Early Outcomes of Endovascular Aneurysm Repair for Abdominal Aortic Aneurysm: First Preliminary Report of National Hospital Organization Network Study in Japan

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Objective: Patients and Methods: In order to assess the early outcomes of endovascular aneurysm repair (EVAR) for abdominal aortic aneurysm (AAA) in the Japanese population, a total of 183 patients who had EVAR at eight medical centers of the National Hospital Organization were retrospectively reviewed and registered. The mean number of registered cases in each center was 23 ± 17 (4–50 cases). Patient characteristics were male sex, 84%; mean age, 77 years; age ≥ 80 years, 40%.

Results: In-hospital mortality was one case (0.5%). Endoleaks were observed at the end of the procedure in 35 patients (19%: type I: n = 4, II: n = 22, III, n = 3, IV: n = 6). Early morbidity included delayed wound healing or infection (n = 7), deterioration of renal dysfunction (n = 3), stroke (n = 2), postoperative bleeding (n = 2), gastrointestinal complications (n = 2), and peripheral thromboembolism (n = 2). Eleven late deaths included one of unknown cause and six cardiovascular causes at a mean follow up of 1.0 year. Survival rates of freedom from all causes of death and from aneurysm-related death at one year were 95.4% ± 1.7% and 99.5% ± 0.5%, respectively.

Interpretation: Although registered patients carry a variety of risks, early outcomes were satisfactory. EVAR is an acceptable alternative treatment modality for treating AAA.

Key words: endovascular aneurysm repair, multicenter study, abdominal aortic aneurysm

INTRODUCTION

From 2004 to 2006, approximately seven to eight thousand cases of infra-renal abdominal aortic aneurysm (AAA) had been repaired annually in Japan.1) The results of open abdominal repair in a nationwide survey by the Japanese Society for Vascular Surgery showed excellent results of early mortality of 2%–3% in whole patients and 0.6%–0.9% in unruptured cases.1) Recent advances of endovascular aneurysm repair (EVAR) for AAA provide a less invasive approach for patients who are ineligible or carry high risks for open abdominal surgery. The advantage and the disadvantage of EVAR in comparison with open abdominal repair have been disputed in many articles outside Japan.2–6) Three prospective randomized trials have been reported which suggested that endovascular approach was superior to open abdominal repair for unruptured AAA in early results, and was not inferior to in mid term results.2–4) It was noted, however, that their reported mortality rates of the open surgical arm ranged from 3.0% to 4.7%, and the EVAR arm ranged from 0.5% to 1.7%. There is criticism among Japanese
vascular surgeons that reported mortalities of EVAR outside Japan are higher than that of open surgical cases in Japan. Unfortunately, the introduction of such products and devices into Japan for endovascular repair of AAA was delayed until July 2007, when they were approved by the Ministry of Labor and Welfare of Japan. As a result, early results of EVAR by a multi-center cooperative study have not been published in the Japanese population at the moment. In the present study, eight centers of National Hospital Organization (NHO) joined to form registration of AAA cases retrospectively. The present interim goal of the study is to report early results of EVAR in Japan by analyzing registered cases collected by NHO Network Study Group for AAA.

**Methods**

The study was a retrospective observational study to review EVAR cases and to form registration at eight participating centers. The study was approved by the human rights ethical committee, and institutional review boards at each participating center. Progress of the study was assessed annually, and an extension of the study was approved by the central human rights ethical committee of NHO. All participating institutions displayed 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 Education, Culture, Sports, Science and Technology, and the Ministry of Health, Labor and Welfare in Japan.

**Patients and registration**

Eligible patients who had endovascular aneurysm repair for abdominal and/or iliac artery aneurysm were registered retrospectively. General indications for treating AAA are as follows: maximum external diameter ≥ 5 cm or 4–5 cm with rapid enlargement, or a saccular morphology, which carries a high risk of rupture. Each patient had a preoperative examination including a multi-detector computed tomography (CT) examination according to the requirements in each participating center. The choice of treatment modality between EVAR and open abdominal repair depended upon the decision making by surgeons and endovascular therapists. Only endovascular systems approved by the Ministry and Welfare of Japan were included in the study. Patients who were treated with a homemade stent graft were excluded from the analysis. A total of 110 variables consisting of preoperative, intra-operative and postoperative variables were collected. Parameters were selected, based on the 10 risk scores previously published for predicting risks of open abdominal repair of AAA. After anonymization in a linkable fashion, all databases at 8 centers were connected into one large database at Nagara Medical Center. A total of 183 patients were registered at the end of March 2010.

**Outcome measures**

The primary outcome measure was in-hospital mortality. Secondary outcome measures included early morbidities, and intermediate term results. Survival rates of freedom from all causes of death, from aneurysm-related death and other events, were calculated with Kaplan-Meier survival analysis. Details of treatments were described such as procedure time, volume of blood transfusion, and process of recovery including hours of respiratory management, intensive care unit stay (ICU stay), procedure failure requiring additional procedure during the same hospitalization, and readmission. Preoperative patient characteristics and intra-operative and postoperative factors are described in Table 1, including preoperative physiological status of American Society of Anesthesiology (ASA), and both preoperative and postoperative Physical Performance Indices (PPI). The ASA classes are as follows; Class 1 = normal healthy, Class 2 = mild systemic disease, Class 3 = severe systemic disease that is not incapacitating, Class 4 = incapacitating systemic disease that is a constant threat to life. Class 5 = moribund, not expected to survive for 24 hours with or without surgery. PPI is defined as follows: Grade 0 = fully active and able to perform all predisease activities without restrictions, Grade 1 = restricted strenuous physical activity but ambulatory and able to perform work of a light or sedentary, Grade 2 = ambulatory and capable of only limited self-care but unable to perform any work activities for up to or more than 50% of waking hours. Grade 3 = capable of limited self-care and confined to bed or chair for more than 50% of waking hours. Grade 4 = completely disabled, unable to perform any self-care and totally confined to bed or chair.

**Results**

**Patient characteristics and preoperative condition**

Patient characteristics are detailed in Table 1. Patients who had EVAR were predominantly of the male gender and were old (male sex: 84%; mean age, 77 years old). About 40% of patients were more than or equal to 80 years old. Distribution of AAA size was shown in Table 1.
The mean diameter was 51.3 ± 9.4 mm. Eleven patients who had an AAA size less than 40 mm were indicated for EVAR because of either a saccular morphology of aneurysm or their location, mainly in common iliac artery. Co-morbid conditions included coronary artery disease (36%), induced myocardial ischemia (17%), history of stroke (25%), and history of abdominal surgery (27%). Preoperative patient condition for procedure and anesthesia was graded by American Society of Anesthesiology, which showed concomitant mild systemic disease (55%), severe systemic disease (21%) and life threatening condition (2%). Physical performance index as an indicator of physical activity before surgery showed that about 50% of folks showed limited physical activity to some degree and that 20% were moderately or severely disturbed as daily activity (Fig. 1).

**Details of EVAR procedure and postoperative recovery**

Devices used for EVAR were as follows: COOK Zenith AAA endoprosthesis 96 cases (52%), Gore Tex Excluder 76 case (46%), and Endologix PowerLink 1 cases (6%). Twenty-eight percent of cases were beyond the manufacturer’s recommendation for use. Causes beyond manufacture’s recommendation were detailed in Table 2. It was noted that angulated neck and short distal landing zone were the two major reasons. Duration of procedure time was 163 ± 64 minutes. Average transfusion volume of banked red blood cell was 94 ± 321 ml. Recovery from procedure was fast and smooth. Mean hours of mechanical ventilation support was 0.3 ± 1.3 hours only. Mean duration from the end of the procedure to start meal and walking were 1.4 ± 2.8 days and 1.3 ± 1.7 days respectively.

**Early results**

Early mortality and morbidity are shown in Table 3. In-hospital mortality was one (0.5%). Endoleaks were observed at the end of the procedure in 35 (19%) patients, (type I: n = 4, type II: n = 22, type III: n = 3, type IV: n = 6). Early morbidity included delayed wound healing or infection, the most frequently observed complication in the study. In addition, three patients required transient dialysis after the procedure. It was noted that two patients each had stroke, re-exploration for bleeding, acute ischemia of the limb and a gastrointestinal complication. Five patients (2.7%) were readmitted within 30 days after EVAR for various reasons. Causes for readmission included acute type B dissection, respiratory insufficiency due to interstitial pneumonia, infection of urinary tract and so on.

**Intermediate term results**

The mean duration of follow-up was only 1.0 ± 0.7 years. Eleven patients died at follow-up. No obvious aneurysm-related death was reported. However, six patients died due to cardiovascular causes (acute myocardial infarction, 2 cases; congestive heart failure, 2 cases; rupture of cerebral aneurysm, 2 cases). Two patients died of malignant neoplasm. One patient had interstitial pneumonitis, which deteriorated and developed into respiratory failure, resulting in death. One patient died of an unknown cause, which was included as an aneurysm-related death.
Survival freedom from all-cause death, from aneurysm-related death and cardiovascular death at one year were 95.4 ± 1.7%, 99.5 ± 0.5% and 96.6 ± 1.5% (Fig. 2a–2c), respectively. Two patients had a secondary procedure after dismissal. One was a coil embolization for expansion of internal iliac artery. The other was an extension of the iliac limb for a type I endoleak. Major morbidities after discharge included renal failure requiring dialysis, aortic valve replacement for severe aortic stenosis and surgery for pancreatic cancer. With respect to late results of endoleak observed at the end of procedure, type I and III endoleak in 7 out of 8 patients had disappeared at 6 months after EVAR. One patient with residual endoleak required the extension of iliac limb for treating type I endoleak. Two out of six patients who had a type IV endoleak had persisted at the most recent follow-up CT examination. About half of the patients who had a type II endoleak were still visualized on the CT examination so far and were currently under observation.

**Pre- and post-operative PPI**

PPI at both preoperative and postoperative conditions were available in only 129 out of 183 patients. Distributions of grade 0–4 were shown in Fig. 1. Five out of 129 patients showed postoperative PPI were downgraded

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**Table 2  Causes beyond manufacture’s recommendation**

<table>
<thead>
<tr>
<th>Cause</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angulated neck</td>
<td>13</td>
</tr>
<tr>
<td>Short distal landing zone</td>
<td>13</td>
</tr>
<tr>
<td>Short neck</td>
<td>10</td>
</tr>
<tr>
<td>Access problem</td>
<td>7</td>
</tr>
<tr>
<td>Circumferential thrombus</td>
<td>4</td>
</tr>
<tr>
<td>Narrow terminal aorta</td>
<td>3</td>
</tr>
<tr>
<td>Others</td>
<td>5</td>
</tr>
</tbody>
</table>

**Table 3  Early results**

<table>
<thead>
<tr>
<th>Event</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Endoleak</td>
<td>35 (19%)</td>
</tr>
<tr>
<td>Type I</td>
<td>4</td>
</tr>
<tr>
<td>Type II</td>
<td>22</td>
</tr>
<tr>
<td>Type III</td>
<td>3</td>
</tr>
<tr>
<td>Type IV</td>
<td>6</td>
</tr>
<tr>
<td>Others</td>
<td>2 (1.1%)</td>
</tr>
<tr>
<td>Delayed wound healing/wound infection</td>
<td>7 (3.8%)</td>
</tr>
<tr>
<td>Re-exploration for bleeding</td>
<td>2 (1.1%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>2 (1.1%)</td>
</tr>
<tr>
<td>Deterioration of renal function</td>
<td>3 (1.6%)</td>
</tr>
<tr>
<td>Intervention of acute ischemia of limb</td>
<td>2 (1.1%)</td>
</tr>
<tr>
<td>Multiple organ failure (Liver, Kidney)</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Gastrointestinal complication</td>
<td>2 (1.1%)</td>
</tr>
<tr>
<td>Others</td>
<td>4 (2.2%)</td>
</tr>
</tbody>
</table>
compared with preoperative PPI. All five patients had peri-procedural complications, including stroke and delayed wound healing. Physical performance was maintained in 59% of patients and was improved in 37%, while physical performance only in 4% of patients was downgraded (Fig. 1).

**DISCUSSION**

The present study showed the results of EVAR cases registered from eight NHO medical centers. It is clear that early mortality of 0.5% is good as a treatment modality, though 40% of patients are more than or equal to 80 years old. Two prospective randomized trials published in 2004 and 2005 elegantly reported the early advantages of EVAR over open surgical repair in unruptured AAA cases, which were updated with the data of long term follow-up. Although most vascular surgeons and endovascular therapists in Japan accepted the results of two studies, they questioned why their mortalities of open surgical results were relatively high. In contrast, the early mortality of open surgical repair surveyed by the Japanese Society for Vascular Surgery was about only 0.6%–0.9% in unruptured AAA. It is our question before the present study was conducted if the result of EVAR in Japan is low enough to be equivalent to the result of open surgical repair in Japan.

Most institutions of the NHO AAA study group were typical regional medical centers to start EVAR after it was authorized for health insurance reimbursement as well as federal approval as a treatment modality. Out of 8 NHO medical centers in the present study, three registered 30–50 cases, three did 10–30 cases and the other two did less than 10 cases. In general, the volume-outcome effect of the institution performing a large number of cases had better results compared with those performing a small number of cases and is also applied in the treatment of AAA. Although they experienced a low to medium volume of EVAR cases, the overall results were excellent, which demonstrated that it is an extremely
safe procedure with a minimal learning curve. It also suggested that the introduction of the treatment modality into Japan has been very successful.\(^{15}\) The Japanese Committee for Stentgraft Management (JACSM) was established to aim at the safe and proper practice standard for EVAR. It was reported recently that early mortality of EVAR in Japan was 0.4% in the first two years, analyzed by The JACSM.\(^{15}\) The lower operative mortality in our study compared with the previous two prospective randomized trials in Europe could result from the difference of devices used when studies were conducted. Three devices currently available in Japan are very sophisticated, reliable and well-tested ones of the third-generation. In our study, treatments were performed more recently, from 2007–2010 compared with 1999–2003 in EVAR-1 and DREAM trials.\(^{11-12}\) The most recent randomized trial from the Veterans Affairs (VA) Cooperative study in the United States was based on data between 2002 and 2007, which showed a 0.5% early mortality in the EVAR group.\(^{4}\) The VA study excluded patients who had previous abdominal surgery or urgent repair. As a new generation of devices becomes available, which are modified, early results may further improve in the future.

With respect to preoperative risk evaluation in the present study, patients who had EVAR carried a variety of risks associated with cardiovascular disease, respiratory insufficiency, hostile abdomen and so on. As a result, the ASA physiological status before surgery showed that three fourths had at least mild systemic disease and 21% had severe systemic disease. In terms of the EVAR procedure and recovery from it, it was noted that the procedure time was short and the average volume of blood transfusion was a small amount. Duration of ventilator management and terms for starting oral intake and walking were very short as well, so that the hospital stay was less than 10 days on average. In addition, readmission within 30 days was required in only 5 cases (2.7%). Postoperative recovery appeared to be fast and smooth, though it was not compared with open surgical patients. With respect to the late results, mean duration of the follow-up term was only 1.0 years which is too short to elucidate a meaningful interpretation. No late re-intervention was reported so far except for two events: coil embolization in one patient and extension of leg for type I endoleak in another. It is, however, noted that the survival rate freedom from aneurysm-related death was 99.6% at one year. It is essential to collect longer follow-up data and to accumulate further case registration. It is also important to compare EVAR with open surgical repair. Prospective randomized trial is required in Japan as well for demonstrating any evidence of relative advantage. At this moment in our study group, retrospective registration of open surgical repair is ongoing. The choice of treatment modality between two may not only depend upon surgical risk, but also upon other factors such as physical activity, quality of life, co-morbid conditions and cost-effectiveness in Japanese health insurance system. In the present study, PPI was used for estimating physical daily activity before and after surgery. Physical performance was maintained in 59% of patients and was improved in 37%. It is suggested that EVAR prevent deterioration of physical activity, while repairing AAA.

Limitation of the study

The present interim report has many limitations. It is obvious that the report is based on the data collected retrospectively. The report is only a descriptive observation without any intergroup comparison. Therefore the results are assessed in comparison with the previously published article outside Japan. The follow-up term was short. A longer follow-up and further accumulation of registered cases were mandatory.

Conclusion

Although a substantial portion of patients carry a variety of risks, good early outcomes were demonstrated in multicenter cooperative study of EVAR registration by eight NHO medical centers. It is suggested from the present data that EVAR is an acceptable alternative treatment modality to maintain physical performance well while repairing AAA.

Acknowledgment

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References

1) Annual survey of vascular surgical cases by The Japanese Society for Vascular Surgery. h\(\text{t}\text{t}\text{p://j\text{svs}j\text{p}/}\text{en\_quete6.php\text{\_result/index.html}}\)
3) De Bruin JL, Baas AF, Bath J, et al. Long-term ou-


APPENDIX

This is a research by National Hospital Organization Network Study Group in Japan for Abdominal Aortic Aneurysm.

Participants

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