◆ CLINICAL INVESTIGATION ◆

Type II Endoleaks After Endovascular Repair of Abdominal Aortic Aneurysms: Fate of the Aneurysm Sac and Neck Changes During Long-term Follow-up

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Purpose: To evaluate the frequency of type II endoleaks after endovascular aneurysm repair (EVAR) and to compare sac diameter and neck changes in patients with type II endoleak to endoleak-free patients with at least 3-year imaging follow-up.
Methods: Among 407 consecutive EVAR patients, 109 patients (101 men; mean age 72.1 years, range 55–86) had at least 3-year computed tomography (CT) data and no type I or III endoleak. In this cohort, 49 patients presented with a type II endoleak at some time and 60 patients had no endoleak. Patients with type II endoleaks were further divided into subgroups based on the vessel origin and the perfusion status (persistent or transient). The course of the perfusion status of type II endoleaks and changes in the aneurysm sac diameters, neck diameters, and renal to stent-graft distances (RSD) were evaluated in the defined groups. Reintervention and death rates were also reported.
Results: The mean follow-up was 68.1±23.8 months. Compared to the no endoleak group, overall sac diameter increased significantly in the type II endoleak group ($p=0.007$), but vessel origin did not have any influence. With regard to the perfusion status of type II endoleaks, aneurysm sac changes were significantly higher ($p=0.002$) in the persistent endoleak group. During the study period, the increase in the proximal neck diameter was significantly higher in the no endoleak group compared to the type II endoleak group ($p=0.025$). No significant difference was found in RSD changes between the defined groups. Reinterventions were performed in 20 (18.3%) patients (13 for type II endoleak); 2 (1.8%) patients without type II endoleak died of ruptured aneurysm.
Conclusion: Persistent type II endoleaks led to significant aneurysm sac enlargement, but without increased mortality or rupture rates.

J Endovasc Ther. 2012;19:193–199

Key words: abdominal aortic aneurysm, endovascular aneurysm repair, endoleak, type II endoleak, persistent endoleak, aneurysm sac, sac diameter, aortic neck, neck diameter

Successful exclusion of infrarenal aortic aneurysms after endovascular aneurysm repair

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(EVAR) is defined by the absence of endoleaks and stable or shrinking aneurysm sacs, as well as freedom from reintervention. In a recent study comprising ≥10,000 patients, Schanzer et al.[1] reported post-EVAR aneurysm sac enlargement in 3%, 17%, and 41% of patients at 1, 3, and 5 years. In this multicenter observational study, the presence of any

The authors have no commercial, proprietary, or financial interest in any products or companies described in this article.

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endoleak was 32%, which resulted in aneurysm sac enlargement in 21%. There is a general consensus that reinterventions are necessary to prevent adverse events, including rupture, in patients with endoleaks.[2,3]

The long-term clinical course of type II endoleak, which is reported in 7% to 42% of EVAR patients, is unclear because of reported heterogeneity in aneurysm sac changes and the need for reinterventions.[4,5] Mean time to reintervention in type II endoleak was 26.1 months in a recent report by Sarac et al.[6] Current data report reintervention rates of 9.8% to 31%.[5,7,8] However, the rupture rate from type II endoleak appears to be low at 0.5% to 2.4%.[8,9] To our knowledge, no one has yet presented long-term data about the influence of type II endoleak on morphological changes in abdominal aortic aneurysms (AAA) after EVAR. Thus, we sought to present our single-center experience in the course of type II endoleak, including aneurysm sac and neck changes, in patients with an at least 3-year computed tomography (CT) follow-up.

METHODS

Study Design

A retrospective study was devised to examine changes in aneurysm sac and proximal neck diameters based on preoperative and >3-year CT data in AAA patients who underwent EVAR and correlate the differences in diameters to the presence or absence of type II endoleak (EL-II). With approval of the local ethics committee, the computerized medical records of all patients undergoing EVAR at our institution were searched to identify patients with at least 3-year CT follow-up and no type I or III endoleak. Data were gathered on presence/absence of EL-II, endoleak perfusion status (persistent or transient), reinterventions, and mortality (the latter was provided by the Statistics Austria, an independent, non-profit federal institution under public law).

Study Cohort

Among 407 consecutive EVAR patients, 109 patients (101 men; mean age 72.1 years, range 55–86) meeting the criteria were identified; 60 had no endoleak and 49 patients presented with an EL-II on at least 1 scan. The other 298 patients were excluded from the evaluation because they did not have ≥3-year CT data (n=251), they had types I/III endoleak (n=33), or they were lost to follow-up (n=14).

In the study group, EVAR was performed with 7 different stent-grafts: Excluder (W.L. Gore & Associates, Flagstaff, AZ, USA; n=60); Talent (Medtronic Vascular, Santa Rosa, CA, USA; n=25); Zenith (Cook Medical, Bloomington, IN, USA; n=13); Vanguard (Boston Scientific, Natick, MA, USA; n=8); TriVascular (Trivascular Inc., Santa Rosa, CA, USA; n=1); Stentor (MinTec, Freeport, Bahamas; n=1); and Powerlink (Endologix, Irvine, CA, USA; n=1).

Measurements

For the diameter analyses, the findings of the pre-discharge (4.0±2.8 days after EVAR) and last available CT scans were compared. The maximum aneurysm diameter and the proximal neck diameter were measured perpendicular to the central lumen line in accordance with the Society for Vascular Surgery reporting standards for EVAR.[10] Aneurysm sac diameter changes were defined as a >4-mm difference in measurements, as proposed by Wever et al.[11]; for the proximal neck, a >3-mm difference between the measurements denoted diameter change. A change in the renal artery to stent-graft distance (RSD) was the reference for migration. All measurements and endoleak classifications were evaluated by 2 independent experienced readers (M.S., R.N.). Interobserver differences in readings were resolved by consensus.

Definitions and Statistical Analyses

Patients were divided according to the presence/absence of EL-II. Patients with EL-II were further categorized according to the vessel origin: lumbar arteries or combined [lumbar arteries and inferior mesenteric artery (IMA), and/or an accessory renal artery, and IMA alone]. For perfusion status of EL-IIs, endoleaks identifiable on the first postoperative and the last CT scans were classified as

persistent; leaks detected on only 1 CT scan were classified as transient.

Continuous data are represented as the mean ± standard deviation or, if appropriate, as the median and range. Comparisons between groups were analyzed for significance using an analysis of variance (ANOVA) with the Tukey correction, the *t* test, or the Fisher exact test, as appropriate. Kaplan-Meier life-table methods were used to determine survival; comparisons of survival between groups were analyzed for significance using the log-rank test. All tests were 2-sided; significance was assumed at $p<0.05$. All statistical analyses were performed using SPSS for Windows, (version 16.0; IBM Corporation, Somers, NY, USA).

RESULTS

Mortality

During a mean follow-up of 68.1±23.8 months, the mortality was 29.4% (n=32). Malignancy was the most frequent cause of death (n=13, 11.9%), followed by cardiovascular events (n=10, 9.2%), renal failure (n=2, 1.8%), pulmonary disease (n=3, 2.8%), gastrointestinal disease (n=2, 1.8%), and aneurysm rupture (n=2, 1.8%). Rupture was due to endotension (sac enlargement without identifiable endoleak on CT and magnetic resonance angiography) in 1 patient 7 years after implantation of an Excluder endoprosthesis. The second patient, who had been treated with an Excluder endoprosthesis, died from rupture after developing a type III endoleak due to disconnection of the iliac limb 5 years after EVAR. In both patients, there was no diagnosis of an EL-II at any time.

The overall cumulative survival rates after 5, 8, and 10 years were 87%, 49.5%, and 39.6%, respectively. In the subgroups, cumulative survival rates (Fig. 1) at the same time point were 87.3%, 45.4%, and 45.4% for patients without EL-II vs. 86.3%, 50.6%, and 33.8% for patient without endoleak (p=0.770).

Endoleak Analysis

The EL-IIs in the study group had origins in the lumbar arteries (n=27), combined lumbar/IMA (n=12), an accessory renal artery (n=2), and the IMA alone (n=8). During the observation period, 18 (36.7%) EL-IIs were transient and 31 (63.3%) persistent. Overall, aneurysm sac changes were significantly higher (p=0.002) in the persistent endoleak group.

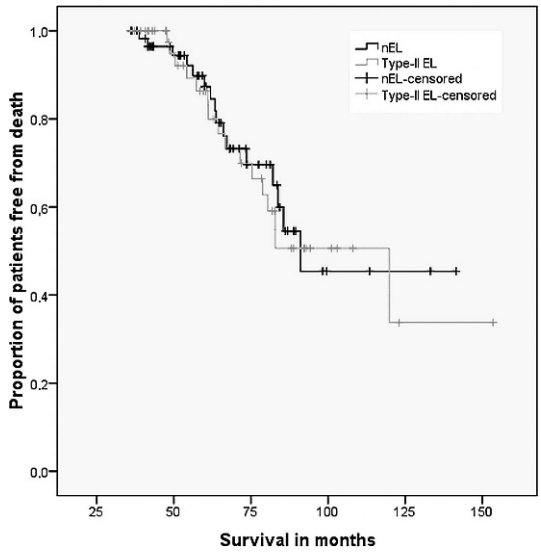

Figure 1 ◆ Freedom from death in patients with and without (nEL) type II endoleak (EL).

In all patients, the aneurysm sac diameter was 58.4±11.4 mm at the pre-discharge CT vs. 57.6±18.0 mm at the last CT, resulting in a diameter difference of −0.7±14.5 mm (p=0.608). During follow-up, mean maximum aneurysm sac diameter in the no endoleak group was significantly decreased (p=0.045), whereas in the EL-II group, there was a significant (p=0.036) enlargement (Table). The distribution of aneurysm sac diameter changes based on the means of the 2 groups is given in Figure 2. At the pre-discharge CT, there was no significant difference in aneurysm sac diameters of patients with and without EL-II (57.1±11.5 vs. 59.4±11.4 mm; p=0.303). However, comparing the aneurysm sac diameter changes at follow-up, the difference was significantly higher in patients with an EL-II compared to patients without (p=0.007).

When sac diameter differences were compared based on the means of the endoleak perfusion status, persistent leaks showed significantly larger sac diameter differences than transient ones (p=0.013; Fig. 3A). Based on the vessel origin, there were no significant

TABLE
Subgroup Analyses of Diameter Differences Between the First Postoperative and the Last CT Scans

Group	Sac Diameter Difference, mm	Proximal Neck Diameter Difference, mm	RSD Difference, mm
Type II endoleak			
No (n=60)	−4.1±16.2 (p=0.045)	2.2±2.3 (p<0.001)	0.8±1.7 (p<0.001)
Yes (n=49)	3.4±11.1 (p=0.036)	1.4±1.2 (p<0.001)	0.5±0.8 (p<0.001)
Vessel origin			
Lumbar (n=27)	1.6±15.5 (p=0.477)	1.5±1.3 (p<0.001)	0.5±0.8 (p<0.001)
Combined* (n=22)	5.6±10.4 (p=0.019)	1.2±1.1 (p<0.001)	0.5±0.9 (p=0.029)
Perfusion status			
Transient (n=18)	−1.7±11.0 (p=0.528)	1.6±1.7 (p=0.001)	0.7±1.0 (p=0.010)
Persistent (n=31)	8.8±14.2 (p=0.005)	1.3±1.0 (p<0.001)	0.4±0.7 (p<0.001)

Data are presented as the means ± standard deviation.
CT: computed tomography, RSD: renal artery to stent-graft distance.
* Lumbar and inferior mesenteric arteries, and/or accessory renal artery, and IMA alone.

differences in sac diameter changes when comparing lumbar endoleaks with combined endoleaks (p=0.986).

Overall, proximal neck diameter dilatation was observed in 11 (10.1%) patients. Of those patients, 8 (7.3%) occurred in the no endoleak group and 3 (2.8%) in the EL-II group (p=0.339). Overall, neck diameter and RSD were 25.4±5.3 mm and 2.7±3.7 mm, respectively, at baseline and 27.2±5.6 mm and 3.3±4.0 mm at the last CT examination, resulting in neck diameter increase of 1.8±1.9 mm (p<0.001) and RSD differences of 0.7±1.4 mm (p<0.001) during a mean follow-up of 68 months. None of these changes resulted in a type I endoleak.

The proximal neck diameter increase was significantly higher in the no endoleak group (p=0.025). However, RSD changes showed no significant difference (p=0.270) between the groups. When the proximal neck diameter changes were compared, the diameter increase was significantly higher in the no endoleak group than in the persistent endoleak group (p=0.040), but there was no significant change between the no endoleak and transient endoleak groups (p=0.424; Fig. 3B).

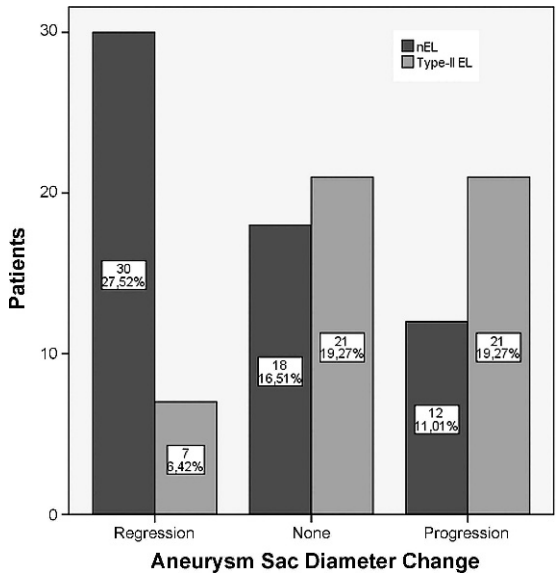

Figure 2 ◆ Distribution of mean aneurysm sac diameter changes in patients with and without (nEL) type II endoleak (EL).

Interventions

Secondary interventions were performed in 20 (18.3%) patients after a mean of 57.6±29.5 months. An additional stent was implanted in 5 (4.6%) patients with a stenosis in the stent-graft limb. A distal extension of the iliac limb was necessary in 2 (1.8%) patients who had progression of their aneurysmal disease. An embolization of either the IMA or the lumbar arteries via the internal iliac artery was performed in 4 (3.7%) and 7 (6.4%) patients, respectively. Two (1.8%) patients were treated for persistent lumbar endoleaks with a percutaneous translumbar thrombin injection. In patients treated for EL-II, mean time to re-intervention was 43.4±5.5 months (range

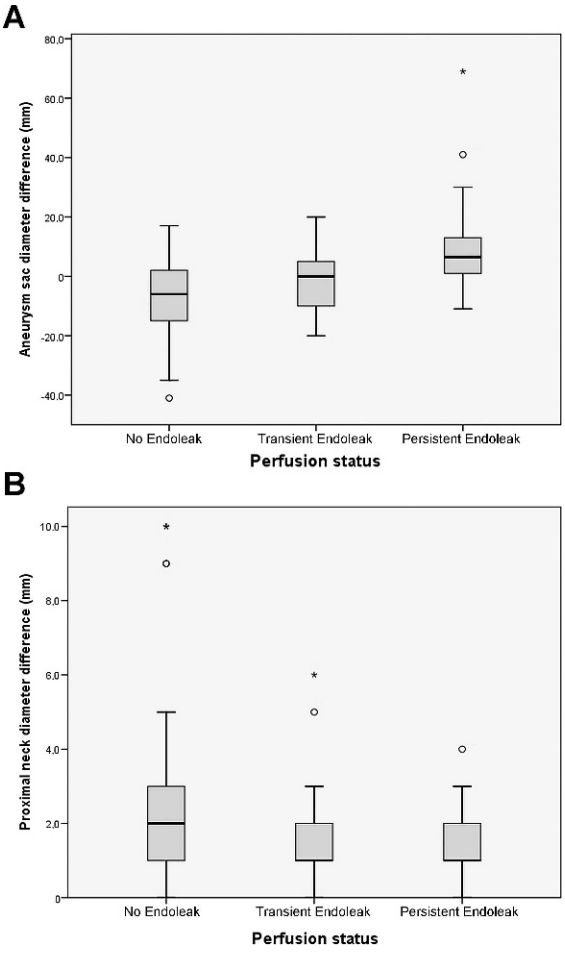

Figure 3 ◆ Box plots of mean (**A**) aneurysm sac diameter and (**B**) proximal neck diameter differences by perfusion status. The box represents the 75th to 25th percentiles, the bar is the median, and the whiskers are the 10th/90th percentiles. The outliers are defined as within 3 standard deviations (°) or >3 standard deviations (*).

36.5–51.1), and the mean aneurysm enlargement was 13.4±7.4 mm (range 5–30). By way of comparison, in the 298 patients excluded from this study (mean survival 32.9±31.1 months), more than half of the patients (159, 53.4%) patients were without an endoleak. Of the 92 (30.9%) patients who had an EL-II, 16 (17.4%) were treated. In all, 33 (11.1%) patients had further interventions for endoleak.

DISCUSSION

The incidence of EL-II ranges widely (7%–42%),[5,7,8] as do the reported rates of persistent EL-II (4% to 23%).[5,8] In our institution, more than a third of all our treated patients (34.6%) have developed an EL-II during the observation period. Among the 49 observed EL-IIs in the study group, more than two thirds were persistent.

The aneurysm-related adverse events and death rates of EL-II during long-term follow-up after EVAR are unclear, and the clinical relevance of persistent EL-II has been the subject of some controversy. Some authors identified persistent EL-II as a significant risk factor for late adverse events, with a rupture rate up to 2.4%[8]; however, in other studies, EL-IIs were not associated with aneurysm sac rupture during midterm follow-up.[4,5] In our study cohort, we observed 2 (1.8%) ruptures; neither patient had an EL-II. Overall, mortality after EVAR is more often caused by cardiovascular events and malignancy than by aneurysm-related death.[12–14] Cumulative survival rates in our study group, which were in accord with the survival rates reported in 2 randomized controlled trials,[13,15] did not differ significantly between the EL-II and the no endoleak groups. In the presence of an EL-II, several authors observed aneurysm sac enlargement in 24% to 55% of patients during midterm follow-up.[4,8,16] Moreover, van Marrewijk et al.[7] found this sac enlargement to be significant.

We observed a significant decrease in aneurysm sac diameters in the no endoleak group, whereas there was a significant sac enlargement in the EL-II group during a mean follow-up of 68 months. Regardless of the fate of the EL-II, an increase in the aneurysm sac was observed in nearly one fifth of our patients. However, there was a tendency toward sac retraction in patients with transient EL-IIs, which Arko et al.[17] also noted in their study of sealed vs. persistent EL-II.

When combined and lumbar endoleaks were compared in our patients, a change in sac diameters was unrelated to the aortic branch vessels involved. Basing the need for reintervention in EL-IIs on increasing aneurysm size, Keedy et al.[18] and Sarac et al.[6] did not report a difference in the reintervention rate based on different branch vessel involvement, although Keedy et al.[18] identified endoleak transverse diameter and communicating vessel

maximum diameter as characteristic features in predicting need for reinterventions, with sensitivity/specificity of 0.74/0.80 and 0.74/0.54, respectively. Moreover, Timaran et al.[16] also found no significant influence of the feeding sac vessels on either an increasing or decreasing aneurysm sac, but reported that a maximum nidus diameter >15 mm increased the risk for aneurysm enlargement. In a later study, the rates of freedom from aneurysm rupture and conversion to open aneurysm repair at 5 years were 92% and 75%, respectively. However, in persistent type EL-IIs, that study found a median increase in aneurysm diameter of 10 mm in 41% of patients. This finding is quite comparable with the mean diameter enlargement of 9 mm in our patients with persistent EL-IIs, which was significantly higher than in transient EL-IIs.

Several reports have focused on the proximal aneurysm neck changes and migration during short- and midterm follow-up.[19–22] However, none of them highlighted the dynamics at the proximal anchoring zone with regard to existing EL-IIs. Cao et al. [22] reported neck enlargement in 13.5% and a migration rate of 4.9% during a mean follow-up of 25 months. In a study by Resch et al.,[21] 50% of patients with migrated stent-grafts had dilatation of the proximal aneurysm neck. Furthermore, Litwinski et al.[19] reported a significant neck diameter increase in patients with complete loss of seal at the proximal anchoring zone. Overall, neck dilatation in our study cohort was found in 10%, which is consistent with other results.[22] Nonetheless, we did not see significant migration during long-term follow-up, and none of our patients developed a type I endoleak. When the no endoleak and the EL-II groups were compared, the proximal neck diameter increase was significantly higher in the no endoleak group. Comparing neck diameter changes in aneurysms with persistent, transient, or no EL-II, Arko et al.[17] did not find a significant change during a mean follow-up of 21.7 months. As mentioned before, Litwinski et al.[19] found significantly greater diameter dilatation in patients with a complete loss of stent-graft fixation within the aneurysm neck compared to patients with incomplete migration; however, the presence of an EL-II was not different between the 2 groups.[19] In a recently published experimental study, peak forces to initiate stent-graft migration were significantly higher in the model with an EL-II, which was associated with significantly higher sac pressure compared to the endoleak-free models.[23] The authors concluded that an increased sac pressure inhibits migration and may stabilize the stent-graft. Therefore, we speculate that the significantly smaller change in neck diameter in the EL-II group could have been caused by restricted pulsatile stent-graft movement. However, this supposition has to be confirmed in a prospective study that assesses endograft deformation and motion.

Limitations

Admittedly, our study is limited by its retrospective nature. Moreover, the study cohort included patients who were treated with the original Excluder endoprosthesis, and the presence of endotension might have influenced diameter changes. Because we observed no rupture in patients with EL-II, we cannot recommend criteria for reintervention.

Conclusion

Persistent EL-II, independent of vessel origin, leads to significant aneurysm sac enlargement compared to aneurysms with transient or no EL-II during long-term follow-up. In our study cohort, EL-IIs, persistent or transient, did not cause an increase in the rupture or mortality rates. Close surveillance in growing aneurysms with persistent EL-II seems to be advisable.

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