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Programvezető: Dr. Merkely Béla, egyetemi tanár

Témavezető: Dr. Csobay-Novák Csaba, egyetemi adjunktus

INITIAL RESULTS OF COMPLEX ENDOVASCULAR INTERVENTIONS FOR THE TREATMENT OF AORTIC DISEASE IN HUNGARY

PhD thesis

Sarolta Borzsák

Doctoral School of Theoretical and Translational Medicine

Semmelweis University

Supervisor: Csaba Csobay-Novák, MD, PhD

Official reviewers: Barnabás Galambos, MD, PhD

Dénes Horváthy, MD, PhD

Head of the Complex Examination Committee:

Tivadar Tulassay MD, DSc

Members of the Complex Examination Committee:

Henriette Farkas, MD, DSc

Charaf Hassan, DSc

Budapest

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List of Abbreviations

AAA	abdominal aortic aneurysm
ASA	American Society of Anesthesiologists
BMI	body mass index
CIA	common iliac artery
CMD	custom-made device
CSFD	cerebrospinal fluid drainage
CTA	computed tomography angiography
EIA	external iliac artery
EVAR	endovascular aneurysm repair
FBEVAR	fenestrated/branched endovascular aortic repair
IBD	iliac branch device.
ICU	intensive care unit
IFU	instructions for use
IIA	internal iliac artery
IQR	interquartile range
MRA	magnetic resonance angiography
N	number
OTS	off-the-shelf
PRA	pararenal aneurysms
SD	standard deviation
TAA	thoracic aortic aneurysm
TAAA	thoracoabdominal aortic aneurysm
TEVAR	thoracic endovascular aortic repair

1. Introduction

1.1. Aortic aneurysms

The word aneurysm evolved from a Greek word (ανευρυσμα - aneurusma), meaning dilatation. Aneurysms are the vessels' irreversible focal dilatation, defined as exceeding the expected normal diameter by at least 1.5 times. A true aneurysm is one that contains all three layers of the vessel, otherwise it is called a pseudoaneurysm. (1) Aneurysms can occur anywhere in the vascular system but can be found most commonly on the arterial side, especially on the aorta. In terms of location, abdominal (AAA), thoracic (TAA) and thoracoabdominal aortic aneurysms (TAAA) are distinguished. The most common form affects the infrarenal abdominal aorta, followed by the ascending thoracic aortic aneurysm. (2)

Based on morphology, we differentiate saccular and fusiform aneurysms. The more common type is the fusiform type, where the whole circumference of the artery is affected, while an aneurysm that includes only a part of the circumference is named saccular, referring to the sac-like appearance. (1)

1.1.1. Abdominal aortic aneurysm

If the aortic diameter is 30 mm or more, the diagnosis of an AAA is conventionally made. (1) In clinical practice, in addition to morphological classification, they are most often classified according to the location of the proximal aneurysm and the renal and visceral arterial branches. These are infrarenal (aneurysm with a proximal neck longer than 10 mm), juxtarenal (aneurysm with a proximal neck shorter than 10 mm but not extending above the renal artery), pararenal (aneurysm located between the superior mesenteric artery and the renal artery) and paravisceral (aneurysm located between the superior mesenteric artery and the celiac trunk). There is also a fifth type, which extends over the celiac trunk, usually classified as type IV thoracoabdominal aneurysm. (3) (Figure 1.)

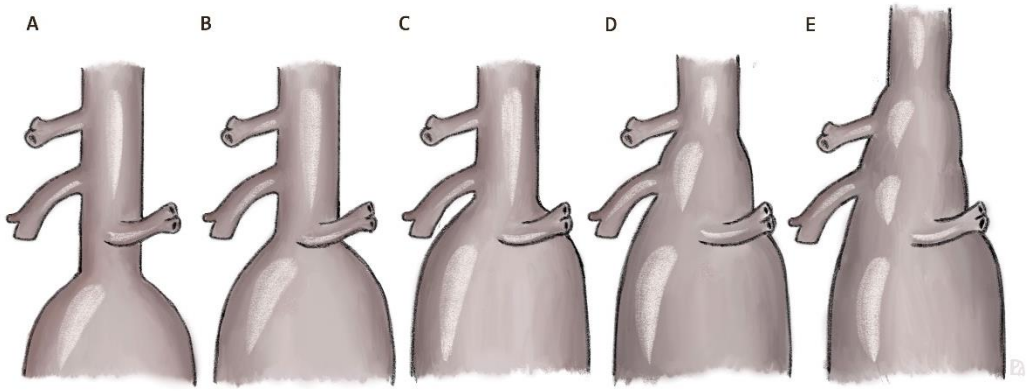


Figure 1. Classification of abdominal aortic aneurysms (AAAs): short-neck (<10 mm) infrarenal (A), juxtarenal (B), pararenal (C), paravisceral (D), and extent IV thoracoabdominal aortic aneurysm (E).

In terms of incidence, the number of abdominal aneurysms has been steadily increasing in recent times, due to an ageing population, an increase in the number of smokers, and improved diagnostic tools. (1) The lifetime risk in men is 8.2%, while in smokers it is 10.5%. (4) The main risk factors include male sex, older age, and smoking. The disease is 4-6 times more common in men than in women. The incidence increases steadily with age, with a significant increase in risk after the age of 60 years. Women develop aneurysms approximately 10 years later than men. (5) Smokers have more than four times the incidence of the disease compared to the non-smoking population. (1) Caucasian populations also have a higher incidence. Other risk factors include hypertension, coronary artery disease, peripheral vascular disease and atherosclerosis. A positive family history and intervention for AAA in a first-degree relative also increase the risk. However, it is less common in patients with diabetes. (5)

Clinically, most aneurysms are asymptomatic, usually discovered incidentally during abdominal ultrasound, computed tomography angiography (CTA) or MR angiography. If the aneurysm compresses surrounding abdominal structures, chronic abdominal or back pain may occur. In addition, distal embolization or acute thrombotic complications and, very rarely, disseminated intravascular coagulation may occur. If the aneurysm spreads to the iliac vessels, ureterohydronephrosis may also develop. One of the most serious complications of abdominal aneurysms is rupture. The risk of this depends mainly on the size of the aneurysm, ranging from an annual risk of 3-15%

between 5 and 5.9 cm, while the risk is 30-50% above 8 cm. The growth rate of the aneurysm, regardless of its initial size, is also an important factor. If this growth exceeds 0.5 cm within 6 months, it is considered to be at high risk of rupture. Growth is generally faster in smokers, but slower in diabetics or peripheral vascular patients. In addition, female gender and a positive family history of aortic aneurysm also increase the risk of rupture. Symptoms of rupture are characterized by a characteristic triad: sudden onset of intense abdominal pain, abdominal pulsation, and hypovolemic shock. The dynamics of the onset of shock depend largely on the location of the rupture. In the case of a rupture of the anterolateral wall of the aorta, the hemorrhage ruptures into the peritoneal space, leading to a rapidly developing shock. Rupture of the posterolateral wall has a more favorable outcome. In this case, the rupture may temporarily seal the bleeding into the retroperitoneum, causing only a small amount of blood loss. (1, 5)

In establishing the diagnosis, abnormalities detected during the physical examination may arouse suspicion before imaging studies are performed. For example, palpation of the pulsatile abdominal terime in the area above the navel. The sensitivity of the physical examination is greatly influenced by the size of the aneurysm and the amount of abdominal fat in the patient. (5) Among imaging studies, abdominal ultrasound is the primary modality for both screening and follow-up. The guideline recommends abdominal imaging every 3 years for aneurysms between 3 and 3.9 cm in diameter, every year between 4 and 4.9 cm in men and 4 and 4.4 cm in women, and every six months for aneurysms over 5 cm in men and 4.5 cm in women. (6) If the aneurysm diameter warrants intervention, CTA or in cases of poor renal function MR angiography should be performed. The main purpose of these imaging techniques is preoperative planning, to help decide whether open or endovascular intervention is warranted, and to assess more accurately the extension of the aneurysm into the proximal neck, iliac arteries and the patency and anatomy of the visceral branches. (1)

1.1.2. Thoracoabdominal aneurysm

To classify aneurysms involving both the thoracic and abdominal segments, we use the Crawford classification modified by Safi. (7, 8) According to this classification, in type I, the aneurysm starts at the level of the left subclavian artery and ends at the level

of the renal artery. In type II, the dilatation also starts at the level of the subclavian artery and involves the whole abdominal aortic segment, often adjacent to the common iliac artery. In type III, the whole abdominal aorta is also involved, but the aneurysm starts at the level of the 6th intercostal space. Type IV involves an aneurysm starting just above the diaphragm and extending throughout the abdominal aorta up to the iliac bifurcation. In type V, the aneurysm extends from the level of the 6th intercostal space to the palate of the renal artery. (Figure 2.) (9)

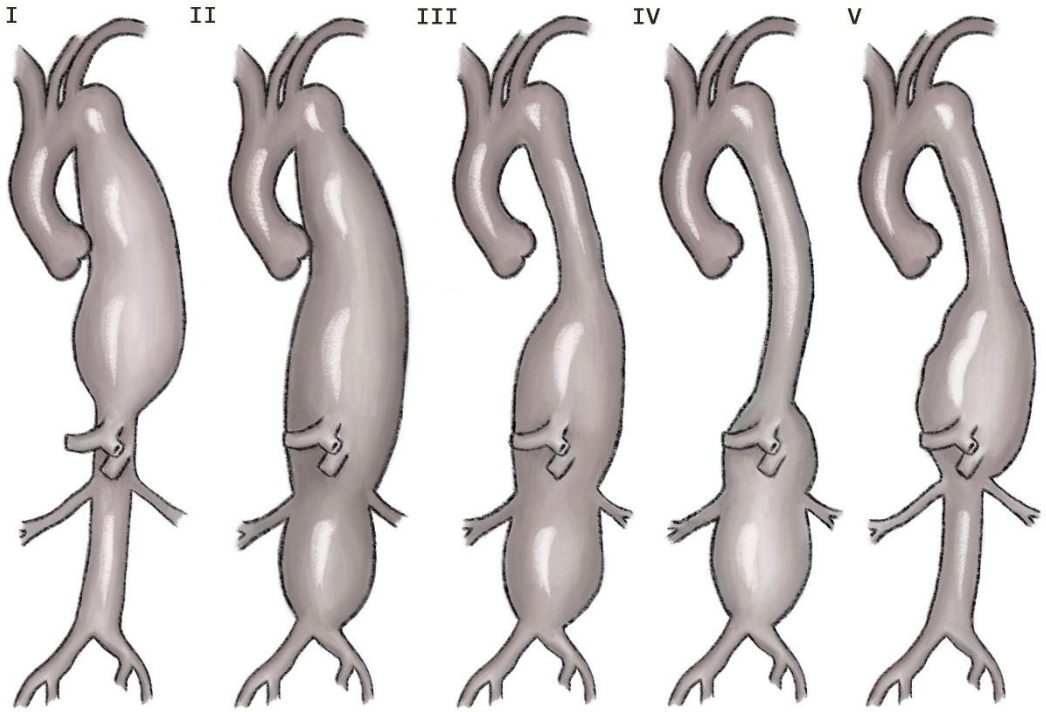


Figure 2. Crawford's classification of thoracoabdominal aneurysms modified by Safi

1.2. Iliac artery aneurysm

Compared to aortic aneurysms, dilatation of the iliac arteries is considered a rare vascular disease, with an isolated iliac aneurysm having a prevalence of 0.03% in the general population. (10) In the isolated form, they account for less than 6-7% of intra-abdominal aneurysms, but more often occur in association with abdominal aortic aneurysms, which are responsible for up to 20% of cases. (11) 70% of iliac aneurysms involve the common iliac artery (CIA), 20% the internal iliac artery (IIA), and the

remaining 10% the external iliac artery (EIA). (12) In about two-thirds of cases, more than one segment of the iliac artery is involved. (13) CIA aneurysms are defined as a vessel diameter of more than 18 mm in men and more than 15 mm in women, while IIA aneurysms are defined as a vessel diameter of more than 8 mm in both men and women. Isolated iliac aneurysms affect predominantly men (90%) and are usually detected between the age 70 and 80 years. (14) The etiological factors are the same as those detailed for abdominal aortic aneurysms, of which atherosclerosis is the primary cause, but it can also develop due to infection, trauma or genetical connective tissue disease. (11, 13)

Isolated iliac aneurysms can be classified in several ways. Reber's classification is based on the anatomical localization of the aneurysm, which can be divided into types I-IV. Type I involves only the common iliac artery, type II only the internal iliac artery, type III both the common and internal iliac arteries, and type IV the external iliac artery in addition to the common and internal iliac arteries (Figure 3). (14, 15)

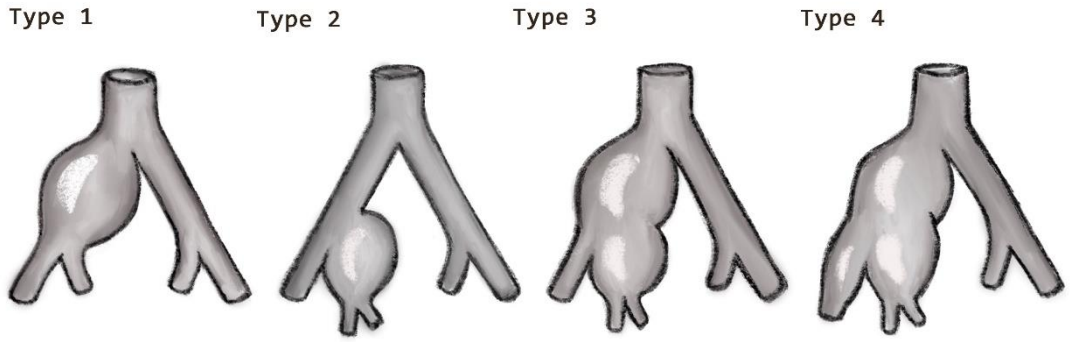


Figure 3. Reber's classification of isolated iliac aneurysm

Another classification system was created by M. Fahrni, which combines anatomical characteristics and endovascular treatment options. Type I involves the common iliac artery and type II the internal iliac artery. Within this type, we can speak of type Ia, in which the proximal aneurysm allows proximal fixation of the iliac stent graft. In type Ib, there is no adequate proximal aneurysm so that a bifurcation aorto-iliac stent graft is required. Type IIa requires distal iliac internal embolization and iliac stent graft implantation due to a too wide iliac internal aneurysm stoma. In type IIb, the proximal neck of the iliac internal iliac is adequate and therefore afferent and efferent

embolization is the treatment option. In type IIc, there is no adequate proximal neck, therefore embolization of the entire aneurysm sac is indicated. (16)

Similar to abdominal aortic aneurysms, iliac aneurysms are typically asymptomatic in clinical presentation, but can sometimes present as more serious complications. These include rupture, distal embolization, thrombosis and various compression symptoms. The most serious complication is aneurysmal rupture, which can have a perioperative mortality of up to 40%. (17) In some cases, the compression symptoms caused by the aneurysm raise the suspicion of the presence of a vessel dilatation. These include pyelonephritis or urinary tract sepsis due to compression of the ureters, pain during defecation due to obstruction of the rectum, paresthesia of the lower limbs due to compression of surrounding nerve formations, and symptoms due to compression of surrounding vascular formations (e.g. the iliac vein). (18)

There is a similarity in growth rate to abdominal aortic aneurysm. The average growth rate is 1-4 mm per year, depending on the size of the aneurysm. (14) One of the most comprehensive retrospective studies has shown that aneurysms smaller than 3 cm have a low growth rate (0.11 mm/year), whereas the growth rate is significantly higher for dilations between 3-5 cm (26 mm/year). (19)

In the case of a large aneurysm, a pulsatile mass may be detected on abdominal or rectal physical examination, but imaging is required to establish an accurate diagnosis. (18) Unlike abdominal aortic aneurysms, ultrasound may be less reliable in depicting iliac aneurysms. For this reason, CTA is the primary imaging modality. (14)

1.3. Treatment of abdominal aortic aneurysms and iliac aneurysms

Treatment options for asymptomatic aortic aneurysms include conservative therapy as well as invasive procedures. The latter includes surgical reconstruction and endovascular stent graft implantation. (14)

1.3.1. Conservative treatment

In asymptomatic, small aneurysms, which do not reach the diameter that would indicate elective surgery, regular imaging and conservative therapy are important. Several classes of drugs have been tested in randomized trials for their ability to reduce the growth

rate of aneurysms, but no single class of drugs has been shown to be effective. In addition, regular exercise has not been shown to reduce growth. However, smoking cessation has a significant growth-reducing effect. Most observational studies show that termination of smoking is associated with a reduction in growth rate of about 20% and also halves the risk of rupture. The growth rate of aneurysms in diabetics is also slower than in non-diabetics, which is presumably related to the use of metformin. Since the cardiovascular risk is higher in patients with aortic aneurysms (annual cardiovascular mortality risk 3%), lifestyle changes (regular exercise, healthy diet, avoidance of smoking) and risk reduction with medication are essential. The latter include adequate blood pressure control with antihypertensive agents, treatment of dyslipidemia with statins, and antiplatelet therapy. (14)

1.3.2. Indication of repair

According to the latest guidelines open surgical of endovascular repair is indicated for abdominal aortic aneurysms in the following cases: symptomatic dilatation regardless of the size of the aneurysm, asymptomatic cases with a diameter of more than 5.5 cm in men, 5 cm in women, saccular type and if the growth rate is greater than 0.5 cm within six months. (14) For iliac artery aneurysms, the threshold for considering invasive treatment is 3.5 cm. (14)

1.3.3. Open surgical techniques

Proximally suprarenal or supracoeliac clamping can be used during the surgical treatment of such aneurysms, in both cases it is important to keep the cross clamping time as short as possible. The fundament of the open surgical technique is tubing, performing mostly end-to-end anastomoses on both sides. In pararenal aneurysms an oblique proximal anastomosis can also be implemented with or without renal reimplantation. Regarding the distal part, there has been a shift from bifemoral to biiliac grafts, latter having a better longterm clinical outcome due to the preservation of the internal iliac artery, and having less infection afterwards, as there is no inguinal incision. The most frequently used graft material is polyester, however, vascular homografts can be also used. (14)

1.3.4. Endovascular options

1.3.4.1. Endovascular aneurysm repair

During endovascular treatment, instead of replacing the dilated vascular segment, the aneurysm sac is excluded from the systemic circulation with the use of a stent graft, which is mostly inserted from the femoral artery, either percutaneously under ultrasound guidance or through a surgical incision. (14)

In the treatment of complex aortic diseases, there has been a significant development of endovascular therapeutic options in recent times. Therefore, the management of aortic and aorto-iliac pathologies shift towards endovascular procedures in patients with suitable anatomy as endovascular treatment possibilities evolve. (20) The safety and efficacy of endovascular aneurysm repair (EVAR) for a suitable aortic anatomy has been demonstrated in several studies, the majority of aortic diseases being successfully treatable using conventional grafts available on the market. (14) (Figure 4.)

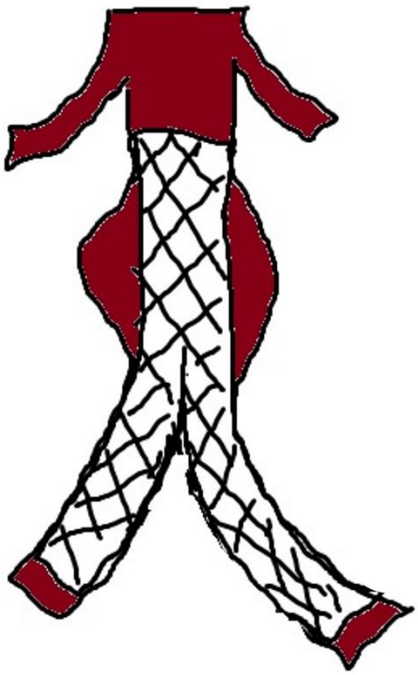


Figure 4. Illustration of an infrarenal aortic aneurysm after a standard EVAR procedure. EVAR: endovascular aneurysm repair

Endovascular complications associated with endovascular intervention include vascular injury during graft deployment, which in some cases can lead to rupture, however, the most common complications following an endovascular procedure are endoleaks. (5) Endoleaks are defined as persistent blood flow in the aneurysm sacs outside the graft after stent graft implantation. They occur in almost one third of cases following endovascular procedures, although their incidence is highly dependent on the type of stent graft used. About half of the cases resolve spontaneously without reintervention. The timing of onset can be divided into primary (detected during the procedure) and secondary (occurring after a negative imaging). The risk of onset is probably increased by anticoagulant therapy. The presence of endoleak increases the risk of rupture by increasing the pressure within the aneurysm. Five different forms of endoleaks are distinguished (Figure 5.) (14)

Type I can be divided into three subtypes. In Ia, the fixation of the proximal graft to the vessel wall is inadequate, whereas in Ib, the fixation of the distal graft to the vessel wall is inadequate. In the case of a problem of the distal attachment of a side branch, a type Ic endoleak may develop. As type I endoleak has a particularly high risk of aneurysm rupture, it requires immediate treatment, mainly by endovascular surgery. This may involve balloon dilatation, metal stent implantation, stapling of the graft tissue to the aortic wall or extension of the proximal/distal fixation zone. Type II endoleak is the most common form, in which the collateral vessels (lumbar arteries, inferior mesenteric artery) fill the aneurysm sac. Most of these types of endoleaks are considered benign, with a risk of rupture of less than 1%, most of them resolve spontaneously, but there are also cases of persistent flow which may lead to sac enlargement and secondary rupture. (14) Risk factors for persistent type II endoleaks include advanced age, previous coil embolization of the internal iliac artery, distal graft extension, and mostly anatomical factors such as aneurysm sac thrombus and, above all, larger number and/or diameter of the branches (inferior mesenteric artery and lumbar arteries) arising from the aneurysm sac. (21-25) For type II endoleaks that do not resolve spontaneously and are associated with sac enlargement, endovascular interventions, such as transarterial embolization should be considered. If this is unsuccessful, transcaval, transsealing or direct translumbar approach may be considered, or open surgical intervention such as ligation of the side branches may be used. Type III endoleaks are caused by separation of the graft components (due

to inadequate overlap or graft migration) or rupture of the graft material. Similar to type I, it is associated to an increased risk of rupture, which warrants immediate intervention. Type IV endoleak, which is caused by porosity of the graft material, is now almost non-existent thanks to modern stent grafts. Type V, also known as "endotension", refers to the growth of aneurysms without a detectable endoleak. Several potential mechanisms have been described for this type, which include, for example, increased graft permeability or endoleaks which are undetectable with current imaging modalities. Treatment is indicated for sac growth greater than 1 cm. In addition to endoleaks, other complications include stent graft migration, infection or thrombosis due to narrowing or occlusion. (14)

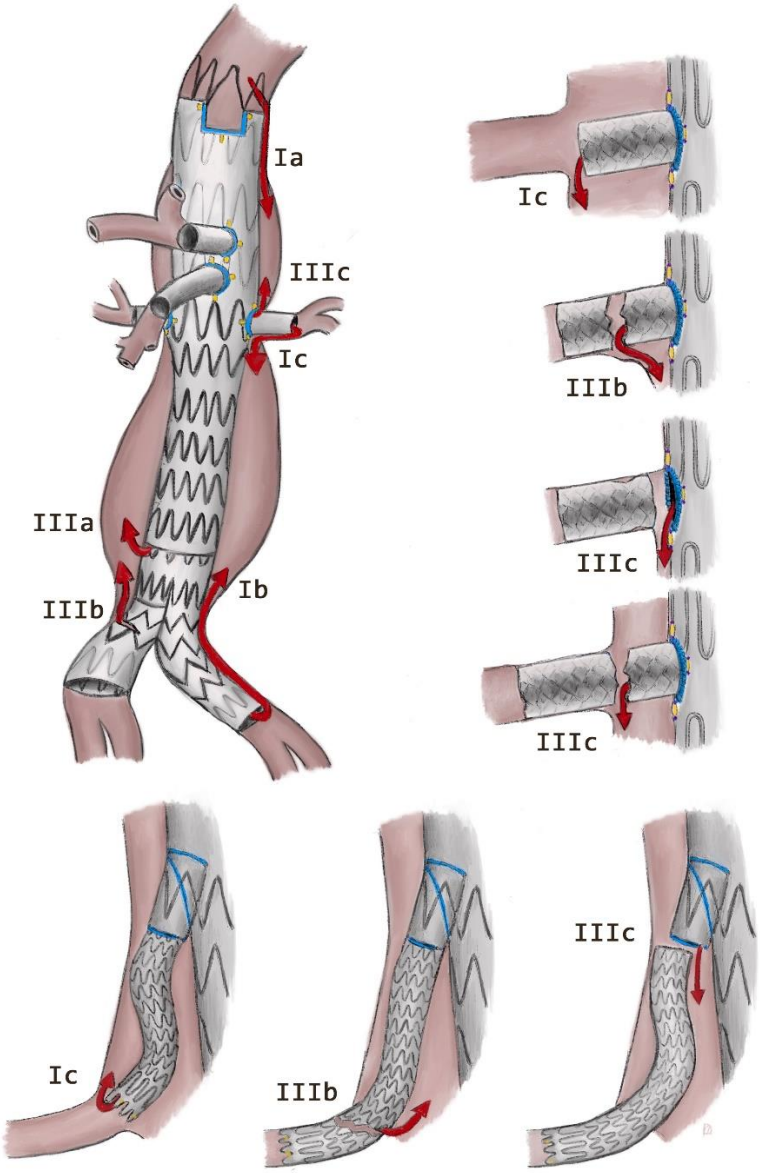


Figure 5. Classification of endoleaks

The three largest randomized controlled trials conducted to date comparing the results of elective open surgery with EVAR have produced consistent results. All three studies found that 30-day morbidity and mortality were significantly lower with EVAR. In addition, the length of hospital stay for patients undergoing EVAR was significantly shorter. However, the short-term survival advantage of patients undergoing EVAR decreased during the follow-up period, so that among patients surviving beyond 2-3 years, survival rates associated with the two procedures were similar, remaining balanced over the 8-10-year follow-up period. (26-28) An argument against EVAR is that reintervention rates were found to be higher in this group of patients, although most of these procedures could be managed endovascularly. Thus, the choice of treatment strategy should take into account the patient's anatomical suitability, the surgical risk and the patients' preference. Patient compliance is also important because patients undergoing EVAR require lifelong imaging monitoring in order to identify any complications (aortic or device-related) and to monitor changes in aneurysm size. (29)

1.3.4.2. Iliac branch devices

In many cases, the dilatation of the aorta and iliac system coexist, but extensive iliac aneurysm repair might not provide a durable exclusion of the aneurysm or might endanger the pelvic circulation. (30) Endovascular treatment of iliac artery aneurysms was originally performed by embolization of the internal iliac artery and stent grafting, where the stent graft is extended so that it ended in the external iliac artery, not in the common iliac artery, covering the internal iliac artery (thus the name coil&cover). Occlusion of the internal iliac is normally compensated by collateral circulation from the contralateral internal iliac artery and the femoral and mesenteric arteries. In the absence of compensation, various complications may occur, such as buttock claudication, erectile dysfunction, pelvic necrosis, and intestinal or spinal ischemia. Of these, buttock claudication is the most common complication, with an incidence of up to 28%. The likelihood and severity of these complications are also higher in bilateral occlusion. To avoid the above-mentioned complications, preservation of at least one of the internal iliac arteries is recommended. (14) The importance of preserving the internal iliac artery was also demonstrated in a retrospective Danish study of 112 patients with aorto-iliac aneurysms. In 38% of the patients treated by occlusion of the internal iliac artery, buttock

claudication developed, whereas in none of those in whom its flow was preserved. (31) In another study in which 71 patients underwent internal iliac occlusion, 2.8% of cases ended in fatal pelvic ischemia, while 25% of patients developed buttock claudication (32) A meta-analysis of 2671 patients revealed that after sacrificing the internal iliac artery, 27.9% of the patients had buttock claudication and 10.2% of the men had erectile dysfunction. (33)

The development of endovascular techniques has led to a paradigm shift in the treatment of iliac aneurysms in recent years as up-to-date guidelines recommend the preservation of at least one internal iliac artery which can be best obtained by the implantation of an iliac branch device (IBD). (14, 20, 34) The concept of this device is that the flow of the internal iliac artery can be preserved using a side branch. (35) (Figure 6) Several studies have already showed encouraging outcomes of IBDs, reporting excellent results. (30, 36-38) Nonetheless, the availability of such devices also shows significant geographical differences due to either the lack of experience of the centers in association with absent or incomplete centralization or the consequence to reimbursement and/or availability issues of the devices. (39)

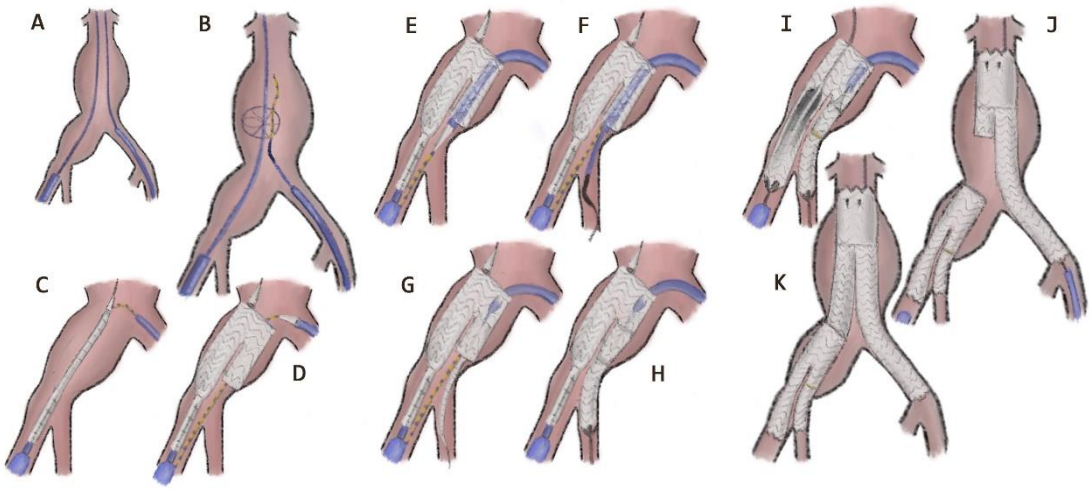


Figure 6. Technique of endovascular repair using the GORE® EXCLUDER® Iliac Branch Endoprosthesis. First, the iliac branch device is deployed via bilateral femoral access. (A-D) Then, the internal iliac component stent is put in and ballooned, which is followed by the deployment of the external iliac limb. (E-H) Afterwards, kissing-balloon angioplasty is performed in the transition of the iliac branch and finally, the EVAR is performed with an iliac extension to reach the iliac branch device. (I-J)

1.3.4.2. Complex endovascular solutions

In a significant proportion of cases, however, the patient's anatomy does not allow a standard EVAR. In such cases, the use of a custom-made device (CMD), off-the-shelf (OTS) branched stent graft, or a physician-modified endograft (PMEG) can provide an endovascular solution. (40)

CMDs are fenestrated and/or branched stent grafts that are adapted to the patient's anatomy, with reinforced fenestrations or directional branches according to the visceral orifices. (34) In addition to their significantly higher price, a major drawback is their typically long manufacturing time, which makes them practically only applicable in elective conditions. (40)

Nowadays technical developments of EVAR and visceral stenting provide a lasting and safe treatment of the visceral aortic segment. Since the first implantation of a fenestrated stent graft in 1998 by Anderson, significant advantages of fenestrated/branched endovascular aortic repair (FBEVAR) have been demonstrated regarding mortality and morbidity compared to open surgical repair. It has opened new dimensions in endovascular treatments, as these devices offer the possibility of an adequate suprarenal proximal landing zone for stent graft implantation and successful aneurysm exclusion at the same time, thus the method can also be used in cases of juxtarenal aneurysms or dilatation of the visceral segment, among others. (41-44) During the last decade FBEVAR has been widely accessible in several countries, which resulted in sufficient scientific evidence to support the recent guideline recommendations of the European Society for Vascular Surgery favoring FBEVAR over open surgery for patients with juxtarenal or thoracoabdominal aortic disease with suitable anatomy. (14) Yet there are compelling regional and geographical alterations regarding the availability of such therapies, especially in Eastern Europe. (45-47) These dissimilarities are likely due to the same reasons as mentioned in the case of the IBDs. However, Eastern European endovascular practice is largely missing in the current international literature.

In patients requiring emergency endovascular intervention, OTS branched stent grafts became available, which have the visceral orifices' branches in a standard position according to normal anatomy. Their immediate availability is a major advantage. Still, their use is limited by aortic diameter discrepancies and visceral anatomy variations. (40)

As another alternative to CMDs, PMEG implantations are being considered in larger centers. The term PMEG was coined by Ben Starnes, with the first technical description by Uflacker et al. (48, 49) In this technique, a straight or bifurcated stent graft is modified by the surgeon/interventionalist to suit the patient's anatomy under sterile conditions prior to the surgery. More complex backtable modifications can also be performed, using a cautery to customize the length of the stent graft, or to form fenestrations at the visceral orifices. PMEG also appears to be a promising technique for elective cases with unusual anatomy or for complex endovascular surgery requiring an urgent intervention and is reported as a safe and effective method by several centers. (43, 48-54) However, one of its known drawbacks is the loss of quality control regarding the modifications. Potential measurement errors, device contamination and alterations in the integrity of the stent graft and delivery system can all lead to complications. (55) Furthermore, the long-term success of the procedure is questionable. Current PMEG practice apply open-ring reinforcements, typically made of guidewire tips and snare loops, which have different mechanical properties than the circular reinforcements of the CMDs. Late dilation of an open-ring fenestration due to fatigue might lead to a type IIIc endoleak in the long term. (56) The indeterminate durability of this method is probably a major reason why it has not been widely adopted despite a high technical success rate and good early results. (57)

PMEG has also been used in our center, e.g. in an 81-year-old female patient who was admitted to our hospital with a type I endoleak associated with an aorto-uni-iliac endograft. The wide juxtarenal aortic diameter together with the short distance between the proximal end of the previously deployed uni-iliac graft and the superior mesenteric artery made the patient unsuitable for conventional endovascular repair, therefore the distal 3 cm was cut from a standard thoracic stent graft, after which the device was reloaded. The modified graft could be positioned below the superior mesenteric artery, while renal perfusion was secured via a chimney graft. (Figure 7.) (58)

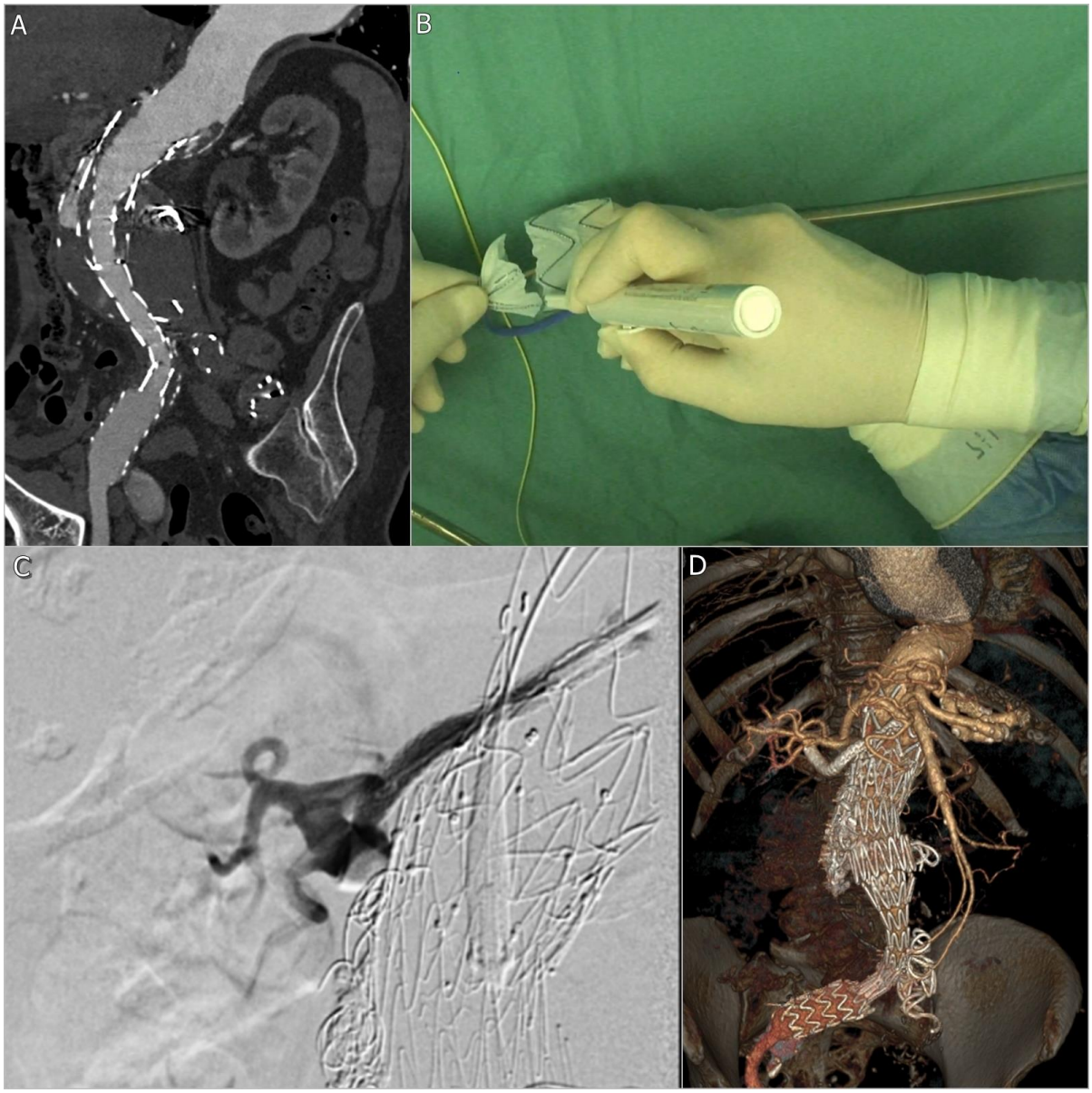


Figure 7. A, Multiplanar reconstruction of a CTA performed prior to the implantation of the physician-modified endograft, where the contrast filling of the aneurysm sac suggests a proximal endoleak. B, Two stents were removed from the distal end of a thoracic stent graft with a cautery. C, Digital subtraction angiography image showing the right renal chimney. D, Three-dimensional reconstruction of the pre-discharge CTA.

CTA: computed tomography angiography (58)

1.4. Complex aortic interventions in Hungary

In recent decades, the surgical management of abdominal aortic aneurysms has changed significantly in many countries to provide more effective care. (59) However, the situation in Hungary in relation to aortic and complex aortic interventions is somewhat

specific, mostly because of the financial background. The first EVAR was performed in 1998 in Miskolc, the first thoracic endovascular aortic repair (TEVAR) was performed in 2000 in our center. Still, the fixed budget of these led to a relatively low number of these procedures in the first approximately 15 years, open surgical repair was the method of choice. Quite impressive surgical techniques could be observed as a result. Between 2002 and 2008 there were 42 patiens with complicated acute type B aortic dissection treated by open surgical suprarenal aortic fenestration. (60) Furthermore, in June 1997 a homograft bank was established in our center being a pioneer in the region, providing an opportunity to use homografts in multiple settings. In patients who underwent aortic replacement using cryopreserved homografts due to infected infrarenal prosthetic reconstruction, the method proved to be durable and eradicated late infection. (61) Homograft use also showed to be a key revascularization method in chronic limb-threatening ischemia. (62)

The first IBD was used in 2010, however after that there was a long gap. The first FEVAR was implanted in 2013, the first BEVAR was deployed in 2015 and even after these only a few cases were performed for years. (Figure 8.) The main reason for this was their high cost. Regarding these complex interventions, the financial problem: having had a fixed cap budget yearly to cover all aortic interventions, was even more pronounced. Complex endovascular interventions cost approximately 5-8 times more than a standard EVAR. Therefore, the endovascular treatment of juxtarenal aneurysms, requiring two fenestrations, which is an important step in the learning curve of complex interventions, was basically skipped, these patients received an open surgical repair with supraceliac clamping. This led to relatively difficult first cases. The fist FEVAR incorporated one vessel, there was another case having only two fenestrations, however the third case was a thoracoabdominal BEVAR with four branches and all other cases incorporated three or more side branches, the average of the vessels integrated was 3.6. The patient population was also at higher risk, there was a high percentage of patients with prior aortic repair and the number of the thoracoabdominal aneurysms was also relatively high. Even though BEVAR is more difficult technically than FEVAR, being an off-the-shelf solution, its lower price led to a more extensive use in the initial patient population, often combined with the off-label use of the device.

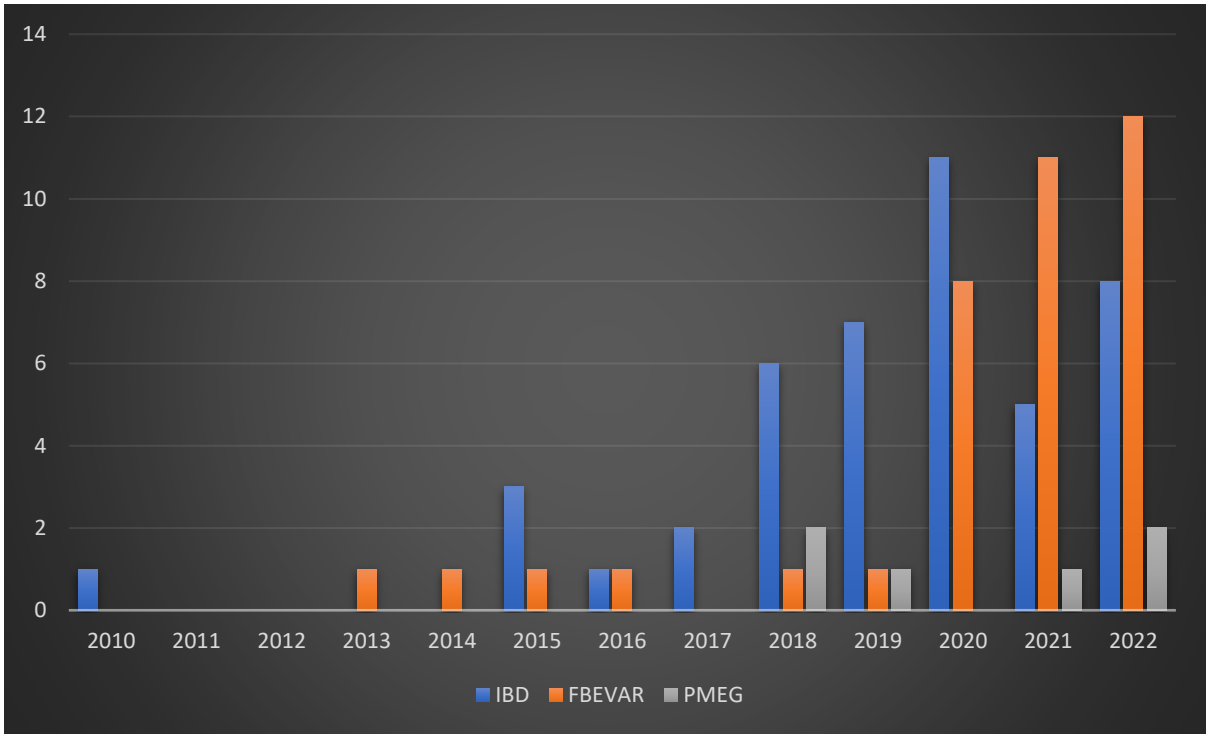


Figure 8. Complex aortic interventions in our tertiary center IBD = iliac branch device, FBEVAR = fenestrated/branched endovascular aortic repair, PMEG = physician-modified endograft

2. Objectives

Several papers have been published on the outcomes and determinants of the above discussed complex aortic interventions, but no data on outcomes in Hungary have been available before. Our objective was to investigate the initial results of the application of these endovascular treatments at a tertiary vascular center in Hungary.

1. **We aimed to study the initial results of FBEVAR and IBD implantation.**
   Our objective was to investigate the short- and mid-term outcomes in patients undergoing FBEVAR and IBD deployment based on a retrospective analysis.

2. **Our purpose was to assess the risk of the introduction of these procedures into our treatment portfolio in special regard to the beforementioned individual situation in Hungary, having a significant drawback in complex endovascular interventions due to the financial background.**
   We hypothesized that our initial results would not be as good as the results obtained in established centers with substantial experience, especially since the step of endovascular treatment of juxtarenal aneurysms, requiring only two fenestrations or branches was missing from our learning curve.

3. Methods

3.1. Fenestrated/branched endovascular aortic repair study

Single center retrospective study was performed in our tertiary vascular center to evaluate the results of complex aortic interventions including our first 20 consecutive patients treated with FBEVAR. The study was approved by the local ethics committee (Semmelweis University Regional and Institutional Committee of Science and Research Ethics: 96/2021) and was performed in accordance with the Helsinki declaration. Informed consent was obtained from all patients.

3.2. Iliac branch device study

To evaluate the results of iliac branch devices, we performed a single center retrospective study in our tertiary vascular center. The analysis contained our first 35 patients receiving IBDs. Local ethics committee approval was obtained (Semmelweis University Regional and Institutional Committee of Science and Research Ethics: 92/2021) and it was performed in accordance with the Helsinki declaration. Each patient provided informed consent.

3.3. Data collection

Demographic data, cardiovascular risk factors, anatomical data, procedural and postoperative variables were collected retrospectively. When performing complex aortic interventions, intraoperative cone beam computed tomography was used to confirm technical success whenever possible. Follow-up clinical examination and imaging were performed according to current guidelines: at 30 days, 6 months, 12 months and annually thereafter. However, in some cases the results of the previous CTA examinations could indicate a more frequent follow-up, in other cases, especially due to the COVID-19 pandemic, some examinations were not performed in the intended time period. In patients with severely impaired kidney function, magnetic resonance angiography (MRA) was performed instead of a CTA. In some cases, duplex ultrasound or contrast-enhanced ultrasound were additionally completed.

3.4. Data analysis

Terminology, end point definitions and measurement techniques were used according to the most recent reporting standards document's definitions, published by Oderich et al.. (3) Technical success was defined if arterial access, delivery and deployment of the stent graft components, side branch cannulation and the placement of the bridging stents were all successful, and if the patency of all target vessels were preserved, furthermore there was no sign of type I or III endoleak on the 30-day follow-up CTA. A clinical success was defined as the absence of disabling clinical complications, such as aortic-related complications or permanent paraplegia, newly onset permanent need for dialysis, and disabling stroke, in addition to the criteria of technical success. Primary endpoints were major adverse events, including the composite endpoints of all-cause mortality, new-onset dialysis, paraplegia, bowel ischemia, myocardial infarction, major stroke, or respiratory failure, and in-hospital and late aortic mortality. Secondary intervention was defined as any unanticipated procedure, which was performed after the index procedure, further classified as minor if percutaneous ≤10 Fr access was obtained, and major if open surgery or large-bore (≥12 Fr) endovascular access was necessary. (3)

Categorical variables were reported as total numbers and percentages, whereas continuous variables as means with standard deviations. Time dependent variables (like patency and survival) were reported using the Kaplan-Meier method. Statistical analyses were performed using IBM SPSS (Armonk, NY, USA, version 27.0) and GraphPad Prism 8 (GraphPad Software, San Diego, CA, USA) and the latter was also used to visualize the data on graphs. A value of $p<0.05$ was considered statistically significant for all measurements. (31, 51)

3.5. Technique

3.5.1. Fenestrated/branched endovascular aortic repair

All procedures were performed by the same interventional radiologist after the initial three cases. The primary operator has 14 years of experience in endovascular procedures and is a proctor for major aortic device companies. The aortic team consists of another interventional radiologist (7 years of experience) and two diagnostic radiologists (4 and 6 years of experience), furthermore two vascular surgeons with > 20 years of experience

in thoracoabdominal open repair, two cardiac surgeons with 35 and 15 years of experience in aortic surgery, and a cardiovascular anesthesiologist with 10 years of experience. All our team members are working in a center, dedicated to cardiovascular care. The procedures were completed in a hybrid endovascular room with a fixed imaging system under general anesthesia. The primary operator performed centerline analyses using 3Mensio Vascular software (Pie Medical Imaging B.V., The Netherlands) in order to decide the stent design. Off-the-shelf (OTS) branched stent graft (Cook t-Branch, Cook Medical Inc., Denmark) or patient-specific custom-made devices (CMDs) with up to five fenestrations or branches (Cook Medical Inc., Denmark and Terumo Aortic, UK) were applied. Reinforced fenestrations were preferred for vessels originating from narrow aortic segments, while directional branches were used to incorporate vessels that originate from wide aortic segments. Fenestrations were aligned to target vessels with balloon-expandable covered stents (Viabahn VBX, W.L. Gore & Associates, USA; Begraft Peripheral or Begraft Peripheral Plus, Bentley InnoMed GmbH, Germany; Atrium V12, Getinge AB, Sweden). Directional branches on the other hand were bridged to target vessels with balloon-expandable (Viabahn VBX, W.L. Gore & Associates, USA; Begraft Peripheral or Begraft Peripheral Plus, Bentley InnoMed GmbH, Germany) or self-expandable covered stents (Viabahn, W.L. Gore & Associates, USA; Fluency or Covera, BD, USA), latters being only used in our early experience. Stent selection was the interventionist's own choosing but had been heavily influenced by device availability of the different devices and budget constraints at the time of implantation. Open surgical cutdown was performed in all cases as suture-mediated closure devices were not reimbursed at the time of the repairs. A shift from transaxillary to transfemoral access can be observed over time, latter being performed in recent times almost exclusively with the help of a 16F steerable sheath (Heli-FX Guide 22, Medtronic plc, Ireland). Wire-loops were not needed, thus not used. In our early experience, when the risk of paraplegia was assumed high, associated with either the extent of the repair or other parameters (subclavian artery patency, internal iliac artery patency, large number and/or large diameter of intercostals/lumbars to be occluded during the operation), prophylactic cerebrospinal fluid drainage (CSFD) was used, based on a multidisciplinary decision. Lately, therapeutic CSFD only is being favored due to the relatively high risk of adverse events associated with CSFD. On-table extubation is being endorsed lately to check if

any neurological complication developed as early as possible. Postoperative period was primarily managed in a dedicated cardiovascular intensive care unit by critical care physicians and nurses experienced in the treatment of vascular disease, with a close collaboration with the primary operators. Lately, the tendency shifts toward managing the postoperative period in the vascular surgery department with close supervision, asking for help from the intensivists only if needed. This helped to reduce complications associated with intensive care unit (ICU) stay. (51)

3.5.2. Iliac branch device

The IBD implantation was performed as a stand-alone procedure, when only an isolated iliac artery aneurysm was repaired, but if aorto-iliac involvement was seen, the deployment was performed as an adjunctive procedure during an endovascular aneurysm repair (EVAR). The choice of implanted branch device was based on the the availability of the different IBDs and the patients' anatomic features. Planning was carried out using IntelliSpace Portal (Philips Healthcare, The Netherlands) or 3Mensio Vascular software (Pie Medical Imaging B.V., The Netherlands). The IBDs used in our institution during the observed time period were Zenith Branch Endovascular Graft (Cook Medical, USA), Gore Iliac Branch Endoprosthesis (IBE; W. L. Gore & Associates, USA) and Jotec E-liac (Jotec GmbH, Germany). Gore implants were used for wider lumina, the Cook device was preferred for smaller common iliac luminal diameters, Jotec devices were chosen when isolated repair was planned, and proximal diameters were suitable. All procedures took place in a room equipped with a fixed X-ray imaging system and were performed by two physicians. (31)

4. Results

4.1. Fenestrated/branched endovascular aortic repair

In our study there were 9 pararenal aneurysms (PRA, 45%) and 11 thoracoabdominal aortic aneurysms (TAAA, 55%), latter including 4 chronic dissection cases (20%) among the initial 20 FBEVAR cases (16 men, 65±11 years). All aneurysms were degenerative, there was no Marfan syndrome patient in the observed patient population. Demographics, clinical and anatomical characteristics can be found in Table 1.

Table 1. Demographics, clinical and anatomical characteristics

Variable		**N (%) or mean ±SD**
Demographics	Male gender	16 (80)
	Mean age, years	65.5 ± 11.2
	BMI, kg/m^2	27.3 ± 4.1
Clinical Characteristics	Hypertension	16 (80)
	Smoking	8 (40)
	Hypercholesterolemia	10 (50)
	Diabetes mellitus	3 (15)
	Coronary heart disease	11 (55)
	Chronic obstructive pulmonary disease	7 (35)
	Chronic kidney disease stage III-V	4 (20)
	eGFR, mL/min/1.73m^2	74.6 ± 16.9
	Prior aortic repair	10 (50)
	Malignant disease	5 (25)
ASA status	ASA II	1 (5)
	ASA III	17 (85)
	ASA IV	2 (10)
Anatomical characteristics	Pararenal aortic aneurysm	9 (45)
	Thoracoabdominal aortic aneurysm	11 (55)
	Chronic dissection	4 (20)
	Average size of the aortic aneurysm, mm	72.5 ± 17.0

Abbreviations: N = Number; SD = Standard deviation; BMI = Body mass index; ASA = American Society of Anesthesiologist's physical status classification

Procedural details are shown in Table 2. The average aortic coverage length was 346.6 ± 132.8 mm. In the majority of the cases (14/20, 70%) custom-made devices were used. Overall, seventy-one renal and mesenteric vessels were incorporated with 46

fenestrations and 25 directional branches. Among the first cases, two cases (10%) were managed via transaxillary access, afterwards there was a shift to a transfemoral only approach using a 16 Fr steerable guide catheter to facilitate target artery cannulation (Heli-FX Guide 22, Medtronic plc, Ireland). All target arteries were successfully cannulated and stented resulting in a 100% per vessel technical success rate. Furthermore, no open surgical conversion was necessary. Cerebrospinal fluid drainage was performed in three patients (15%), two cases were prophylactic, one therapeutic. Lately, therapeutic only approach was being preferred. In four patients (20%), who were regarded high risk for spinal cord ischemia, perfusion branches were used. The use of two (out of six) OTS devices were off-label, one with a narrow visceral aortic segment, and one with a chronic occlusion of the celiac trunk. In the latter urgent case, the occlusion of the corresponding portal was managed using a combination of a covered stent an Amplatzer plug (Amplatzer Vascular Plug II, Abbott Laboratories, USA) after neither the antegrade, nor the retrograde recanalization attempt of the celiac trunk through the gastroduodenal arcade were successful. Six adjunctive procedures were necessary in the management of five cases (5/20, 25%): two iliac bifurcation device implantations, two left subclavian transposition/bypass (zone 2 debranching), a prophylactic internal iliac artery recanalization and a branch portal embolization. Preloaded catheters were not available and therefore were not used.

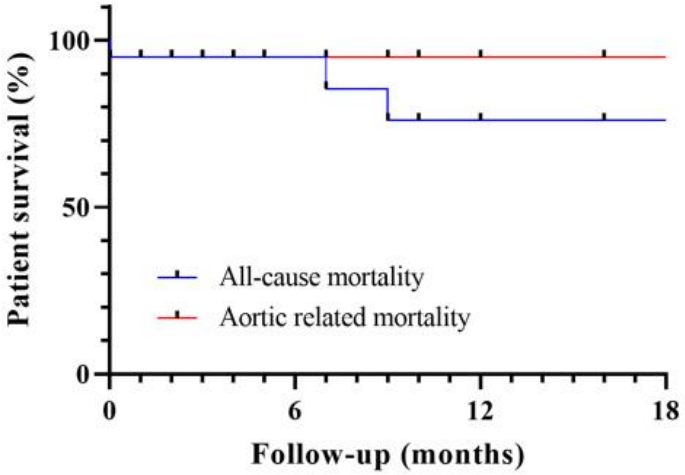
The per patient technical success rate was 65% (13/20). Technical failure was mainly caused by the need for an early reintervention (minor: 5/20, 25%, major: 1/20, 5%). There was one in-hospital death due to the unintended coverage of a common hepatic artery arising from the superior mesenteric artery. The average length of stay (LoS) in the intensive care unit (ICU) was 0.8 ± 1.2 days, the average total LoS was 5.9 ± 2.4 days.

Table 2. Procedural details

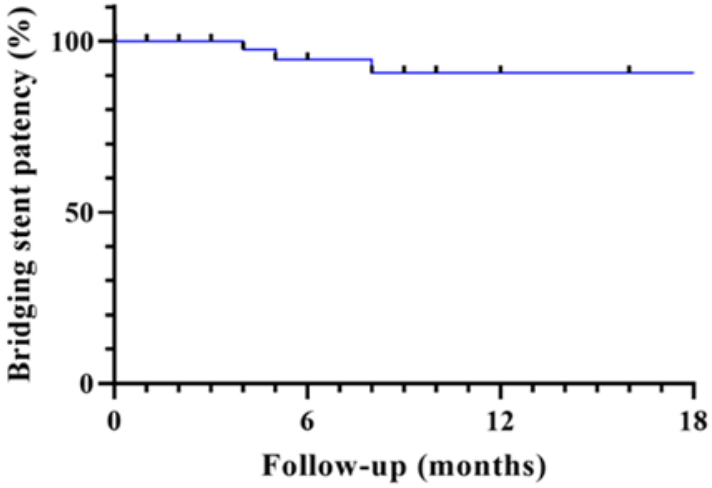
Variable		N (%) or mean ±SD /[IQR]
Device design	Off-the-shelf device	6 (30)
	Patient-specific device	14 (70)
Proximal sealing zone	zone 2-4	10 (50)
	zone 5	7 (35)
	zone 7	1 (5)
	zone 8	2 (10)
Distal sealing zone	zone 9	3 (15)
	zone 10	11 (55)
	zone 11	6 (30)
Aortic coverage length, mm		346.6 ± 132.8
Total incorporated vessels		71
Incorporated vessels per patient	Total	3.6 ± 0.9
	1 vessel	1 (5)
	2 vessels	1 (5)
	3 vessels	5 (25)
	4 vessels	12 (60)
	5 vessels	1 (5)
Type of incorporation	Fenestrations	46 (65)
	Directional branches	25 (35)
Procedural data	Contrast volume, ml	285.4 ± 124.0
	Fluoroscopy time, min	69 ± 39
	Cumulative air kerma, Gy	3.6 ± 2.5
ICU length of stay, d		0.8 [0-1]
Total length of stay, d		5.9 [4-6]
Staged repair		6 (30)
Cerebrospinal fluid drainage		3 (15)
Temporary aneurysm sac perfusion		4 (20)
Technical success per vessel		71 (100)
Primary technical success per patient		13 (65)

Abbreviations: N = Number; SD = Standard deviation; ICU = Intensive care unit; IQR = interquartile range

Primary clinical success rate was 45% (9/20) at an average follow-up of 14.0 ± 21.9 months. Secondary clinical success was achieved in 75% (15/20) observing the same time period. In-hospital mortality was 5% (1/20), all-cause mortality was 20% (4/20), with only one case being aortic related (5%). In that case, the above-mentioned coverage of an atypical common hepatic artery led to the patient's death. During the follow-up one celiac and three renal stent occlusions were found (4/71, 5,6%, Figure 9). In the other cases, which were not a technical success, the cause of this was type I or III endoleak and/or the need of reintervention.



	Number at risk	20	11	6	5
	Kaplan-Meier estimate survival rates	1	0.950	0.760	0.760
	Standard error	0	0.048	0.126	0.126
	Number at risk	20	11	6	5
	Kaplan-Meier estimate survival rates	1	1	1	1
	Standard error	0	0	0	0



	Number at risk	70	29	17	13
	Kaplan-Meier estimate rates	1	0.945	0.907	0.907
	Standard error	0	0.024	0.038	0.051

Figure 9. Patient survival (up) and bridging stent patency (down) at an average follow-up of 14 ± 22 months.

Stroke, myocardial infarction, or aortic rupture were not detected. Spinal cord injury was discovered in two patients, one paraparesis occurred, and one paraplegia was found because of a spinal epidural hematoma due to a prophylactic CSFD. Three cases of new-onset permanent dialysis were observed (15%), two of them associated with renal stent occlusions.

4.2. Iliac branch device

In our study aiming to evaluate the midterm results of IBD implantations a total of 37 IBDs were implanted in 35 patients, between 14. December 2010 and 23. July 2021 in our tertiary vascular center. In 19 cases the primary disease was aorto-iliac aneurysm, in 11 cases isolated iliac aneurysm, in 3 cases a chronic aortic dissection and in 2 cases a Ib endoleak following an EVAR. In the 11 cases, where the indication of the IBD implantation was an isolated common iliac aneurysm, a stand-alone IBD deployment was carried out. The other patients were treated in conjunction with an EVAR. In addition to the EVAR-IBD implantation three patients also underwent a thoracic endovascular aortic repair (TEVAR) for a thoracic aortic aneurysm. The patients were mostly male (89%), the mean age was 67.9 ± 8.5 years. The patient population and aneurysm characteristics are reported in Table 3, respectively. Detailed procedural data are presented in Table 4.

Based on the instructions for use (IFU), only the Jotec E-iliac graft should be used in isolated iliac aneurysms, however in 6 cases a ZBIS Cook or a Gore IBE endograft were implanted isolated, due to proximal landing zone diameter issues. There were 14 other patients treated outside the IFU, either because they didn’t meet the anatomical requirements of the IFUs or because of aortic dissection as their primary disease. In all of these cases an aortic team decision was made to recommend IBD implantation, to which the patient consented.

Table 3. Baseline patient and anatomical characteristics.

Variable		N (%) or mean ±SD
Demographics	Male gender	31 (89)
	Mean age, years	67.9 ± 8.5
	BMI, kg/m^2	28.5 ± 5.7
Cardiovascular risk factors	Hypertension	35 (100)
	Smoking	13 (37)
	Hypercholesterolemia	16 (46)
	Diabetes mellitus	6 (17)
	Peripheral artery disease	7 (20)
	Cardiac disease	18 (51)
	Chronic obstructive pulmonary disease	10 (29)
	Chronic kidney disease stage III-V	11 (31)
	Previous aortic repair	12 (34)
	Prior malignancies	11 (31)
Anatomical characteristics	AAA diameter - mm	46.9 ± 15.2
	Left CIA aneurysm diameter - mm	32.3 ± 14.1
	Right CIA aneurysm diameter - mm	35.0 ± 13.5

Abbreviations: N = Number; SD = Standard deviation; BMI = Body mass index; AAA = abdominal aortic aneurysm, CIA= common iliac artery.

None of the internal iliac arteries were lost, the per vessel technical success rate was 100%. The overall technical success rate was 88.2%, the primary clinical success was 82.4%, the assisted primary clinical success was 88.2%.

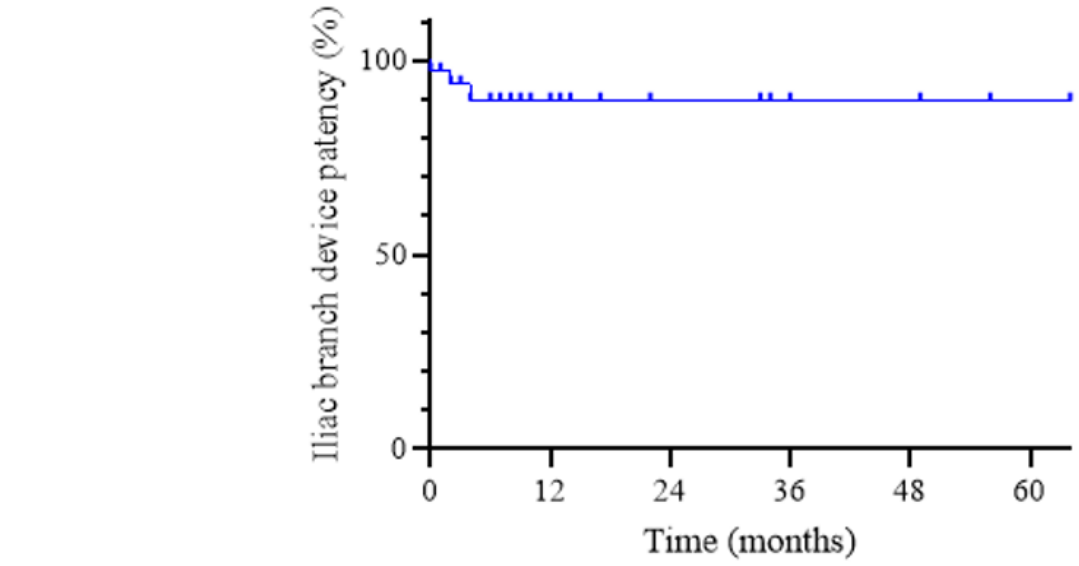
The mean length of the ICU LoS was 0.3 ± 0.5 days, the average total hospitalization duration was 4.6 ± 0.7 days. No surgical conversion was needed. The average follow-up time was 20.1 ± 26.2 months, during which one patient was lost to follow-up. No peri-operative or in-hospital death was recorded, there was no stroke, myocardial infarction, new-onset renal failure, mesenteric or spinal cord infarct, or significant buttock claudication.

Using the Kaplan-Meier estimates, freedom from IBD occlusion was 97.2%, 93.9%, 89.6% at 1, 2 and 4 months, respectively. (Figure 10.) During the follow-up, 3 iliac occlusions were detected, only the internal branch was affected. Each occlusion was left untreated.

Table 4. Baseline procedural characteristics.

Variable		N (%) or mean ±SD / [IQR]
Implanted devices	ZBIS Cook	20 (54)
	Gore IBE	12 (32)
	Jotec E-iliac	5 (14)
	Isolated IBD	11 (31)
	Bilateral IBD	2 (6)
Procedural data	Contrast dose - ml	139.25 ± 71.36
	Fluoroscopy time - s	2832.55 ± 1656.08
	Dose area product - Gy*cm^2	294.45 ± 442.74
	Hospitalization - days	4.60 [4-5]
	Intensive care unit stay - days	0.3 [0-0]
Complications	Type I endoleak	1 (3)
	Type II endoleak	10 (29)
	Type III endoleak	2 (6)
	Type V endoleak	1 (3)

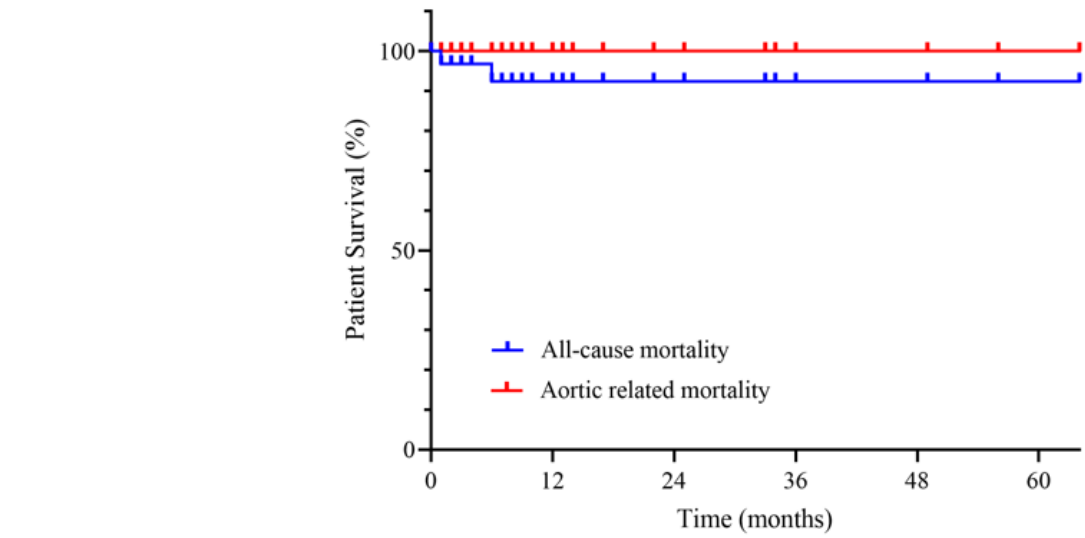
Abbreviations: N = Number; SD = Standard deviation; IBD = iliac branch device, IQR = interquartile range



Number at risk	36	12	7	4	4	2
Kaplan-Meier estimate rates	0.972	0.896	0.896	0.896	0.896	0.896
Standard error	0.027	0.058	0.058	0.058	0.058	0.058

Figure 10. Kaplan-Meier estimates of iliac branch patency treated by iliac branch devices

In the observed time period, seventeen endoleaks were observed in 14 patients. One type I and type V, two type III endoleaks were detected, ten patients had type II endoleak. Five reinterventions were needed, all for endoleaks (14.7%). The need for reintervention was associated with the IBD device in 4 patients (11.8%). Two late deaths were registered, neither of them related to the aneurysm or the endovascular procedure. Both cases occurred months after the implantations, one was due to a Clostridium sepsis, the other to a gastro-intestinal bleeding. The freedom from all-cause mortality and aneurysm related mortality were 92.4% and 100%, respectively. (Figure 11.) Clinical success was not obtained in cases, where technical success was not achieved, as detailed above, in the two patients who died, and in the three patients in whom we observed growing aneurysm sacs.



Number at risk	34	15	10	6	6	4
Kaplan-Meier estimate survival rates	1	1	1	1	1	1
Standard error	0	0	0	0	0	0
Number at risk	34	15	10	6	6	4
Kaplan-Meier estimate survival rates	1	0.924	0.924	0.924	0.924	0.924
Standard error	0	0.053	0.053	0.053	0.053	0.053

Figure 11. Kaplan-Meier estimates of all-cause mortality and aortic related mortality treated by iliac branch devices

5. Discussion

More and more portion of aortic pathologies can be treated endovascularly. In specialized centers, performed by experienced teams, FBEVAR has advanced to a widely accepted alternative to open surgery for complex aortic pathologies in all patients, even though it was developed only to extend the indications of EVAR in high-risk patients with insufficient proximal landing zone. (14, 46) IBD treatment, aiming to preserve the internal iliac artery while still allowing an adequate distal landing zone during EVAR, has been applied over a decade with excellent results. (37, 63) In urgent cases, or in patients with unusual aortic anatomy with complex aortic pathologies, PMEG implantation can provide an effective alternative to endovascular procedures using the available endovascular toolkit. (58)

In developed countries FBEVAR and IBD are accessible, however, significant geographical disparities remain, especially in less developed countries, e.g. the Eastern European countries like Hungary. A slow dissemination of FBEVARs was seen in the United States after the Food and Drug Administration approval of the Zenith Fenestrated endovascular graft (ZFEN, Cook Medical) in 2012. 30% of the physicians who received ZFEN training did not order a single device and 81% of those who ordered, ordered ≤5 devices/year. (46, 64) The barriers of more widespread use were attributed to several factors: greater technical complexity of the procedures requiring advanced endovascular skills, greater reliance on a complicated preoperative planning and for this the need of advanced imaging equipment. (64) The demand for highly specialized imaging and for precise complex planning of FBEVAR limit the adaptation of these techniques, as the procedural planning requires not only measurements, but comprehensive knowledge of parameters which affect device delivery, deployment, and target artery cannulation. (65) Moreover, restricted access to appropriate devices remains a limiting factor in the adoption of novel endovascular techniques in the Eastern European countries. Dissemination of the FBEVAR procedure is even slower in the majority of Central and Eastern European countries, with a very few exceptions only. In Hungary, less than 10 complex aortic procedures were performed altogether by the tertiary centers until 2019, due to the missing reimbursement of complex aortic procedures paired with the lack of centralization due to political reasons. Our institution is a pioneer in the aortic field in

Hungary, regarding both standard and complex aortic interventions: more than 80% of the Hungarian IBD cases and 90% of the Hungarian complex aortic procedures were performed in our tertiary vascular center. (59)

In 2020, the Semmelweis Aortic Center was established in our tertiary vascular center. This resulted in an outbreak of complex aortic procedures compared to earlier years despite the ongoing struggle with the limited budget for aortic procedures. (47)

Centralization and multidisciplinary teams result in a better care for the patients. The outcome of an open abdominal aortic aneurysm repair is considered by most authors to be associated with surgeon and hospital caseload. (66-71) McPhee et al. observed that after an elective open abdominal aortic aneurysm repair, surgeon case volume is the primary determinant of in-hospital mortality (66). An analysis of 178 860 EVAR patients found no volume effect on in-hospital or 30-day mortality. (70) In the Australian population researched by Sawang et al., the mortality after EVAR was unaffected by either surgeon, or hospital volume. However, hospital volume showed a strong inverse correlation with mortality in the TEVAR subgroup. (67) Complication rates and in-hospital mortality rates after abdominal aortic aneurysm repairs were found to be inversely associated with annual hospital volume in Germany. (71) Zetterwall et al. reported no association between mortality following an EVAR procedure and surgeon, but hospital volume was associated with slightly higher perioperative mortality in the same patient population. (68) The beforementioned recent Dutch analysis also showed a significant effect of hospital volume on perioperative mortality following complex EVAR, with high volume centers demonstrating lower mortality rates. Their study found a perioperative mortality following FBEVAR of 9.1% in hospitals with a yearly volume of <9, while 2.5% in hospitals performing more than 13 complex endovascular aneurysm repairs in a year. (72). D'Oria et al. examined the association between hospital volume and failure to rescue after EVAR and open aortic repair of intact abdominal aortic aneurysms and observed a significant association: hospitals in the top volume quartiles achieve the lowest mortality after a complication has developed. (73) To the best of our knowledge, no data on the effect of surgeon case volume or hospital volume are presently available regarding the outcomes of IBD deployments. Nonetheless, our cases being performed by only two physicians and our results being slightly better than other center's

initial data, suggest that the operator's experience (both prior endovascular expertise and practice obtained during the IBD procedures) may have an effect in decreasing the learning curve. In spite of having a case load of complex aortic procedures (ca. 10/year) way less than ideal (3/month) to obtain lower adverse event rates, we were able to observe an outcome at least non-inferior to the most experienced centers of open repair of thoraco-abdominal aortic aneurysms (TAAA). (74) The in-hospital mortality rate detected in our study analyzing the initial cases (5%) compares favorably to the operative mortality of 6.2% published by Coselli et al., a benchmark of elective thoracoabdominal open repair. (75)

The results of our initial cases compare well with other reported data from experienced aortic centers of Western Europe. Up to the present, no unconnected fenestrations or branches occurred during FBEVAR procedures, and none of the internal iliac arteries were lost whilst IBD deployments, resulting in a 100% per vessel technical success rate, which is rather unusual in the initial cases of a newly established center. (76) On the other hand, Schanzer et al. reported a 2.3% failure to cannulate and bridge any targeted artery resulting in a 97.7% per vessel technical success rate. (65) Our per patient technical success rate (65%) regarding the FBEVAR cases was compromised mostly by a relatively high reintervention rate (30%), although the majority of these were classified as minor and values compare well with literature data. (64, 74) A technical success of 88.2% was observed in our IBD study. In a systematic review Kouvelos et al. reported a technical success of endovascular internal iliac artery preservation in 96.2% of the cases. (77) Simonte et al. found a technical success of 97.5% in a study with a median follow-up of 34.0 months including 149 patients with 157 IBD deployments. (37) Parlani et al. detected a technical success of 95%, Haulon et al. reported technical success in 94% of the cases. (30, 34) An outstanding technical success rate of 100% was detected by Mylonas et al., although the results were reported in accordance with more permissive criteria. (78)

Our internal iliac artery occlusion rate of 8.8% at 2-5 years is comparable to a few other studies in the literature. Haulon et al. and Karthikesalingam et al. both found similar, slightly elevated occlusion rates of 11.3-12.2% (34, 35) However, a lower iliac patency rate was found in our IBD patient cohort, than mostly reported in other similar studies, where the internal iliac branch patency was between 89.7% and 100%. (78, 79) Our

reintervention rate of 14.7% following IBD implantations is also comparable to the results of previous studies. Verzini et al. found a reintervention rate of 18.2%. (80) Gibello et al. reported a reintervention rate of 11.8% in patients with a common iliac artery diameter < 18 mm and 19.1% in those with a common iliac artery diameter ≥18 mm. (81) Altogether, 42 reinterventions were performed among the 575 patients (7.3%) in the patient cohort analyzed by Donas et al. (82)

The existence of a learning curve is a well-known fact regarding all procedures. Simonte et al. conducted a subanalysis comparing outcomes observed in the first 25 IBD implantations, and those achieved in the later phase. Significant difference was found, the perioperative success rate was 84.0% in the early period, and it was 97.7% after the first 25 patients. (37) Parlani et al. also found evidence of the existence of a learning curve as four out of the five technical failures occurred during their first year of experience with IBDs. Compared to their five intraoperative IBD internal limb occlusions, our technical outcome regarding the per vessel technical success rate of 100% shows better results. (30) Mirza et al. reported significant improvement in perioperative mortality regarding FBEVAR cases at the Mayo Clinic, Schneider et al. found a similar, 6% perioperative mortality rate of the initial 50 FBEVAR cases performed in New York - Presbyterian Hospital. Our mortality rate observed in our FBEVAR experience compares well to these above-mentioned data, especially since our initial patient cohort, and thus our experience is significantly smaller than that of the cited authors' (64, 74). Furthermore, we detected a lower in-hospital mortality rate than observed in the WINDOWS trial (10.1%), a study that was planned to minimize center effect and evaluate the real-world mortality of FBEVAR procedures. (83) Still, lower mortality rates were also detected, e.g. Schanzer et al.'s single center experience of the first 100 consecutive FBEVAR cases showed a mortality rate of 3%. (65) The initial risk, which is associated with the starting of a complex aortic program is profoundly dependent on the operating team's skills. Previous experience with crural angioplasty and EVAR might be associated with a steeper learning curve in both FBEVAR and IBD deployments. (84) Our center has more than two decades of experience in aortic interventions and operations with numbers approaching 100/year in the previous five years. We were also one of the very first centers in Europe to perform angioplasty of the branches of the aorta, which skill is essential to accomplish success in complex aortic repair. (85)

It is common knowledge that early experience usually involves very high-risk patients, who are unfit for open repair. (64, 74, 84) Our initial patient cohort almost exclusively consisted of patients deemed unfit for major surgery, the vast majority (95%) of them being ASA class III-IV, which is among the highest values reported in association with early experience. (74) Another usual finding is that the complexity of the FBEVAR deployments increases with the growing experience of the team. (74, 84) Due to our small patient cohort, the trends regarding the complexity of our repairs cannot be evaluated, but more vessels were incorporated per patient (3.6 ± 0.9) in our present study than in the early period of Mirza et al. (2.8 ± 0.9). (74) Prior aortic surgery (50%) and postdissectional TAAA repair (20%) occurred with a frequency that is comparable to that reported by Oderich et al. very recently, which also suggests that the complexity of our initial cases was higher than what is usual to start with. (86)

When interpreting our IBD outcome rates, another factor must be taken into account: the high number of patients treated outside the instruction for use (IFU) of the devices (57.1 %), most commonly in association with a reduced diameter of the common iliac bifurcation. An interesting study by Tomczak et al. aimed to evaluate the number of patients with asymptomatic abdominal aortic aneurysms, regardless of the actual treatment plan, who theoretically could be treated by EVAR with stent graft devices commercially available in East–Central Europe in conformity with the IFU. The suitability rates of the examined devices were 20-65%, 32% of the patients were not suitable for any of the examined stent grafts, assuming a rigorously followed IFU. (87) Similar difficulties could be present regarding the armamentarium of IBDs, limiting the patients who can be endovascularly treated within the IFU. Liberalization of morphology indications may result in increased failure rates and higher endoleak rates. (30) Donas et al. conducted a comparative study where minimal anatomical characteristics were used for IBD deployment and challenging anatomies of the internal iliac artery were also included. They found a higher endoleak rate (12.5%) compared to the average literature data. (82)

On the contrary, Simonte et al. observed similar results comparing the long-term outcomes of IBD implantations performed in an experienced center as per or outside manufacturer's IFU. (88) Rodriguez et al. reported similar results: in a study where 15 patients were treated within the IFU and 24 patients' IBD implantations were non-IFU,

no significant difference was observed regarding technical success and device-related reintervention in the short term. (89)

Staged repair, which was performed in twenty percent of our FBEVAR cases, is widely accepted to be associated with reduced rates of neurological complications such as paraplegia and paraparesis. These symptoms remain a feared complication of extensive aortic repair. (90)

Regarding the PMEGs, mentioned in the introduction, most publications on their use are mostly case reports or retrospective studies, with only one or two prospective studies available to date. (91-94) In addition to these, two large-item summary studies provide an overview of the outcomes of PMEG implantations. (40, 95)

The meta-analysis of 20 papers published in 2021 described a technical success rate of 87.5-100% and a 30-day mortality rate of 0-8%. The primary patency of the visceral branches affected by the treatment in one year was 96.3-100%, during a follow-up of 14.8 months, 0-14.3% patients were observed to have a type I or type III endoleak. (95)

In 2012, a retrospective study by Starnes reviewed 47 cases of juxtarenal aortic aneurysms treated with PMEG implantation. The technical success rate in this study was also high (98%) with a low complication rate. (48)

Oderich is the author of the study with the largest number of PMEG cases, analyzing data from 145 PMEG implantations between 2007 and 2016. The technical success rate was 98% and the 30-day mortality rate was 5.5%. After three years, they detected a primary patency of 94% and a secondary patency of 98% for the affected visceral branches. (96)

Comparing our own initial experience with these is not feasible due to the small number of elements in our patient cohort. Examples of technical solutions of a similar nature to the cases detailed above can be found in the literature. In 2009, Leon et al. reported on the successful exclusion of an iliac artery aneurysm using a reverse iliac leg stent graft. (97) Song et al. used reversely positioned iliac grafts during the treatment of three isolated internal iliac artery aneurysms. (98) Gemayel successfully treated a life-threatening rupture of the internal iliac artery in an unstable patient using reversely positioned iliac leg stent graft and embolization. (99)

Erben et al. used a unique solution for a 6 cm pseudoaneurysm with recurrent coarctation. Proximally, an inverted iliac leg stent graft and distally an inverted aortic stent graft were implanted into the aorta, resulting in an "hourglass" configuration. During 5 years of follow-up, no complications occurred and the pseudoaneurysm was reduced from 61 mm to 25 mm. (100) Peppelenbosch et al. summarized the treatment of 12 cases of various aorto-iliac pathologies treated with inverted iliac grafts. They described an immediate postoperative technical success rate of 100% and satisfactory mid-term results. (101) Higashigawa and van der Steenhoven have also successfully used reverse-positioned iliac grafts to treat infrarenal aortic aneurysms to accommodate the existing diameter discrepancies. (102, 103) Stent graft shortening was used by Wada et al. for an ascending aorta pseudoaneurysm. Commercially available thoracic stent grafts are typically too long for this procedure, so the half of a 10 cm-long stent graft was cut off. (104)

In 2017, Dossabhoy compared the use of PMEGs and CMDs. The retrospective cohort analysis observed 82 cases, including 41 patients treated with PMEGs and 41 patients treated with a factory-produced stent graft. Primary differences were seen only in surgical metrics, and in the need for reintervention. Longer fluoroscopy times and operative times were found with PMEG implantations using more contrast media, and more reoperations were required after implantation. No significant difference was found between the two groups in terms of perioperative complications, length of hospital stay, type I or type III endoleak, or mortality. (105) A comparative study by Oderich et al. reported that CMDs were performed with higher technical success (99.5% vs. 98%; $p=0.02$), lower early mortality (0% vs. 5.5%; $p=0.0018$) and fewer serious adverse events (28% vs. 48%; $p<0.001$). Survival at 3 years and survival without reintervention were similar, with no difference in aneurysm-related mortality in the long term. When evaluating these results, it should be kept in mind that, in addition to the limitations of a retrospective and non-randomised study, patients typically belonged to different risk groups (the PMEG group had significantly more aneurysms, more chronic lung and kidney disease, and higher comorbidity severity scores). Furthermore, PMEGs were used for the majority of the patients in the first half of the study and CMDs were implanted in substantially more patients in the second half, so the favorable results found regarding the

CMD implantations may be partly due to the increase in the experience of the physicians performing the procedure. (96)

Georgiadis' meta-analysis also compared PMEGs and OTS fenestrated stent grafts. Although both methods were found to be effective and safe, the former group had a slightly lower clinical success rate (91.4% vs 95%), a slightly higher rate of serious adverse events (12.8% vs 7.4%) and a slightly higher mortality rate (3.2% vs 0%). (40) However, it is important to recognize that the comparability of physician-modified stent grafts with OTS fenestrated stent grafts is limited due to the following main factors. They have slightly different indications, partly due to the fact that prefabricated devices incorporate more visceral branches on average. Adverse outcomes observed in the literature with physician-modified endograft devices are probably under-represented. Moreover, physicians with highly variable routine performed modifications on stent grafts, while OTS fenestrated stent grafts were mostly provided to centers with high practice. (55) In Hungary, OTS devices are not available except for one branched graft (t-Branch; Cook Medical; Bloomington, Indiana, USA).

The need for PMEGs is justified both by the presence of different anatomical configurations and the need to treat complex cases with short time windows, and they will certainly continue to play a major role in the future. (48) Their use is considered a well-established and useful technique that should be part of the toolbox of physicians dealing with high-risk complex aortic aneurysms. (55) Recently, there has been a growing number of publications on the treatment of thoracic aortic aneurysms with a physician-modified stent graft. (95, 106) The use of physician-modified endografts has declined significantly in one of the leading United States centers for endovascular interventions, driven by the availability of CMDs and the significant development of off-the-shelf devices. (95) Oderich et al. used PMEGs in 66% of cases between 2011 and 2013, compared to 100% between 2007 and 2010, and in 4% of cases between 2014 and 2016. (96) Nevertheless, limited access to CMDs and the significantly lower cost of PMEGs in centers in other countries may play an important role, not only in emergency situations. Their more widespread use in Hungary would allow endovascular treatment of more patients with aortic pathologies.

Almost all publications stress the question of the long-term success of this technique, but to date there is limited data available.

5.1. Study limitations

The limitations of our studies have to be acknowledged. Single-center, retrospective studies were performed with a moderate sample size. Regarding the FBEVAR cases, the follow-up was relatively short. Given the several long-term complications of FBEVARs, a longer follow-up would be necessary to evaluate the durability of the treatments. The IBD patient cohort had a relatively longer follow-up, but since the vast majority of the IBDs were implanted in the past few years, the COVID-19 pandemic delayed many control examinations. The patient cohorts were heterogeneous regarding the patients' gender and the pathology treated. Patient and material selection for intervention was determined based on a team decision, therefore the lack of a standardized approach might also limit the generalizability of our findings. Moreover, three different manufacturer's endograft models were utilized in our IBD study. We didn't have enough data in that study to perform subgroup analyses and although to our best knowledge, no relevant differences were identified among the current IBDs regarding the implantations' outcome, it is possible that differences among the grafts may exist. (78, 79)

6. Conclusions

Based on our three studies the following statements can be made:

1. The initial outcome of the FBEVAR and IBD procedures showed high technical success with high freedom from disease-related mortality.
2. The per vessel technical success rates of the FBEVAR and IBD deployments were exceptional.
3. In spite of the special funding situation in Hungary which led to the absence of a significant proportion of the learning curve of interventions and to technically demanding initial complex endovascular cases, the outcomes of these implantations were comparable to other reported data.
4. The safe introduction of FBEVAR and IBD treatment could be a result of the few physicians performing the implantations and their previous expertise in the endovascular field.
5. PMEG can be used effectively in high-volume aortic centers in elective cases in patients with unusual anatomy or in urgent cases of complex aortic pathologies.

7. Summary

As endovascular treatment possibilities emerge, management of aortic and aorto-iliac pathologies shifts towards endovascular procedures in patients with suitable anatomy. Recent developments involve fenestrated and branched endovascular aneurysm repair (FBEVAR), which provide an opportunity to use a suprarenal proximal landing zone, iliac branch devices (IBD), which preserve the internal iliac arteries even if there is a coexisting dilatation of the aorta and the iliac system, and physician modified endografts (PMEG), which are of great use when treating urgent cases, especially if unusual anatomy is present.

We aimed to evaluate the risk associated with the learning curve of starting a complex aortic program in a tertiary vascular center in Hungary. Therefore, we performed retrospective studies to assess the initial- and midterm results of the first twenty FBEVAR and first thirty-seven IBD implantations in our institution.

The initial outcome of the FBEVAR and IBD procedures showed high technical success with high freedom from disease-related mortality. The 100% per vessel technical success rates of the FBEVAR and IBD deployments were exceptional, especially since this was observed among the initial cases of a newly established center.
Regarding our incipient PMEG cases, excellent technical and clinical success was achieved.

The safe introduction and favorable outcomes of FBEVAR and IBD treatment in our institution could be a result of the few physicians performing the implantations and their previous expertise in the endovascular field. Despite the drawback related to the financial background of these procedures in Hungary, the implantations showed good results and were safe.
Additionally, based on our first PMEG cases, we believe that PMEG can be used effectively in high-volume aortic centers in elective cases in patients with unusual anatomy or in urgent cases of complex aortic pathologies.

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life

MDPI

Article

Complex Aortic Interventions Can Be Safely Introduced to the Clinical Practice by Physicians Skilled in Basic Endovascular Techniques

Sarolta Borzsák [1,2], András Szentiványi [1], András Süvegh [1], Daniele Mariastefano Fontanini [1,2], Milán Vecsey-Nagy [1], Péter Banga [2,3], Zoltán Szeberin [2,3], Péter Sótonyi [2,3] and Csaba Csobay-Novák [1,2,*]

[1] Department of Interventional Radiology, Semmelweis University, 1122 Budapest, Hungary; borzsak.sarolta@med.semmelweis-univ.hu (S.B.); sz.andris1@gmail.com (A.S.); suviandris@gmail.com (A.S.); fontanini.daniele@med.semmelweis-univ.hu (D.M.F.); vecsey_nagy.milan@med.semmelweis-univ.hu (M.V.-N.)
[2] Semmelweis Aortic Center, Heart and Vascular Center, Semmelweis University, 1122 Budapest, Hungary; banga.peter@med.semmelweis-univ.hu (P.B.); szeberin.zoltan@med.semmelweis-univ.hu (Z.S.); sotonyi.peter@med.semmelweis-univ.hu (P.S.)
[3] Department of Vascular and Endovascular Surgery, Semmelweis University, 1122 Budapest, Hungary
* Correspondence: csobay.csaba@med.semmelweis-univ.hu; Tel.: +361-458-6870

Abstract: Our purpose was to evaluate the risk associated with the learning curve of starting a complex aortic programme in an Eastern European country. A retrospective study was conducted involving the initial 20 patients (16 males, mean age: 65 ± 11 years) undergoing fenestrated/branched endovascular aortic repair in a single centre. Demographic, anatomical, procedural, and postoperative variables were collected. Our elective patient cohort consisted of 9 pararenal aneurysms (45%) and 11 thoracoabdominal aortic aneurysms (55%), with the latter including 4 chronic dissection cases (20%). A total of 71 branch vessels were incorporated (3.5 ± 0.9 per patient). The per vessel technical success rate was 100%. In-hospital mortality was 5% (1/20). At an average follow-up of 14 ± 22 months, the primary clinical success rate was 45% (9/20) and the secondary clinical success was achieved in 75% of cases (15/20). All-cause mortality at 14 months was 20% (4/20; aortic related: 1/20, 5%). Four bridging stent occlusions were found (5.6%). Mortality and reintervention rates were comparable to the initial results of high-volume centres, while the complexity of our cases and the per vessel technical success rate was comparable to the values reported as late experience. The morbidity of the learning curve could be decreased if operators are skilled in basic endovascular procedures.

Keywords: aortic aneurysm; endovascular aneurysm repair; stentgraft; fenestrated; branched

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1. Introduction

Technical developments of endovascular aortic repair (EVAR) and visceral stenting nowadays allow the safe and durable treatment of the visceral aortic segment. Since the first implantation of a fenestrated stent graft in 1998 by Anderson, significant advantages of fenestrated/branched endovascular aortic repair (FBEVAR) have been shown regarding mortality and morbidity compared to open surgical repair [1–3]. FBEVAR has been widely adopted in several countries during the last decade, which provided scientific evidence to support the recent guideline recommendations of the European Society for Vascular Surgery favouring FBEVAR over open surgery for patients with a suitable anatomy [4]. However, there are significant regional and geographical alterations regarding the availability of such therapies, especially in Eastern Europe [5,6]. These disparities can either be attributed to the lack of experience of the centres in association with incomplete or absent centralization, or due to reimbursement and/or availability issues of such devices. Nonetheless, Eastern European endovascular practice is largely missing in the current literature. The aim of our

study was to evaluate the risk associated with the learning curve of starting a complex aortic programme in a pioneer centre of Hungary.

2. Materials and Methods

This study is a single centre retrospective analysis conducted under the Semmelweis University Regional and Institutional Committee of Science and Research Ethics 96/2021. Current analysis includes our first 20 consecutive patients treated with FBEVAR. Informed consent was obtained from each patient.

2.1. Data Collection

Cardiovascular risk factors, demographics, anatomical, procedural, and postoperative variables were collected retrospectively. Follow-up clinical examination and imaging for all patients included in the complex endovascular aortic programme was performed at baseline, 30 days, 3 to 6 months, 12 months, and annually thereafter. Imaging included computed tomography angiography (CTA), magnetic resonance angiography (MRA), duplex ultrasound (DUS), or contrast-enhanced ultrasound (CEUS) studies. Intraoperative cone-beam computed tomography (CBCT) was used to confirm technical success whenever possible.

2.2. Data Analysis

Terminology, measurement techniques, and endpoint definitions were used according to the reporting standards of the Society for Vascular Surgery. This recently published document defines technical success if arterial access, delivery, and deployment of the stent graft, side branch cannulation, and the placement of the bridging stents are all successful, and if all target vessels are patent and there is no sign of type I or III endoleak on the 30-day follow-up CTA [7]. Primary endpoints were in-hospital and late aortic mortality and major adverse events, including the composite endpoints of all-cause mortality, new-onset dialysis, paraplegia, bowel ischemia, myocardial infarction, major stroke, or respiratory failure. Any unanticipated procedure performed after the index procedure was considered a secondary intervention, further classified as major if open surgery or large-bore ($\geq$12 Fr) endovascular access was needed, and minor if percutaneous $\leq$10 Fr access was obtained. Categorical variables were reported as total numbers and percentages and continuous variables as means with standard deviations. Time-dependent variables were reported using the Kaplan–Meier method. Statistical analyses were carried out using IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism 8 (GraphPad Software, San Diego, CA, USA), and the latter was also used to graph data.

2.3. Technique

After the initial three cases, all procedures were performed by the same interventional radiologist (CCN). The primary operator is a proctor for the majority of aortic device companies and has 13 years of experience in endovascular procedures. The aortic team consists of another interventional radiologist (7 years of experience) and two diagnostic radiologists (4 and 6 years), two vascular surgeons with >20 years of experience in thoracoabdominal open repair, two cardiac surgeons with 35 and 15 years of experience in aortic surgery, and a cardiovascular anaesthesiologist with 10 years of experience. All of our team members are working in an institute dedicated to cardiovascular care. All procedures were performed under general anaesthesia in a hybrid endovascular room with a fixed imaging system. Decision on stent design was based on centreline analyses performed by the primary operator (CCN) using 3Mensio Vascular software (Pie Medical Imaging B.V., Maastricht, The Netherlands). Off-the-shelf (OTS) branched stent graft (Cook t-Branch, Cook Medical Inc., Bjaeverskov, Denmark) or patient-specific custom-made devices (CMDs) with up to five fenestrations or branches (Cook Medical Inc., Bjaeverskov, Denmark and Terumo Aortic, Inchinnan, UK) were used in the following fashion: reinforced fenestrations were

preferred for vessels originating from narrow aortic segments, whereas directional branches were used to incorporate vessels that originate from wide aortic segments. Fenestrations were aligned to target vessels with balloon-expandable covered stents (Begraft Peripheral or Begraft Peripheral Plus, Bentley InnoMed GmbH, Hechingen, Germany; Atrium V12, Getinge AB, Gothenburg, Sweden; Viabahn VBX, W.L. Gore & Associates, Newark, DE, USA), whereas directional branches were bridged to target vessels with balloon-expandable (Begraft Peripheral or Begraft Peripheral Plus, Bentley InnoMed GmbH, Germany; Viabahn VBX, W.L. Gore & Associates, USA) or self-expandable covered stents (Viabahn, W.L. Gore & Associates, USA; Fluency or Covera, BD, USA), the latter being used in our early experience only. Stent selection was at the discretion of the interventionist but had been heavily influenced by device availability of the different devices and budget constraints at the time of implantation.

Open surgical cutdown was performed in all cases, suture-mediated closure devices not being reimbursed. A shift from transaxillary to transfemoral access can be observed through the years, with the latter being performed lately almost exclusively with the help of a 16F steerable sheath (Heli-FX Guide 22, Medtronic plc, Dublin, Ireland). Wire-loops to increase the support of the steerable sheath were not needed nor used.

Prophylactic cerebrospinal fluid drainage (CSFD) was used selectively in our early experience when the risk of paraplegia was deemed high, associated with either the extent of the repair or other parameters (subclavian artery patency, internal iliac artery patency, large number and/or large diameter of intercostals/lumbars to be occluded during the operation), based on aortic team decision. Lately, therapeutic CSFD is preferred due to the relatively high risk of adverse events associated with CSFD.

On-table extubation is preferred lately to check for neurological complications as early as possible. Postoperative period was primarily managed in a dedicated cardiovascular intensive care unit by intensivists and nurses experienced in the treatment of vascular disease and with a close collaboration with the primary operators. Lately, we prefer to manage the postoperative period in the vascular surgery department with close supervision and with the help of the intensivists only if needed. This helped to reduce complications associated with the ICU stay.

3. Results

Among the initial 20 cases (16 men, 65 $\pm$ 11 years) enrolled in this study and treated by FBEVAR, there were 9 pararenal aneurysms (PRA, 45%) and 11 thoracoabdominal aortic aneurysms (TAAA, 55%), the latter including 4 chronic dissection cases (20%). There was no Marfan syndrome patient in this group, and all aneurysms were degenerative. Demographics, clinical, and anatomical characteristics are shown in Table 1.

Procedural details can be found in Table 2. Average aortic coverage length was 346.6 $\pm$ 132.8 mm. Custom-made devices were used in the majority of cases (14/20, 70%). Seventy-one renal and mesenteric vessels were incorporated with forty-six fenestrations and twenty-five directional branches. Two cases (10%) were managed via transaxillary access, after which we shifted to a transfemoral only approach using a 16 Fr steerable guide catheter to facilitate target artery cannulation (Heli-FX Guide 22, Medtronic plc, Ireland). All target arteries were successfully cannulated and stented and no open surgical conversion was needed. CSFD was used in three cases (15%) based on aortic team decision, two were prophylactic, one was therapeutic. The therapeutic-only approach was preferred lately over prophylactic insertion. Perfusion branches were used in four patients (20%) deemed high risk for spinal cord ischemia (SCI). Two out of the six OTS devices were used off-label, one due to a narrow visceral aortic segment and another with the chronic occlusion of the celiac trunk. The latter urgent case was managed with the occlusion of the corresponding portal using a combination of a covered stent and an Amplatzer plug (Amplatzer Vascular Plug II, Abbott Laboratories, Chicago, IL, USA) after antegrade and retrograde recanalization attempt of the celiac trunk through the gastroduodenal arcade both failed. Five cases were managed with six adjunctive procedures (5/20, 25%): two

iliac bifurcation device implantations, two left subclavian transposition/bypass (zone 2 debranching), a prophylactic internal iliac artery recanalization, and a branch portal embolization. Preloaded catheters were not available and thus were not used.

Average total length of stay (LoS) was 5.9 ± 2.4 days with an intensive care unit (ICU) LoS of 0.8 ± 1.2 days. Per patient technical success rate was 65% (13/20). Technical failure was mostly due to the need for an early reintervention (major: 1/20, 5%, minor: 5/20, 25%), with one in-hospital death associated with the unintended coverage of a common hepatic artery arising from the superior mesenteric artery. At an average follow-up of 14.0 ± 21.9 months, primary clinical success rate was 45% (9/20), whereas secondary clinical success was achieved in 75% (15/20). In-hospital mortality was 5% (1/20). All-cause mortality at 14 months was 20% (4/20), with only one case being aortic-related (5%). In that case, the coverage of an atypical common hepatic artery led to the patient's death. One celiac and three renal stent occlusions were found (4/71, 5,6%, Figure 1).

Spinal cord injury occurred in two patients (10%), one paraplegia occurred in association with spinal epidural hematoma as a complication of a prophylactic CSFD, and a case of a paraparesis. Three cases of new-onset permanent dialysis were found (15%), two of them associated with renal stent occlusions. Aortic rupture, stroke, and myocardial infarction was not discovered.

Table 1. Demographics, clinical, and anatomical characteristics.

Variable		*n* (%) or Mean ± SD
Demographics	Male gender	16 (80)
	Mean age, years	65.5 ± 11.2
	BMI, kg/m^2	27.3 ± 4.1
Clinical Characteristics	Hypertension	16 (80)
	Smoking	8 (40)
	Hypercholesterolemia	10 (50)
	Diabetes mellitus	3 (15)
	Coronary heart disease	11 (55)
	Chronic obstructive pulmonary disease	7 (35)
	Chronic kidney disease stage III–V	4 (20)
	eGFR, mL/min/1.73 m^2	74.6 ± 16.9
	Prior aortic repair	10 (50)
	Malignant disease	5 (25)
ASA status	ASA II	1 (5)
	ASA III	17 (85)
	ASA IV	2 (10)
Anatomical characteristics	Pararenal aortic aneurysm	9 (45)
	Thoracoabdominal aortic aneurysm	11 (55)
	Chronic dissection	4 (20)
	Average size of the aortic aneurysm, mm	72.5 ± 17.0

Abbreviations: *n* = Number; SD = Standard deviation; BMI = Body mass index; ASA = American Society of Anesthesiologist's physical status classification.

Table 2. Procedural details.

Variable		*n* (%) or Mean ± SD
Device design	Off-the-shelf device	6 (30)
	Patient-specific device	14 (70)
Proximal sealing zone	zone 2–4	10 (50)
	zone 5	7 (35)
	zone 7	1 (5)
	zone 8	2 (10)

Table 2. *Cont.*

Variable		*n* (%) or Mean ± SD
Distal sealing zone	zone 9	3 (15)
	zone 10	11 (55)
	zone 11	6 (30)
Aortic coverage length, mm		346.6 ± 132.8
Total incorporated vessels		71
Incorporated vessels per patient	Total	3.6 ± 0.9
	1 vessel	1 (5)
	2 vessels	1 (5)
	3 vessels	5 (25)
	4 vessels	12 (60)
	5 vessels	1 (5)
Type of incorporation	Fenestrations	46 (65)
	Directional branches	25 (35)
Procedural data	Contrast volume, ml	285.4 ± 124.0
	Fluoroscopy time, min	69 ± 39
	Cumulative air kerma, Gy	3.6 ± 2.5
ICU length of stay, d		0.8 ± 1.2
Total length of stay, d		5.9 ± 2.4
Staged repair		6 (30)
Cerebrospinal fluid drainage		3 (15)
Temporary aneurysm sac perfusion		4 (20)
Technical success per vessel		71 (100)
Primary technical success per patient		13 (65)

Abbreviations: *n* = Number; SD = Standard deviation; ICU = Intensive care unit.

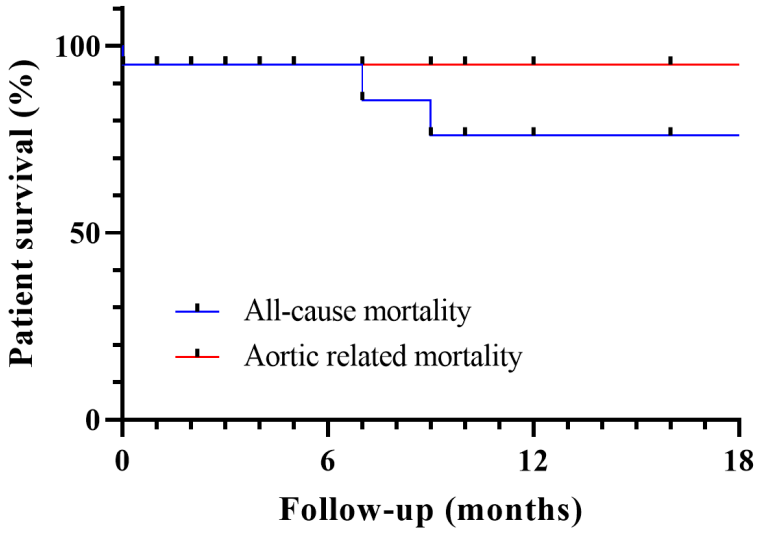

Figure 1. *Cont.*

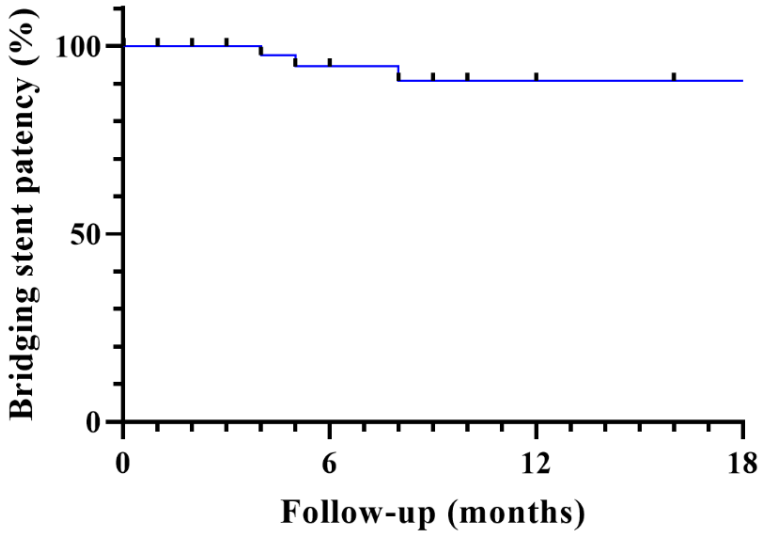

Figure 1. Patient survival (**upper**) and bridging stent patency (**lower**) at an average follow-up of 14 ± 22 months.

4. Discussion

Initially developed to extend the indications of EVAR in high-risk patients with insufficient proximal landing zone, FBEVAR has recently matured to a widely accepted alternative to open surgery for complex aortic pathologies in all patients, regardless of surgical risk. Although FBEVAR is widely available for patients in developed countries, significant geographical disparities remain, especially in less-developed countries, e.g., the Eastern European countries.

The slower adoption of this technology can be attributed to several factors. A slow dissemination was seen in the US after the Food and Drug Administration approval of the Zenith Fenestrated endovascular graft (ZFEN, Cook Medical) in 2012, with 30% of the physicians who received ZFEN training not ordering a single device and 80% ordering <five devices/year [8,9]. The greater technical complexity of these demanding procedures requiring advanced endovascular skills, greater reliance on a complicated preoperative planning, and the need of advanced imaging equipment were identified as barriers of more widespread use, resulting in a reduced number of cases performed [8]. The need for a highly specialised imaging and for precise complex planning limiting the adaptation of FBEVAR techniques as the procedural planning requires not only measurements but extensive knowledge of the parameters, which affect device delivery, deployment, and target artery cannulation [10]. Furthermore, restricted access to appropriate devices remains a limiting factor in the adoption of novel endovascular techniques in the Eastern European region. Dissemination of the FBEVAR technique is even slower in the vast majority of Central and Eastern European countries, with a very few exceptions only. In Hungary, the missing reimbursement of complex aortic procedures is paired with the lack of centralisation due to political reasons, despite the provided evidence, resulting in less than 10 complex aortic procedures performed altogether by the tertiary centres until 2019 [11]. Being a tertiary vascular centre in Hungary, we established the first Aortic Centre of Hungary in early 2020, which resulted in an outbreak of complex aortic procedures compared to earlier years, despite the ongoing struggle with the limited budget for aortic procedures. Centralisation and treating patients in multidisciplinary teams provide a better care for the patients. Alberga et al. showed an association of hospital volume with perioperative mortality of complex endovascular repairs. In this Dutch nationwide study, they detected a perioperative mortality following FBEVAR in 9.1% in hospitals with a yearly volume of <9, while 2.5% in hospitals were performing more than 13 complex endovascular aneurysm repairs [12].

Despite having a case load (ca. 10/year) way less than ideal (3/month) to achieve lower adverse event rates, we were able to deliver an outcome at least noninferior to the most experienced centres of open repair of TAAA [13]. The in-hospital mortality rate found in our initial series (5%) compares favourably to the operative mortality of 6.2% reported by Coselli et al., a benchmark of elective thoracoabdominal open repair [14]. Mirza et al. reported the learning curve at the Mayo Clinic with a 6% mortality rate of the initial patient cohort (n = 81), while Schneider et al. reported a similar 6% perioperative mortality rate of the initial 50 FBEVAR cases performed in New York-Presbyterian Hospital. Our mortality rate compares well to these data, especially since our initial patient cohort, and thus our experience, is much smaller than that of the cited authors' [8,13]. Furthermore, we achieved a lower in-hospital mortality rate than reported in the WINDOWS trial (10.1%), a study that was planned to minimize centre effect and evaluate the real-world mortality of FBEVAR [15]. However, some authors reported lower mortality rates, e.g., Schanzer et al. evaluated their single centre's experience of the first 100 consecutive FBEVAR of complex aortic aneurysms. In their observational cohort study, a mortality rate of 3% was shown [10].

Staged repair, which was performed in one-fifth of our cases, is widely accepted to be associated with reduced rates of neurological complications such as paraparesis and paraplegia. These neurologic symptoms remain a dreaded complication of extensive aortic repair [16].

Initial risk associated with the starting of a complex aortic programme is heavily dependent on the operating team's skills. Previous experience with EVAR and crural angioplasty may be associated with a steeper learning curve [17]. Our centre has more than two decades of experience in aortic interventions, with numbers approaching 100/year in the last five years. We were also one of the very first centres in Europe to perform angioplasty of the branches of the aorta, a skill that is essential to achieve success in complex aortic repair [18]. Up to now, no unconnected fenestrations/branches occurred, resulting in a 100% per vessel technical success rate, which is rather unusual in the initial cases of a newly established centre [19]. In comparison, Schanzer et al. reported a 2.3% failure to cannulate and bridge any targeted artery resulting in a 97.7% per vessel technical success rate [10]. Per patient technical success rate (65%) was compromised mostly by a rather high reintervention rate (30%), although the vast majority of these were classified as minor and values compare well with literature data [8,13].

It is well known that early experience usually involves very high-risk patients unfit for open repair [8,13,17]. Our initial cohort almost exclusively consisted of patients deemed unfit for major surgery, 95% of them being ASA class III-IV, which is among the highest values reported in association with early experience [13]. It is also usual that the complexity of the FBEVAR implants increases with the growing experience of a team [13,17]. The trends regarding the complexity of our repairs cannot be evaluated due to our very small patient cohort; however, more vessels were incorporated per patient (3.5 $\pm$ 0.9) in our present study than in the early period of Mirza et al. (2.8 $\pm$ 0.9) [13]. Prior aortic surgery (50%) and postdissectional TAAA repair (20%) occurred with a frequency that is comparable to that reported by Oderich et al. very recently, also suggesting that the complexity of our initial cases was somewhat higher than what is usual to start with [20].

There are limitations of our study. This is a single-centre, retrospective study which includes only twenty FBEVAR cases and has a relatively short follow-up. Since FBEVAR has several long-term complications, a longer follow-up would be necessary to evaluate the durability of these repairs. The lack of a standardized approach for patient selection might also result in patient and material selection. Furthermore, the heterogeneity of the patients regarding the gender and the pathology treated also limits the generalisability of our findings.

5. Conclusions

The initial outcome of our complex aortic programme showed high technical success and a low complication rate with a high freedom from disease-related mortality. Mortality and reintervention rates were comparable to the initial results of high-volume centres, while the complexity of our cases and the per vessel technical success rate are comparable to the values reported as late experience. The late addition of FBEVAR to our treatment portfolio and the advanced skills of our team in standard aortic and visceral interventions may have helped us to avoid the higher mortality and morbidity associated with the learning curve of our complex aortic programme.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Semmelweis University Regional and Institutional Committee of Science and Research Ethics (96/2021, date of approval: 6 May 2021).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Not applicable.

Conflicts of Interest: Csaba Csobay-Novák—training, consultation, and proctoring for W. L. Gore & Associates and Cook Medical. Zoltán Szeberin—training, consultation, and proctoring for W. L. Gore & Associates and Cook Medical.

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Midterm Results of Iliac Branch Devices in a Newly Established Aortic Center

Sarolta Borzsák [1,2], András Süvegh [1], András Szentiványi [1], Daniele Mariastefano Fontanini [1,2], Milán Vecsey-Nagy [1], Péter Banga [2,3], Péter Sótonyi [2,3], Zoltán Szeberin [2,3] and Csaba Csobay-Novák [1,2,*]

[1] Department of Interventional Radiology, Semmelweis University, 1122 Budapest, Hungary; borzsak.sarolta@med.semmelweis-univ.hu (S.B.); suviandris@gmail.com (A.S.); sz.andris1@gmail.com (A.S.); fontanini.daniele@med.semmelweis-univ.hu (D.M.F.); vecsey_nagy.milan@med.semmelweis-univ.hu (M.V.-N.)
[2] Semmelweis Aortic Center, Heart and Vascular Center, Semmelweis University, 1122 Budapest, Hungary; banga.peter@med.semmelweis-univ.hu (P.B.); sotonyi.peter@med.semmelweis-univ.hu (P.S.); szeberin.zoltan@med.semmelweis-univ.hu (Z.S.)
[3] Department of Vascular and Endovascular Surgery, Semmelweis University, 1122 Budapest, Hungary
* Correspondence: csobay.csaba@semmelweis.hu; Tel.: +36-1-458-6870

Abstract: The first-line treatment of common iliac artery aneurysms is endovascular repair. International guidelines recommend the preservation of the internal iliac artery, which is best achieved by the implantation of an iliac bifurcation device (IBD). Our aim was to evaluate the initial midterm results of IBDs in the leading vascular center of Hungary. In this single-center retrospective study, relevant clinical data and the results of the imaging examinations were collected and analyzed in all patients who underwent IBD implantation between December 2010 and July 2021. Thirty-five patients (31 males, mean age: 67.9 ± 8.5 years) underwent endovascular treatment with 37 IBD implantations. Technical success was achieved in 88.2% of the patients, with no perioperative mortality or open surgical conversion. One patient was lost during follow-up. Internal iliac artery occlusion was detected in three (8.8%) patients, and reintervention was performed in five (14.7%) patients. Primary patency of the internal iliac branch was 97.1% at 1 month, 93% at 2 months, and 89.0% at 5 years. The average follow-up time was 20.1 ± 26.2 months, during which two (5.9%) deaths occurred. Our initial experience with iliac branch devices was associated with a low complication rate and a favorable outcome, which confirms the midterm success of this intervention.

Keywords: iliac aneurysm; endovascular procedures; iliac branch device

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1. Introduction

As endovascular treatment possibilities evolve, the management of aortic and aortoiliac pathologies is shifting towards endovascular procedures in patients with suitable anatomy [1]. On the other hand, extensive iliac aneurysm repair might not provide a durable exclusion of the aneurysm, or it might endanger pelvic circulation [2]. Recent guidelines recommend the preservation of at least one internal iliac artery to minimize the risk of ischemic complications following the loss of the internal iliac arteries. In addition to a surgical approach, various endovascular techniques can be used to preserve hypogastric anatomy, e.g. the bell bottom technique, sandwich technique, and multiple side branch techniques. However, it can be best obtained by the implantation of an iliac branch device (IBD) [1,3,4]. Several studies have reported on the outcomes of IBDs, demonstrating favorable results [2,5,6]. However, the availability of such devices shows significant geographical differences due to the lack of reimbursement and/or centralization, especially in Eastern European countries [7]. Therefore, as such data are currently missing from the literature, we aimed to evaluate the initial experience of IBD implantations regarding the short- and midterm results at a pioneer aortic center in Hungary.

Our aim was to examine the results of these interventions, above all the per vessel technical success rate, technical success rate, and clinical success rate, and to describe the outcome parameters at follow-up, such as aortic-related and all-cause mortality, need for reintervention, and patency of the iliac arteries.

2. Materials and Methods

2.1. Study Population

We performed a retrospective analysis of all consecutive patients who underwent IBD implantation between December 2010 and July 2021. The study was approved by the local ethics committee (Semmelweis University Regional and Institutional Committee of Science and Research Ethics: 92/2021) and performed in accordance with the Declaration of Helsinki. All patients provided informed consent.

Demographic data and cardiovascular risk factors, as well as anatomical, procedural, and postoperative variables, were collected retrospectively. Follow-up clinical examinations and imaging were performed according to current guidelines: first at 30 days, then at 6 months, and then yearly depending on the results of the computed tomography angiography (CTA) examination completed during the first follow-up. In patients with severely impaired kidney function, magnetic resonance angiography (MRA) was performed instead of a CTA.

2.2. IBD Procedure

The IBD deployment was performed as an adjunctive procedure during an endovascular aneurysm repair (EVAR) if aorto-iliac involvement was seen, or as a stand-alone procedure, when only an isolated iliac artery aneurysm was repaired. The choice of implanted bifurcation device was based on the patients' + anatomic features and the availability of the different IBDs. Planning was performed using IntelliSpace Portal (Philips Healthcare, Best, The Netherlands) or 3Mensio Vascular software (Pie Medical Imaging B.V., Maastricht, The Netherlands). Zenith Branch Endovascular Graft (Cook Medical, Bloomington, IN, USA), Gore Iliac Branch Endoprosthesis (IBE; W.L. Gore & Associates, Newark, DE, USA), and Jotec E-liac (Jotec GmbH, Hechingen, Germany) were used. The Cook device was preferred for smaller common iliac luminal diameters, whereas Gore implants were used for wider lumina. Jotec devices were preferred when isolated repair was planned, and proximal diameters were suitable.

All procedures were performed by two physicians (CCN, ZSz), both of whom are proctors of a firm. A fixed X-ray imaging system was used, and latter cases were performed in a hybrid operating room. Open surgical cutdown was preferred in our early experience, with a shift towards the percutaneous technique using Perclose Proglide (Abbott Laboratories, Abbott Park, IL, USA) suture-mediated closure system. Additional collagen-plug based vascular closure devices (AngioSeal VIP; Terumo Corporation, Tokyo, Japan) were used liberally if suture-mediated vascular closure failed. General or locoregional anesthesia was used at the discretion of the anesthetist. Postoperative course was usually managed outside the intensive care unit. Dual antiplatelet therapy was maintained postoperatively for three months followed by lifelong aspirin or clopidogrel monotherapy.

2.3. Data Analysis

In terms of terminology, measurement techniques, and outcome parameters, we followed definitions within the most recent reporting standards document published by Oderich et al. Technical success was considered to be achieved if successful access to the arterial system was obtained, the stent graft components were deployed, and the preservation of all branches was successful, and no type I or III endoleak was seen on the 30-day follow-up imaging study. A clinical success was defined as the absence of important disabling permanent clinical sequelae, such as aortic-related complications or permanent paraplegia, disabling stroke, or permanent dialysis in addition to technical success [8]. Primary endpoints in this study were aortic-related and all-cause mortality,

need for reintervention, and patency of the iliac arteries. Secondary outcomes were technical and clinical success, detection of endoleaks, and major adverse events, including new-onset renal failure, major stroke, myocardial infarction, respiratory failure, and significant buttock claudication.

2.4. Statistical Analysis

Categorical variables are presented as numbers and percentages, and continuous parameters are reported as mean ± standard deviation (SD). Kaplan–Meier survival estimates were calculated to assess long-term outcomes (patency, re-intervention, and survival); the curve is displayed up to a value of standard error (SE) < 0.10. A value of $p < 0.05$ was considered statistically significant for all measurements. Statistical analyses were carried out using IBM SPSS (Armonk, NY, USA, version 27.0) and GraphPad Prism 8 (GraphPad Software, San Diego, CA, USA), and the latter was used to graph data.

3. Results

Between 14 December 2010 and 23 July 2021, 37 IBDs were implanted in 35 patients in a tertiary care university medical center. The primary disease was aorto-iliac aneurysm in 19 cases, isolated iliac aneurysm in 11, chronic aortic dissection in 3 and Ib endoleak following an EVAR in 2 cases. In the 11 cases where the indication of the IBD deployment was an isolated common iliac aneurysm, a stand-alone IBD implantation was performed. The remaining 24 patients were treated in conjunction with an EVAR. Three patients also underwent a thoracic endovascular aortic repair (TEVAR) procedure for a thoracic aortic aneurysm in addition to the EVAR-IBD implantation. The mean age was 67.9 ± 8.5 years, and patients were mostly male (89%). The population and aneurysm characteristics of patients undergoing IBD implantations are reported in Table 1. Detailed procedural data are shown in Table 2.

Twenty patients (57.1%) were treated outside of the instructions for use (IFU). Based on the IFU, only the Jotec E-iliac graft should be used in isolated iliac aneurysms; however, in six cases, a Cook ZBIS or a Gore IBE endograft was placed and isolated, due to proximal landing zone diameter issues. The other 14 patients were outside of the IFU, either because of aortic dissection as their primary disease or because they did not meet the anatomical requirements of the IFUs. In these cases, an aortic team decision was made to recommend IBD implantation, to which the patient consented. Off-label/non-IFU repairs were equally prevalent throughout the study period.

Table 1. Baseline patient and anatomical characteristics.

Variable		N (%) or Mean ± SD
Demographics	Male gender	31 (89)
	Mean age, years	67.9 ± 8.5
	BMI, kg/m^2	28.5 ± 5.7
Cardiovascular risk factors	Hypertension	35 (100)
	Current smoking	13 (37)
	Hypercholesterolemia	16 (46)
	Diabetes mellitus	6 (17)
	Peripheral artery disease	7 (20)
	Cardiac disease	18 (51)
	Chronic obstructive pulmonary disease	10 (29)
	Chronic kidney disease stage III-V	11 (31)
	Previous aortic repair	12 (34)
	Prior malignancies	11 (31)
Anatomical characteristics	Left CIA aneurysm diameter, mm	32.3 ± 14.1
	Right CIA aneurysm diameter, mm	35.0 ± 13.5

Abbreviations: N = number; SD = standard deviation; BMI = body mass index; CIA = common iliac artery.

Table 2. Baseline procedural characteristics.

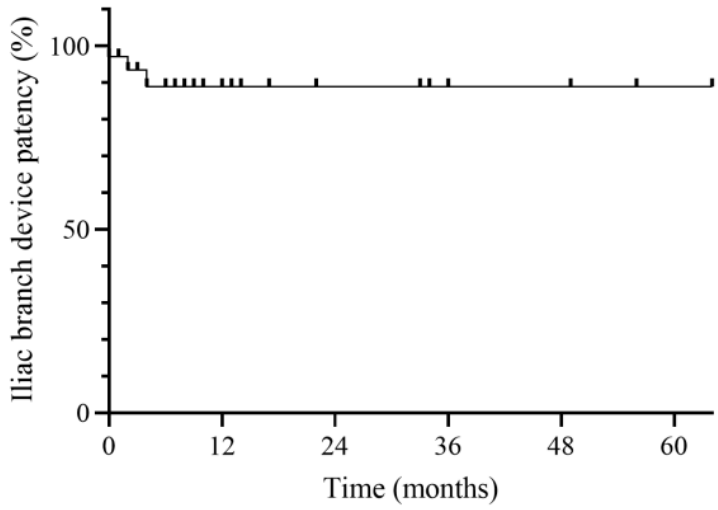
Variable		N (%) or Mean ± SD
Implanted devices	Cook ZBIS	20 (54)
	Gore IBE	12 (32)
	Jotec E-iliac	5 (14)
	Isolated IBD	11 (31)
	Bilateral IBD	2 (6)
Procedural data	Contrast dose, mL	139.25 ± 71.36
	Fluoroscopy time, s	2832.55 ± 1656.08
	Dose area product, Gy*cm^2	294.45 ± 442.74
	Total length of hospital stay, days	4.60 ± 0.69
	Length of intensive care unit stay, days	0.3 ± 0.51
Complications	Type I endoleak	1 (3)
	Type II endoleak	10 (29)
	Type III endoleak	2 (6)
	Type IV endoleak	0 (0)
	Type V endoleak	1 (3)

Abbreviations: N = number; SD = standard deviation; IBD = iliac branch device.

Our per vessel technical success rate was 100%, and none of the internal iliac arteries were lost. The overall technical success rate was 88.2%. The primary clinical success rate was 82.4%, while the assisted primary clinical success rate was 88.2%.

The mean postoperative hospitalization duration was 4.6 ± 0.7 days, and the average length of the intensive care unit stay was 0.3 ± 0.5 days. The mean follow-up time was 20.1 ± 26.2 months. One patient was lost during follow-up. During the follow-up period, no peri-operative or in-hospital deaths were recorded, nor was surgical conversion needed. There was no myocardial infarction, stroke, new-onset renal failure, mesenteric or spinal cord infarction, respiratory failure, or significant buttock claudication.

Freedom from IBD occlusion values were 97.1%, 93.5%, and 89.0% at 1, 2, and 4 months using Kaplan–Meier estimates, respectively (Figure 1). In total, three iliac occlusions were observed, and only the internal iliac branch was affected. All the occlusions were left untreated.

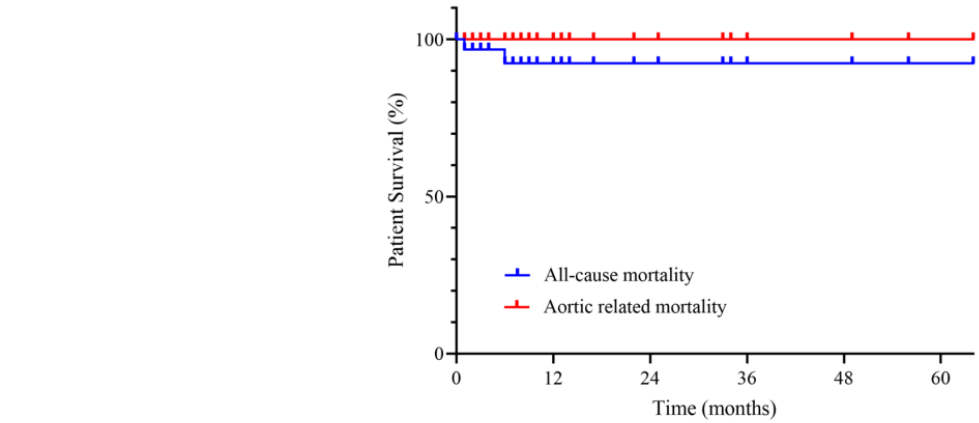


Number at risk	34	12	7	4	4	2
Kaplan-Meier estimate survival rates	0.971	0.890	0.890	0.890	0.890	0.890
Standard error	0	0.061	0.061	0.061	0.061	0.061

Figure 1. Kaplan-Meier estimates of iliac branch patency treated by iliac branch devices.

Seventeen endoleaks were detected in 14 patients. One type I, one type V, and two type III endoleaks were found, while 10 of the patients had a type II endoleak. Five re-interventions were necessary (14.7%). Endoleaks were managed when a significant aneurysm sac growth (>5 mm) was seen (4 cases, 11.4%). In three cases, successful embolization was performed (using histoacryl and lipiodol), but in one case, the source of the endoleak could not be clearly identified. The need for re-intervention was related to the IBD device in four patients (11.8%).

Two late deaths were recorded, neither of them related to the endovascular intervention or the aneurysm. The cause of death was gastro-intestinal bleeding in one case and Clostridium sepsis in the other case, both of which occurred months after the IBD procedure. The freedom from all-cause mortality and freedom from aneurysm-related mortality was 92.4% and 100%, respectively (Figure 2).



	Number at risk	34	15	10	6	6	4
	Kaplan-Meier estimate survival rates	1	1	1	1	1	1
	Standard error	0	0	0	0	0	0
	Number at risk	34	15	10	6	6	4
	Kaplan-Meier estimate survival rates	1	0.924	0.924	0.924	0.924	0.924
	Standard error	0	0.053	0.053	0.053	0.053	0.053

Figure 2. Kaplan-Meier estimates of all-cause mortality and aortic related mortality treated by iliac branch devices.

4. Discussion

Preserving the internal iliac artery during EVAR or during an isolated iliac aneurysm treatment is advocated to minimize the risk of pelvic ischemic complications [9]. IBDs have been used as an adjunctive procedure during an EVAR and as a stand-alone procedure for over a decade with excellent results [6,10].

In recent years, the numbers of IBDs started to rapidly increase due to the establishment of a multidisciplinary aortic center. In Figure 3, we provide a graph demonstrating the number of IBD implantations performed at our institution each year. Despite the lack of formal centralization in Hungary regarding both standard and complex aortic procedures, our institute is a pioneer in the aortic field. We have performed 90% of the complex aortic procedures for more than 80% of IBD cases in Hungary so far [11].

The results of our initial series of patients are favorably compared with other reported data from experienced aortic centers in Western Europe. The technical success rate was 88.2% in our study. In their systematic review, Kouvelos et al. reported a technical success rate of endovascular internal iliac artery preservation in 96.2% of cases [9]. In a study by Simonte et al., including 149 patients with 157 IBD implantations and a median follow-up of 34.0 months, the technical success rate was 97.5% [6]. Parlani et al. reported a

technical success rate of 95% [2]. Haulon et al. achieved a technical success rate of 94% [4]. Mylonas et al. demonstrated an outstanding technical success rate of 100%, although they reported their results in accordance with more permissive criteria [12].

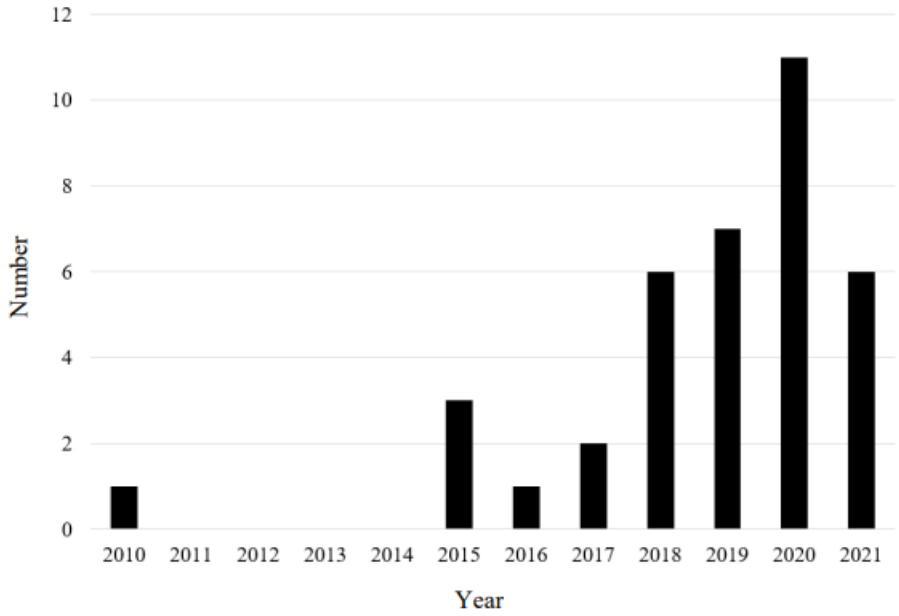


Figure 3. IBD implantations in our institution.

However, the existence of a learning curve is a well-known fact regarding all procedures, which explains our slightly inferior outcome parameters. Simonte et al. performed a sub-analysis comparing outcomes achieved in the first 25 IBD deployments, and those observed in the later phase. Significant differences were detected—the peri-operative success rate was 84.0% in the first period, and it was 97.7% after the first 25 cases [6]. The study of a 5-year experience on IBD implantations conducted by Parlani et al. also confirmed the important role of the learning curve effect, as they detected four out of the five technical failures during their first year of experience with IBDs [2]. Compared to their five intra-operative IBD internal limb occlusions, our per vessel technical success rate of 100% shows a better technical outcome.

Another factor that might explain the slightly inferior outcome rates of the devices is the high number of patients treated outside the IFU (57.1%). Off-label use was most commonly associated with a reduced diameter of the common iliac bifurcation. In particular, we believe the 16 mm threshold for the Cook ZBIS device is rather strict, and narrow iliac bifurcations down to 12–13 mm may be treated successfully with an acceptable outcome. These procedures are technically more demanding, but outcomes may not be inferior to on-label cases once the technical difficulties are managed intraoperatively and proper post-dilation is performed, most commonly with a kissing balloon maneuver. Similarly, narrow aortic bifurcation was found to be non-inferior regarding long-term outcome if a proper implantation technique was used [13].

There is an interesting study by Tomczak et al. that aimed to evaluate the number of patients with asymptomatic abdominal aortic aneurysms, regardless of the treatment plan, who can be treated by EVAR with stentgraft devices commercially available in East–Central Europe in conformity with the IFU. The suitability rates of the examined devices varied from 20% to 65%. It was found that 32% of the patients were not suitable for any of the analyzed stentgrafts, assuming a rigorously followed IFU [14]. Similar difficulties could be present regarding the armamentarium of IBDs, limiting the patients who can be endovascularly treated within the IFU. The liberalization of morphology indications might result in increased failure rates and higher endoleak rates [2]. In a comparative study by Donas et al., where minimal anatomical characteristics were used for IBD implantation and

challenging anatomies of the internal iliac artery were also included, a higher endoleak rate was observed (12.5%) than the average literature data [15].

On the other hand, Simonte et al. found similar results when comparing the long-term outcomes of IBD implantations performed in an experienced center as per or outside manufacturer's IFU [16]. Rodriguez et al. reported similar findings: in a study where 15 patients were treated within the IFU and 24 patients' IBD implantations were non-IFU, no significant difference was found regarding technical success and device-related reintervention in the short term [17]. Another approach, when patients with challenging anatomy require iliac aneurysm treatment, could be the use of a custom-made iliac branch device. Huang et al. found non-inferior results when comparing their custom-made devices to commercial devices in a cohort of 46 patients [18].

Our internal iliac artery occlusion rate of 8.8% at 2–5 years is comparable to a few other studies. Haulon et al. and Karthikesalingam et al. both reported similar, slightly elevated occlusion rates of 11.3–12.2% [4,19]. However, our iliac patency rate was lower than what was mostly found in other similar studies, where the internal iliac branch patency was between 89.7% and 100% [12,20].

Our endoleak rate with 17 detected endoleaks was higher than the literature data. We detected 10 type II endoleaks in our patient cohort of 35 compared with the results of the D'Oria et al. study on the bilateral use of IBDs within the pELVIS registry, where only 17 persistent type II endoleaks were seen in 96 patients [21]. However, the number of endoleaks, which required invasive therapy, did not differ much from the existing data. We only treated endoleaks with a significant aneurysm sac growth, which was the case in four patients. We find it important to try to manage complications conservatively, especially in fragile patients. One possibility is to modify the patient's medication; e.g., we had a case, in which a type I endoleak disappeared after the dual antiplatelet therapy was changed to a mono antiplatelet therapy.

The re-intervention rate of 14.7% is also comparable to the existing data in the literature. Verzini et al. reported a re-intervention rate of 18.2% [22]. Gibello et al. found a re-intervention rate of 11.8% in patients with a common iliac artery diameter <18 mm and 19.1% in those with a common iliac artery diameter ≥18 mm [23]. Overall, 42 re-interventions were performed among the 575 patients (7.3%) in the patient cohort analyzed by Donas et al.

Most authors agree that the outcome of an open abdominal aortic aneurysm repair is associated with surgeon and hospital caseload [23–28]. McPhee et al. found that after an elective open abdominal aortic aneurysm repair, surgeon case volume is the primary determinant of in-hospital mortality [24]. An international analysis of 178,860 patients found no volume effect on in-hospital or 30-day mortality after EVAR for abdominal aortic aneurysm [26]. Mortality after EVAR was unaffected by either surgeon or hospital volume in the Australian population studied by Sawang et al., but hospital volume in the TEVAR subgroup showed a strong inverse correlation with mortality [25]. Complication rates and in-hospital mortality following abdominal aortic aneurysm repairs were found to be inversely associated with annual hospital volume in Germany [29]. After EVAR, hospital volume was associated with slightly higher perioperative mortality in the study of Zettervall et al., but no such association was observed for surgeon volume [26].

A recent Dutch analysis also showed a significant effect of hospital volume on peri-operative mortality following complex EVAR, with high volume centers demonstrating decreased mortality rates [30]. D'Oria et al. investigated the association between hospital volume and failure to rescue after EVAR and open aortic repair of intact abdominal aortic aneurysms and found a significant association: hospitals in the top volume quartiles achieve the lowest mortality after a complication has occurred [31].

To our best knowledge, no data on the effect of surgeon case volume or hospital volume are available regarding the outcomes of IBD implantations. However, our cases being analyzed by only two physicians, both of whom are proctors, and our results being slightly better than other centers' initial data, suggest that the operator's experience (both

prior endovascular experience and practice obtained during the IBD implantations) might have an effect on decreasing the learning curve.

Study Limitations

We acknowledge the limitations of our study. Our single-center, retrospective analysis includes a relatively small sample size of patients, and since the vast majority of these IBDs were deployed in the past three years, and the COVID-19 pandemic delayed many control examinations, we have a significant number of patients with short follow-up data; the follow up completion rate has been relatively low recently. Patient and material selection for intervention were derived from team discussions; we did not have a standardized approach. The heterogeneity of the patients regarding the type of treated pathology also limits the generalizability of our results.

Furthermore, three different manufacturer's endograft models were utilized in our study. It is possible that differences in peri-operative or late performances among the grafts may exist, but we did not have enough data in this study to perform subgroup analyses. Nonetheless, to our best knowledge, no relevant differences were detected among the current IBDs regarding patient outcomes [12,18]. Finally, the low event rate did not make the evaluation of the adjusted risk factors for the primary and secondary endpoints possible.

5. Conclusions

In this retrospective study, a high technical success rate and low complication rate were found with a high freedom from disease-related mortality when analyzing our short- and midterm results, despite observing the initial cases of our center. The safe introduction of IBDs for the treatment of iliac aneurysms could be the result of the few physicians performing the implantations and their previous expertise in endovascular procedures.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Not applicable.

Conflicts of Interest: Csaba Csobay-Novák—training, consultation, and proctoring for W. L. Gore & Associates and Cook Medical. Zoltán Szeberin—training, consultation, and proctoring for W. L. Gore & Associates and Cook Medical.

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Kezdeti tapasztalataink az orvos által módosított sztentgraftok alkalmazásával

Borzsák Sarolta dr.[1, 2] ▪ Péter Csongor dr.[1] ▪ Suhai Ferenc dr.[1]
Szeberin Zoltán dr.[2, 3] ▪ Csobay-Novák Csaba dr.[1, 2]

[1]Semmelweis Egyetem, Általános Orvostudományi Kar, Városmajori Szív- és Érgyógyászati Klinika, Intervenciós Radiológiai Tanszék, Budapest
[2]Semmelweis Egyetem, Általános Orvostudományi Kar, Városmajori Szív- és Érgyógyászati Klinika, Semmelweis Aortacentrum, Budapest
[3]Semmelweis Egyetem, Általános Orvostudományi Kar, Városmajori Szív- és Érgyógyászati Klinika, Érsebészeti és Endovaszkuláris Tanszék, Budapest

Bevezetés: Az aortabetegségek kezelése során az orvos által módosított sztentgraftok alkalmazása vitatott. Döntően sürgősségi esetben, nagy rizikójú nyitott műtét alternatívájaként vagy nehéz anatómiai konfigurációk esetén alkalmazzák őket.
Módszer: Cikkünkben három eseten keresztül klinikánk kezdeti tapasztalatait mutatjuk be az orvos által a műtét során módosított sztentgraftokkal kapcsolatosan.
Eredmények: Első esetünkben egy 75 éves férfi beteg 50 mm-es saccularis infrarenalis aortaaneurysma miatt került felvételre. A rövid infrarenalis tágulat proximalis rögzítési zónájának átmérője lényegesen nagyobb volt, mint a terminális aortaszakasz. A kaliberdiszkrepancia megoldására a legalkalmasabb egy reverz helyzetű iliacagraftszár volt, így egy graftszárat a felvezetőrendszeréről eltávolítottunk, majd megfordítva az aorta tágulatába deponáltuk. Hasonló megoldást választottunk egy 67 éves férfi beteg jobb oldali, 65 mm-es arteria iliaca communis aneurysmájának kezelése során. Egy 81 éves nőbeteg hasi aortaaneurysma tartott rupturája miatt korábban behelyezett unilateralis graft proximalis endoleakjének megoldása miatt érkezett. Az ectaticus aorta, valamint az arteria mesenterica superior és a primer intervenció során bekerült unilateralis graft elkeskenyedő része közti rövid távolság miatt konvencionális sztentgraft beültetése nem volt lehetséges. A szituáció egy rövid thoracalis sztentgrafttal volt megoldható: egy thoracalis sztentgraft distalis végéből 3 cm-t kauter segítségével levágtunk, majd az eszközt a felvezetőrendszerbe visszatöltöttük. A módosított sztentgraftot az arteria mesenterica superior alá pozicionáltuk, egy 'chimney' sztentgraft segítségével biztosítottuk a jobb vese perfúzióját. Technikailag mindhárom beavatkozásunk sikeres volt.
Következtetés: Az endovascularis aortaműtétek azonnal elérhető eszközparkja a típusos anatómiájú betegek megoldására általában alkalmas. A szokatlan anatómiával rendelkező elektív esetek, illetve a sürgető beavatkozást igénylő komplex endovascularis műtétek során az orvos által módosított sztentgraftok hatékonyan alkalmazhatók. Alkalmazásuk nagy forgalmú aortacentrumokban javasolt.
Orv Hetil. 2022; 163(3): 109–115.

Kulcsszavak: endovascularis technikák, abdominalis aortaaneurysma, endoleak

Initial experiences with physician-modified endo grafts

Introduction: Physician-modified endografts are mainly used in urgent cases of aortic disease as an alternative to high-risk open surgical repair or in difficult anatomical configurations.
Method: We present our initial experiences with physician-modified stent graft implantation.
Results: A 75-year-old male patient was admitted with a 50 mm saccular infrarenal aortic aneurysm. However, the diameter of the proximal sealing zone was significantly larger than that of the distal sealing zone, so we decided to use an iliac limb stent graft with reverse mounting resulting in an upside-down configuration to accommodate this diameter mismatch. A similar approach was used to treat a 67-year-old male patient with a 65 mm right common iliac artery aneurysm. An 81-year-old female patient was admitted with a type I endoleak associated with an aorto-uni-iliac endograft. The wide juxtarenal aortic diameter together with the short distance between the superior mes-

enteric artery and the proximal end of the previously deployed uni-iliac graft made the patient unsuitable for conventional endovascular repair, thus the distal 3 cm was cut from a standard thoracic stent graft and the device was reloaded. The modified graft was positioned below the superior mesenteric artery, while renal perfusion was secured by a chimney graft. Technical success was obtained in all three cases.
Conclusion: The available toolkit of endovascular aortic surgery is generally suitable for the treatment of patients with typical anatomy. In elective cases of patients with unusual anatomy, or in urgent cases with complex aortic pathologies, physician-modified endovascular graft implantation can be used effectively.

Keywords: endovascular techniques, abdominal aortic aneurysm, endoleak

Borzsák S, Péter Cs, Suhai F, Szeberin Z, Csobay-Novák Cs. [Initial experiences with physician-modified endo grafts]. Orv Hetil. 2022; 163(3): 109–115.

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Rövidítések

CMD = (custom-made device) egyedileg gyártott eszköz; CT = (computed tomography) komputertomográfia; EVAR = (endovascular aneurysm repair) az aortaaneurysma endovascularis kezelése; MRA = mágneses rezonanciás angiográfia; OSFG = (off-the-shelf fenestrated and branched graft) készen kapható fenesztrált és elágazó endograft; PMEG = (physician-modified endograft) orvos által módosított sztentgraft

Az aortaaneurysma endovascularis kezelésének (endovascular aneurysm repair – EVAR) biztonságosságát és hatékonyságát arra alkalmas aortaanatómia esetén több tanulmány igazolta, a piacon elérhető konvencionális graftok alkalmazásával az aortabetegségek többsége sikeresen kezelhető [1]. Az esetek egy jelentős hányadában azonban az anatómia nem teszi lehetővé ezen eszközök használatát. Ilyenkor – az endovascularis terápia elvetése, nyitott műtét mérlegelése mellett – egyedileg gyártott eszköz (custom-made device – CMD), készen kapható fenesztrált vagy elágazó sztentgraft (off-the-shelf fenestrated and branched stentgraft – OSFG), illetve orvos által módosított endograft alkalmazása lehetséges [2]. Ezek többek között juxtarenalis aneurysmák esetén vagy a visceralis ágakat is érintő tágulat esetén is megoldást kínálhatnak azzal, hogy suprarenalis proximalis landing zóna alkalmazására biztosítanak lehetőséget [3].

A CMD-k a páciens anatómiájához illeszkedő fenesztrált vagy elágazó sztentgraftok, melyeken megerősített fenesztrációk vagy direkt ágak figyelhetők meg a zsigeri szájadékoknak megfelelően, ezzel biztosítva a sztentgraft-implantációhoz szükséges adekvát landing zónát és a sikeres aneurysmakirekesztést [4]. Lényegesen magasabb áruk mellett jelentős hátrányuk a jellemzően hosszú gyártási idő, mely miatt gyakorlatilag csak elektív körülmények között alkalmazhatók [2].

A sürgősségi endovascularis beavatkozást igénylő betegek terápiájára OSFG-k is megjelentek a piacon, melyeken fix helyeken találhatók a visceralis ágak fenesztrációi, illetve ágai. Hatalmas előnyük az azonnali elérhetőség. Alkalmazásukat átmérőbeli diszkrepanciák és a konvencionálistól nagyban eltérő zsigeri anatómia limitálja a leginkább, emellett használatukhoz kiváló kateteres gyakorlat szükséges [2].

A CMD-k másik alternatívájaként nagyobb centrumokban az úgynevezett orvos által módosított sztentgraftok (physician-modified endograft – PMEG) alkalmazása merül fel. A PMEG kifejezés *Ben Starnes* nevéhez fűződik, az első technikai leírás *Uflacker és mtsai* nevéhez köthető [5, 6]. Ilyenkor a műtét előtt steril körülmények között egy egyenes vagy bifurkációs sztentgraftot a beavatkozást végző orvos a beteg anatómiájának megfelelően módosít. A módszer egyszerűbb változata a fordított betöltés (reverse mounting), melynek során a graftot a felvezetőrendszerről eltávolítjuk, majd fejjel lefelé implantáljuk. Bonyolultabb műveletek is elvégezhetők, kauter segítségével a visceralis szájadékoknál fenesztrációt is képezhetünk. Ígéretes módszernek tűnik a szokatlan anatómiával rendelkező elektív esetek, illetve a sürgető beavatkozást igénylő komplex endovascularis műtétek esetén is, több centrum biztonságos és hatékony módszerként számol be róla [5–12]. Ugyanakkor egyik ismert hátránya, hogy a minőségkontroll a modifikációk kapcsán megszűnik. Potenciális mérési hibák, eszközkontamináció és a sztentgraft, valamint a felvezetőrendszer integritásának megváltozása egyaránt komplikációkhoz vezethet [4]. Emellett az eljárás hosszú távú sikeressége is kérdéses – valószínűleg jelentős részben ez áll annak a hátterében, hogy a magas technikai sikerarány és a jó korai eredmények ellenére a módszer nem terjedt el széles körben [13].

Reverz betöltés (reverse mounting)

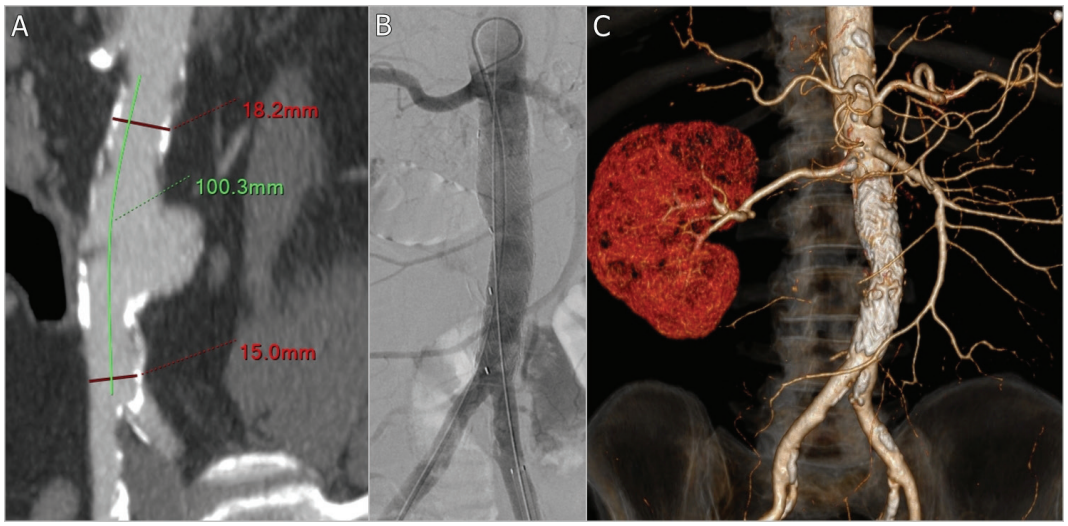
A 75 éves férfi betegünk anamnéziséből a hypertonia, a nem inzulindependens diabetes mellitus, a mélyvénás thrombosis és az évtizedekkel korábban tuberkulózis miatti balvese-eltávolítás emelendő ki. Felvételére 2018 tavaszán egy 50 mm-es saccularis infrarenalis abdominalis aortaaneurysma miatt került sor.

Multidiszciplináris konzílium alapján endovascularis beavatkozásra készültünk. A proximalis rögzítési zóna átmérője azonban lényegesen nagyobb volt, mint a distalis, az aorta átmérőinek megfelelő sztentgraft nem volt készen elérhető. Az átmérők közötti diszkrepancia megoldására reverz helyzetű iliacakomponens beültetését javasoltuk, ezt a beteg elfogadta.

A műtét során kétoldali, ultrahangvezérelt percutan femoralis punkciót követően képerősítő alatt vezettük fel a vezetődrótot az aortába. Bal oldalon merev vezetődróton egy 12 F kaliberű, 45 cm hosszúságú sheath-et (hüvelyt) (Gore DrySeal, W. L. Gore & Associates, Inc.; Newark, DE, USA) vezettünk az arteria (a.) renalisok szájadékáig. A reverz betöltéshez egy Gore Excluder (W. L. Gore & Associates, Inc .) iliacakomponenst használtunk fel, melynek cranialis vége 16 mm, distalis vége 20 mm, hossza pedig 95 mm volt. A kioldózsinór elvágását, a felvezetőrendszer olívájának levágását követően a graftot a felvezetőrendszerről eltávolítottuk, majd fordított helyzetben a bal femoralis felől felvezetett merev vezetődrótra fűztük. A 12 F sheath dilatatorának elkeskenyedő végéből mintegy 3 cm-t levágtunk; az így kapott, tompa végű eszközt ugyancsak felfűztük a vezetődrótra, és ezzel toltuk előre a graftot a sheath cranialis végéig. A jobb femoralis felől végzett angiográfiával pozicionáltuk a sheath-en belül lévő graftot az a. renalis szájadékok alá. Ezt követően a graft kioldózsinórját meghúzva – még a sheath-en belül – nyitottuk a graftot, majd a sheath-ben lévő graftról a sheath-et fokozatosan hátrahúzva, a dilatatort mozdulatlanul tartva a graftot optimális pozícióban deponáltuk, egy perifériás öntágúló sztenthez hasonlóan. Így végül a beteg anatómiája számára optimális graftot helyeztünk el, melynek cranialis vége 20 mm, caudalis vége 16 mm volt. A záró angiográfián szövődményt nem észleltünk. Jobb oldalon Angio-Seal (Terumo; Tokió, Japán), bal oldalon 2 db ProGlide (Abbott; Chicago, IL, USA) eszközzel végeztünk zárást. Eseménytelen posztoperatív szakot követően a beteget a negyedik posztoperatív napon otthonába bocsátottuk. Hároméves kontroll-CT-vizsgálaton endoleak nem látszik, az aneurysmazsák zsugorodott *(1. ábra)*.

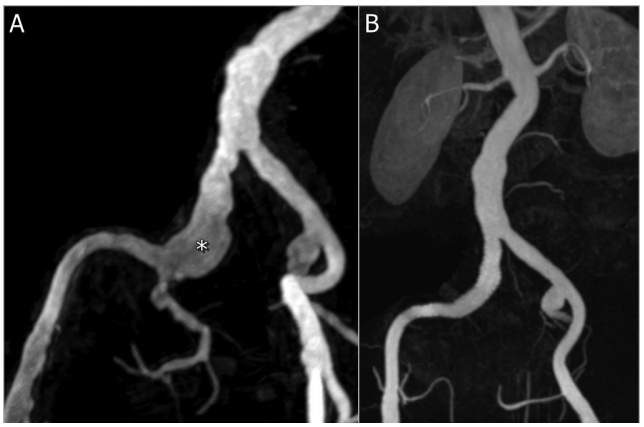
Hasonló megoldást választottunk egy 67 éves férfi beteg jobb oldali a. iliaca communis aneurysmájának kezelése során 2019 őszén. A beteg anamnézisében myasthenia gravis, lumbalis compressiós csigolyatörés, hasfali sérv, valamint súlyos fokú aortabillentyű-stenosis szerepelt. Jobb oldali, tünetmentes, 65 mm-es átmérőjű a. iliaca communis aneurysma miatt került felvételre, mely az a. iliaca interna eredését is érintette. Multidiszciplináris team a beteg endovascularis kezelése mellett döntött. A páciens alapbetegsége (myasthenia) miatt jódos kontrasztanyagot sem a preoperatív, sem a posztoperatív diagnosztika során nem alkalmaztunk, és az endovascularis beavatkozások alkalmával is csak neurológiai szakvéleményt követően, a minimálisan szükséges mennyiségben használtunk.

Staging beavatkozásként először a jobb a. iliaca interna embolisatióját végeztük Amplatzer dugókkal (Abbott). Később hibrid műtétet végeztünk a jobb a. femoralis feltárásából, bal oldalon percutan femoralis punkcióból. Merev vezetődrót felvezetését követően 12 F kaliberű, 45 cm hosszúságú DrySeal sheath-et (W. L. Gore & Associates, Inc.) vezettünk a bifurkációig. A reverz betöltéshez egy 120 mm hosszúságú Gore Excluder (W. L. Gore & Associates, Inc.) iliacakomponenst hasz-



1. ábra A) Saccularis infrarenalis aortaaneurysma CT-angiográfiás felvételének multiplanáris rekonstrukciója látható, ahol a rövid infrarenalis tágulat proximalis rögzítési zónájának átmérője lényegesen nagyobb, mint a terminális aortaszakasz. B) Az endovascularis beavatkozás záró angiográfiás képén a sztentgraft homogén telődését láthatjuk, az anerysma kirekesztődött. C) A posztprocedurális CT-angiográfia háromdimenziós rekonstrukciója azonosítható, melyen az aneurysma nem telődött

CT = komputertomográfia



2. ábra A) MR-angiográfiás kép a jobb oldali arteria iliaca communist érintő aneurysmáról (csillaggal jelölve). B) Az endovascularis terápiát követő kontroll-MR-angiográfiás vizsgálaton jó helyzetű sztentgraft látszódott, endoleak nem volt megfigyelhető

MR = mágneses rezonancia

náltunk fel, melynek cranialis vége 16 mm, distalis vége 20 mm volt. Az eszközt a fent leírtaknak megfelelően reverz betöltést követően fejjel lefelé nyitottuk. Utótágítást követően jó morfológiai eredmény ábrázolódott. A bal a. femoralist 6 F Angio-Seal VIP (Terumo) eszközzel, a jobb oldali sebet tovafutó, intracutan, felszívódó varrattal zártuk. Eseménytelen posztoperatív időszakot követően a beteget a negyedik napon otthonába bocsátottuk. A két hónap elteltével végzett MRA-vizsgálat jó helyzetű sztentgraftot mutatott endoleak nélkül *(2. ábra)*.

Sztentgraft rövidítése

81 éves nőbetegünk anamnézisében hypertonia, szürke hályog miatti kétoldali cataractaműtét és kompressziós csigolyatörés szerepelt. 2011-ben nem komplikált, atípusos, csak a hasi aortát érintő dissectio igazolódott, amelyet konzervatív módon kezeltek. 2016-ban ruptura miatt sürgősségi körülmények között unilateralis sztentgraft-implantációra és jobbról balra vezetett femorofemoralis crossover bypass implantációjára volt szükség. Utánkövetése során I/a típusú endoleak igazolódott, mely miatt proximalis kiegészítés történt egy újabb unilateralis grafttal. Perzisztáló endoleak, illetve további aneurysmazsák-növekedés miatt nonadhezív ágenssel végrehajtott embolisatio is történt, mely azonban szintén sikertelen volt.

További követése során változatlanul jelen lévő proximalis endoleak, illetve tovább táguló aneurysmazsák miatt reintervencióra kényszerültünk. Multidiszciplináris konzílium a páciens előrehaladott életkora és a nyitott műtét extrém nagy rizikója miatt endovascularis beavatkozást javasolt, melyet a beteg elfogadott.

Fenesztrált, illetve elágazó thoracoabdominalis graft implantációjára azonban az anatómiai helyzet alkalmatlan volt, a 42 mm átmérőjű visceralis segmentum miatt csak thoracalis sztentgraft implantációja jött szóba. Az a. mesenterica superior, illetve az unilateralis sztentgraft elkeskenyedő része közötti, mintegy 7 cm-es távolság miatt azonban a legrövidebb thoracalis sztentgraft is túl hosszú lett volna, ezért PMEG implantációja mellett döntöttünk. A renalis perfúziót párhuzamos sztentgraftokkal terveztük biztosítani 'chimney' konfigurációban.

A műtét elején steril körülmények között kinyitottunk egy 46 mm átmérőjű, 100 mm hosszúságú Valiant (Medtronic; Dublin, Írország) thoracalis sztentgraftot, majd distalis végéből két sztentsort steril kauter segítségével eltávolítottunk, végül a sztentgraftot visszatöltöttük a felvezetőrendszerbe.

Ezt követően bal a. subclavia feltárás történt a renalis sztentgraftok felvezetésére. A nagyfokú elongáció és a bal a. renalis szájadékának ismert dissectiója miatt stabil pozíciót biztosítani csak a jobb oldalon lehetett, így a bal a. renalis feláldozása mellett döntöttünk. Ezt követően jobb femoralis feltárás következett az aortasztentgraft felvezetése céljából. A sztentgraftot az a. mesenterica superior szájadéka alá pozicionáltuk, majd nyitottuk. Ezután végeztük el a jobb a. renalisba helyezett 'chimney' sztentgraft beültetését. Kontrollangiográfián a proximalis endoleak záródása látszódott a vesék megtartott perfúziójával *(3. ábra)*.

A posztoperatív szakban szövődményt nem észleltünk, a vesefunkció nem romlott. A beteg elbocsátása előtt készített kontroll-CT-angiográfia a proximalis endoleak záródását igazolta jó helyzetű sztentgraftrendszerrel, megtartott kétoldali renalis keringéssel. A beteget jó általános állapotban otthonába bocsátottuk.

A beteg fél évvel később akut, Stanford A típusú aortadissectio szövődményei miatt elhunyt.

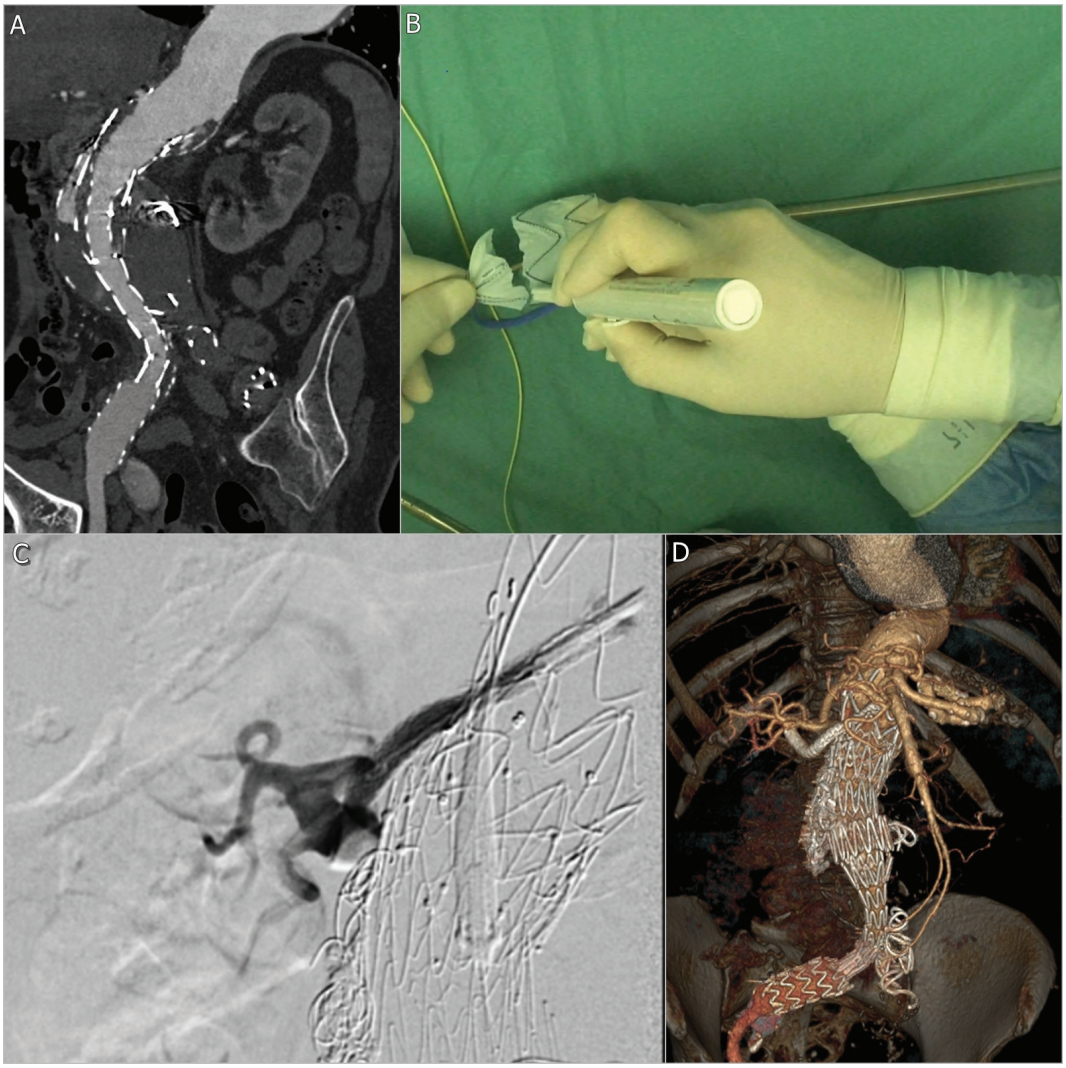
Megbeszélés

A PMEG-k alkalmazásáról szóló publikációk javarészt esetleírások vagy retrospektív vizsgálatok, egy-két prospektív vizsgálat áll csak ez idáig rendelkezésre [14–17]. Ezek mellett két nagy elemszámú, összefoglaló tanulmány segíti a témában született jelentősebb közleményekből származó eredmények áttekintését [2, 18].

Az idén megjelent, 20 publikációt magában foglaló metaanalízis 87,5–100%-os technikai sikert és 0–8%-os 30 napos mortalitást írt le. A kezelés által érintett visceralis ágak tekintetében a primer átjárhatóság egy évnél 96,3–100% volt, a 14,8 hónapos utánkövetés során 0–14,3%-ban találtak I-es vagy III-as típusú endoleaket [18].

2012-ben *Starnes* retrospektív vizsgálatában 47, PMEG-beültetéssel kezelt juxtarenalis aortaaneurysma esetét dolgozta fel. A technikai sikerarány ebben a tanulmányban is magas (98%) volt, alacsony szövődményráta mellett [5].

A legnagyobb esetszámú vizsgálatot *Oderich és mtsai* végezték, a 2007 és 2016 közötti időszakban történt 145 PMEG-beültetés adatait elemezték. A technikai si-



3. ábra A) Multiplanáris rekonstrukció az orvos által módosított sztentgraft behelyezése előtt készült CT-angiográfiás vizsgálatról, ahol az aneurysmazsák mellett proximalis endoleakre utaló telődési többlet látható. B) A thoracalis sztentgraft distalis végéből két sztentsort steril kauter segítségével eltávolítottunk. C) A jobb arteria renalisba helyezett 'chimney' sztentgraft beültetését követő angiográfián az arteria renalison számottevő szűkület nem látszik, a jobb vese perfúziója megtartott. D) A posztprocedurális CT-angiográfia háromdimenziós rekonstrukciója látható

CT = komputertomográfia

ker 98%-os, a harmincnapos mortalitás 5,5%-os volt. Három év elteltével 94%-os primer és 98%-os szekunder átjárhatóságot találtak az érintett visceralis ágak tekintetében [19].

A mi kezdeti tapasztalatunkon alapuló saját adataink ezekkel való összevetése a kis elemszám miatt nem kivitelezhető. A fent részletezett eseteinkhez hasonló jellegű technikai megoldásokra olvasható már példa az irodalomban. *Leon és mtsai* 2009-ben egy sikeres a. iliaca aneurysma kirekesztésről számolnak be reverz iliacagraftszár használatával [20]. *Song és mtsai* három izolált a. iliaca interna aneurysma kezelése során alkalmaztak reverz helyzetű iliacagraftszárat [21]. *Gemayel* egy instabil beteg életét veszélyeztető a. iliaca interna rupturát látott el sikeresen reverz helyzetű iliacagraftszár beültetése és embolisatio segítségével [22]. *Erben és mtsai* recidív coarctatio mellett jelentkező, 6 cm-es pseudoaneurysma kapcsán alkalmaztak egyedi megoldást. Proximalisan egy invertált iliacagraftszárat, distalisan egy megfordított aortasztentgraftot ültettek be az aortába, mely „homokóra-" konfigurációt eredményezett. Az ötéves utánkövetés során komplikáció nem fordult elő, a pseudoaneurysma 61 mm-ről 25 mm-re csökkent [23]. *Peppelenbosch és mtsai* 12 esetet foglaltak össze különböző aortoiliacalis patológiák reverz iliacagraftszárakkal történő kezeléséről. 100%-os közvetlen posztoperatív technikai sikert, valamint kielégítő középtávú eredményeket írtak le [24]. *Van der Steenhoven* és *Higashigawa* is sikeresen alkalmaztak infrarenalis aortaaneurysmák kezeléséhez reverz helyzetű iliacagraftszárat, hogy a fennálló átmérőbeli diszkrepanciához alkalmazkodjanak [25, 26]. Sztentgraftrövidítést *Wada és mtsai* alkalmaztak egy aorta ascendens pseudoaneurysma esetén. A kereskedelmi forgalomban kapható mellkasi sztentgraftok ehhez az

eljáráshoz jellemzően túl hosszúak, ezért egy 10 cm-es sztentgraft felét levágták [27].

2018-ban *Dossabhoy* összevetette a PMEG-k és a CMD-k használatát. A retrospektív kohorszanalízisben 82 esetet vizsgáltak, ezekben 41, PMEG-vel és 41, gyári sztentgrafttal kezelt beteg szerepelt. Elsődleges különbségek csak a műtéti mérőszámokban és a reintervenció szükségességében látszottak. PMEG-implantáció során hosszabb fluoroszkópiás időt és műtéti időt találtak több kontrasztanyag alkalmazásával, valamint a beültetést követően több reoperációra volt szükség. A perioperatív szövődmények, a bent fekvés időtartama, az I-es vagy III-as típusú endoleak, illetve a mortalitás tekintetében nem volt kimutatható szignifikáns eltérés a két csoport között [28]. *Oderich és mtsai* összahasonlító vizsgálata azt mutatta, hogy a CMD-ket nagyobb technikai sikerrel (99,5% *vs.* 98%; p = 0,02), kisebb korai halálozással (0% *vs.* 5,5%; p = 0,0018) és kevesebb súlyos nemkívánatos eseménnyel (28% *vs.* 48%; p<0,001) végezték. A hároméves túlélés és az újbóli beavatkozás nélküli túlélés hasonló volt, aneurysmával összefüggő halálozásban hosszú távon sem találtak különbséget. Ezen eredmények értékelésekor szem előtt kell tartani a retrospektív és nem randomizált vizsgálat limitációin túl azt is, hogy a betegek jellemzően eltérő kockázati csoportba tartoztak (a PMEG-csoportban szignifikánsan nagyobb aneurysmák, több krónikus tüdő- és vesebetegség, valamint magasabb komorbiditási súlyossági pontszám volt). Ezenkívül a vizsgálat első felében többségében PMEG-t, második felében jelentős részben CMD-t használtak, így a CMD-implantációknál talált kedvező eredmények részben a beavatkozást végző orvosok tapasztalatának növekedéséből is adódhatnak [19].

Georgiadis metaanalízise is a PMEG-ket és az OFSG-ket hasonlította össze [2]. Bár mindkét módszert hatékonynak és biztonságosnak találta, az előbbi csoportban a klinikai siker valamelyest alacsonyabb volt (91,4% *vs.* 95%), illetve a súlyos nemkívánatos események bekövetkezte (12,8% *vs.* 7,4%), valamint a halálozás (3,2% *vs.* 0%) kissé magasabb volt. Fontos ugyanakkor annak ismerete, hogy a PMEG-k OSFG-kkel való összehasonlíthatósága az alábbi főbb tényezők miatt limitált. Kissé eltérő az indikációs körük, részben ebből adódóan az előregyártott eszközök átlagosan több visceralis ágat inkorporálnak. Az irodalomban az orvos által módosított endograftok kapcsán észlelt kedvezőtlen kimenetelű esetek valószínűleg alulreprezentáltak. Emellett rendkívül eltérő gyakorlatú orvosok végezték a sztentgraftokon a modifikációkat, míg az OSFG-ket többnyire nagy gyakorlattal rendelkező centrumok részére biztosítottak [4]. Hazánkban OSFG-eszközök egy 'branched' graft kivételével (t-Branch; Cook Medical; Bloomington, IN, USA) nem érhetők el.

A PMEG-k szükségességét a különböző anatómiai konfigurációk jelenléte és a rövid időablakos komplex esetek ellátása egyaránt indokolja, minden bizonnyal a jövőben is jelentős szerepet játszanak majd [5]. Használatukat jól bevált, hasznos technikaként tartják számon, melynek szerepelnie kell a magas kockázatú, komplex aortaaneurysmák kezelésével foglalkozó orvosok eszköztárában [4]. A thoracalis aortaszakasz PMEG-vel történő kezeléséről az utóbbi időben egyre több publikáció jelent meg [18, 29]. A PMEG-k használata az endovascularis beavatkozások tekintetében vezető egyik amerikai centrumban jelentősen csökkent, aminek hátterében a CMD-k elérhetővé válása és az 'off-the-shelf' eszközök jelentős fejlődése áll [18]. *Oderich és mtsai* a 2007 és 2010 közötti időszak 100%-ához képest 2011 és 2013 között 66%-ban, 2014 és 2016 között az esetek 4%-ában alkalmaztak PMEG-t [19]. Ennek ellenére más országok centrumaiban a CMD-khez való korlátozott hozzáférés, illetve a PMEG-k jelentősen alacsonyabb ára miatt ezek továbbra is kiemelt jelentőséggel bírhatnak, nem csak sürgősségi helyzetekben. Elterjedtebb hazai alkalmazásuk több aortabeteg endovascularis kezelését tenné lehetővé.

Csaknem valamennyi közlemény hangsúlyozza a módszer hosszú távú sikerességének kérdésességét, melyről azonban eddig kevés adat áll rendelkezésre.

Következtetés

A típusos anatómiájú aortabetegek endovascularis kezelése mellett a komplexebb esetek endovascularis kezelésére is egyre több lehetőség kínálkozik. A PMEG-k a bonyolult anatómiai konfigurációjú betegek terápiáján túl olyan, kihívást jelentő feladatok esetén is hatékonyan alkalmazhatók, mint például a hasi aortaaneurysmák endovascularis kezelését követő proximalis rögzítési zóna tágulatával összefüggésbe hozható endoleakek ellátása. Használatukhoz elengedhetetlen a különböző eszközök és felvezetőrendszerek mélyreható ismerete és a kiváló katéteres gyakorlat. Nagy forgalmú aortacentrumokban történő alkalmazásuk az irodalmi adatok és saját kezdeti biztató tapasztalataink alapján is kedvező eredményt biztosíthat a szokatlan anatómiával rendelkező elektív esetek, illetve a sürgető beavatkozást igénylő komplex endovascularis műtétek során egyaránt.

Anyagi támogatás: A közlemény megírása, illetve a kapcsolódó kutatómunka anyagi támogatásban nem részesült.

Szerzői munkamegosztás: A beavatkozások elvégzése: Cs.-N. Cs., Sz. Z., S. F., B. S. A képalkotó vizsgálatok elkészítése, értékelése: Cs.-N. Cs., S. F., B. S. Irodalomkutatás, a kézirat megírása, szerkesztése: B. S., P. Cs., S. F. A képek kiválasztása: B. S., S. F., Cs.-N. Cs. A kézirat átnézése, javítása, jóváhagyása: Cs.-N. Cs., S. F., Sz. Z., P. Cs. A cikk végleges változatát valamennyi szerző elolvasta és jóváhagyta.

Érdekeltségek: A szerzőknek nincsenek érdekeltségeik.

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(Csobay-Novák Csaba dr.,
Budapest, Határőr út 18., 1122
e-mail: csobay.csaba@med.semmelweis-univ.hu)