra-renal EVR

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of SR-EVR</th>
<th>Mean/Median Follow-Up (months)</th>
<th>Renal Assessment</th>
<th>No. IR ‘controls’</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malina et al. 1997</td>
<td>18</td>
<td>6</td>
<td>sCr</td>
<td>Spiral CT</td>
<td>13</td>
</tr>
<tr>
<td>Marin et al. 1998</td>
<td>37</td>
<td>10.3</td>
<td>sCr</td>
<td>CT Angiography</td>
<td>6</td>
</tr>
<tr>
<td>Kichikawa et al. 2000</td>
<td>18</td>
<td>14</td>
<td>BUN</td>
<td>Duplex Angiography</td>
<td>16</td>
</tr>
<tr>
<td>Bove et al. 2000, 2003</td>
<td>28, 37</td>
<td>6, 29</td>
<td>sCr</td>
<td>Duplex CT Angiography</td>
<td>18,22</td>
</tr>
<tr>
<td>Lobato et al. 2000</td>
<td>35</td>
<td>11</td>
<td>sCr</td>
<td>CT</td>
<td>15</td>
</tr>
<tr>
<td>Izzedine et al. 2002</td>
<td>39</td>
<td>6, 30</td>
<td>sCr CrC (Cockroft-Gault)</td>
<td>Duplex Renal Tomography</td>
<td>19</td>
</tr>
<tr>
<td>Kramer et al. 2002</td>
<td>69 ‘overstented renal arteries’</td>
<td>12</td>
<td>sCr CrC (Cockroft-Gault)</td>
<td>Spiral CT ‘124 uncovered arteries’</td>
<td>14</td>
</tr>
<tr>
<td>Mehta et al. 2004</td>
<td>111</td>
<td>19</td>
<td>sCr CrC (Cockroft-Gault)</td>
<td>CT</td>
<td>385</td>
</tr>
<tr>
<td>Alric et al. 2003</td>
<td>169</td>
<td>30</td>
<td>sCr CrC (Cockroft-Gault)</td>
<td>–</td>
<td>146</td>
</tr>
<tr>
<td>Cayne et al. 2003</td>
<td>69</td>
<td>17</td>
<td>sCr CrC (Cockroft-Gault)</td>
<td>Contrast enhanced CT</td>
<td>61</td>
</tr>
<tr>
<td>Lau et al. 2003</td>
<td>32</td>
<td>12</td>
<td>sCr CrC (Cockroft-Gault)</td>
<td>CT Angiography</td>
<td>57</td>
</tr>
<tr>
<td>Surowiec et al. 2004</td>
<td>60</td>
<td>23</td>
<td>sCr CrC (Cockroft-Gault)</td>
<td>Contrast enhanced CT</td>
<td>53</td>
</tr>
<tr>
<td>Grego et al. 2004</td>
<td>47</td>
<td>16</td>
<td>sCr CrC (Cockroft-Gault)</td>
<td>99Tc-DTPA</td>
<td>–</td>
</tr>
<tr>
<td>Parmer et al. 2006</td>
<td>91</td>
<td>7.3</td>
<td>sCr CrC (Cockroft-Gault)</td>
<td>CT Angiography</td>
<td>192</td>
</tr>
</tbody>
</table>

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Much recent interest has focused on the potential application of a low molecular weight protein, cystatin C as a marker of renal function. It has been validated by various gold-standard clearance analyses that are inappropriate for routine clinical use, and shown to be superior to sCr measurement in this respect. Contrary to sCr, serum cystatin C levels remain unaffected by the physiological variables of sex, muscle mass and dietary intake. Finally and most importantly, significant increases in serum cystatin C have been reported with minimal, currently subclinical mild GFR reduction, allowing a more sensitive and possibly an earlier detection of renal dysfunction than with sCr methods. In view of this, its measurement in a prospective study assessing the potential silent renal injury following SR-EVR is proposed.

In conclusion, this present work adds further supporting biochemical evidence that EVR in the treatment of AAA is indeed safe for the kidneys to mid-term follow-up. Furthermore, this preservation of renal function is independent of proximal fixation designs incorporating uncovered supra-renal fixation. This modification in endograft design to improve both the durability and applicability of EVR in AAA management is not apparent at the expense of mid-term renal function.

References


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