Early Outcomes of Open Abdominal Repair Versus Endovascular Repair for Abdominal Aortic Aneurysm: Report from National Hospital Organization Network Study in Japan

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Objective: Early outcomes of open abdominal repair (OS) versus endovascular repair (EVAR) for abdominal aortic aneurysm were retrospectively analyzed, after commercialized devices for EVAR had become available in Japan.

Patients and Methods: A total of 781 consecutive patients (OS, n = 522; EVAR, n = 259) were treated at ten medical centers between January 2008 and September 2010. The OS group comprised patients with preoperative shock (SOS, n = 34) and without shock (NOS, n = 488).

Results: Patients in the EVAR group were 3 years older than those in the NOS group. There was greater prevalence of hostile abdomen, on dialysis, chronic obstructive pulmonary disease on inhaled drug, and cerebrovascular disease in the EVAR group than in the NOS group. Surgical mortality was 16 cases (2.0% in all patients, EVAR: 0.8%, NOS: 1.4%, SOS: 21%). Hospital stay >30 days was documented in 52 (11%) with NOS, 11 (33%) with SOS, and 8 (3%) with EVAR. Thirty late deaths included 6 aneurysm related death and 14 cardiovascular causes at a mean follow up of 1.0 year. The survival rates freedom from all cause death at one year, were 95 ± 1% in NOS and 94 ± 2% in EVAR respectively.

Conclusion: Though significant differences in patient characteristics among three groups were noted, early results were satisfactory.

Keywords: abdominal aortic aneurysm, endovascular aneurysm repair, open surgical repair, multicenter cooperative study, less invasive approach

Introduction

Since commercial devices to treat endovascular aneurysm repair (EVAR) for infra-renal abdominal aortic aneurysm (AAA) were approved for use in Japan in June 2007, both patients and physicians had acquired to choose appropriate treatment from two modalities, open surgical repair (OS) and EVAR. The relative advantage of each treatment strategy was disputed in Europe and North America including three prospective randomized trials. However, there is no such trial conducted at the moment in Japanese population. In addition, contemporary
reports regarding open surgical repair of infra-renal AAA were scarce\(^7,8\) after EVAR was introduced into Japan. A
nationwide survey by the Japanese Society for Vascular Surgery provided valuable information over several years, 
though it is voluntarily collected and thus, potentially 
biased.\(^9\) Ten medical centers of the National Hospital Organization (NHO) conducted a multicenter cooperative 
study to register AAA cases retrospectively. The interim 
goal of the present study was to report differences in 
patient backgrounds and preoperative surgical risks, as 
well as to compare treatment outcomes between two 
treatment modalities.

**METHODS**

The study was conducted at 10 national medical centers 
participating NHO network study (Fig. 1a). It was a retro-
spective observational study to review and collect clinical 
data of AAA cases. All 10 databases were gathered to one 
large database of registration, which was analyzed. The 
study was approved by human rights ethical committee and 
the institutional review boards at each participating center. 
Progress of the study was assessed annually, and extension 
of the study was approved by central human rights ethical 
committee of NHO. All 10 participating institutions dis-
played the notice that they joined the NHO network study 
of AAA in the center according to the ethical guidelines for 
epidemiological research published by the Ministry of Ed-
cuation, Culture, Sports, Science and Technology, and the 
Ministry of Health, Labor and Welfare in Japan.\(^10\) Patient 
registration Patient registration and management of the 
database were detailed elsewhere.\(^10\) In brief, indications for 
treating AAA were as follows: maximum external diam-
eter $\geq 5$ cm or 4–5 cm with rapid enlargement, or saccular 
morphology, which carried a high risk of rupture. Some 
patients were treated for main location of common iliac 
artery aneurysm if their maximum size were more than 
twice the normal diameter. Each patient had a preoperative 
examination, including a multi-detector CT examination, 
according to the requirements of each participating center. 
The choice of treatment modality, EVAR or OS, depended 
upon the decision of surgeons and endovascular therapists 
(Fig. 1b). A total of 110 preoperative, intra-operative, and 
postoperative variables were collected. Parameters were 
selected, based on 10 risk scores previously published, 
for predicting risks of open abdominal repair of AAA.\(^12\) 
After anonymization in a linkable fashion, all databases 
at 10 centers were connected into a large database at the 
Nagara Medical Center, which was shared by participants 
at ten NHO medical centers. From January 2008 through 
September 2010, a total of 786 patients were treated and 
registered. Of these patients, 5 had concomitant surgeries, 
such as coronary bypass surgery, or had scheduled sur-
gery, which was not associated with AAA repair during 
the same hospitalization; thus, they were excluded from 
the present analysis. Accordingly, the study population 
was 781 patients. Of these, 259 patients underwent EVAR 
(EVAR group), and 522 patients had open surgical repair 
(OS group). In the OS group, 34 patients experienced pre-
operative shock due to a ruptured AAA and were treated 
emergently (SOS group), while the rest of 488 patients were 
treated electively without shock (NOS group).
Outcome measures

The primary outcome measure was surgical mortality. It is defined as either any cause of death within 30 days after operation or in-hospital mortality without discharge at any time. The secondary outcome measures included early morbidities, and intermediate term results. Details of treatments were procedure time, volume of blood transfusion, and process of recovery, including hours of respiratory management, length of intensive care unit stay (ICU stay), procedure failure requiring additional procedure during the same hospitalization, and re-admission within 30 days. Preoperative patient characteristics and intra-operative and postoperative factors are described in Table 1.

Statistical analysis

Statistical analysis of the intergroup comparison was conducted mainly between the EVAR group and NOS.
group because no patients had EVAR under preoperative shock state in the present study population. Statistical software package, JMP version 8 (SAS, Institute Japan, Tokyo) was used for statistical analysis. The characteristics of the patients between two treatment modality were compared by using chi-square tests for categorical variables and t-tests for continuous variables. Survival proportion rates freedom from all cause death, cardiovascular death, aneurysm related death and other events were estimated with the use of Kaplan–Meier method, and comparisons were made with the use of log-rank analysis. P values of less than 0.05 were considered to indicate statistical significance.

RESULTS

Patient characteristics and preoperative condition

Patient characteristics are detailed in Table 1. Patients who underwent EVAR were significantly older than those in NOS group (P <0.001), while patients in SOS were almost same age compared with those in EVAR. Approximately 42% of patients were 80 years old or older in EVAR group, while 24% in NOS group. Maximum diameter of AAA size is shown in Table 1, as well. Mean diameter was significantly smaller in the EVAR than in the NOS group (51 ± 10 mm vs 55 ± 12 mm). It was noted that patients who were currently smoking were less prevalent in the EVAR group than in the NOS group (21% vs 10%). It was realized as well that the following risk factors were more prevalent in EVAR group than NOS group: on dialysis, previous history of stroke, history of abdominal surgery and chronic obstructive lung disease (COPD) on inhaled drug.

Treatments and postoperative recovery

Devices used for EVAR were as follows: COOK Zenith AAA endoprosthesis in 127 cases (49%), Gore Tex Excluder in 111 cases (43%), and Endologix PowerLink in 19 cases (7%). Eighty-nine patients (34%) who had EVAR were for the case beyond the manufacturer’s Instructions for Use (IFU). With respect to procedure-related factors, results are shown in Table 2. NOS group required a longer procedure time, increased blood transfusion, and longer respiratory management. Recovery from the procedure, such as duration until walking and duration to resume meal, was faster in the EVAR group than in the NOS group. As a result, a long hospital stay, defined as >30 days, was significantly reduced in the EVAR group than in the NOS group.

Early results

Early mortality and morbidity are detailed in Table 3. In-hospital mortality was 16 cases (2.0% in all patients, EVAR: 0.8%, NOS: 1.4%, SOS: 21%). Early morbidity included delayed wound healing or infection (n = 14), deterioration of renal dysfunction (n = 34), stroke (n = 3), gastrointestinal complications (n = 34), and peripheral thromboembolism (n = 10) congestive heart failure (n = 8), prolonged ventilation (>72 hours, n = 9). It was noted that postoperative stroke was more frequent in the EVAR group, while gastrointestinal complications were more common in the NOS group. Unexpectedly, deterioration of renal dysfunction either a new event from dialysis or a twofold rise in the creatinine level was more frequent in the NOS group than in the EVAR group. Hospital stays >30 days was
52 patients (11%) in the NOS group, 11 (33%) in the SOS and 8 (3%) in the EVAR. In the EVAR group, endoleaks were observed at the end of the procedure in 70 (27%) patients (type I, n = 9; type II, n = 52; type III, n = 4; type IV, n = 5). The secondary procedure performed during index hospitalization is summarized in Table 3, as well. Interventions for postoperative leg ischemia were required in 15 patients (2 in SOS group, 8 in NOS group, 5 in EVAR group). With respect to readmission within 30 days, 15 patients (7 in NOS and 8 in EVAR) were readmitted. Causes of readmission within 30 days after EVAR were, in 2 patients, late intervention for type I endoleaks, and in 1 patient each, a wound problem, allergic reaction to follow-up CT at the outpatient clinic, urinary tract infection, new type B dissection, surgery for colon cancer, and deterioration of concomitant interstitial pneumonia.. Causes of readmission within 30 days after open surgery were, in 2 patients, wound infection and in 1 patient each, surgery for colon cancer, ileus, graft infection, surgery for peripheral arterial disease and cerebral bleeding.

**Intermediate term results**

Mean duration of follow-up was only 1.0 ± 0.8 years.

<table>
<thead>
<tr>
<th>Secondary procedure before dismissal</th>
<th>OS n = 522</th>
<th>SOS n = 34</th>
<th>NOS n = 488</th>
<th>EVAR n = 259</th>
<th>P value (NOS vs EVAR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative death</td>
<td>14 (2.7%)</td>
<td>0 (0%)</td>
<td>14 (3%)</td>
<td>2 (0.8%)</td>
<td>0.3095</td>
</tr>
<tr>
<td>Endoleak</td>
<td></td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.0172</td>
</tr>
<tr>
<td>Type I</td>
<td>3 (0.6%)</td>
<td>0 (0%)</td>
<td>3 (0.6%)</td>
<td>0 (0%)</td>
<td>0.2061</td>
</tr>
<tr>
<td>Type II</td>
<td>8 (2%)</td>
<td>0 (0%)</td>
<td>7 (1%)</td>
<td>0 (0%)</td>
<td>0.0528</td>
</tr>
<tr>
<td>Type III</td>
<td>6 (1%)</td>
<td>2 (6%)</td>
<td>4 (0.8%)</td>
<td>0 (0%)</td>
<td>0.8960</td>
</tr>
<tr>
<td>Type IV</td>
<td>6 (1%)</td>
<td>1 (3%)</td>
<td>5 (1%)</td>
<td>2 (0.8%)</td>
<td>0.3333</td>
</tr>
<tr>
<td>EVAR leg occlusion or stenosis</td>
<td>3 (1%)</td>
<td>0 (0%)</td>
<td>7 (1%)</td>
<td>0 (0%)</td>
<td>0.0054</td>
</tr>
<tr>
<td>Delayed wound healing/ infection</td>
<td>14 (3%)</td>
<td>0 (0%)</td>
<td>14 (3%)</td>
<td>7 (3%)</td>
<td>0.9341</td>
</tr>
<tr>
<td>Stroke</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>3 (1%)</td>
<td>0.9341</td>
</tr>
<tr>
<td>Perioperative myocardial infarction</td>
<td>3 (0.6%)</td>
<td>0 (0%)</td>
<td>3 (0.6%)</td>
<td>0 (0%)</td>
<td>0.2061</td>
</tr>
<tr>
<td>Congestive Heart failure</td>
<td>8 (2%)</td>
<td>1 (3%)</td>
<td>7 (1%)</td>
<td>0 (0%)</td>
<td>0.0528</td>
</tr>
<tr>
<td>Intervention for arrhythmia</td>
<td>6 (1%)</td>
<td>2 (6%)</td>
<td>4 (0.8%)</td>
<td>0 (0%)</td>
<td>0.3333</td>
</tr>
<tr>
<td>Dialysis (postoperative new event)</td>
<td>6 (1%)</td>
<td>1 (3%)</td>
<td>5 (1%)</td>
<td>2 (0.8%)</td>
<td>0.7333</td>
</tr>
<tr>
<td>Deterioration of renal function</td>
<td>34 (7%)</td>
<td>5 (15%)</td>
<td>29 (6%)</td>
<td>4 (2%)</td>
<td>0.0054</td>
</tr>
<tr>
<td>Prolonged respiratory management</td>
<td>9 (2%)</td>
<td>3 (9%)</td>
<td>6 (1%)</td>
<td>0 (0%)</td>
<td>0.0732</td>
</tr>
<tr>
<td>Thoracostomy</td>
<td>4 (0.8%)</td>
<td>1 (3%)</td>
<td>3 (0.6%)</td>
<td>0 (0%)</td>
<td>0.2061</td>
</tr>
<tr>
<td>Peripheral vascular malperfusion</td>
<td>10 (2%)</td>
<td>2 (6%)</td>
<td>8 (2%)</td>
<td>5 (2%)</td>
<td>0.7721</td>
</tr>
<tr>
<td>Postoperative liver dysfunction</td>
<td>6 (1%)</td>
<td>4 (12%)</td>
<td>2 (0.4%)</td>
<td>1 (0.4%)</td>
<td>0.9611</td>
</tr>
<tr>
<td>Multiple organ failure</td>
<td>6 (1%)</td>
<td>2 (6%)</td>
<td>4 (0.8%)</td>
<td>1 (0.4%)</td>
<td>0.4891</td>
</tr>
<tr>
<td>Gastrointestinal complication</td>
<td>34 (7%)</td>
<td>9 (26%)</td>
<td>25 (5%)</td>
<td>4 (2%)</td>
<td>0.0160</td>
</tr>
<tr>
<td>Postoperative pneumonia</td>
<td>4 (0.8%)</td>
<td>1 (3%)</td>
<td>3 (0.6%)</td>
<td>0 (0%)</td>
<td>0.2061</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>2 (0.4%)</td>
<td>0 (0%)</td>
<td>2 (0.4%)</td>
<td>0 (0%)</td>
<td>0.3022</td>
</tr>
<tr>
<td>Prosthetic graft infection</td>
<td>2 (0.4%)</td>
<td>1 (3%)</td>
<td>1 (0.2%)</td>
<td>0 (0%)</td>
<td>0.4660</td>
</tr>
<tr>
<td>Allergic reaction to contrast medium</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (0.4%)</td>
<td>0.1696</td>
</tr>
</tbody>
</table>

| Management for endoleaks            | ――         | ――        | ――         | 3           |
| Intervention for leg ischemia        | 10 (1%)    | 1 (3%)    | 9 (1%)     | 5 (0.8%)    | 0.9341               |
| Delayed wound closure or repair      | 4 (0.8%)   | 3 (1%)    | 1 (0.2%)   | 1 (0.2%)    | 0.6483               |
| Ileus/gastrointestinal complication  | 4 (0.8%)   | 0 (0%)    | 4 (0.8%)   | 0 (0%)      | 0.1440               |

Operative death is defined as death within 30 days or death during index hospitalization.

OS: open surgery; SOS: open surgery with preoperative shock; NOS: open surgery without preoperative shock

Deterioration of renal dysfunction is defined as that highest postoperative creatinine level was higher than the twofold of preoperative creatinin level.
Twenty-four patients died during the follow-up term. One patient in the NOS group died of prosthetic graft infection. Five patients (3 in NOS group and 2 in EVAR group) died of unknown causes. These 6 patients were considered as aneurysm related death. Additional 14 patients died of cardiovascular causes, which were not directly related to the AAA and its repair. Kaplan Meier survival analysis freedom from all cause death showed good 1 year survival rates of 95% for NOS patients and 94% for EVAR patients (Fig. 2a). Survival rates freedom from cardiovascular death and aneurysm-related death at one year were 95% and 96% for the NOS group and 97% and 99% for the EVAR group at one year (Fig. 2b and 2c).

**DISCUSSION**

The present results of this multicenter cooperative study regarding AAA repair provides contemporary surgical outcomes of open abdominal repair as well as initial results of EVAR after it was introduced into Japan. First of all, it is clearly recognized that surgical mortalities of 0.8% in EVAR group, 1.4% in NOS group and 21% in SOS group were all satisfactory. Early mortality for elective AAA repair was reported as 1.6%–4.7% with open abdominal repair and 0.5%–1.7% with EVAR.¹⁻⁶ Our results are equivalent to or even better than these results. In the current study, it may be inappropriate to compare these 2 groups because the study is a retrospective observational study and patient characteristics and background were significantly different between them. It was also suggested that the vascular surgeon or endovasculartherapist selected the treatment modality for each patient, according to their institutionalized criterion or preference. In fact, some institutions treated most patients with open surgery, while others did so with EVAR (Fig. 1b). The multicenter database, however, revealed that patients in the EVAR group were three years older than those in the NOS group, on average. They were also characterized with a greater prevalence of history of stroke, previous abdominal surgery, on dialysis and COPD on inhaled drug.

Secondly, regarding patients in the SOS group, a small number of patients that had an episode of preoperative...
shock without rupture might have been included in the group. However, most patients in the group were referred to as having a ruptured AAA and were treated only with open abdominal repair in the present study population. Recently, surgical management of ruptured AAA was systematically reviewed and was discussed elsewhere, based on the reports, mainly from Europe and USA.\(^{13,14}\) In the review, the 30-day mortality rate of open abdominal repair in this subset of patients ranged from 13.6% to 75%, mostly between 20% and 50%.\(^{13}\) The large study of a cooperative multicenter cohort study comprising 49 institutions in 13 countries compared EVAR with open abdominal repair for ruptured AAA, reporting 30-day mortality of 19.7% in patients treated with EVAR compared with 36.3% in those with open abdominal surgery.\(^{14}\) However, it was pointed out as well that there was selection bias as patients who had EVAR were hemodynamically stable enough to select it as a treatment strategy with radiological evaluation by CT scan. \(^{13,14}\) Although emergent EVAR for ruptured AAA was widely applied with excellent results in U.S. and European countries, no such cases were reported and registered from NHO medical centers at present.

Third, several interesting observations were realized in the study results. Factors associated with the procedure or surgery demonstrated that patients in the EVAR group recovered earlier than those in the NOS group, resulting in a significant reduction in the duration of hospital stay. Patients who were hospitalized for more than 30 days were more frequently observed in the NOS group than in the EVAR group. With respect to early morbidity, as anticipated, incidence of stroke was more common in the EVAR group, while gastrointestinal complication was in the NOS group. Increased incidence of stroke might have been related with increased prevalence of preoperative history of stroke. However, in order to reduce it, manipulations of wire and catheter around ascending aorta or aortic arch should be gentle and cautious. Preoperative assessment of atheroma by CT is helpful. Unexpectedly deterioration of renal dysfunction was more frequent in the NOS group than in the EVAR group, though contrast medium was inevitably used in the EVAR group. Preoperative renal dysfunction has been considered as a relative contraindication for EVAR. The results of the present study, however, suggest that EVAR is the choice of treatment rather than open surgical repair in patients with mild to moderate renal dysfunction if treatment for AAA is unavoidable. A comparison between groups in a well-controlled manner will be required to have conclusion in this subset of patients.

Fourth, the present report must be the first one of multicenter cooperative study consisting of a consecutive series of patients having open surgical repair of AAA for Japanese population. The clinical studies regarding a large number of open surgical repair of AAA were reported from England, U.S. and other countries.\(^{1-6,12}\) However, no English literature of such study for Japanese population was found within our investigation. It was only available that the nationwide survey by Japanese Society for Vascular Surgery.\(^{9}\) It provided extremely valuable information in Japanese population that the surgical mortality of elective AAA repair ranged from 0.6% to 0.9% over several years.\(^{9}\) However, it must be taken into account as well that data were collected on voluntarily fashion by yearly questionnaire so that it was potentially biased. Single institutional reports of a consecutive series over several years were available recently in Japan. The Kureme University was congratulated to report no mortality for elective open abdominal repair of AAA over 6 years of their experience.\(^{7}\) Their experience included 13% of patients over 80 years of age.\(^{7}\) The other literature from Nagoya University reported 2.2% of in-hospital mortality in patients with elective open surgical repair of infra-renal or juxta-renal AAA over 6 years.\(^{8}\) As institutions of NHO AAA study group were typical regional medical centers in Japan, it is supposed that the results of the present study must be representative data in Japanese population. With respect to early results in EVAR, The Japanese Committee for Stentgraft Management (JACSM) reported its successful role of introducing EVAR into Japan safely and early mortality of 0.4% in the first two years.\(^{15}\)

Finally with respect to late mortality, follow-up term was limited as 1.0 years on average at present. Therefore, meaningful interpretation was not elucidated. Under the limited follow-up term at present, survival rates freedom from all cause death, cardiovascular death and aneurysm related death were satisfactory in both group. However, five out of six patients who died of unknown causes were considered to be aneurysm-related deaths, according to the reporting standard of the cardiovascular society. Real causes might have been cardiovascular or non-cardiovascular, which may change the interpretation of follow-up data between groups. In addition, late morbidity has not been collected sufficiently, so far. Only cases of readmission within 30 days were completed in the present study, which included two late interventions for type I endoleaks in EVAR. It is absolutely required to collect information on late morbidity and secondary interventions during follow-up.
Limitation of the study

The present interim report had many limitations. It is obvious that the result was based on data collected retrospectively. The NOS and EVAR groups were not comparable, in terms of patient background and characteristics, as well as anatomy of the aneurysm. The follow-up term was short and insufficient. Longer follow-up and further accumulation of registered cases are mandatory. In particular, late morbidity and secondary intervention at follow up need to be collected.

CONCLUSION

The present multicenter, cooperative study provides contemporary outcomes of AAA repair, either open abdominal repair or endovascular repair, in Japan. Although the process of selecting the treatment modality was different in each medical center, early outcomes were satisfactory, overall.

REFERENCES

3) Lederle FA, Freischlag JA, Kyriakides TC, et al. Open Versus Endovascular Repair (OVER) Veterans Affairs Cooperative Study Group Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. JAMA 2009; 302: 1535-42. [Medline] [CrossRef]

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