Assessing volumetric changes in abdominal aortic aneurysms following endovascular repair

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Abstract
Objective: Volumetric changes in the aneurysm sac were evaluated following endovascular aortic repair (EVAR) in intact abdominal aortic aneurysm (AAA) patients who underwent EVAR.

Methods: Fifty-two patients, who underwent EVAR from 2015 to 2019, were analysed retrospectively. A total of 158 computed tomography angiography scans was examined by performing reconstructive volumetric calculations. Total aneurysm volume (TAV), patent lumen volume (PLV) and thrombus-coated aneurysm wall volume (TCAWV) were calculated. The results obtained at six, 12 and 24 months postoperatively were compared with those of the pre-operative period.

Results: Mean TAV had regressed 7% by the sixth month ($p=0.1$), 27% by the 12th month ($p=0.0003$) and 19% by the 24th month ($p=0.0008$). Mean TCAWV had increased 2% by the sixth month ($p=0.3$), and regressed 26% by the 12th month ($p=0.3$) and 14% by the 24th month ($p=0.8$). Mean PLV had regressed by 20% by the sixth month ($p=0.008$), 29% by the 12th month ($p=0.0002$) and 26% by the 24th month ($p=0.0006$). For each individual proximal, middle and distal measurement, regression was observed at six and 12 months; however, an increase was observed at 24 months compared to the previous follow ups.

Conclusion: The expansion measurements of TAV in the 24th month support the doubts on the medium- to long-term results of EVAR. The largest regression in the aneurysm sac was observed in the distal portion, then in the proximal portion, and the least regression was observed in the middle section.

Keywords: endovascular aneurysm repair, abdominal aortic aneurysm, volumetric measurement, endotension, endoleak

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Nowadays, endovascular aortic aneurysm repair (EVAR) is a common method for the treatment of abdominal aortic aneurysm (AAA). Lifelong follow up is necessary for EVAR patients since the aneurysm diameter may increase or an endoleak may develop over time. Changes in aneurysm volume are also critically important as they indicate the long-term success of EVAR. Computed tomography angiography (CTA) is commonly used for patient follow up. The status of stent grafts and aneurysms can be evaluated through observing two-dimensional axial sections or three-dimensional volumetric measurements of CTA scans.

Reconstructive volumetric measurement is the process of combining two-dimensional axial sections taken from different reference levels, converting these sections into a three-dimensional image and obtaining volumetric measurements from the newly formed three-dimensional image. Volumetric measurements are considered to be more reliable than measurements obtained from two-dimensional diameter changes.

In this study, volumetric changes in the aneurysm sac following EVAR were examined in AAA patients. The aim was to investigate to what extent an expected volumetric regression occurred following EVAR, when expansion occurred again, whether the stent graft placed in the patient’s lumen changed over time, and in which part of the aneurysm sac the process was more effective.

Methods
In this study, 132 intact infrarenal AAA patients, who had elective EVAR surgery between November 2015 and May 2019 in our clinic, were retrospectively analysed. Fifty-two patients who had had EVAR and CTA scans performed in the sixth, 12th and 24th months postoperatively were included in the study. Retrospective information of the patients was obtained from the hospital software system.

The local ethics committee (2019/1946) approved the study and all patients provided their written informed consent. The
study was performed in accordance with the principles of the Helsinki Declaration.

EVAR was performed on patients whose infrarenal aortic diameter was 5.5 cm or more. Patients who had CTA imaging in the postoperative sixth, 12th and 24th months were included in the study. Exclusion criteria were as follows: emergency surgery due to AAA rupture or dissection, and renal function impairment preventing CTA scans in routine control follow ups (a creatinine value of 1.5 mg/dl or above). Three different stent graft systems were used for EVAR, Medtronic (Endurant II Stent Graft), Jotec (E-vita abdominal Stent Graft) and Lifetech (Ankura AAA Stent Graft) brand devices.

Reconstructive volumetric measurements were performed to assess total aneurysm volume (TAV), patent lumen volume (PLV) and thrombus-coated aneurysm wall volume (TCA WV). In addition, individual measurements were performed at the proximal, distal and middle sections of the aneurysm. The impact of pre-operative thrombus load and the brand of the stent device on volumetric regression were also examined.

The impact of pre-operative thrombus load on TAV change was examined at three different postoperative periods. To do this, the median TCA WV value was measured pre-operatively (131 cm³) and used as a threshold, and patients who were below or above the threshold were divided into two groups. Postoperative TAV was then measured at three different time points in the two patient groups.

TAV was determined as the total volume of the aortic segment starting from the distal end of the left renal artery to the distal iliac bifurcation. PLV was the open lumen volume through which blood passed. TCA WV was defined as the total thrombus volume smeared on the aneurysm wall between the aneurysm outer wall and the patent lumen (Fig. 1A, B). The measurements were performed with the Syngo.via software (VB20B version; Siemens Health, Erlangen, Germany), which was integrated with the PACS imaging system belonging to the Department of Radiology of our hospital. The measurements were carried out jointly by a radiologist and a cardiovascular surgeon.

Reconstructive volumetric TAV measurements were performed as follows: after the axial section scan was opened and enlarged in ‘MM reading’ mode, axial sections were taken at 3-mm intervals starting from just below the left renal artery outlet to the beginning of the distal iliac artery bifurcation, and the image borders were drawn manually. Then the software’s ‘create voi’ feature combined semi-automatically drawn segments to make a three-dimensional reconstruction that provided the volume of the three-dimensional structure in cm³ (Fig. 2A, B).

In some patients, tortuous areas were present in the sagittal and coronal sections. While creating the reconstruction, in areas with aortic tortuosity, measurements were made with 1-mm slices instead of 3 mm in the axial sections. For each TAV measurement, a three-dimensional view was obtained by reconstructing axial sections taken from 30 to 40 different segments, depending on the aneurysm length.

A low molecular-weight heparin (Enoxaparin, 1 mg/kg every 12 hours) was administered to patients for one or two days following the surgery. After hospital discharge, clopidogrel (75 mg/day), acetylsalicylic acid (100 mg/day) and a β-blocker (50–100 mg/day) were prescribed. At the six-month follow up, clopidogrel was terminated and the patients were continued on acetylsalicylic acid and a β-blocker.

Statistical analysis
For continuous variables, mean and standard deviation are used as descriptive statistics. Likewise, for categorical variables, number and percentage are provided. The changes of numerical variables over time were compared using mixed-effects models. Multiple comparisons were performed using Dunnett’s adjustments. Analyses were performed using SAS University edition 9.4. A p-value < 0.05 was considered statistically significant.

Results
The mean age of patients was 66.9 years (range 61–73). A total of 158 CTA scans was examined pre-operatively (n = 52), and six (n = 49), 12 (n = 35) and 24 months postoperatively (n = 22). In two patients, a type 1 endoleak was detected and in four, a type 2 endoleak. In nine patients (17%), sac enlargement was observed compared to the pre-operative period. Demographic data of patients are provided in Table 1.

Mean TAV had regressed at six (p = 0.1), 12 (p = 0.0003) and 24 months (p = 0.0008) compared to the pre-operative period (Fig. 3). Mean TCA WV had increased at six months (p = 0.3), while it had regressed at 12 (p = 0.3) and 24 months (p = 0.8) compared to the pre-operative period (Fig. 4). Mean PLV had

Fig. 1. A. Components of an AAA. B. Transverse plane image of an AAA.
regressed at six ($p = 0.008$), 12 ($p = 0.0002$) and 24 months ($p = 0.0006$) compared to the pre-operative period (Fig. 5).

Mean proximal measurements suggested a regression at six ($p = 0.4$), 12 ($p = 0.08$) and 24 months ($p = 0.1$) compared to the pre-operative period (Fig. 6). Likewise, mean middle measurements demonstrated a regression at six ($p = 0.2$), 12 ($p = 0.007$) and 24 months ($p = 0.1$) compared to the pre-operative period (Fig. 7). Mean distal measurements had also regressed at six ($p = 0.3$), 12 ($p = 0.001$) and 24 months ($p = 0.0004$) compared to the pre-operative period (Fig. 8). Volume measurements of patients taken at three different postoperative time points compared to the pre-operative period are provided in Table 2.

In the high pre-operative TCAWV (> 131 cm$^3$) group, postoperative TAV at six ($p = 0.008$), 12 ($p < 0.0001$) and 24 months ($p = 0.0004$) were significantly different. On the other hand, in the low TCAWV group, no significant change was observed (Fig. 9).

Five patients died during the study, seven, 10, 12, 13 and 18 months postoperatively. The causes of death were found to be due to co-morbidities. Four patients had hypertension, three had coronary artery disease, three had chronic lung disease, and one had both coronary artery and chronic lung disease.

Table 1. Demographic data

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>Patient number (n = 52)</th>
<th>%</th>
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<tbody>
<tr>
<td>Gender: female/male</td>
<td>4/48</td>
<td>8/92</td>
</tr>
<tr>
<td>Hypertension</td>
<td>23</td>
<td>44</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>22</td>
<td>42</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>37</td>
<td>71</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>18</td>
<td>34</td>
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<tr>
<td>Peripheral artery disease</td>
<td>10</td>
<td>19</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>History of malignancy</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Body mass index, kg/m$^2$</td>
<td>27.8 (23–39.5)</td>
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</table>

Table 2. The change in aneurysm volume measurement over time

<table>
<thead>
<tr>
<th>Volume</th>
<th>Pre-operative, cm$^3$</th>
<th>6th month, cm$^3$ (%)</th>
<th>12th month, cm$^3$ (%)</th>
<th>24th month, cm$^3$ (%)</th>
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<tbody>
<tr>
<td>TAV</td>
<td>276</td>
<td>254 (7)</td>
<td>291 (27)</td>
<td>222 (19)</td>
</tr>
<tr>
<td>TCAWV</td>
<td>158</td>
<td>162 (2)</td>
<td>116 (26)</td>
<td>135 (14)</td>
</tr>
<tr>
<td>PLV</td>
<td>118</td>
<td>94 (20)</td>
<td>83 (29)</td>
<td>87 (26)</td>
</tr>
<tr>
<td>Proximal</td>
<td>34</td>
<td>32 (6)</td>
<td>24 (27)</td>
<td>25 (24)</td>
</tr>
<tr>
<td>Distal</td>
<td>59</td>
<td>53 (10)</td>
<td>42 (28)</td>
<td>47 (21)</td>
</tr>
<tr>
<td>Middle</td>
<td>182</td>
<td>168 (7)</td>
<td>131 (27)</td>
<td>149 (18)</td>
</tr>
</tbody>
</table>

Discussion

In order to detect potential complications that may develop following EVAR, CTA follow up is suggested at one, six and 12 months postoperatively. In patients without any complications, lifelong annual CTA follow up is recommended. Moreover, assessment of the axial sections of CTA scans or reconstructive volumetric measurements could also be performed.

It has previously been reported that volumetric measurements could more precisely detect the size of the AAA and result in less variation between observers. Since volumetric measurements are three dimensional, they can detect minor changes compared to two-dimensional diameter changes. Two-dimensional measurements are inadequate, especially in areas with an irregular aneurysm wall; they can be used for the assessment of a single section instead of examining the whole structure. Therefore, in our study, we preferred assessment of volumetric changes rather than changes in diameter.

When volumetric CTA scans were performed in the third, sixth and 12 months, any increase in the volume more than 2% from the previous examination could be associated with endoleaks. A volume regression of 10% or more within six months and continuous decline over time was considered a successful endovascular repair. In the present study, mean TAV had regressed at six and 12 months, while expansion was observed at 24 months compared to the previous follow-up examination, but this expansion was not comparable to that of the pre-operative period.

A decrease in regression at 24 months, or in other words, restart of the expansion was associated with a TCAWV increase. Since no endoleak was observed, this could have been associated with endotension, which is defined as persistent pressure in the aneurysm and continued expansion of the sac with no endoleak. This may be caused by high hydrostatic pressure in the graft and its associated impact on porosity and transmission. In addition to hydrostatic pressure, recent data suggest that a fluid called ‘permeat’, which is accumulated inside the sac due to thrombolytic activity but is located outside of the graft, could also be involved in endotension.

Mean TCAWV, which indicates changes in thrombus load, partially increased at six months compared to the pre-operative period, but then started to decline at 12 and 24 months. However, the increase at 24 months was similar to that of the TAV. The increase in the sixth month could have been associated with inferior mesenteric and lumbar arteries causing a type II endoleak. The use of anti-aggregants by the patients could also have caused these results.

Mean PLV was significantly reduced at six months compared to the pre-operative period. Similar mean PLV were obtained from six-, 12- and 24-month measurements. The first measurement showing the internal volume of the stent graft following EVAR was performed at six months, therefore it could be expected that there would be a decline in volume at six months. Similar results obtained at six, 12 and 24 months suggest that there were no major changes in PLV following the stent graft placement.

In order to observe in which region and to what extent the volume change occurred in the aneurysm sac, it was divided into three regions: proximal, middle and distal. The results obtained from these regions were similar to that obtained from the TAV. There was a regression at six and 12 months and an expansion at 24 months compared to the previous follow up. However, the expansion observed at 24 months was not comparable to that of the pre-operative period.

Even though the total regressions were similar, the distal portion displayed the largest regression, followed by the proximal and then the middle portions. The least regression observed in the middle portion could be associated with the weakest aneurysm sac present in this location.

It is known that EVAR reduces mortality rate in the peri-operative period and first six months compared to open surgery. Controversial results have been reported regarding
long-term effects of EVAR. Similar mortality rates have been reported from six months to eight years. However, after eight years, the EVAR group showed higher mortality rates.10

In another study, the first three years’ survival rate was significantly higher in EVAR compared to open surgery. Thereafter, similar survival rates were reported. In the same study, higher complications and interventions were reported in the EVAR group after an eight-year follow-up period. This eight-year follow-up period also revealed that the aneurysm rupture rate in the EVAR group was 5.4% compared to 1.4% in the open-surgery group.11 The EVAR group displayed higher complication rates, secondary interventions, delayed aneurysm ruptures, and long-term aneurysm-associated mortality rates compared to the conventional surgery groups.12

Endoleaks are the most frequent complications of EVAR and the frequency has been reported to range from 2.4 to 45.5%.13 The continuum of aneurysm expansion, rupture development and associated mortalities following EVAR has been reported to be correlated with endoleaks.14,15 Therefore, endoleaks require a close follow up and the frequency should depend on the endoleak type. The most common endoleaks are types I and II.15

In one study, type I and III endoleaks were reported to have higher sac expansion rates. They were suggested to be high-pressure endoleaks and early medical intervention was advised.16 On the other hand, type II and V endoleaks were considered lower pressure and therefore less urgent for medical intervention.17 If aneurysm volume is not increased significantly in type II endoleaks, they can be resolved without any medical treatment. Therefore, in such cases a ‘wait and see’ approach has been suggested.18

The importance of pre-operative opening of inferior mesenteric and lumbar arteries has been documented in EVAR-associated type II endoleaks.19 In the current study, 3.8 and 7.6% of the patients displayed type I and II endoleaks, respectively. Additional interventions were performed in patients who displayed a type I endoleak. In the follow up of patients with type II endoleaks, abnormal sac expansion was not observed, therefore additional interventions were not performed. The reduced endoleak rates in the present study compared to the other published studies in the literature could be associated with the short follow-up period.

In our study, the impact of the device used on the observed differences in endoleak, graft migration and sac regression following EVAR was also investigated and a potential impact of the device was found.19 However, opposite results stating no effect of the device has also been reported.19 The impact of three different devices was investigated on the volumetric regression following EVAR and no significant difference was found. However, irregularities in the number of devices distributed may have impacted on the current results.

The correlation between pre-operative thrombus load and sac regression has been investigated and controversial results have been reported. Some studies report an increased sac expansion with lower thrombus load.1 After eight years, the EVAR group showed higher mortality rates.20 However, there are some studies that do not suggest any association between thrombus load and sac regression.21 In the present study, volumetric regression of TAV was significantly higher in all three postoperative periods, with a higher thrombus load.

It is well known that development of an aneurysm is a chronic condition and may continue after EVAR. Therefore, CTA scans should be performed during the early and late postoperative period in order to determine expansion and the elimination of potential endoleaks. Lifetime CTA monitoring however is a disadvantage.22 The results of our study suggest the use of three-dimensional reconstructive volumetric measurements that show all surfaces of the aneurysm instead of using two-dimensional longitudinal sections that only allow assessment of diameter.

The main limitations of our study were the retrospective nature of data collection, the relatively small sample size, and lack of long-term follow up. Other limiting factors that could have affected regression or enlargement and were largely unknown were patient-related factors, such as smoking, hypertension and medication used. Also the number of CTA images done decreased, especially by the 24th month postoperatively.

Conclusion
Even though mean TAV displayed volumetric regression for the first 12 months, the re-start of expansion at 24 months supports the long-term doubts about EVAR. PLV measurements demonstrated that six-, 12- and 24-month measurements did not show significant differences after the placement of a stent. However, increased expansion of TAV while PLV were not significantly different at 24 months suggests pathological processes had continued outside the stent graft. The most regression of the aneurysm sac was detected in the distal portion, followed by the proximal and then the middle sections. Future long-term studies are required to determine when sac expansion will reach the pre-operative state and what course this expansion will take in the period after 24 months.

References
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