Does Gender Influence Outcome of AAA Endoluminal Repair?

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Background: it has been suggested that female patients have a less favourable outcome of endoluminal repair of abdominal aortic aneurysms. Yet, data on stratified per gender are lacking.

Methods: we reviewed our prospective database of 402 endografts over a 4-year period and the peri- and postoperative course in the 25 (6%) female patients was compared with the 377 (94%) male patients. Median follow-up was 24 months (range 1–56 months). Logistic regression analysis was performed to test the effect of five confounding variables (gender, age, ASA grade IV, EUROSTAR class D or E, AAA diameter) on failure of AAA exclusion.

Results: there were no perioperative deaths in the female group and 5 (1.3%) in the male group (p ‡ 0.8). Major perioperative morbidity occurred in 17% versus 6% (OR 3.7; 95% CI 1.2–10.6; p = 0.026). There were 1 (4%) and 5 (1%) conversions to open repair in the female and male groups, respectively (p = 0.3). Late failure of AAA exclusion occurred in 5 (21%) and 26 (7%) patients, respectively (p = 0.03). Of the five variables examined for their influence on failure of AAA exclusion, female gender (hazard ratio 4.42; 95% CI 1.4–13.4; p = 0.009) and AAA diameter (hazard ratio 1.05; 95% CI 1.009–1.09; p = 0.017), were positive independent predictors of late failure of AAA exclusion on multivariate analysis.

Conclusion: endoluminal AAA repair in female patients appear associated with a less favorable outcome when compared to their male counterparts. These data may be taken into consideration when endoluminal AAA repair is suggested to a female patient.

Key Words: Gender; Aortic aneurysm; Endovascular.

Introduction

Despite an increased interest in abdominal aortic aneurysm (AAA) Endovascular Repair (EVAR) outcome data, few studies have addressed specifically the issue of whether gender might represent a proxy for other confounding variables in EVAR outcomes. It is well known that there are gender differences in the prevalence and severity of arterial disease. This difference is supported by the increased prevalence of aneurysms and occlusive disease in men as compared with women.1–4 Evidence also exists that gender difference in the prevalence of disease is accompanied by different treatment outcome.4–7 However, whether gender-related differences in arterial morphology may preclude applicability and technical success of aortic endografting in women, remains controversial.

The aim of this study was to determine whether women are at increased risk of early and late failure after EVAR.

Patients and Methods

Between April 1997 and April 2002, 402 consecutive patients underwent elective EVAR for AAA at our Unit and represent the cohort of the present study. Twenty-five patients (6%) were female and were compared with 377 (94%) male patients. Median follow-up was 24 months (range 1–56 months). Preoperative, operative, and follow-up data were prospectively collected. Indications for treatment of AAA at our Unit included AAA of 5 cm or greater, or AAA 4 cm that increased rapidly in size (>0.5 cm in the previous 6 months), or became tender, or associated with an iliac aneurysm greater than 3 cm. AAA diameter at computed tomography (CT) was assessed considering the maximum external diameter of the vessel. Measurements were always carried out at the widest portion of the aneurysm. When the aneurysm circumference had an elliptical shape, the smaller diagonal was considered, thus avoiding errors in size evaluation due to aortic tortuosity.8 Selection criteria for EVAR included a proximal aneurysm neck length of 15 mm or greater and a neck diameter of 30 mm or less, aortic neck angulation <75°, iliac artery of >7 mm in diameter without excessive tortuosity, calcification, or stenosis.

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Anatomical features were evaluated by a combination of pre-procedural imaging techniques including contrast-enhanced, conventional, or spiral CT scan with 5 mm cuts or less, color duplex scan, and angiography or angio-magnetic resonance with gadolinium. Aneurysm extension was recorded according to the EUROSTAR classification.9

The AneuRx stent graft (Medtronic, Santa Rosa, CA, U.S.A.) was implanted in 231 procedures, the Excluder (WL Gore and Associates, Flagstaff, AZ, U.S.A.) in 53, the Talent graft (World Medical-Medtronic, Sunrise, FL, U.S.A.) in 51, the Zenith graft (William Cook Europe, Biaeverskow, Denmark) in 52, the Anaconda in 11 (Sulzer Vascutek, Edinburgh, U.K.), Endologix (Bard, Irvine, CA, U.S.A.) in 3, Endofit (Endomed, Phoenix, AZ, U.S.A.) in one. Endograft configuration included three tubes, 393 bifurcated grafts, and six aortouniliac grafts combined with contralateral iliac occlusion and femoral–femoral bypass.

EVAR was performed in an operating room by a team of vascular surgeons and interventional radiologists under general or epidural anesthesia. The decision to perform epidural anesthesia was left to the discretion of the anesthesiologist and/or patient choice.

Intraoperative radiological imaging was performed with a portable C-arm fluoroscopic device (9000 OEC, Diasonics) with digital imaging and road mapping capability on a compatible operating table. Initial assessment of endograft function and position, and verification of satisfactory exclusion of the AAA were evaluated by intraoperative post-deployment angiography, pre-discharge color duplex scan and plain abdominal radiographs.

Physical examination, color duplex scan, and plain abdominal radiography were repeated at 1, 6, 12 months after the procedure and annually thereafter. Contrast-enhanced CT scan was repeated 1 month after surgery and then annually.

Outcome measures were survival, early failure (i.e., death or conversion within 30 days) and late failure of AAA exclusion (i.e., AAA rupture, conversion to open repair, increase in AAA diameter ≥3 mm after ER or persisting graft-related endoleak). Other outcome measures included major perioperative morbidity (i.e., life threatening complications and those resulting in permanent injury or disability or arterial occlusion that occurred within 30 days after procedure), blood loss, operative time, and length of hospital stay. Endoleak detected either on CT or color duplex scan was defined as the presence of contrast enhancement or color and doppler signal within the aneurysmal sac and outside the endograft, respectively.10

Comparison between male and female patients was performed by the two-sample t-test for continuous variables and chi-squared or Fisher exact test for discrete variables. Life table method with log rank test for significance was used for survival. The influence of five confounding variables (gender, age, ASA grade, EUROSTAR class D or E, AAA diameter) on outcome measures was tested by Cox regression analysis. Statistical analysis was conducted with SPSS software (SPSS Inc., Chicago, IL, U.S.A.). p ≤ 0.05 was considered statistically significant.

There were no perioperative deaths in the female group and five (1.3%) in the male group (p = 0.8), one due to intraoperative aortic neck rupture. Clinical and anatomical features of male and female patients are shown in Tables 1 and 2.

There was one (4%) perioperative conversion to open repair in the female group while five (1.3%) conversions were performed in the male group (p = 0.3). Intraoperative details stratified per study groups are displayed in Table 3. Overall perioperative major morbidity rate was 6.2%. Major perioperative morbidity occurred in five (17%) female patients and in 20 (5.7%) male patients (OR 3.7; 95% CI 1.2–10.6; p = 0.026); causes of morbidity are displayed in Table 4.

### Table 1. Risk factors in 402 patients.

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>%</th>
<th>Male</th>
<th>%</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>25</td>
<td></td>
<td>377</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age</td>
<td>75.3</td>
<td>71.3</td>
<td>0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>10</td>
<td>40</td>
<td>230</td>
<td>61</td>
<td>0.03</td>
</tr>
<tr>
<td>Hypertension</td>
<td>22</td>
<td>88</td>
<td>238</td>
<td>63</td>
<td>0.02</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2</td>
<td>8</td>
<td>33</td>
<td>9</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>13</td>
<td>52</td>
<td>182</td>
<td>48</td>
<td>NS</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>12</td>
<td>48</td>
<td>203</td>
<td>54</td>
<td>NS</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>2</td>
<td>8</td>
<td>41</td>
<td>11</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS, not significant.

### Table 2. Anatomical features in 402 patients.

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>%</th>
<th>Male</th>
<th>%</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>n</td>
<td>25</td>
<td></td>
<td>377</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean AAA diameter</td>
<td>52.2</td>
<td>50.8</td>
<td>0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mm (range)</td>
<td>(40–86)</td>
<td>(40–84)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EUROSTAR class D or E</td>
<td>3</td>
<td>10</td>
<td>58</td>
<td>15</td>
<td>NS</td>
</tr>
<tr>
<td>Severe iliac calcification</td>
<td>4</td>
<td>14</td>
<td>53</td>
<td>14</td>
<td>NS</td>
</tr>
<tr>
<td>Proximal neck thrombus</td>
<td>1</td>
<td>3</td>
<td>32</td>
<td>8</td>
<td>NS</td>
</tr>
<tr>
<td>Short proximal neck (&gt;1.5 cm)</td>
<td>2</td>
<td>7</td>
<td>35</td>
<td>9</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS, not significant.
At a median follow-up of 24 months (range 1–56 months), overall late mortality occurred in 42 patients (9.5%): three patients (12%) died in the female group and 39 (11%) in the male group. Causes of late mortality included three AAA ruptures, seven cardiac failures, one bowel occlusion, one pulmonary embolism, eight myocardial infarctions, 11 cancers, two traumas, one renal failure, one suicide, two strokes, three respiratory insufficiencies, one intracranial haemorrhage, and one bleeding duodenal ulcer. Survival at 42 months was 83.5% in women and 79.1% in men based on Kaplan–Meier analysis (Fig. 1).

Late failure of AAA exclusion occurred in five patients (21%) in the female group and in 26 patients (7%) in the male group (p = 0.03). Causes of late failure listed for male and female patients are displayed in Table 5.

Overall, 4 AAA ruptures occurred: all associated with secondary endoleak (one of Type I and three of Type III) not evident on the first postoperative CT scan; two of the patients had refused subsequent follow-up examinations prior to AAA rupture. Elective late conversion to open repair was performed in 14 patients: two in the female group (8%) and 12 (3.1%) in the male group. Conversion was not accomplished in two patients with persisting Type I endoleak, because one patient refused open treatment while the other died for congestive heart failure before the planned conversion. AAA growth (>3 mm) occurred in 18 patients, seven required treatment. Growth by itself was not considered an indication for conversion in 11 patients because it ranged between 3 and 5 mm and was not associated with endoleak or other abnormalities suggesting impending graft failure.

Of five variables examined for their influence on failure of AAA exclusion, female gender (hazard ratio 4.42; 95% CI 1.4–13.4; p = 0.009) and AAA diameter (hazard ratio 1.05; 95% CI 1.009–1.09; p = 0.017), were positive independent predictors of late failure of AAA exclusion on multivariate analysis. AAA diameter was also found the only independent predictor of early failure (hazard ratio 1.05; 95% CI 1.009–1.09; p = 0.017). Female gender (hazard ratio 3.2; 95% CI 1.02–10.2; p = 0.04), age (hazard ratio 1.07; 95% CI 1.01–1.14; p = 0.03) and EUROSTAR Class D or E (hazard ratio 2.5; 95% CI 1.04–6.3; p = 0.04) were positive independent predictors of perioperative complications.

Cumulative probability of failure at 42 months was 28% in female patients and 14% in men (p = 0.01) (Fig. 2).

**Discussion**

Although the number of endoluminal procedures for AAA has increased considerably in the recent years, the proportion of operations on women has remained
Our data indicate that although female patients undergoing EVAR are at no greater risk of perioperative death or conversion, they are at greater risk of major intra-operative complications. Late results in women were not comparable with those recorded in men. Some differences may be due to the discrepancy in numbers of men with respect to female patients. In general AAA occurs five to six times more commonly in men than in women. Consequently, many series of patients with AAA undergoing endovascular or open repair include a relatively small number of women.

In our series freedom from failure was 72% for female and 86% for males undergoing EVAR at 42 months, a difference that reached statistical significance ($p = 0.01$). Analysis beyond 42 months was not performed with Kaplan–Meier analysis, as the number of endovascular patients with >4-year follow-up was small. It is possible that the female gender has more than a propensity for complex aortic aneurysm morphologic features. In general women are known to have smaller arteries. EVAR eligibility rate with respect to men is controversial. Previous studies using different type of aortic devices showed conflicting conclusions: Carpenter et al. in analysing exclusion criteria for EVAR on 307 patients (43 women), found a disproportionate number of women were to be excluded because of anatomic findings (24/43), the most determinant of which was the aneurysm neck. Similar conclusions were detected by Velazquez et al. who found the proximal neck significantly wider, shorter and angulated in women than in men undergoing EVAR with Ancure or Talent endografting. In addition, the authors found a significant smaller diameter in iliac arteries among female. Based only on unsuitable anatomy for EVAR, rejection rate was about two-fold for women than for men: 63.2% versus 38.6%. Differently, Wolf et al. analysing a different type of aortic device in 26 women and 161 men, concluded that the eligibility rate for women was lower but not significantly different from that of men: 49% versus 57%. However, women experienced more intraoperative complications (31% vs 13%, $p < 0.05$) primarily related to arterial access and needed more frequent arterial reconstructions. We did not found significantly morphological differences in women except for the AAA diameter that was significantly larger. Women were similar to men with respect to aortic neck characteristics, vessel calcification or aneurysmal extension (see Table 2). Although we did not measure specifically iliac external size, our female patients experienced only one intraoperative iliac artery rupture. Rupture occurred in an ASA IV female patient with severe cardiac disease (congestive heart failure after cardiac revascularization), 6 cm AAA and 3 cm common left iliac aneurysm. Endovascular repair was attempted with 32/15 mm Talent stentgraft using right side branch for principal access (right iliac femoral bypass). Unfortunately, left external iliac rupture occurred intraoperatively and a left iliac femoral bypass was immediately performed for repair.

Similarly, only one early conversion to open repair for impossibility to advance the device through the arterial tree was needed in the women subgroup. It is possible to hypothesize that arterial morphology may not have a role on early outcomes in female patients undergoing EVAR when an appropriate device was selected. Furthermore, in our experience, EVAR was not technically more demanding in women: special exposure techniques (e.g., iliac femoral conduit for access, etc.) were not more frequently employed in these patients with respect to male counterpart. EVAR in women did not require a higher number of extender cuffs nor longer procedural or fluoros times, greater contrast volumes or blood replacements than men (see Table 4). Obviously, we could not detect significant correlation between a particular brand device and EVAR complications for women patients, due to the wide variability of devices used in a small sample size.

From the analysis of our patient characteristics, women were older than men and showed aneurysms with a larger diameter. This may be the result of late diagnosis or late referral for surgical treatment in women with AAA. Likely, the older age and the more complex anatomical features may have played a key role on the higher peri-procedural morbidity and late technical failure rates. However, our numbers are too small to draw strong conclusions.

Women were more prone to late failure also after successful AAA repair was performed. We found that female patients undergoing EVAR had a four-fold higher risk of late failure than men. Although there
are a small number of reports focusing specifically on gender in endovascular AAA repair, our findings agree with other experiences. Bath et al., reporting data from a large registry on 1554 patients undergone EVAR (EUROSTAR), found that female gender and age <75 years were independent risk factors for primary endoleak (p = 0.02; OR 1.7; 95% CI 1.1–2.7 and p = 0.009; OR 1.9; 95% CI 1.3–2.9, respectively).\textsuperscript{15}

Because of the limited number of our female cohort and the relatively small size of aneurysm treated, our data confirm that large AAA diameter and female sex are independent positive predictors of late outcome of endovascular AAA repair (i.e., 5.5 cm). Our data justify a more aggressive repair also in women with AAA diameter smaller than common accepted threshold for repair (i.e., 5.5 cm).

In conclusion, gender influences the late outcome of EVAR. Women with AAA in our series were older with larger AAA diameter yet, their immediate EVAR success rate did not differ significantly from that of men. On the other hand, EVAR in female patients was associated with a significantly worse late outcome when compared to their male counterparts. These findings may be considered when suggesting endoluminal AAA repair to female patients.

References