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ENDOLEAK EVALUATION AFTER ENDOVASCULAR REPAIR OF ABDOMINAL AORTIC ANEURYSM

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Abstract

Background: One of the main limitations of EVAR during the long-term follow-up is the rate of re-intervention mainly caused by the development of endoleaks (EL). The aim of this study was to analyse the characteristics of patients who developed endoleaks at the CHUV after EVAR.

Method: Data of all patients who underwent EVAR and who were subject to treatment for endoleaks at the CHUV from 2013 to 2017 were retrospectively collected and analysed. All the parameters at the time of EVAR were analysed

Results: The 25 patients were mainly men (80%) with a mean age of 75 years (62-87) at the time of EVAR. The mean aneurysm diameter was 64 mm (40-100) with a neck of 22.7 mm in length. The mean oversizing was 12.8%, and 805 of the stent grafts used were Excluder and Endurant.

During the mean follow-up of 58 months (4-164), 47 re-interventions were required after a median time of 13 months following EVAR. Most re-interventions were performed during the first two years after EVAR. There was a majority of type 2 ELs (84% of patients) followed by type 1 (48%). Patients with type 1 EL had the shortest neck (17mm) and mean oversizing inferior to 10%. In the group of patients with type 2 EL, the ratio of circulating blood volume compared to total sac volume was the highest and the thrombus the thinnest and these patients had bigger lumbar arteries.

Conclusion: This single-centre study found type II endoleaks to be the most common type of endoleak and associated with less thrombus and higher ratio of circulating blood. We support the hypothesis that all EVAR should be followed. The preferable way to treat ELs was translumbar embolotherapy for type II endoleaks and prosthetic elongation for type I and III endoleaks. The findings of this study, in parallel to an extensive literature review, enabled a better understanding of local management of endoleaks after EVAR but further studies on bigger population are mandatory.

TABLE DES ABBREVIATIONS:

EVAR: Endovascular aortic repair
AAA: Aortic aneurysm rupture
IMA: Inferior mesenteric artery
CHUV: Centre hospitalier universitaire Vaudois
CEUS: Contrast enhanced ultrasound
DUSS : Duplex Ultrasound scanning
ABI : Ankle-Brachial index
CRP: C-reactive protein
ASA : acetylsalicylic acid
CTA : Computed tomography angiography
US : Ultrasound
MRA : Magnetic resonance angiography
PTA: Percutaneous transluminal angioplasty
T1E: type 1 endoleak
T2E : type 2 endoleak
T3E: type 3 endoleak
T4E : type 4 endoleak
COPD : Chronic obstructive pulmonary disease
EL : endoleak
IFU: Instruction for use

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Introduction

1. Background

Due to the lower peri-operative mortality and morbidity, endovascular aortic repair (EVAR) has become the preferred method to treat abdominal aortic aneurysms (AAA) in our developed countries.[1] In the United States, EVAR represents around 80% of all interventions performed for AAA repair. EVAR involves excluding the aneurysm by positioning a stent graft along the internal lining of the aorta. The endograft is implanted through the femoral artery under fluoroscopic guidance through a catheter. Once the stent graft has been placed, it fastens to the aortic wall, excluding blood from the aneurysm sac, which decreases the pressure in the aneurysm and consequently reduces the risk of rupture, as shown in Figure 1A. The stent graft is composed of a metallic body covered with a nonporous fabric, and exists in three different types, the bifurcated system, the aorto-uniliac and the tube, as illustrated in Figure 1B.

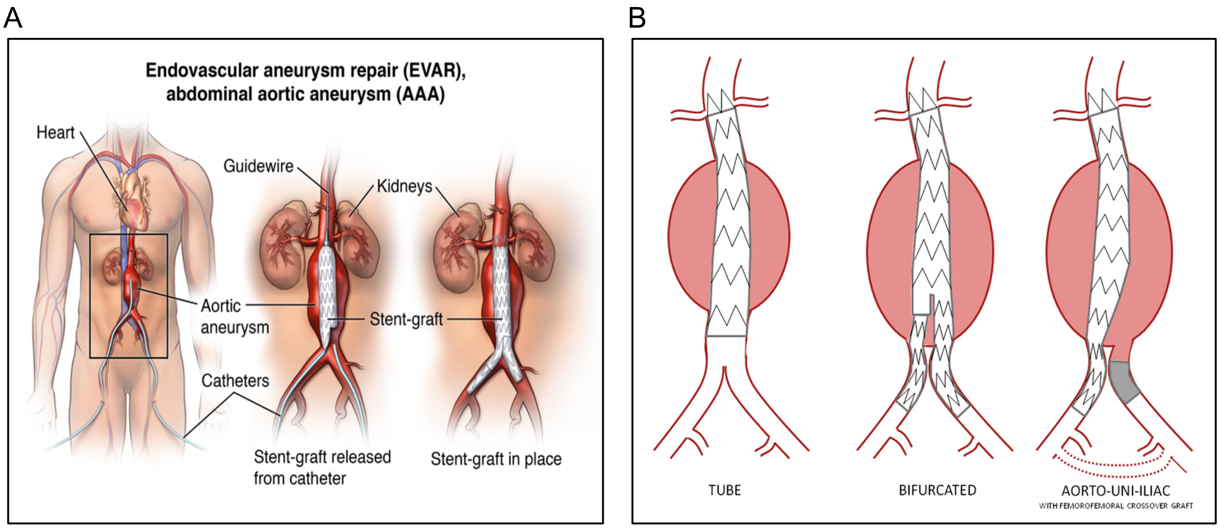

Figure 1. A. Schematic illustration of the positioning of a stent using EVAR. Reproduced from https://www.elcaminohospital.org/library/abdominal-aortic-aneurysm-repair.2 B. Schematic illustration of the different types of stent grafts used in EVAR. Reproduced from Endovascular Aortic Aneurysm Repair (EVAR) Andrew England1, Richard McWilliams2.[3]

As shown by Greenhalgh et al. in EVAR-1 trial[4] and by De Bruin et al. in DREAM[5], EVAR reduces 30-day operative mortality by two thirds in comparison to the more invasive open repair of AAAs (Figure 2). However, this early advantage is lost in the long-term outcome. The survival rates after either EVAR or open repair, 2 years and 6 years after the intervention, do not show any significant difference, as seen in the survival curves (Figure 2). EVAR was proven to be associated with a higher rate of re-intervention, as well as graft related complications, and was revealed to be more costly than open repair in the long term (Figure 3)[6].

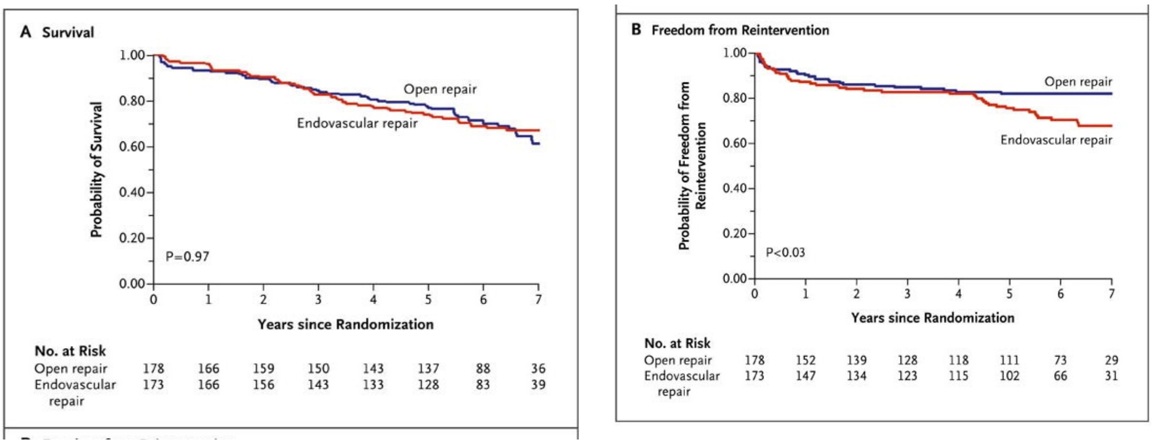

Figure 2: Kaplan–Meier Estimates for Total Survival and Aneurysm-Related Survival during 8 Years of Follow-up. Reproduced from De Bruin et al.[5]

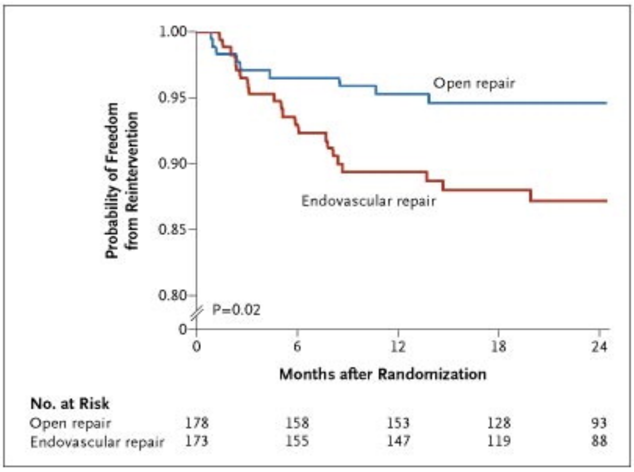

Figure 3: Kaplan–Meier Estimates of Freedom from Reintervention among Patients Assigned to Undergo Open or Endovascular Aneurysm Repair. Reproduced from Blankenjstein et al.[6]

2. Endoleak

An endoleak is defined as persistent circulation of blood into the aneurysmal sac, despite placement of the endograft.[9] There are different types of endoleaks, shown schematically in Figure 4, each one of which requires a specific type of surveillance. Type I endoleaks occur due to attachment site leaks, whereas type III endoleaks are a consequence of graft misoverlapping and the endoleak appears between the different modules. Both of them require urgent attention due to high potential for rupture of the aneurysm.[10] Type IV endoleaks are due to porosity of the graft wall but almost totally disappeared since the development of late-generation devices. The most common endoleaks are type II (T2E). They are caused by retrograde flow from aortic collaterals, most frequently the inferior mesenteric artery (IMA) and the lumbar arteries, but also the renal and hypogastric arteries. They occur with an estimated prevalence of up to 40%[11]. Despite many various studies conducted on the subject of endoleaks, the clear identification of their risk factors and the determination of an efficient treatment option remain unknown. Indeed, when comparing studies undertaken in the early days after the first EVAR operations and the ones launched during the more recent years, little progress was made concerning the medical care of endoleaks. Data concerning the risk factors, surveillance and management of endoleaks are still scarce.

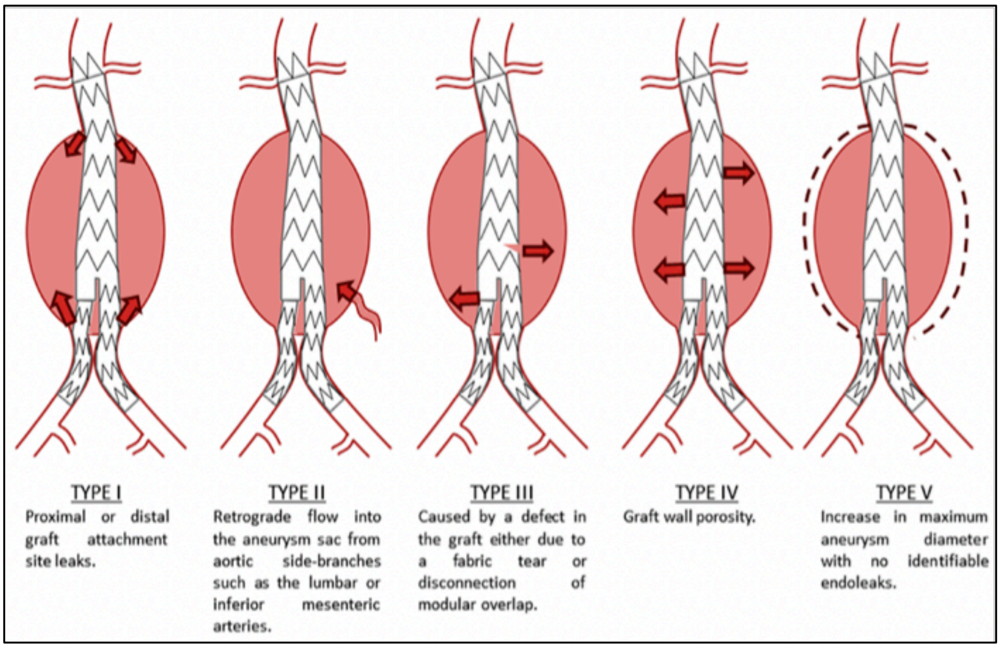

Figure 4: Schematic illustrations of the types of endoleak associated with endovascular aortic repair.

3. Objectives of the study

The aim of this retrospective study was to evaluate the endoleaks occurring after the implantation of the latest generation of stentgrafts, the patient's risk factors, as well as the various approaches to the management and treatment of endoleaks.

Material and Methods

1. Study design

All patients who underwent EVAR and who were later subject to treatment for endoleaks at the Centre Hospitalier Universitaire Vaudois (CHUV) were retrospectively selected from 2013 to 2017. Thirty-three patients treated for post-EVAR endoleaks were found and 25 were included in the study. Two of the patients had been treated initially outside of Switzerland, and the medical records were undiscoverable. They were excluded from the study. We also excluded 6 more patients due to a large amount of missing information concerning their pre-operative, intra-operative and post-operative characteristics.

Study protocol was in accordance with the Declaration of Helsinki and approved by the local Ethical Committee.

2. Patient characteristics

Details about the pre-operative, intra operative, post-operative and late follow-up characteristics were collected in each patient's medical record and entered into an electronic database. The date of birth, gender and tobacco use of each patient was reviewed. Comorbidities including COPD, hypertension, diabetes, hyperlipidaemia, liver diseases, cardiac diseases, cerebrovascular diseases, and peripheral vascular disease were also investigated.

3. Aneurysm anatomical features

The pre-operative anatomic features were determined on a pre-operative CT scan, with the 3mensio Vascular sizing software (Pie Medical Imaging, Bilthoven, The Netherlands). They included the diameter of the aneurysm, the ratio between the circulating blood volume and the total volume of the aneurysm, the maximum thrombus thickness, the diameter and the length of the proximal neck, the maximum diameter of the iliac arteries and the angulation of the infra-renal aorta. Some pre-operative CTs were missing, therefore the maximum thrombus thickness could only be determined in 22 patients and the ratio between the circulating blood in the aneurysm and the total volume of the aneurysm was only calculated in 21 patients. The number of patent lumbar arteries as well as their diameter was analysed, along with the patency of the inferior mesenteric artery (IMA). The evaluation of the diameter of the patent lumbar arteries was only possible for 20 of the patients and the number of lumbar arteries could be determined in 22 patients. The average number of patent lumbar arteries was calculated with the data of 20 patients. Additional patient information such as anticoagulation and antiplatelet therapy, statin or Plavix therapy were also reviewed. The ankle-brachial index was also recorded. Only 15 patients had data available concerning the ankle brachial index due to the impossibility of retrieving pre-operative angiological work ups for certain patients, the average was therefore calculated in regards to 15 patients and not 25 Whether patients underwent elective surgery, or were subject to emergency treatment following a ruptured aneurysm was also distinguished.

The pre-operative characteristics of the aneurysms were also analysed for each type of endoleak that developed during late follow-up.

4. Intra-operative characteristics

The evaluation of intra-operative data for the initial EVAR procedure was done by collecting data found in the operative protocols of each patient. The date of procedure, the type of endograft and its proximal diameter were included. Oversizing was calculated by subtracting the value found for the diameter of the proximal neck of the aneurysm to the value of the diameter of the proximal neck of the endograft used for the EVAR and divided by the diameter of the proximal neck of the aneurysm. The oversizing was evaluated for 24 patients as one patient was treated with a Nellix endograft and oversizing is not relevant for this type of endograft. The operating time was recorded in every patient but one. The use of intra operative adjuncts such as iliac branch device, and embolization of the IMA, side branches or hypogastric arteries, was recorded. Use of intra operative blood transfusion, the type of anaesthesia and both femoral accesses were also analysed.

5. Early follow-up analysis

The early follow-up analysis was defined as the period of 30 days following the intervention and/or the intra-hospital period. The occurrence of endoleaks, medical complications, surgical complications, reintervention, and death were also considered. Medical complications were divided into pulmonary, renal, digestive, cerebral and cardiac complications. On the other hand, surgical complications were separated into vascular and non-vascular surgical complications. Non-vascular complications included failure to heal of the incision wound, infection of the wound, hematomas and the development of seromas. Bleeding issues including coagulopathies (thrombosis) and the necessity for post-operative transfusions were also recorded in this category. Vascular surgical complications consisted of ischaemic complications, caused by thrombosis, embolization, dissection or occlusion of vessels. They can also consist in the failure of grafts and occlusion or infection of the grafts.

Finally, post-operative inflammatory syndrome defined by fever, maximum C-reactive protein levels and maximum leucocyte levels was investigated.

6. Late follow-up analysis

During the follow-up period, any type of imaging performed (CT-scan, duplex ultrasound (DUSS), contrast-enhanced ultrasound (CEUS), plain radiography, conventional angiogram or magnetic resonance angiography), as well as any endoleaks detected was analysed.

However, in 5 patients, some data were missing such as the sac diameter, the type of endoleak and the vessels involved due to suboptimal image quality. In 4 of these patients, another imaging technique was used to visualize the aneurysm.

Complications involving the stent graft, such as stenosis, thrombosis, migration and rupture, and the need for reintervention were also described. Reintervention for endoleaks included transarterial embolotherapy, translumbar embolotherapy, percutaneous transcaval embolotherapy, and the use of endostapling (Aptus), prosthetic elongations, thrombectomies, bypass techniques, angioplasties with and without stent coverage, and conversion to open repair. Death and any other complications reported were also included.

7. Statistical analysis

Data were analysed using Excel software, which allowed us to calculate the means, ranges and percentages of the different events. Kaplan-Meier life tables and figures were performed with Stata (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC) and used to analyse correlations between early endoleaks (<30 days) and late endoleaks (>30 days). The time patients went without reintervention was analysed (as a function of each type of endoleak). The correlation coefficients, the p-values and the Kaplan Meier curves were calculated using STATA version 15.0. A p-value < 0.5 was considered significant, and results were expressed as n (percentage) and mean (range).

Results

The data acquired in this way are summarized in Table 1,2, 3, 4, 5,6 and 7 and the results illustrated in these tables are described in this section.

1. Pre-operative characteristics (Tables 1,2)

Characteristics		n	%	Range
Age (average)		75		62-87
M		21	84	
F		4	16	
COPD		5	20	
Hypertension		21	84	
Liver disease		2	8	
Smoking		17	68	
Peripheral vascular disease		4	16	
Hyperlipidemia		19	76	
Diabetes		7	28	
Cardiac disease		16	64	
Cerebrovascular disease		7	28	
*Average ABI	Left	1,12		0,75-1,42
	Right	1,11		0,7-1,39
*Pre-operative Embolization	IMA	2	9	
	Other side branches	0	0	
Statin		17	68	
Anticoagulation		2	8	
ASA		18	72	
Plavix		5	20	
Elective		20	80	
Ruptured/Emergency		5	20	

Table 1: Patient demographics and medical history. All percentages were calculated in relation to 25 patients except for the data with an associated *(see method).

The 25 patients were mainly men (84%) with a mean age at the time of EVAR of 75 years (range 62-87 years). The most frequent comorbidities observed were smoking (68%), hypertension (84%), hyperlipidaemia (76%), and cardiac disease (64%). The average ankle-brachial index (ABI) was 1.1 on both sides (range 0.8-1.4 for the left and 0.7-1.4 for the right). The most frequently medication was ASA (72%) followed by statins (68%). Only 20% of the patients benefited from Clopidogrel. Finally, 5 patients underwent emergency treatment of their aneurysms, whilst the 20 others were all planned for elective repair. Two patients underwent pre-operative embolization of the IMA (9%) whereas no patients were submitted to the embolization of other side branches.

The mean aneurysm sac diameter was 64 mm (range 40-100 mm). Five patients (20%) had conical necks. The mean diameter and the mean length of the proximal neck were 24,8 mm (range 19-32 mm) and 22,7 mm (range 5-54 mm), respectively. The mean maximum thrombus thickness of the aneurysm was 22,8 mm (range 0-52). The ratio between the circulating blood in the aneurysm and the total volume of the aneurysm was identified to be of 66% (range 35-100%).

An average of 6 patent lumbar arteries per patient was found (range 4-9) with a mean maximal diameter of 3,7 (range 1,5-5,2). The IMA was patent in 95% of the population.

Characteristics		%	Range
Average Aneurysm sac diameter (mm)	64		40-100
Conical neck (n)	5	20	
Average proximal neck diameter(mm)	24,8		19-32
Average proximal neck length(mm)	22,7		5-54
Average infra renal angulation(degrees)	45,2		5-90
Average diameter of the iliac arteries (mm)	20		11-38
*Average Diameter of patent lumbar arteries (mm)	3,7		1,5-5,2
*Patent lumbar arteries (n)	6		4-9
*Patency of the IMA (n)	21	95	
Ratio between circulating blood volume and total volume of the aneurysm	66		35-100
*Average maximum thrombus thickness	22,8		0-52
*Percentage of oversizing	12,8		0-33

Table 2: Characteristics of the pre-operative aneurysm. * see method

2. Intra-operative parameters (Table 3)

The mean operating time was 132 minutes (range 83-226). The endografts used for EVAR were equally Excluder (Gore) (40%) and Endurant (Medtronic) (40%). The other types of grafts were significantly less common: 2 Zenith (Cook), 1 Talent (Medtronic), 1 Nellix (Endologix) and 1 Endofit (LeMaitre Vascular). No patients with AFX (Endologix) or Jotec grafts were seen. The mean number of modules of endografts used was 3 per patient (range 1-8). The mean diameter of the proximal body of the endograft was 28 mm (range 23-33). The mean oversizing was 12,8% (range 0-33). Only 2 patients for whom iliac branching was necessary and one patient who needed the use of one chimney were found.

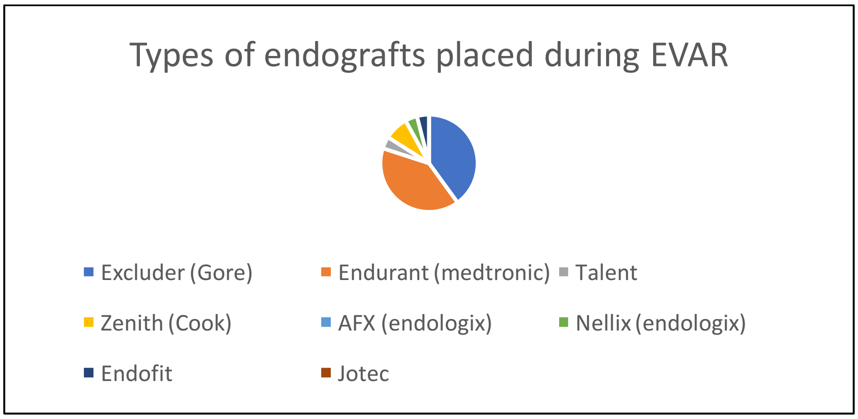

Figure 5: Graphical representation of the distribution of endografts

Intra-operative embolization of the internal iliac artery was undertaken for 3 patients. There were no embolization of the IMA and other side branches. The large majority of grafts placed in the patients included in this study had a bifurcated system. Indeed 24 patients beneficiated of an aorto-bi-iliac graft whereas the aorto-uni-iliac graft was used in one patient only.

Left and right open femoral cut-down was performed in the majority of cases (80%). The great majority of interventions were carried out under general anaesthesia (92%). Loco-regional anaesthesia was very uncommon in the cohort (8%).

Characteristics		n	%	Range
*Average operating time (min)		132	40	83-226
Type of endoprosthesis	Excluder (Gore)	10	40	
	Endurant (medtronic)	10	40	
	Talent (Medtronic)	1	8	
	Zenith (Cook)	2	0	
	AFX (endologix)	0	4	
	Nellix (endologix)	1	4	
	Endofit(LeMaitre)	1	0	
	Jotec	0	8	
Iliac branching		2	4	
Chimneys		1	4	
Number of chimneys		1	4	
Embolization	IMA	0	0	
	side branches	0	12	
	hypogatsric (internal iliac)	3	12	
*Number of endografts		3		1-8
*Average diameter of the proximal end of the endograft		28		23-33
Blood transfusion		2	8	
Device design	Aortouniiliac	1	4	
	Bifurcated system	24	96	
General Anesthesia		23	92	
Loco -regional anesthesia		2	8	
Left percutaneous		5	20	
Right Percutaneous		5	20	
Open surgery Left		20	80	
Open surgery right		20	80	

Table 3: Intra-operative characteristics.

3. Post- operative characteristics (Table 4).

Characteristics		n	%	Range
Length of hospital stay (days)		9,6		3 - 43
US		24	96	
Patients with endoleaks (Early <30 days)		17	68	
	Type 1	6	24	
	Type 2	12	48	
	Type 3	1	4	
	Type 4	1	4	
Patients with no endoleaks		8	32	
Patients with one type of endoleak		14	56	
Patients with more than one type of endoleak		3	12	
CTA within 30 days		21	84	
Vessels involved	IMA	5	20	
	lumbar arteries	5	20	
	IMA and lumbar arteries	2	8	
	Internal iliac artery	1	4	
Early medical complications		7		
	Cardiac	5	20	
	Pulmonary	1	4	
	Renal	3	12	
	Digestive	0	0	
	Cerebral	1	4	
Early surgical complications		7		
	Vascular	2	8	
	Non- vascular	6	24	
Revision Surgery		1	4	
Death		0	0	
Fever		4	16	
*CRP (max) mg/L		132,6		21-316
Leucos (max) G/L		11,3		6,8-21,7

Table 4: Post-operative characteristics. The average CRP levels were calculated for 22 patients.

The mean length of hospital stay was 9,6 days (range 3-43). There was a significative difference between women and men with an average of 15,5 days versus 8.5 days for men ($p<0.05$).

During the post-operative period, an ultrasound was performed in 96% of the population n and an angio-CT in 84% of the population. Each patient had at least one of this exam.

In this study, only 8 patients (32%) did not manifest any early endoleaks. Among the 17 patients with early endoleaks, 3 patients (12%) had more than one type of endoleak. When looking at the number of endoleaks occurring in the first 30 days, 48% of the population were found to developed type 2 endoleaks making them the most common type of early endoleak. Type 1 endoleak was seen in 24% of the population, and type 3 and 4 endoleaks were noticed to be much rarer in only 1 patient each.

The inferior mesenteric artery and the lumbar arteries were each responsible for type 2 endoleaks in 20 % of the population respectively. Eight percent of the patients had type 2 endoleaks caused by both the IMA and the lumbar arteries. The internal iliac artery was only responsible for 1 of the type 2 endoleaks. In this patient, a lumbar artery was also involved in the type 2 endoleak.

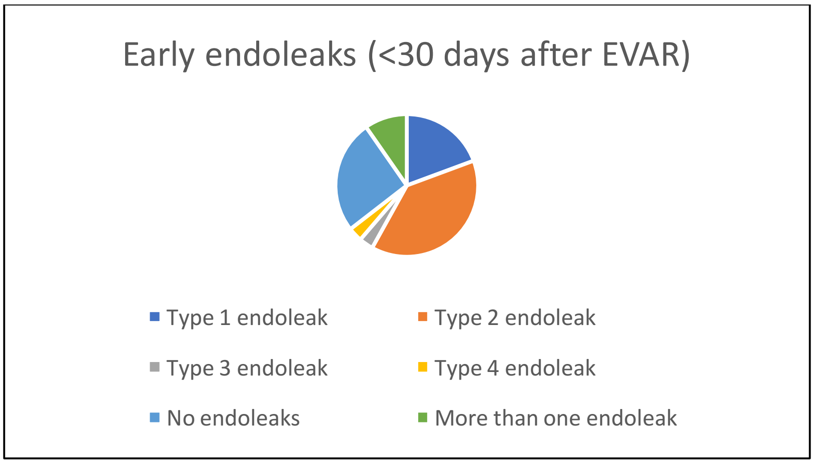

Figure 6: Graphical representation of the distribution of early endoleaks.

In this study, 28% of patients presented medical complications. Two patients developed more than one type of medical complication and the most frequent types of complications found were cardiac (20%). During the post-operative period, 28% of patients manifested surgical complications. Two of these patients developed vascular surgical complications, and one patient required a re-intervention for a type 4 endoleak that was treated endovascularly with a cuff. One occlusion at the origin of the internal iliac arteries in 1 patient was left untreated due to downstream vascularization taken over by the gluteal artery.

The 6 remaining surgical complications were not vascular. There were 3 hematoma at the puncture site, an inguinal wound dehiscence, and a inguinal seroma. One bleeding at the site of incision and the necessity for a post-operative transfusion following a significant decrease in haemoglobin levels were also observed.

The mean CRP value was 133 mg/L (range: 21-316) and the mean leucocytes value was 11.3 G/L (range: 6.8-21.7). In this study, 4 patients had fever (16%), and no deaths were recorded during early follow-up in the cohort.

4. Long-term follow-up (Tables 5,6)

The mean length of follow-up was 58 months (range 4-164). The most common types of imaging used to evaluate the status of the treated aneurysms were ultrasound and CT scans. All patients (100%) were submitted to at least one CT scan and 96% of the study cohort also underwent an ultrasound. A total of 174 Ultrasounds and 154 CT scans was seen with an average of 6 CT scans (range 2-16) and 7 ultrasounds (range 0-19) per patient.

The use of other types of imaging including contrast enhanced US performed in 24% of the population as well as conventional angiograms found in 40% of the population. In this study group, no plain radiographs were performed, nor any MRAs.

	Characteristics	n	%	Range
Average follow-up time (months)		58		4-164
CT scan		154	100	
DUSS		179	96	
Plain radiograph		0	0	
Contrast enhanced US		11	24	
Conventional angiogram		16	40	
Magnetic resonance angiography		0	0	
Endoleak (>30 days)	Type 1	12	48	
	Type 2	21	84	
	Type 3	6	24	
	Type 4	3	12	
	one type of endoleak	13	52	
	two types of endoleak	8	32	
	more than two type s of endoleak	4	16	
Vessels involved (>30 days)	IMA	9	36	
	Lumbar	20	80	
	Hypogastric	2	8	
Average sac growth (mm)		11,8	0	
Late complications		9	36	
Re-intervention		47	100	
Delay between initial EVAR and the first re-intervention (months)		Median 13		1-143
Embolization failure		5	20	
Thombectomy		2	8	
PTA+/- stent		3	12	
Bypass		1	4	
Other		14	56	
Death		0	0	

Table 5: Long term follow-up characteristics

During the long-term follow-up, type 2 endoleaks were discovered to be the large majority (84% of patients) of all endoleaks occurring, representing 50% of all endoleaks (Figure 7). The second most frequent type of endoleak was type 1 endoleak with 48% of the study group. The less frequent type 3 and 4 endoleaks were manifested in 24% and 12% of the population, respectively. Eight patients had two types of endoleaks during follow-up, 4 patients had more than two and 13 patients had one type of endoleak. Most type 2 endoleaks were due to lumbar arteries (80%). The inferior mesenteric artery was less frequently involved (36%) and the inferior iliac artery was rarely implicated in these types of endoleaks (8%).

The average sac growth over the whole follow up period was 11.8 mm (range 1-28 mm).

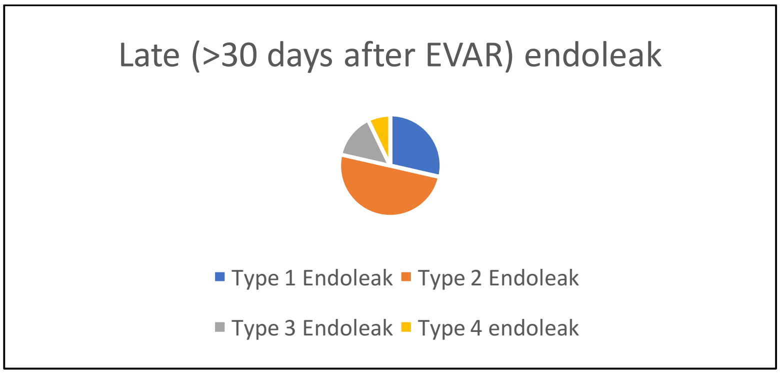

Figure 7: Graphical representation of the distribution of late endoleaks

The aneurysm characteristics specific to each endoleak were analysed (Table 6). The mean oversizing was the lowest for T1, T3 and T4 endoleaks, being inferior to 10%. The neck length was the shortest in patients with T1 endoleaks. Patients with T2 endoleaks had the highest ratio of circulating blood, the largest average lumbar artery diameter and were more prone to have patent IMA. When excluding the patients with T4 endoleaks, the thrombus was thinner in patients with T2 as compared to T1 and T3 endoleaks. T3E's are found to have the largest aneurysm sac diameter (67,2 mm), the widest proximal neck (27mm), the longest average neck length (24mm) and the most important angulation of the infra-renal aorta (54 degrees). Moreover, they were more prone to have iliac diameter superior to 20 mm. An equal amount of Excluder and Endurant endografts were seen in patients developing T2Es, whereas patients with type 1 and 3 endoleaks had a majority of Endurant grafts used for EVAR. This was not statistically significant in our study.

Aneurysm characteristics		T1E	%	T2E	%	T3E	%	T4E	%
Average aneurysm sac diameter (mm)		58,1		64,2		67,2		68	
Average proximal neck diameter (mm)		26		24		27		23	
Average proximal neck length (mm)		**17**		23		24		20	
Average infra renal angulation (degrees)		45		42		54		50	
Ratio between circulating blood volume and total blood volume		53		**68**		64		65	
Average diameter of patent lumbar arteries (mm)		3,4		**3,6**		3,3		2,9	
Average number of patent lumbar arteries		6		6		6		6	
Number of patients with patent IMA		8	67	18	**86**	4	67	3	100
Number of patients with an iliac artery diameter >20mm		2	17	5	24	3	**50**	0	0
Average Maximum thrombus thickness(mm) *		24,8		**22,8**		26,8		16,1	
Average diameter of proximal neck of endograft(mm)		29		27		29		25	
Average oversizing percentage		**9**		13		8,4		**8,7**	
Type of endograft	Endurant	7	58	8	38	3	50	3	100
	Excluder	3	25	8	38	2	33	0	0

Table 6: aneurysm characteristics specific to each type of endoleak. The average maximum thrombus was available for 10 patients.

The rate of reintervention in this study population was 100% with an average of 2 reinterventions per patient (range 1-5). The median time between the initial EVAR intervention and the first re-intervention for the treatment of an endoleak was 13 months (range 1-143).

As illustrated in Table 7, the most frequent type of treatment for endoleaks observed was embolization in 84% of patients. The most common type of embolization was transarterial (44%) followed by translumbar embolotherapy (36%) and percutaneous transcaval embolotherapy (4%). Prosthetic prolongation was done in 52% of the population. Endostapling (12%) and conversions to open repair (12%) were rarer. No patient underwent laparoscopy for the treatment of their complications. Twelve percent of the cohort was noted to have an angioplasty associated or not to stenting for the treatment of complications. Eight percent of the study population underwent thrombectomies and the use of a bypass was reported in 4 % of the patients.

Type of treatment for endoleaks	Type of treatment for endoleaks	n	%
Embolization	Transarterial Embolotherapy	14	44
	Translumbar Embolotherapy	12	36
	Percutaneous transcaval embolotherapy	1	4
Endostapling (aptus)		3	12
Laparoscopic		0	0
Prosthetic prolongation		16	52
Conversion to open repair		3	12

Table 7: Type of treatments for endoleak

During the follow-up period, 36% of the cohort manifested endograft-related complications, other than endoleaks. The most common complication was the development of thrombosis at the location of the stent graft (16%) followed by stenosis of the stent grafts (16%), and migration of the stent-graft (4%). No aneurysm ruptures were observed.

Fifty-six percent of the population manifested complications which were not endoleaks and that did not involve the stent graft. These included dissections, false-aneurysms, anaemia, thrombocytopenia, stenosis of the IMA and the renal artery, kidney atrophy, aneurysm of the iliac artery, seromas and pseudo-aneurysms. An occlusion of the femoral artery, a contrast agent leak into the ilio-psoas muscle and an acute ischaemia of the leg were also noted.

During the follow-up period, no deaths were observed.

5. Correlation analysis

Our analysis of the relationship between the early endoleaks and the late endoleaks revealed no significant association (the correlation coefficient was of -0.0454 and the p-value of 0.8293).

The Kaplan- Meier life curves showed that 72% of the study cohort did not have re-interventions 6 months after EVAR, 60% after 1 year and 28% after 3 years. Most reinterventions were performed during the first two years after EVAR.

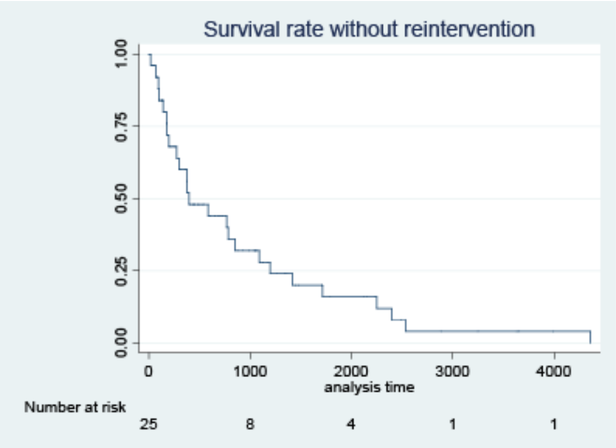

Figure 8 Kaplan-Meier life curve illustrating the survival rate of patients, without re-intervention

Another Kaplan-Meier life curve analysed the rate of re-intervention as a function of the different types of endoleaks. Ninety percent of patients with a Type 2 endoleak did not have a re-intervention 6 months after the initial EVAR in comparison to 33% for patients with type 1 and 3 endoleaks. One year after EVAR, 60% of patients with type 2 endoleaks did not have re-interventions and 33% of patients with type 1 and 3 endoleaks did not have re-interventions. Three years after EVAR, 12% of patients with type 2 endoleaks did not have re-interventions whereas 20% of patients with type 1 and 3 endoleaks did not have re-interventions.

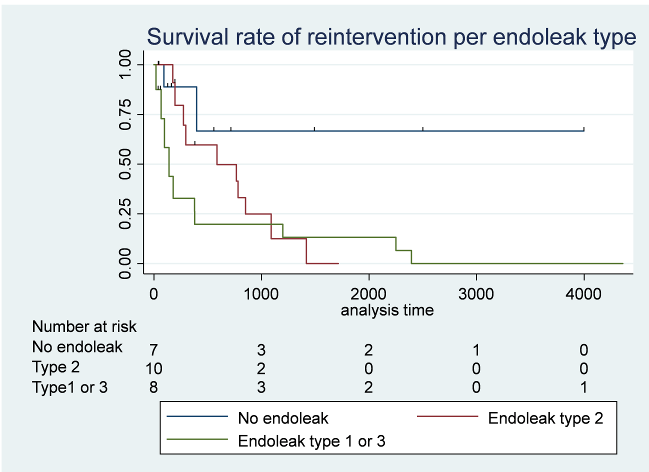

Figure 9 Kaplan-Meier survival curve illustrating the survival rate of patients, without re-intervention

Discussion

Over the last decades, the treatment of AAA has shifted from open repair to EVAR. This was a consequence of early findings showing decreased morbidity and mortality associated to EVAR.[4] However, it was later shown that this early advantage was lost during long term follow-up.[6] This is essentially due to the development of endoleaks and the high rate of reinterventions they induced and to the risk of late rupture.[10] Although it seems rather clear that patients have to be followed after EVAR, the way and the frequency of follow-up remains matter of debate. Moreover, data remains discordant concerning the predictive factors, detection and treatment of these endoleaks. This single-centre retrospective study aimed to clarify the impact of EVAR on the CHUV's patients and enable a better targeting of the medical care in relation to endoleaks and their complications. More significantly, in the longer term, if the reasons for endoleaks can be identified and the rate of endoleaks reduced, then the EVAR approach should lead to better long-term outcomes than open repair.

In this study, type 2 endoleaks were established to be the most common. This was concordant with findings made by other groups.[11] Past studies have identified predictive factors for the development of type 2 endoleaks such as older age,[12] anticoagulation therapy[13] and larger aneurysm diameters.[14] [15,16] The findings found in this study were similar, although a small number of this study's patients were under anticoagulation therapy.

Abularrage et al described that active tobacco use was associated with lower rates of endoleak occurrence.[12] However, smokers represent a large proportion of our study population which is in contradiction with other findings. COPD, and an ABI < 0.87, were also considered a protective factor for endoleaks.[17,18,19] A small number of the patients in our study had COPD and their mean ABI was significantly higher than 0.87. The interpretation of the mean ABI in this study must be made with caution as only few ABI values were possible to collect.

Other factors such as hypertension, hyperlipidaemia and cardiac disease, which concerns a large number of the patients in this study, were not found to be associated to a higher risk of endoleaks. However, it was noticed by Powell et al that coronary artery disease was associated to an increased post-operative mortality which could indicate a need for better peri-operative care for these patients.[20] Pre-operative statin and aspirin treatment was also present in many of the patients in this study, but has not been proven to be associated to higher rates of endoleaks.

Being a female patient was found in previous studies to be associated with a higher risk of reinterventions and rupture whereas male patients seemed to have better post-operative outcomes.[21,15] This study was mainly composed of male patients, and analysing the impact of gender on endoleaks would necessitate a larger number of patients.

Concerning the role of the pre-operative anatomical characteristics of the aneurysm, Petrik et al determined that there was no significant association established between the anatomical properties of the aneurysm and the probability of developing endoleaks during the late follow-up.[22] Indeed, Chuter et al had previously reported that the diameter of the proximal neck of the aneurysm, the angulation of the infrarenal aorta, or the difference between the diameter of the endograft and the diameter of the aorta didn't have any impact on the appearance of endoleaks during follow-up.[23] Although our study showed very spread out values regarding the anatomical characteristics of the aortic aneurysms, some interesting associations could be done. Type 1 EL was associated with shorter neck length and a mean oversizing inferior to 10%. This is in accordance with most of the IFUs given by the companies. Abularrage et al reported that patients with a low percentage of thrombosis in the aneurysm sac were more at risk of developing endoleaks during follow-up. The percentage of thrombosis in the aneurysm sac was also low in this study, especially in the group of type 2 EL. Moreover, type 2 ELs were associated with the highest ratio of circulating blood volume compared to total aneurysmal volume. Nevertheless, to better understand the importance of the anatomical features of abdominal aortic aneurysms in the development of endoelaks, it would be interesting to study a larger cohort over a significant amount of time.

It has been previously described that a patient with a patent IMA and more than 2 patent lumbar arteries is more at risk of developing a type II endoleak.[24] The higher the number of patent lumbar arteries are, the higher the risk for type II endoleaks.[25] The patency of the lumbar arteries was proven to be a more important risk factor for the persistence of endoleaks, more so than the patency of the IMA. This study's population manifested a significant number of patent arteries and a large majority of the patients had a patent IMA. It was also seen that T2Es had the largest number of patients with patent IMAs and patents lumbar arteries in comparaison to other types of endoleaks. This confirms that patent lumbar arteries represent a risk factor for the development of endoleaks. In light of these findings, the increased use of pre-operative embolization of the IMA as a preventive measure against type 2 endoleaks could be envisaged. However, in our study, IMA was responsible for only 36% of type 2 ELs, raising the question of the necessity of pre-operative embolization. Indeed, the preventive benefit of pre-operative embolization of the IMA is a source of controversy. Its benefit was disproven by Velazquez et al, as a significant number of patients with pre-operative patent IMAs do not develop post-operative type 2 endoleaks.[26,27] On the other hand, other studies did demonstrate an advantage of pre-operative embolization. Therefore, the routine use of this technique is still a subject of discussion and would need further work with a larger cohort of patients to determine if it's use should be recommended. We could also raise questions concerning the role of pre-operative embolization of lumbar arteries, or envisage a translumbar embolization to target the nidus of flow between lumbar arteries and the IMA. It must be taken into consideration that these techniques are not trivial and have severe associated risks such as paraplegia.

As for intra-operative factors, Lo et al determined that intra-operative embolization of the hypogastric artery, and graft design being aorto-uniiliac or bi-iliac does not have any impact on the development of post-operative endoleaks.[28] This study only identified a small number of intra-operative embolizations of the hypogastric artery. Further use of this method is no longer recommended. A large majority of the patients had bifurcated endografts and the evaluation of their impact on the occurrence of endoleaks would need a larger cohort of patients.

It was also described in multiple studies that the Endurant graft was considered as a protective factor against endoleaks, whereas the Excluder graft was considered a risk factor.[28,29] On the basis of this observation, it was expected to find a larger amount of Excluder grafts used in the patients included in this study. The Excluder and the Endurant graft were found in equal quantities amongst this cohort. However, the Endurant device was used in more than 50% of patients with type 1 ELs. One hypothesis could be that more Endurant grafts are used outside the IFUs, in order to push the limits. This would need to be compared to the rate of usage of the two types of graft in the general EVAR population at the CHUV. The Talent graft was also associated to a larger chance of endoleaks. However, this was only described in the earlier follow-up and the discrepancy between endografts was lost during later surveillance.[30,31] Only one Talent endograft was identified in this study making it difficult to conclude on its role in the occurrence of endoleaks. The Nellix endograft, by definition, should not be responsible for the development of type 2 endoleaks. Therefore, the more extensive use of the Nellix endograft could be envisaged. Still, in this study the only patient who beneficiated of a Nellix did develop a type 1 and a type 2 endoleak. Further investigations are needed to determine whether the Nellix endograft could have an advantage over other types of grafts on the development of type 2 endoleaks.

Lo et al also described the persistence of an early endoleak for over 6 months as a predictor of reinterventions and aneurysm sac changes.[28] On the other hand, it was found in this study, that there was no statistically significant association between early endoleaks and late endoleaks and it was concluded that the occurrence of an endoleak less than 30 days post-op is not a predictor for the development of an endoleak during later follow-up. This was also seen in previous studies and explained by the high rate of spontaneous resolution of certain endoleaks.[26] Because this population consists of patients with treated endoleaks only, it was no possible to asses the rate of spontaneous resolution of endoleaks. This will be the subject of further work.

Although performing CT scans for the detection and the surveillance of endoleaks is currently the most widespread imaging technique, it has been shown it may not be the most reliable tool for the classification of endoleaks. Indeed, Stravopoulos et al described that although CTA seems to be an efficient technique for the visualisation of endoleaks, it is less reliable for determining the flow of the leaks. [32] As type I, II and III endoleaks may cause the opacification of the lumbar arteries as well as of the IMA, it can make the classification of endoleaks challenging.[33] These observations have raised doubts concerning the efficiency of CTA in post-operative surveillance. Angiography on the other hand can detect the direction of blood flow. In this study, a large number of patients with simultaneously more than one type of endoleak were found. It is difficult to determine whether this phenomenon is accurate, or whether the imaging techniques used have not been able to determine the true type of endoleak. This is why the increased use of angiography could be proposed. However, consensus was established on CTA being an effective technique for the surveillance of endoleaks after their treatment.[34] Furthermore, angiography is time consuming, and necessitates additional hospitalisation days, making it more costly than CT scanning. It has been recommended to use angiography only during interventions, and not as a pre-operative classification method.

The team of Wolf et al showed that the use of Duplex ultrasound for the detection and follow-up of endoleaks after EVAR was equivalent to CT scanning.[35] Despite DUSS being highly dependent on the operator and on the morphology of the patient, it was found that there was no difference in clinical management following the use of these two imaging techniques. This population mostly underwent CT scanning and DUSS at similar rates. Considering the higher radiation-exposure and costs induced by CT-scanning and the proven equal performance of DUSS, the diminished use of CT scanning and the more extensive use of DUSS is recommended.

CEUS was found to be as efficient as CT scanning for the detection of endoleaks during follow-up surveillance, and was also proven to be superior to DUSS. This is due to the reduced impact of artefacts on the CEUS image.[36] CEUS was also proven to be superior to CTA for the classification of endoleaks due to its capacity for haemodynamic analysis. Despite the strong dependency on the operator, Stefaniak et al determined that CEUS was the most efficient technique for the detection and classification of endoleaks.[37,38,39] At the CHUV, low rate of CEUS were seen for follow-up surveillance. In light of this information the promotion of the use of CEUS in the CHUV for the surveillance of patients having undergone EVAR is encouraged.

MRA has also been found to be superior to CTA in its detection of endoleaks, but it's execution is more time-consuming, more expensive and not always available.[37]

In consideration of these different analyses, the increased use of CEUS and DUSS as reliable techniques for the detection of endoleaks during follow-up and for the determination of the type of endoleak is recommended.

Concerning the treatment of endoleaks, controversy particularly surrounds the treatment of type 2 endoleaks. It is difficult to know which type II endoleaks need urgent attention. Some patients with asymptomatic endoleaks presented sudden aneurysm rupture despite the absence of significant sac growth. On the other hand, some patients with persistent endoleaks and important sac growth did not show signs of rupture during follow-up. Some advocate a conservative management due to the absence of significant change despite the presence of a persistent aneurysm sac perfusion.[40,41] Still it has been shown that all endoleaks can cause persevering systemic pressure in the aneurysm sac with a significant risk of rupture.[26,42,43] Another team demonstrated that sac shrinkage and the risk of rupture was the same for patients having had successful treatment of their endoleaks and for patients who never had endoleaks. [44] It was also proven that certain endoleaks that resolve spontaneously, reopen in 20 % of the population. This is an argument for more aggressive treatment of endoleaks.[17] The treatment of all endoleaks for the complete exclusion of all abdominal aortic aneurysms is therefore recommended.

This study showed a majority of patients having transarterial embolotherapy. However, it has been shown by Baum et al that translumbar embolotherapy shows lower rates of recurrence of endoleaks following the treatment.[45] This was explained by the resemblance observed between the mechanism of endoleaks and arterio-venous malformations. Indeed, transarterial embolotherapy only occludes the identified vessel involved with the CT scan but does not enable the occlusion of the outflow vessels which can be responsible for the persistence of endoleaks. Whereas going directly into the aneurysm sac with a translumbar method allows the targeting of the nidus of the endoleak and therefore induces less embolization failures. In this study, 3 embolization failures in relation to transarterial embolotherapy were observed and no embolization failures for translumbar embolotherapy. Some embolizations failed on more than one occasion, which could be explained by an erroneous identification of the vessels involved. This could motivate a change in practice so as to privilege translumbar embolotherapy for the treatment of type II endoleaks.

The treatment of Type I and III endoleaks has achieved consensus. It is accepted practice that type I and III endoleaks be treated with prosthetic elongation. In this study, only one patient with a type I endoleak was not treated. Still the visualization of endoleaks in this patient was unreliable, and the later imaging examination revealed no persisting endoleak. All other patients underwent treatment for their type I endoleaks. As for Type III endoleaks, all but one patient were treated with prosthetic elongation. The type III endoleak detected in the untreated patient was identified at the last follow-up event which was in 2017. Longer follow-up will determine if the patient will be treated or not.

Nolz et al demonstrated that patients with only type 2 endoleaks seem to have no increased mortality, and a higher survival rate than patients with other types of endoleaks.[46] This is only the case for patients with no other associated endoleaks. In this study, almost half of patients had other endoleaks associated to their type 2 endoleaks. It is therefore difficult to assess which type of endoleak is responsible for sac enlargement. [47,48]

Limitations of our study:

It was not possible to compare this group of patients to a control group, free of endoleaks. The analysis of a group of patients presenting endoleaks and who were not the subjects of reintervention was unattainable. Both of these will be the subject of future work.

This study was undertaken using a retrospective method. This induced the lack of some data, limiting the impact of the study. This study was based on a small cohort of patients making the evaluation of the data difficult to interpret. A much larger cohort is needed in order to confirm the preliminary correlations observed and discussed here. This will be undertaken during later work.

Towards this end we have initiated a comprehensive database of patient information, and carried out a preliminary analysis of correlations, so as to be able to target future research on eliminating these types of leaks and to provide the best management of endoleaks.

Conclusions:

An association between this single-centre study and an extensive literature review enabled a better understanding of local management of endoleaks after EVAR. Type II endoleaks were identified as the most common type of endoleak amongst the patients in this study. The presence of certain predictive factors in our cohort such as pre-operative I lumbar artery patency, older age, and large aneurysm sac diameter were assessed. The pre-operative embolization of the IMA was not identified as necessary, and the greatest number of reinterventions was caused by type II endoleaks. Following this study, a reinforced post-operative surveillance along can be recommended. The hypothesis that when endoleaks should be treated, it seems preferable to use translumbar embolotherapy for type II endoleaks and prosthetic elongation for type I and III endoleaks can be emitted based on the findings of this study.

However further work comparing this data with a cohort free of endoleaks is necessary for more detailed interpretation.

Finally, it was noted that in recent years the rate of secondary interventions has been significantly diminished, which could be explained by the progress in device design and the constant evolution of surgical techniques. Therefore, it can be imagined that EVAR will cause reduced secondary interventions in the future, following further progress in the understanding of endoleaks.[49]

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