Identification of Predictive CT Angiographic Factors in the Development of High-Risk Type 2 Endoleaks after Endovascular Aneurysm Repair in Patients with Infrarenal Aortic Aneurysms

Identifikation prädiktiver CT-angiographischer Faktoren für die Entstehung eines Hochrisiko Typ-2 Endoleaks nach endovaskulären Aortenrepair bei Patienten mit infrarenalen Bauchaortenaneurysmen

Abstract

Purpose: An extensive analysis of the value of computed tomography (CT) parameters as potential predictors of the clinical outcome of type 2 endoleaks after endovascular aortic aneurysm repair (EVAR).

Materials and Methods: Initial CT scans of 130 patients with abdominal aortic aneurysms (AAAs) were retrospectively reviewed. On the basis of postoperative CT scans and angiographies, patients were stratified into a low-risk group (LRG; without or transient type 2 endoleak; n = 80) and a high-risk group (HRG; persistent type 2 endoleak or need for reintervention; n = 50). Statistical analysis comprised a univariate and multivariate analysis.

Results: Anatomical, thrombus-specific, as well as aortic side branch parameters were assessed on the initial CT scan. Of all anatomical parameters, the diameter of the immediate infrarenal aorta was significantly different in the univariate analysis (LRG 2.1 ± 0.4 mm; HRG 2.4 ± 0.7 mm; p = 0.01; multivariate: p = 0.006) as well as aortic side branch parameters were unsuitable as predictors. Evaluation of the thrombus-specific parameters showed a trend towards statistical significance for the relative thrombus load (LRG 22.4 ± 3.8 mm; HRG 23.6 ± 2.5 mm; p = 0.03). The investigation of the thrombus-specific parameters revealed only for the univariate analysis significant differences in the patency of the inferior mesenteric artery (LRG 71.3 %; HRG 92.0 %; p = 0.003) and their diameter (LRG 3.3 ± 0.7 mm; HRG 3.8 ± 0.9 mm; p = 0.004). Assessment of aortic side branches revealed only for the univariate analysis significant differences in the patent of the inferior mesenteric artery (LRG 71.3 %; HRG 92.0 %; p = 0.003) and their diameter (LRG 3.3 ± 0.7 mm; HRG 3.8 ± 0.9 mm; p = 0.004). In contrast, the number of lumbar arteries (LAs; LRG 2.7 ± 1.4; HRG 3.6 ± 1.2; univariate: p = 0.01; multivariate: p = 0.006) as well as their diameter (LRG 2.1 ± 0.4 mm; HRG 2.4 ± 0.4 mm; univariate: p < 0.001; multivariate: p = 0.006) were highly significantly associated with the development of type 2 endoleaks of the HRG.

Conclusion: The most important predictive factors for the development of high-risk type 2 endoleaks were mainly the number and the diameter of the LAs which perfused the AAA.

Key Points:
- This study is a very detailed and comprehensive analysis of the value of various CT parameters as potential predictors of the clinical outcome of type 2 endoleaks after EVAR.
- Anatomical as well as thrombus-specific parameters were unsuitable as predictors.
- The most important predictive factors were mainly the number and the diameter of the LAs which perfused the AAA.

Citation Format:

Zusammenfassung


Material und Methoden: Retrospektiv wurden die präoperativen CT-Angiografien von 130 Patienten mit einem infrarenalen Bauchaortenaneurysma (BAA) ausgewertet. Anhand postoperativer CT und angiographischer Verlaufskontrollen wurden die Patienten einer Niedrigrisikogruppe (NRRG) ohne bzw. mit transientem Typ-2 Endoleak; n = 80) oder einer Hochrisikogruppe (HRG) mit persistentem bzw. behandlungsbedürftigem Typ-2 Endoleak; n = 50) zugeordnet. Die statistische
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Introduction

Since the first description by Parodi et al., endovascular aortic aneurysm repair (EVAR) of infrarenal abdominal aortic aneurysms (AAAs) has become established as an accepted alternative to open surgery [1, 2]. An inherent problem of EVAR of infrarenal abdominal aortic aneurysms (AAAs) has become established as an accepted alternative to open surgery [1, 2]. An inherent problem of EVAR is the development of endoleaks due to perivascular collateral flow [3, 4]. Type 2 endoleaks are usually associated with a higher probability of a complicated course and risk of aneurysm rupture [5]. This is caused by a retrograde flow via the lumbar arteries (LAs), inferior mesenteric artery (IMA), or other aortic collaterals [3]. Type 2 endoleaks are usually only transient and thrombose spontaneously within the first 6 months in up to 80% of cases [3, 6]. On the other hand, type 2 endoleaks that persist longer than 6 months are associated with a higher probability of a complicated course and risk of aneurysm rupture due to an intrasaccular increase in pressure [5–11]. This increase in the size of the aneurysmal sac is observed significantly more often in patients with a persistent type 2 endoleak (24–52%) than in patients without a type 2 endoleak (13%) [5, 6].

In the follow-up of patients after EVAR, increase in the size of the aneurysmal sac is a generally accepted criterion for reintervention [12]. On the other hand, the treatment of type 2 endoleaks without changes in the aneurysmal sac is controversial [4, 8, 13–15]. While some authors are in favor of an aggressive approach particularly due to the high reintervention rate in persistent type 2 endoleaks [8, 13, 15], other authors advocate a conservative strategy due to the low probability of aneurysm rupture [4, 14].

It would be of extreme clinical relevance to be able to identify a high-risk group for the development of a type 2 endoleak that is persistent or requires treatment on the basis of the initial computed tomography (CT) scan. Preoperative embolization of aortic side branches could then be performed in these patients to counteract the development of a type 2 endoleak [16, 17]. The size of the intra-aneurysmatic thrombus volume [18, 19] and the number of aortic side branches [20–22] on the basis of the initial CT scan were identified as prognostic factors in previous studies. Since such parameters can affect one another, the goal of this study was to perform a comprehensive analysis of all factors previously identified as potentially predictive on the basis of preoperative CT in order to predict the clinical course of type 2 endoleaks after EVAR.

Materials and Methods

Study criteria

From December 2004 to December 2011, 161 patients were treated via EVAR for AAA. Patients without a corresponding preoperative CT scan (time between CT and implantation >1 month; n = 7) or a lack of long-term follow-up (<12 months, n = 14) were excluded. In addition, patients with a covered ruptured AAA (n = 4) were also excluded. All available postoperative examinations, CT and angiography, were used for reliable classification of the endoleak type. The relationship between periprosthesis contrast accumulation and the aortic side branches and the AAA was decisive. An association of the endoleak with LAs or the IMA was a reason for the classification as a type 2 endoleak. In the case of contrast accumulation around the ends of the prosthesis, a type 1 endoleak (n = 5) was suspected. Contrast accumulation around the connection between the main body and limb of the prosthesis was seen in one patient and a type 3 endoleak was suspected. Angiographies were available for further clarification in all patients with suspicion of a type 1 or type 3 endoleak and confirmed these assumptions. These patients were excluded from further analysis.

Patient data

Under consideration of the inclusion and exclusion criteria, 130 patients could be included in the study (121 men; 9 women; average age 71.9 years; 48–88 years). The evaluation of this patient data was approved by the local ethics committee. An Excluder prosthesis (W.L Gore & Associates, Flagstaff, USA) was implanted in the majority of patients (n = 99; 76%). The remaining 31 patients received the following prosthesis types: Anaconda (Vascutek Inc., Terumo Company, Scotland; n = 15; 12%), Endurant (Medtronic Inc., Minneapolis, USA; n = 12; 9%), Zenith (Cook Medical Bloomington, USA; n = 3; 2%), Talent (Medtronic Vascular, Santa Rosa, USA; n = 1; 1%).

CT protocol

The CT protocol included a two-phase technique with reconstructed slice thicknesses of 5 and 1 mm. 120 kV and modulated mA (Aquilion 16 rows; Toshiba Medical Systems, Netherlands). Iodinated contrast agent (80–100 ml; Imeron 300 Altana, Germany) was injected at a rate of 4 ml/s followed by 30 ml of a saline solution. The arterial phase started in the “sure start” mode followed by the venous phase after a delay of 70 s.

Data evaluation

After the evaluation of all available follow-ups (average length of the observation period after EVAR: 22 months; 12–64 months), the patients were assigned to either a
low-risk group (LRG) or a high-risk group (HRG). Patients without an endoleak (n = 68) and with only a transient type 2 endoleak not requiring treatment (endoleak stopped within 6 months; n = 12) were assigned to the LRG (n = 80), while patients with an endoleak that was persistent (endoleak lasting > 6 months) or required treatment were assigned to the HRG (n = 50). As a rule, the indication to treat a type 2 endoleak was determined on an interdisciplinary basis at the local vascular center with a progressive increase in the size of the aneurysmal sac of > 5 mm compared to the preoperative measurement being viewed as a decisive criterion.

The preoperative CT examinations were evaluated without knowledge of the follow-ups and clinical data in consensus by 2 radiologists (D.L. and O.D.) and a vascular surgeon (Z. H.) using a PACS console (software: Infinitt®). In addition to axial slices, multiplanar reconstructions were also taken into consideration. The following parameters were organized thematically and evaluated:

- General anatomical variables. The diameter of the directly infrarenal aorta, the length of the AAA, the maximum axial diameter of the AAA and the perfused lumen, and the surface area in the region of the maximum axial diameter were determined.

- Intra-aneurysmatic thrombus parameter. This evaluation included the determination of the absolute thrombus surface area in the region of the maximum extension of the AAA and the relative percentual thrombus surface area calculated as the ratio of the thrombus surface area to the surface area of the aortic lumen according to the following formula (19):

\[
\text{thrombus surface area} = \frac{\text{surface area of the aortic aneurysm} - \text{surface area of the aneurysm lumen}}{\text{surface area of the aortic aneurysm}}
\]

In addition, the maximum thickness of the thrombus within the AAA and in the branch area of the IMA and the LAs within the AAA was also documented.

- Aortic side branches. The patency and the diameter of the IMA and the number and diameter of the perfused LAs inside and outside of the AAA were determined.

The data were the basis of a complex statistical analysis using SPSS software version 21.0 (SPSS, Statistical Package for the Social Science, Chicago, IL) for Windows (Microsoft, Redmond, WA). Metric variables of both groups were compared via T-test and categorical variables via Fisher’s exact test (univariate analysis). A linear logistic regression analysis (multivariate analysis) of the potentially most predictive univariate variables was performed for further evaluation. In a subsequent ROC (receiver operating characteristic) curve analysis (AUC), the significant multivariate variables were evaluated with respect to their prediction accuracy regarding the development of a high-risk type 2 endoleak and the suitable limiting value was determined via the Youden index (YY = sensitivity + specificity – 1). A p-value of < 0.05 was viewed as a statistically significant difference.

### Results

80 of a total of 130 patients were assigned to the LRG (61.5%). No endoleak was detected postoperatively or on all additional follow-up CT scans in 68 of these patients (52.3%). A transient type 2 endoleak was found in 12 patients (9.2%), 50 patients (38.5%) were assigned to the HRG. This group was comprised of 35 patients (26.9%) with a persistent type 2 endoleak and 15 patients (11.5%) with a type 2 endoleak requiring treatment.

The univariate analysis of the morphological parameters yielded a significant difference in the diameter of the directly infrarenal aorta with 22.4 ± 3.8 mm in the LRG and 23.6 ± 2.5 mm in the HRG (p = 0.03). The multivariate analysis showed only a tendency toward statistical significance (p = 0.06). There were no differences between the two risk groups with respect to the length (LRG 64.2 ± 25.0 mm; HRG 68.0 ± 21.0 mm; p = 0.3), diameter (LRG 54.3 ± 14.1 mm; HRG 56.4 ± 11.9 mm; p = 0.3) and surface area (LRG 22.2 ± 12.5 cm²; HRG 23.4 ± 10.3 cm²; p = 0.5) of the AAA. The diameter and the surface area of the perfused aneurysm lumen did not show any significant differences (see Table 1).

The evaluation of thrombus-specific parameters also did not show any significant differences between the two groups with respect to the absolute thrombus surface area (LRG 11.1 ± 10.6 cm²; HRG 9.3 ± 9.0 cm²; p = 0.4), the relative thrombus surface area (LRG 31.7 ± 18.0 %; 25.3 ± 17.5 %; p = 0.09), and the maximum thrombus thickness (LRG 18.3 ± 13.1 mm; HRG 14.6 ± 11.3 mm; p = 0.2). Moreover, the thrombus thickness in the branch area of the IMA (LRG 4.3 ± 7.5 mm; HRG 3.1 ± 7.4 mm; p = 0.5) and in the branch area of the LAs within the AAA (LRG 3.1 ± 5.2 mm; HRG 2.7 ± 4.9 mm; p = 0.8) did not yield a significant difference between the two risk groups (see Table 2).

The analysis of the number and size of aortic side branches showed that the presence of a perfused IMA is significant as a predictive factor for the development of a type 2 endoleak of the HRG according to univariate criteria (n = 57; 71.3% in the LRG compared to n = 46; 92.0% in the HRG; p = 0.003; see Table 3). This connection could not be confirmed in the multivariate analysis (p = 0.2). The same is true for the average diameter of the IMA that was significantly different in the univariate analysis (3.3 ± 0.7 mm in the LRG versus 3.8

### Table 1: Anatomical parameters of the low-risk group (LRG) and high-risk group (HRG) for the development of a type 2 endoleak after EVAR.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LRG (n = 80)</th>
<th>HRG (n = 50)</th>
<th>p (univariate)</th>
<th>p (multivariate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>diameter of the directly infrarenal aorta (mm)</td>
<td>22.4 ± 3.8</td>
<td>23.6 ± 2.5</td>
<td>0.03</td>
<td>0.06</td>
</tr>
<tr>
<td>AAA length (mm)</td>
<td>64.2 ± 25.0</td>
<td>68.0 ± 21.0</td>
<td>0.3</td>
<td>n. e.</td>
</tr>
<tr>
<td>AAA diameter (mm)</td>
<td>54.3 ± 14.1</td>
<td>56.4 ± 11.9</td>
<td>0.3</td>
<td>n. e.</td>
</tr>
<tr>
<td>AAA surface area (cm²)</td>
<td>22.2 ± 12.5</td>
<td>23.4 ± 10.3</td>
<td>0.5</td>
<td>n. e.</td>
</tr>
<tr>
<td>diameter of the perfused aneurysm lumen (mm)</td>
<td>40.0 ± 10.4</td>
<td>43.4 ± 12.7</td>
<td>0.1</td>
<td>0.6</td>
</tr>
<tr>
<td>surface area of the perfused aneurysm lumen (cm²)</td>
<td>11.1 ± 7.0</td>
<td>14.2 ± 9.9</td>
<td>0.08</td>
<td>0.5</td>
</tr>
</tbody>
</table>

AAA: Abdominal aortic aneurysm; n. e.: not evaluated.

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± 0.9 mm in the HRG; p = 0.004). However, the significance level was again not reached in the multivariate analysis (p = 0.1; see Table 3). The average number of LAs outside the AAA also only showed significant univariate differences between the two groups (LRG 2.6 ± 1.4 mm; HRG 1.9 ± 1.5 mm; univariate: p = 0.04; multivariate: p = 0.6; see Table 3). In contrast, the average number of LAs within the AAA, i.e., the lumbar vessels supplying the aneurysm, was significantly different in both groups in both the univariate and multivariate analysis (LRG 2.7 ± 1.4 mm; HRG 3.6 ± 1.2 mm; univariate: p = 0.01; multivariate: p = 0.006). This was also true for the average diameter of the LAs (LRG 2.1 ± 0.4 mm; 2.4 ± 0.4 mm; univariate: p < 0.001; multivariate: p = 0.006; see Table 3).

As a result, of all examined parameters, only the number and average diameter of the LAs within the AAA were suitable as predictive factors for the development of a high-risk type 2 endoleak. An ROC curve analysis that yielded an area under the curve (AUC) of 0.73 (95 % confidence interval 0.64 – 0.82) and a limiting value (Youden index) of 0.45 (sensitivity of 0.71 and a specificity of 0.66; positive predictive value of 0.57; negative predictive value of 0.78) was performed to define threshold values for these two parameters that mutually affect one another (see Table 4).
Discussion

The development of an endoleak following EVAR remains an inherent problem of the technique [6]. While type 1 and type 3 endoleaks should undergo immediate reintervention, the treatment of type 2 endoleaks continues to be controversial [3, 5, 6, 8, 14, 23–27]. Type 2 endoleaks have a high rate of spontaneous thrombosis of up to 80% so that a conservative approach is favored by some authors [3, 26], while persistent type 2 endoleaks are often associated with an increase in the aneurysmal sac over time and thus require reintervention [6, 27]. Based on these studies, it seems useful to differentiate between type 2 endoleaks that are benign, i.e., transient, and those that are malignant, i.e., persistent and in need of treatment. In light of this, patients were categorized into an LRG and an HRG in this study to be able to identify predictive factors associated with the development of a type 2 endoleak in the HRG on the basis of the preoperative CT scan.

Diverse morphological-anatomical parameters of the AAA, the influence of the intra-aneurysmal thrombus mass, and the number and diameter of aortic side branches were evaluated here. With respect to the morphological parameters, only the diameter of the directly infrarenal aorta differs significantly between the two groups in the univariate analysis (p = 0.03). Interestingly, this observation coincides with the results of another workgroup [20]. Additional morphological parameters, such as the length, diameter, and surface area of the AAA and of the perfused aneurysm lumen, did not differ between the two groups. These results corresponded with those of other authors [6, 18, 28, 29]. Therefore, Higashura et al. were able to show in a prospective study on the basis of 273 patients that both the diameter of the AAA with an average of 56 mm (range: 40 – 93 mm) and the length of the aneurysm neck have no relevant effect on the development of a persistent type 2 endoleak [28]. In summary, no morphological parameter of the AAA proved suitable in this study as a predictive factor for the development of a type 2 endoleak in the HRG.

In a previous analysis of 100 patients, a connection between the size of the intra-aneurysmatic thrombus on the preoperative CT scan and the regression of the size of the aneurysmal sac over time after EVAR was able to be created [19]. In dependence on this study, we also determined a relative thrombus surface area of the AAA with an average of 56 mm (range: 40 – 93 mm) and has a certain risk of complications [35]. The non-critical parameter of the AAA proved suitable as a predictive factor for the development of a type 2 endoleak in the HRG. Undoubtedly there is often a persistent IMA typically with retrograde perfusion in a type 2 endoleak after EVAR [20, 22]. However, the number of LAs involved in such an endoleak is usually numerically superior. To what extent do the initial patency of the IMA and its diameter have a prognostic effect on the later development of a type 2 endoleak in the HRG? This relationship has been a subject of controversy in previous studies [6, 18, 20, 22, 29, 30]. In an analysis to identify preoperative predictors, the patency of the IMA was more common in persistent than in transient type 2 endoleaks (81% versus 43%; p < 0.001) [20]. In contrast, Sampiao et al. were able to identify a perfused IMA but not its diameter as a predictive factor [29]. An initially perfused IMA did not play a role in the later development of a type 2 endoleak in other studies [6, 18, 22, 30]. This coincides with the results of the present study in which the patency of the IMA in the HRG of 92.0% was higher than the value of 71.3% in the LRG but was only significantly different in the univariate analysis with p = 0.003 but not in the multivariate analysis (p = 0.2). This is not surprising because at least one inflow and one outflow vessel must be present for the development of a type 2 endoleak and the IMA can only cause an endoleak in interaction with perfused lumbar arteries. In contrast, both the number and the average diameter of perfused LAs within the aneurysmal sac were prognostically relevant parameters for the later development of a high-risk type 2 endoleak. The probability of the development of an endoleak of the HRG was directly related to the number of perfused LAs and their diameter (see Table 4). These data are in good agreement with the results of other authors [18, 20, 22, 29 – 31]. Interestingly, there is agreement regarding the critical number of perfused LAs for the development of a persistent endoleak which has been defined as 4 in preceding studies [22, 31]. On average, there were 3.6 ± 1.2 LAs in the HRG in the present study. An analysis of CT scans acquired directly after EVAR yielded similar results with respect to the development of a type 2 endoleak requiring treatment [32]. This study found significantly more perfused aortic side branches (4.2 ± 1.4 versus 2.9 ± 1.2; p < 0.001) in patients who had to undergo reintervention due to a type 2 endoleak requiring treatment. What is the explanation for this special significance of LAs for the development of an endoleak that is persistent or requires treatment? A type 2 endoleak usually has a nidus that is typically surrounded by a complex angioarchitecture consisting of multiple inflow and outflow vessels [8]. These vessels are usually the IMA and the LAs as aortic side branches in a type 2 endoleak with at least 2 vessels needing to be perfused and then functioning as an inflow and outflow vessel for an endoleak to even be able to develop. Due to the greater anatomical number of LAs, it seems plausible for the LAs to play a more important role than the IMA.

What do these results mean for the endovascular treatment of patients with an AAA? Systematic preoperative embolization of all aortic side branches in the region of the aneurysm reduces the number and size of type 2 endoleaks after EVAR [33, 34]. On the other hand this means another intervention that is technically demanding, time-consuming, and has a certain risk of complications [35]. The non-critical implementation of preoperative embolization in the clinical
routine is controversial due to the high rate of spontaneous thrombosis in type 2 endoleaks [36]. However, based on the results of this study, the number and diameter of LAs can be used to identify high-risk patients in whom it seems helpful and justified to perform preoperative embolization (see Table 4).

### Clinical Relevance

- A number of potentially predictive CT parameters were analyzed in this study to determine their ability to predict the clinical course of type 2 endoleaks after EVAR.
- None of the thrombus-specific parameters proved to be a useful predictor while among anatomical parameters only the aortic diameter showed a trend toward statistical significance.
- The analysis of parameters of the aortic side branches showed that the number and diameter of perfused lumbar arteries can be used to identify patients who are at a high risk for the development of type 2 endoleaks requiring treatment and in whom preoperative embolization seems useful.

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