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Chapter 9

Midterm reinterventions and survival after endovascular versus open repair for a ruptured abdominal aortic aneurysm

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On behalf of the Amsterdam Acute Aneurysm Trial Collaborators

Submitted
Abstract

Background
In elective aortic surgery, the midterm risk of reintervention is higher after endovascular aneurysm repair (EVAR) than after open repair (OR). In the present study we compared the reintervention and survival rates after EVAR and OR for ruptured abdominal aortic aneurysms (RAAA).

Methods
An observational cohort study was carried out including all consecutive surgically treated RAAA patients between 2004 and 2011 in ten hospitals in the Amsterdam ambulance region. The primary end points were reinterventions and death within five years after the primary intervention. The outcomes were estimated by Kaplan-Meier survival analyses and compared with use of the logrank test. Outcomes were estimated in all patients and in patients who survived their hospital stay.

Results
Of 467 patients with an RAAA, 73 were treated with EVAR and 394 with OR. Five years after primary intervention, the rates of freedom from reintervention were 49% for EVAR (30/73, 95% confidence interval (CI) 36 to 63%) and 60% for OR (128/394, 95% CI 55 to 66%, P=.31). The survival rates were 36% for EVAR (45/73, 95% CI 24 to 47%) and 38% for OR (235/394, 95% CI 33 to 43%, P=.83). In 297 patients who survived their hospital stay, the rates of freedom from reintervention were 66% for EVAR (15/54, 95% CI 52 to 81%) and 90% for OR (20/243, 95% CI 86 to 95%, P<.01). In these patients, the survival rates were 48% (26/54, 95% CI 34 to 62%) for EVAR and 62% for OR (84/243, 95% CI 56 to 69%, P=.04).

Conclusion
Five years after the primary intervention, endovascular and open repair for a ruptured abdominal aortic aneurysm resulted in similar reintervention and survival rates. However, in patients who survived their hospital stay the reintervention rate was higher for EVAR than for OR.
EVAR versus OR for RAAAs; midterm reinterventions and survival

**Introduction**

Patients with a ruptured aneurysm of the abdominal aorta (RAAA) can be treated with endovascular (EVAR) or open repair (OR). So far no significant difference in the 30-day death rate between these interventions has been reported in randomized controlled trials.\(^1\)\(^-\)\(^3\) For this reason midterm outcomes are starting to be of interest in the debate on whether EVAR or OR is to be preferred for patients with an RAAA.\(^2\)\(^-\)\(^6\) Midterm encompasses the period between the primary intervention and five years thereafter. In elective aortic surgery, the midterm risk of reintervention and aneurysm rupture is higher after EVAR than after OR.\(^6\) Midterm outcomes after acute intervention may also differ. Therefore, midterm outcomes may give new insights into the preferred intervention in patients with an RAAA or guide post-intervention surveillance strategies. In the present study we compared the reintervention and survival rates five years after EVAR and OR for an RAAA.

**Methods**

The present study was an observational cohort study and reports follow-up data from the previously published Amsterdam Acute Aneurysm (AJAX) trial which was conducted in the Amsterdam ambulance region which comprises ten hospitals and 1.38 million inhabitants.\(^3\)\(^,\)\(^7\) Between April 2004 and February 2011, all consecutive patients with an RAAA in the region were registered prospectively and of these, all who underwent surgical treatment were included in the present study. Only patients whose demographics or short-term outcome were unknown were excluded. Patients suitable for both EVAR and OR were randomized to either intervention in the AJAX trial. Details of patient identification, the randomization procedure and the informed consent procedure have been published previously.\(^3\)\(^,\)\(^7\) After discharge patients had routine follow-up according to local practice. EVAR follow-up included either yearly computed-tomographic angiography (CTA) or duplex ultrasound combined with plain abdominal x-ray.

The study was conducted in accordance with the principles of the Declaration of Helsinki and the present report includes all items recommended by the STrengthening the Reporting of Observational studies in Epidemiology (STROBE) statement.\(^8\)
End point
The primary end points were reinterventions and death within five years after the primary intervention. Reinterventions were defined according to the reporting standards. Indications for reinterventions were categorized as abdominal compartment syndrome, access site infection, anastomosis aneurysms, re-bleeding, bowel ischemia, endograft migration, endoleaks (type I – IV), false aneurysms, graft thrombosis or obstruction, graft infection, incisional hernia, ischemia of lower limbs, secondary aneurysm rupture, secondary symptomatic aneurysm and symptomatic adhesions.

Data collection
Data were collected up to January 2014 using Microsoft Office Access 2003 (Microsoft Corporation, Redmond, Washington, USA) and included field limits and multivariate checks. Dates of death were obtained stepwise from the hospital registries (1), from the registry of the general practitioner (2) or from the communal registry of death certificates (3). Data regarding reinterventions and their indications were collected from hospital medical records and the general practitioners were asked for information on reinterventions in other hospitals. Patients whose follow-up was unknown were censored in the analysis at the last point of contact. The data collection was done in the same way in patients treated with EVAR and OR.

Statistical analysis
Continuous data were described by the mean with corresponding standard deviation (SD) for data normally distributed, and by the median with corresponding inter-quartile range for data with a skewed distribution. Baseline characteristics were compared using the chi-square test and the Mann-Whitney U test (two-sided; \( \alpha = .05 \)). The reintervention and survival rates were estimated by Kaplan-Meier survival analyses and EVAR and OR compared using the logrank test. Reintervention rates were reported as freedom from reintervention with corresponding events and surrounding 95% confidence interval (CI). In the Kaplan-Meier survival analyses of the reintervention rates, patients who died were censored.

Two subgroup analyses were conducted. The first subgroup included patients who survived their hospital stay and the first 30 days after the primary intervention. The second subgroup included patients from the AJAX trial in whom
EVAR versus OR for RAAAs; midterm reinterventions and survival

treatment allocation was done using randomization. This subgroup analysis was

done according to the intention-to-treat principle.

**Results**

Between 2004 and 2011, 539 patients with an RAAA were admitted to one of the ten

hospitals in the Amsterdam ambulance region. Six patients whose demographics

or outcome were unknown and 66 patients without surgical intervention were

excluded from the analysis (Figure 1). The baseline characteristics of 467 patients

included in the analysis are shown per type of intervention in Table 1. Patients

treated with EVAR showed a tendency towards higher preoperative systolic blood

pressure (P=.07), and required less preoperative cardiopulmonary resuscitation

(P=.05). Five years after the primary intervention, the overall survival rate was

38% (280/467, 95% CI 33 to 43%) and the median follow-up was 2.2 years (inter-

quartile range 0.0-5.0 years). Eighteen patients (3 for EVAR, 15 for OR) were lost

to follow-up and censored at the last point of contact.

**Figure 1.** Flowchart of inclusion.

EVAR = endovascular aneurysm repair
Table 1. Baseline characteristics.  
CPR = cardiopulmonary resuscitation, SBP = systolic blood pressure

<table>
<thead>
<tr>
<th>Variable</th>
<th>EVAR (n = 73)</th>
<th>OR (n = 394)</th>
<th>P</th>
<th>Missing data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>76 (69-80)</td>
<td>76 (69-82)</td>
<td>.70 a</td>
<td>0</td>
</tr>
<tr>
<td>Male : Female</td>
<td>82% : 12% (64 : 9)</td>
<td>80% : 20% (314 : 80)</td>
<td>.11 b</td>
<td>0</td>
</tr>
<tr>
<td>Cardiac co-morbidity</td>
<td>48% (35/73)</td>
<td>42% (158/379)</td>
<td>.32 b</td>
<td>3% (15/467)</td>
</tr>
<tr>
<td>Pulmonary co-morbidity</td>
<td>27% (20/73)</td>
<td>20% (76/376)</td>
<td>.17 b</td>
<td>4% (18/467)</td>
</tr>
<tr>
<td>Renal co-morbidity</td>
<td>10% (7/73)</td>
<td>12% (45/377)</td>
<td>.57 b</td>
<td>4% (17/467)</td>
</tr>
<tr>
<td>Cerebrovascular co-morbidity</td>
<td>15% (11/73)</td>
<td>15% (58/378)</td>
<td>.95 b</td>
<td>3% (16/467)</td>
</tr>
<tr>
<td>CPR</td>
<td>4% (3/73)</td>
<td>12% (45/374)</td>
<td>.05 b</td>
<td>4% (20/467)</td>
</tr>
<tr>
<td>Lowest in-hospital SBP (mmHg)</td>
<td>90 (75-129)</td>
<td>90 (69-125)</td>
<td>.07 a</td>
<td>11% (50/467)</td>
</tr>
</tbody>
</table>

Continuous data are presented as median (inter-quartile range) and categorical data as percentage (number).  
a Mann-Whitney Test  
b Chi-squared statistic

All patients

Five years after the primary intervention, the rates of freedom from reintervention were 49% for EVAR (30/73, 95% CI 36 to 63%) and 60% for OR (128/394, 95% CI 55 to 66%, P=.31) (Figure 2A). The indications for the first reinterventions are shown in Table 2. The survival rates after five years were 36% for EVAR (45/73, 95% CI 24 to 47%) and 38% for OR (235/394, 95% CI 33 to 43%, P=.83) (Figure 3A).

Discharged patients

In 297 patients who survived their hospital stay, the rates of freedom from reintervention were 66% for EVAR (15/54, 95% CI 52 to 81%), and 90% for OR (20/243, 95% CI 86 to 95%, P<.01) (Figure 2B). In these patients, the survival rates were 48% for EVAR (26/54, 95% CI 34 to 62%) and 62% for OR (84/243, 95% CI 56 to 69%, P=.04) (Figure 3B).

Randomized patients

Of 467 patients included in the analysis, 113 were randomized between EVAR and OR in the AJAX trial and were studied in the subgroup analysis. Because of the intention-to-treat principle, 3 patients with a discharge diagnosis other than RAAA were also included in the AJAX trial and therefore added to the subgroup analysis. In patients who survived their hospital stay, the rates of freedom from reintervention were 63% for EVAR (13/41, 95% CI 47 to 80%) and 81% for OR (7/42,
EVAR versus OR for RAAAs; midterm reinterventions and survival

95% CI 68 to 94%, \( P=.14 \) (Table 3). The overall survival rates were 38% for EVAR (34/57, 95% CI 25 to 51%) and 42% for OR (33/59, 95% CI 29 to 55%, \( P=.81 \)).

**Table 2.** Indications of the first reintervention after EVAR and OR.  
EVAR = endovascular aneurysm repair, OR = open repair

<table>
<thead>
<tr>
<th>Condition</th>
<th>All patients</th>
<th>Patients who survived their hospital stay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal compartment syndrome</td>
<td>1 EVAR n = 73</td>
<td>0 OR n = 394</td>
</tr>
<tr>
<td>Access site infection</td>
<td>0 EVAR n = 73</td>
<td>0 OR n = 394</td>
</tr>
<tr>
<td>Anastomosis aneurysm</td>
<td>0 EVAR n = 73</td>
<td>0 OR n = 394</td>
</tr>
<tr>
<td>Re-bleeding</td>
<td>1 EVAR n = 73</td>
<td>38 OR n = 394</td>
</tr>
<tr>
<td>Bowel ischemia</td>
<td>3 EVAR n = 73</td>
<td>28 OR n = 394</td>
</tr>
<tr>
<td>Endograft migration</td>
<td>4 EVAR n = 73</td>
<td>0 OR n = 394</td>
</tr>
<tr>
<td>Endoleak</td>
<td>12 EVAR n = 73</td>
<td>0 OR n = 394</td>
</tr>
<tr>
<td>False aneurysm</td>
<td>1 EVAR n = 73</td>
<td>0 OR n = 394</td>
</tr>
<tr>
<td>Graft thrombosis or obstruction</td>
<td>1 EVAR n = 73</td>
<td>2 OR n = 394</td>
</tr>
<tr>
<td>Graft infection</td>
<td>5 EVAR n = 73</td>
<td>6 OR n = 394</td>
</tr>
<tr>
<td>Incisional hernia</td>
<td>0 EVAR n = 73</td>
<td>9 OR n = 394</td>
</tr>
<tr>
<td>Ischemia of lower limbs</td>
<td>2 EVAR n = 73</td>
<td>22 OR n = 394</td>
</tr>
<tr>
<td>Secondary ruptured aneurysm</td>
<td>0 EVAR n = 73</td>
<td>0 OR n = 394</td>
</tr>
<tr>
<td>Secondary symptomatic aneurysm</td>
<td>0 EVAR n = 73</td>
<td>1 OR n = 394</td>
</tr>
<tr>
<td>Symptomatic adhesions</td>
<td>0 EVAR n = 73</td>
<td>5 OR n = 394</td>
</tr>
<tr>
<td>Other</td>
<td>0 EVAR n = 73</td>
<td>2 OR n = 394</td>
</tr>
<tr>
<td>Unknown</td>
<td>0 EVAR n = 73</td>
<td>6 OR n = 394</td>
</tr>
</tbody>
</table>

**Table 3.** Subgroup analysis of the AJAX trial with Kaplan–Meier estimates of the freedom from reintervention and of the overall survival rates during five years of follow-up in all patients and in patients who survived their hospital stay.  
EVAR = endovascular aneurysm repair, CI = confidence interval, OR = open repair

<table>
<thead>
<tr>
<th></th>
<th>EVAR (events, 95% CI)</th>
<th>OR (events, 95% CI)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedom from reintervention in all patients</td>
<td>45% (26/57, 30 to 60%)</td>
<td>59% (20/59, 45 to 74%)</td>
<td>.23</td>
</tr>
<tr>
<td>Freedom from reintervention in patients who survived their hospital stay</td>
<td>63% (13/41, 47 to 80%)</td>
<td>81% (7/42, 68 to 94%)</td>
<td>.14</td>
</tr>
<tr>
<td>Overall survival in all patients</td>
<td>38% (34/57, 25 to 51%)</td>
<td>42% (33/59, 29 to 55%)</td>
<td>.81</td>
</tr>
<tr>
<td>Overall survival in patients who survived their hospital stay</td>
<td>53% (18/41, 36 to 69%)</td>
<td>59% (16/42, 43 to 75%)</td>
<td>.62</td>
</tr>
</tbody>
</table>
Figure 2. Kaplan–Meier estimates of the freedom from reintervention during five years of follow-up in all patients (A, left) and in patients who survived their hospital stay (B, right). OR = open repair, EVAR = endovascular aneurysm repair.

Figure 3. Kaplan–Meier estimates of the overall survival during five years of follow-up in all patients (A, left) and in patients who survived their hospital stay (B, right). OR = open repair, EVAR = endovascular aneurysm repair.
Discussion

The present study in patients with a ruptured abdominal aortic aneurysm shows that five years after the primary intervention the reintervention and survival rates for endovascular and open repair are similar. In patients who survive their hospital stay the reintervention rate for EVAR is higher than for OR.

Midterm outcomes

The majority of studies comparing EVAR and OR for RAAA focus on short-term outcomes and only five studies\textsuperscript{10-14} have reported midterm outcomes so far. The present study expands on these studies by the prospective patient identification, by the multi-center design representing ten hospitals from one ambulance region and by the subgroup analysis with randomized treatment allocation. Several conclusions can be drawn by interpreting our results in the light of the previous studies.

It is known that in elective aortic surgery, the midterm risk of reintervention is higher after EVAR than after OR.\textsuperscript{6} In agreement with a previous study\textsuperscript{13}, the present study shows that there is no difference in reintervention rates after an acute intervention. Because our study (n = 73) and the previous study (n = 62) included a limited number of patients treated by EVAR, more data is required before definite conclusions can be drawn. An interesting observation from both these studies is that during the in-hospital period there were fewer reinterventions after EVAR and during follow-up there were fewer reinterventions after OR (Figure 2A).

Our results confirm previous results that in patients who survived their hospital stay the reintervention rate is higher after EVAR than after OR.\textsuperscript{10, 13} Although not statistically significant, the large difference with the subgroup analysis in the AJAX trial (63% vs. 81%, respectively) also confirms that the reintervention rate is higher after EVAR than after OR. This conclusion echoes the results after elective aortic surgery.\textsuperscript{6} We did not determine if the indications for reintervention were found by routine follow-up or by an acute event. For this reason, no definite conclusions could be drawn about the need for routine follow-up after EVAR for an RAAA.

The overall survival rate of all patients in the present study (38%, 95% CI 34 to 43%) corresponds to a previously reported 5-year survival of 44% (99% CI 40 to 47%).\textsuperscript{11} This indicates that the 5-year survival after an RAAA is low; approximately 40%.
In the present study, results regarding the midterm survival after EVAR and OR were conflicting. In all patients, the survival rates five years after the primary intervention were similar for EVAR and for OR (Figure 2A). In patients who survived their hospital stay, there was a conspicuously higher survival rate for OR (Figure 3B). Conversely, the subgroup analysis in the AJAX trial showed similar survival rates for both interventions in all patients and in patients who survived their hospital stay (Table 3). The same conflicting results can be found on assessing the outcomes of previous studies. One study\textsuperscript{13} reported similar survival rates, while other studies reported lower survival rates for EVAR.\textsuperscript{10-12, 14} It appears probable that patient selection for EVAR significantly influences these midterm survival rates. Because randomized treatment allocation adjusts for this patient selection, the results of the subgroup analysis in the AJAX trial guide us towards the conclusion that the midterm survival rates for EVAR and for OR are comparable.

Preferred intervention
The present study adds to the debate on whether EVAR or OR is to be preferred for patients with an RAAA. The randomized trials reported a similar short-term survival rate for both EVAR and OR.\textsuperscript{5} EVAR appears to be beneficial on secondary outcomes such as less blood loss, less need for mechanical ventilation and temporary dialysis, a shorter intensive care and hospital stay, and more patients were discharged home.\textsuperscript{2, 3} With the results of the present study in mind, when deciding between EVAR and OR in the acute setting, caregivers have to balance the short-term benefit of secondary outcomes after EVAR with the lower midterm risk of reintervention after discharge for OR.

Limitations
A limitation of the present study was that complications that did not require surgical intervention were not included. For example, an incisional hernia in a patient who was considered to be unfit for reintervention was not included. Hence, the incidence rates of individual complications do not reflect the true incidence of these complications.

There are also some limitations to the external validity of our results. In general, indications for reintervention vary between hospitals and over time. As mentioned before, the number of patients treated with EVAR was low (n = 73). Of those patients evaluated with a CTA in the Amsterdam ambulance region,
only 49% were considered to have aortoiliac anatomy suitable for EVAR.\textsuperscript{15} This is rather low compared with the suitability rate of the IMPROVE trial of 64%.\textsuperscript{2} Caregivers in the Amsterdam region adhered mostly to the instructions for use (IFU) because few data or guidelines are available on the use of endografts outside the IFU. In elective aortic repair, patients treated outside the IFU have a higher risk of adverse events.\textsuperscript{16} For this reason, the midterm reintervention rates in the Amsterdam region were probably low compared with hospitals pushing the anatomical limits of EVAR for RAAAs. In the present study, an aorto-uni-iliac endograft with a contralateral iliac occluding device was to be used for EVAR. Fifty-eight patients received the Talent endograft (Medtronic AVE Europe), seven patients the Endurant endograft (Medtronic BV, Heerlen), and the remaining eight patients received another or unknown endograft. The outcomes for EVAR are therefore predominantly limited to the Talent aorto-uni-iliac endograft. Other and more recent endografts may have better midterm outcomes.

Conclusions
Five years after the primary intervention, endovascular and open repair for a ruptured abdominal aortic aneurysm resulted in similar reintervention and survival rates. However, in patients who survived their hospital stay the reintervention rate was higher for EVAR than for OR.
Reference List


