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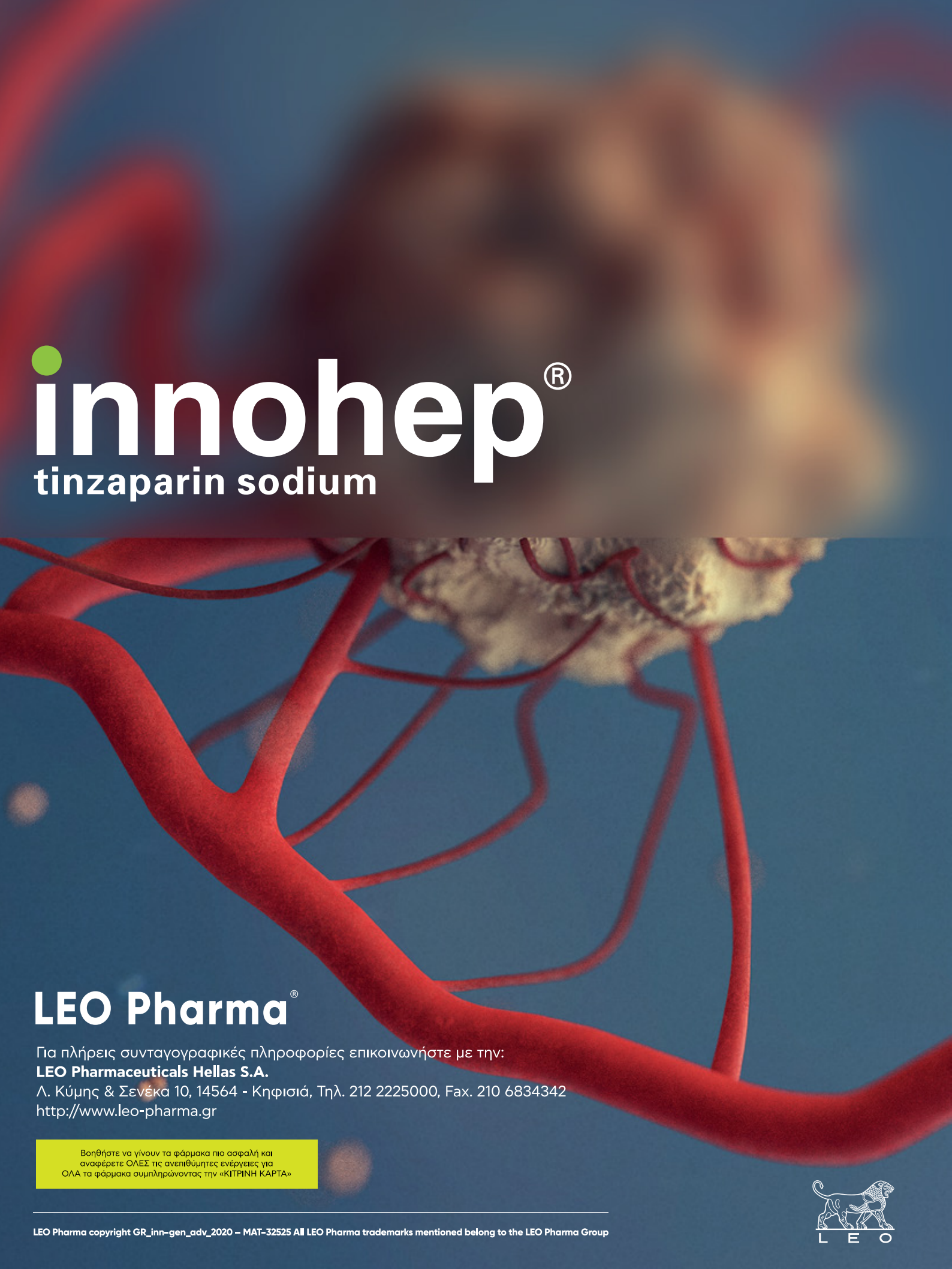
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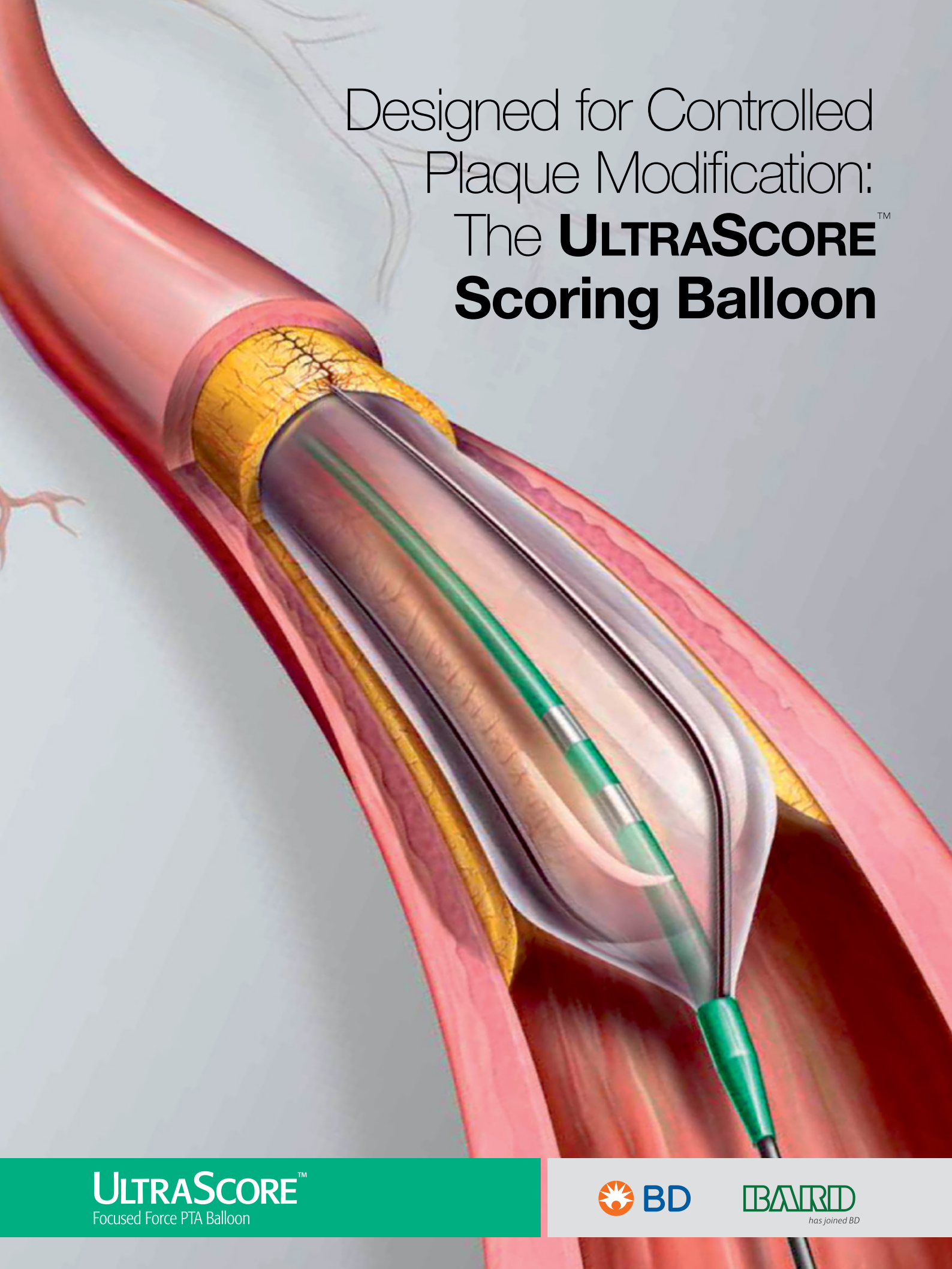

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EDITORIAL

Abdominal aortic aneurysm disease and cancer

Konstantinos Spanos, MD, MSc, PhD, Petroula Nana, MD, MSc, Miltiadis Matsagkas, MD, PhD, FEBVS

Vascular Surgery Department, University Hospital of Larissa, Faculty of Medicine, School of Health Sciences, University of Thessaly, Larissa, Greece

The incidence of concomitant abdominal aortic aneurysm (AAA) and cancer is around 6%.[1] It is an issue of controversy in terms of treatment timing, priority and clinical outcomes. In the recent European Society for Vascular Surgery (ESVS) guidelines it is recommended that patients with AAA and concomitant cancer are not recommended prophylactic aneurysm repair on a different indication (diameter threshold) from patients without cancer, including cases of chemotherapy (III C). Additionally, in patients with concomitant malignancy, a staged surgical approach, with endovascular repair of a large or symptomatic abdominal aortic aneurysm first, to allow for treatment of malignancy with minimal delay, is recommended (I C).

In a recent systematic review of the literature,[2] it was highlighted that decisions about management of AAA and cancer should be based on clinical judgment applied individually in a multidisciplinary setting ("treat first what kills first"). A two-stage treatment seems reasonable and ideally the AAA should be treated by endovascular means if anatomically suitable. The initiation of international registries would shed more light on the management and outcomes of patients with AAA and concomitant cancer.[2]

In clinical practice synchronous cancer in patients with AAA increases morbidity and mortality after AAA repair. However, the role of cancer history on AAA mortality is not clear. Recently, Ahn et al.[3] demonstrated that history of cancer in AAA patients increases long-term mortality, but does not affect short-term mortality after AAA repair.

On the other hand, a recent study[4] showed that small aortic aneurysms with concomitant malignancies are discovered at smaller initial sizes, grow at similar rates, require fewer interventions, and have fewer ruptures and acute dissections than patients without malignancy. Even in cancer patients with AAA that were treated with chemotherapy for their cancer, chemotherapy did not increase aneurysm growth compared with patients not undergoing treatment for malignancy.[5]

Evidence on the risk of malignancy in patients with AAA is scarce. Cardiovascular disease and malignancy have numerous similarities and possible interactions, as these diseases share several risk factors, epidemiological features and biological signaling pathways.[6] Wang et al.[6] showed that patients with an AAA have a substantially increased risk of developing a variety of malignancies compared with patients without AAA. Even after AAA treatment there might be an association with increased risk of cancer in AAA patients. In a population-based cohort study,[7] it was demonstrated that increased risk of abdominal cancer exists after endovascular aortic aneurysm repair (EVAR) compared with open AAA repair. The differential cancer risk needs further exploration in alternative national populations, and radiation exposure during EVAR should be measured as a quality metric in the assessment of EVAR centers.

AAA has been associated with chronic inflammation, cells apoptosis, and impairment of autophagy. Similar pathological pathways exist in the development of various malignancies.[8] Recently, there is an interest on the potential association between cancer and AAA. Studies have identified potential similar pathophysiological mechanisms for each pathology separately. For example, a study showed that BP-1-102 inhibits vascular inflammation and AAA progression through decreasing STAT3 and NF-κB activation and maintaining autophagy.[8] Compelling evidence also exists for the critical role of aberrant STAT3 activity in malignant transformation and tumor progression.[9] The complement pathway is another pathophysiological mechanism which may be involved in both pathological conditions. These are strong evidence that the complement cascade plays a role in human AAA. Based on microarray studies, the pathway is activated in AAA, particularly via the lectin and classical pathways.[10] Similarly, although the mechanisms by which complement is activated and affects tumor progression are not well understood, still there is a strong impact of complement pathway on malignancies.[11]

Another potential association between cancer and AAA is on a genetic level. In recent Society for Vascular Surgery (SVS) guidelines[12] it was reported that there are known genes are implicated in the pathogenesis of an AAA. In a recent study, results suggested that reduced CDKN2B expression and increased smooth muscle cell apoptosis may have an association with aneurysmal disease.[13] Another study showed that

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there is a similar critical role of CDKN2B inactivation in pancreatic carcinogenesis.[14]

The potential association of AAA and cancer is of great interest and future studies should focus on this research on a genetic, biochemical and clinical practice level.

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A pilot study on the predictive role of CD105 in the development of abdominal aortic aneurysms

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Abstract:

Introduction: The progress and the risk factors of an abdominal aortic aneurysm (AAA) is well described in the literature. The exact pathophysiological mechanism that triggers the development of an AAA in some individuals and lies behind the gradual dilatation of the aorta and the consequent rupture still remain unknown. A connection is known to exist between AAA and CD105 through the TGF-βR pathway. Our aim is to study the potential predictive role of CD105 in aortic dilatation and the development of AAA in an animal model using porcine pancreatase under pressure.

Methods & Materials: Thirty-two wild-type male Wistar rats were recruited, weighted and then equally distributed in the study and control groups. In the study group, animals were subjected to laparotomy under general anesthesia and their aortas were perfused with Type I porcine pancreatic elastase (PPE) under hydrostatic pressure. The perfusion time was defined as T0. In a similar manner, the aortas of the control group were perfused with natural saline. On day 7 (T7) and day 14 (T14), each animal underwent additional laparotomies, the aortic diameters were measured and blood samples were drawn. CD105 serum levels were quantified using the ELISA technique and CD105 concentrations were calculated. Matrix metalloproteinase 9 (MMP9) serum concentrations were also measured and compared to CD105 concentrations.

Results: After the intervention, significantly higher levels of CD105 were recorded in the study group at T14. MMP9 levels were significantly higher in this group at both T7 and T14. CD105 could potentially act as biomarkers of the development of AAA.

Conclusions: CD105 has a prognostic value for the reconstruction of the vessel, but it doesn't reflect the destruction of the aortic well as MMP9 does.

Keywords: aneurysm, rupture, animal model, aorta, biomarker, endoglin, metalloprotease, MMP

INTRODUCTION

Abdominal aortic aneurysm (AAA) is a potentially lethal disease affecting a significant percentage of males over the age of 65 and especially those individuals in this age and gender group who are smokers.[1-3] Aortic aneurysm is defined as aortic diameter growth more than 50% compared to the expected normal diameter for the same segment of the aorta. The development of AAA is a continuous process frequently leading to aortic rupture, a life-threatening event that is still linked to significant morbidity and mortality.[4] According to the existing guidelines, AAA repair is necessary only if the AAA is large (≥55mm), symptomatic, or rapidly growing by ≥10mm annually.[5] Based on the current guidelines, asymptomatic aneurysms smaller than 55mm should be subjected to annual follow-up imaging, but not to elective repair.[6,7] Despite what the international guidelines recommend and the existence of screening programs, a debate regarding the cost-effectiveness and technical or logistical feasibility to screen smaller aneurysms exists. In some countries there is a clear benefit from small AAA screening, while others do not see this benefit.[8-10] This gap could be potentially be filled-in by the use of financially and logistically easier to deploy blood biomarkers providing a prognosis of future aortic dilatation. The World Health Organization defines a biomarker as any structure, substance, or process that can be measured in the human body and influences or predicts the incidence of outcome or disease.[11] A number of biomarkers has been suggested, but no biomarker has been validated to enter clinical practice to date.[12-15] Matrix Metalloproteinase 9 (MMP9) is already established as a biomarker for the progressive destruction of the aortic wall elements (elas-

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tin and collagen fibers).[2,16-19] In this study, we use MMP9 as an indirect sign of aortic wall destruction, in order to examine the role of CD105. CD105 or endoglin is a homodimeric transmembrane protein that has a similar structure in humans, rodents and pigs. Through the Tissue Growth Factor-β receptors (TGF-βR) there is a connection between AAA and CD105 and this potential biomarker is also linked to neoangiogenesis. The aim of this study is to report on the potential predictive role of CD105 in aortic diameter growth and the development of AAA in an animal model

METHODS & MATERIALS

This animal model protocol was approved by the General Directorate of Veterinary Services, National Bioethics Commission, according to Greek legislation regarding ethical experimental procedure, in compliance with the European Law (European Economic Community Directive 86/609) the Hellenic National Law (Act 2015/1992) and in conformance with the European Convention on the protection of vertebrate animals used for experimental or other scientific purposes. All animal research also complied with the *Animal Research: Reporting of In Vivo Experiments* (ARRIVE) guidelines.[20] The study was performed at the Laboratory for Experimental Surgery and Surgical Research "N.S. Christeas"; recognized by the European Union (reference number EL 25 BIO 005). Handling and care of the animals were in accordance with the National guidelines for Ethical Animal Research and the Principles of Replacement, Reduction and Refinement (3Rs).[7] All animals were housed in a specially prepared pathogen-free environment with ad libitum access to water and food. Lighting conditions mimicked the daily variation of light in nature. All efforts possible were made to minimize the suffering of animals.

The murine model used in this study is a variant of the experimental *in vivo* model of aortic aneurysm development with PPE infusion under hydrostatic pressure, initially developed by Anidjar et al.[21] Our modified experimental protocol has been previously published in details.[22]

Thirty-two wild-type male Wistar rats were recruited, weighted and then equally distributed in two groups - study and control groups. In the study group, animals were subjected to laparotomy under general anesthesia and their aortas were perfused for 5-15 minutes with a solution of 4.5 U/mL Type I porcine pancreatic elastase (PPE) under hydrostatic pressure of 100mmHg. The perfusion aimed in dilating the aorta by a further 50% of its original diameter. The perfusion time was defined as T0. In a similar manner, the aortas of the control group were perfused with natural saline 0.9% solution. On day 7 (T7) and day 14 (T14), each animal underwent additional laparotomies aiming in measuring the aortic diameter and blood sampling for future analysis. CD105 serum levels were quantified using the ELISA technique (CD105 ELISA Kit, # E02E0186, BlueGene, China) and CD105 concentrations are reported as μg/L. We evaluated the correlation between CD105 and the development and progression of an AAA within a period of time of 14 days.

At the same intervals, the levels of MMP9 were simultaneously measured in the serum samples of the rats of both groups. As mentioned earlier, MMP9 is a biomarker that is linked to the progression of AAA and the continuous dilatation of the infrarenal aorta.

Statistical analysis

All continuous variables are expressed as mean ± standard deviation (SD). The distributions normality was assessed using Kolmogorov-Smirnov's test and graphical methods. Between-group comparisons were performed using student's T-Test and Mann-Whitney U test, where appropriate. Comparisons between multiple time points were performed using repeated ANOVA and Friedman's test with Wilcoxon's Signed Ranks test. Pearson's correlation coefficient and Spearma's rho were calculated in order to examine relationships between variables. Differences were considered significant if the null hypothesis could be rejected with >95% confidence (two-sided $p<0.05$).

RESULTS

Not significant change of the animals' weights was demonstrated within each group at different time points (437.4±55.2 vs 429.1±65.9 at T0, 457.4±55.3 vs 415.1±62.5 at T7, 468±50.4 vs 416.4.1±67.4 at T14; $p>0.05$ for all).

At T0, there was no significant difference in the diameter of the infrarenal aorta between the two groups: 0.94±0.1mm and 0.909±0.08mm for the study and the control groups, respectively (Figure 1). Similarly, at T7, there was no significant difference between the two groups: 2.51±0.4mm and 1.13±0.1mm for the study and the control groups, respectively. At T14, the mean aortic diameter of the study group was significantly higher compared to the control group: 3.04±0.45 versus 1.17±0.12mm, respectively ($p<0.05$). In the study group, the aortic dilatation at T7 was significantly higher compared to T0, and at T14 was significantly higher compared to both T7 and T0 ($p<0.05$ for all in-group comparisons). The diameter of the infrarenal aorta of the control group did not grow significantly in any time point ($p>0.05$ for all in-group comparisons).

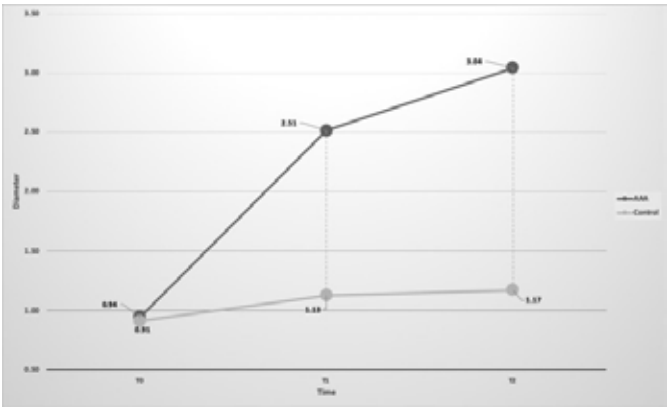

Figure 1. Diameter (in mm) of the infrarenal aorta for the study (AAA) and the control groups.

At T0 the concentrations of CD105 were 0.764±0.021 μg/l and 0.773±0.026 μg/l for the control and study groups, respectively (p>0.05) (Figure 2, Table 1). Similarly, at T7, the CD105 concentration of the two groups were not significantly different: 0.866±0.045 vs 0.816±0.016 for the control and study groups, respectively. At T14, the concentration of CD105 of the study group was significantly higher compared to the control group: 1.261±0.246 vs 0.815±0.031 (p<0.05). The CD105 concentration in the study group did not rise significantly between T0 and T7 (p>0.05). In the study group, the CD105 concentration at T14 was significantly higher compared to both T7 and T0 (p<0.05). The concentration of the control group did not rise significantly at any time point (p>0.05 for all in-group comparisons).

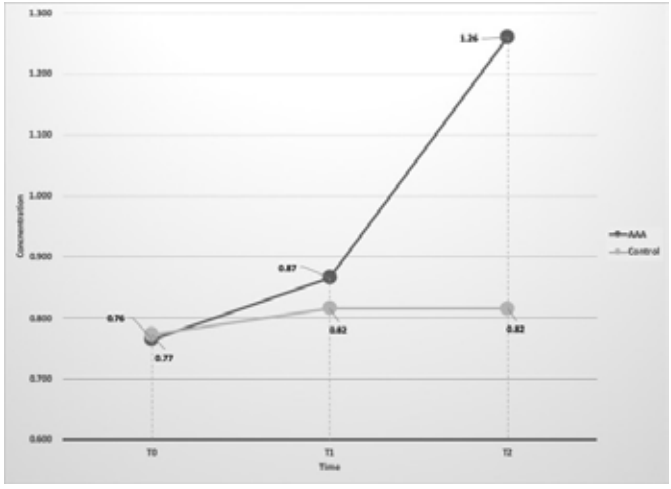

Figure 2. CD105 concentration (μg/L) of the study (AAA) and the control groups.

Time point	Study group		Control Group		p
	Concentration	SD	Concentration	SD	
T0	0.764	0.021	0.773	0.026	NS
T7	0.866	0.045	0.816	0.016	NS
T14	1.261	0.246	0.815	0.031	p<0.05

Table 1. CD105 concentrations (μg/L)

At T0, MMP9 concentrations were 149.385±62.387μg/l and 187.187±61.906μg/l for the study and control groups, respectively (p<0.05) (Figure 3, Table 2). These two concentrations were similar without any statistically significant difference. At T7, the MMP9 concentrations of the two groups were not significantly different: 208.306±52.669 vs 187.100±61.9 for the study and control groups, respectively. At T14, the concentration of MMP9 of the study group was significantly higher compared to the control group: 230.661±40.745 vs 187.091±61.89 (p<0.05). The concentration MMP9 in the study group did not rise significantly between T0 and T7 (p>0.05). At T14, the MMP9 concentration of the study group was significantly higher compared to both T7 and T0 (p<0.001). The concentration of the control group was almost constant at all time points (p>0.05 for all in-group comparisons).

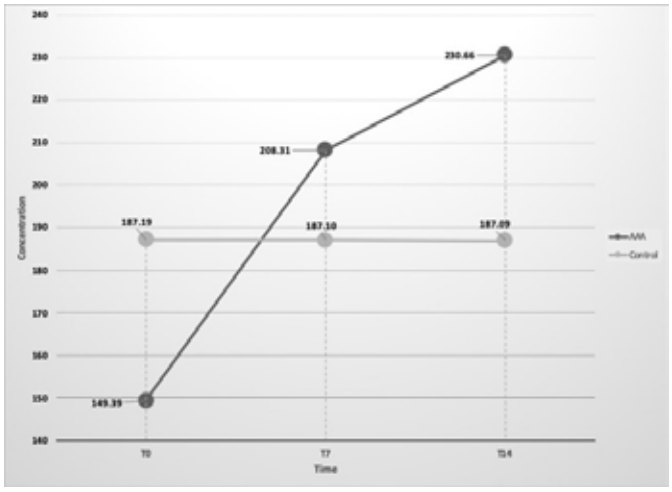

Figure 3. MMP9 concentrations of the study (AAA) and the control groups.

Time point	Study group		Control Group		p
	Concentration	SD	Concentration	SD	
T0	149.385	62.387	187.187	61.906	NS
T7	208.306	52.669	187.100	61.900	NS
T14	230.661	40.745	187.091	61.890	P<0.05

Table 2. Matrix MetalloProteinase 9 (MMP9) concentrations (μg/L)

DISCUSSION

CD105 or endoglin is a homodimeric transmembrane glucoprotein consisted of 633 aminoacids and with a molecular mass of 180kDa.[23-26] CD105 has short endocellular and transmembrane domain, while its extracellular domain is large.[23-25] The intracellular domain can be phosphorylated at multiple points.[24,27-29] CD105 has four points for N-glycozylation and one point for O-glycozylation, rich in serine and threonine.[24,30] Human CD105 has a similar aminoacid sequence to that of pigs and rodents with the exception of the extracellular domain that is significantly different.[31] Another significant difference of the human CD105 is the existence of the tripeptide RGD, which makes human endoglin unique.[30] The transmembrane and the cytoplasmic parts of CD105 demonstrate similarities to the β-glycane of the type III TGF-b receptor.[32] The human gene coding endoglin is located at chromosome 9q34->qter24 and is fourteen exons long.[33-35] Mutations of this gene usually lead to alterations of the extracellular domain.[36,37] Two isomorphs of CD105 exist: L- and S-CD105.[38] These two isoforms differ in the length of the cytoplasmic domain and their distribution in various tissues.[33] Apart its presence in human tissues, a soluble form of CD105 exists in human blood.[39] CD105 plays a major role in homeostasis, the development of blood vessels and the formation of the heart from gestational weeks four to eight.[40,41] In adult humans, CD105 is mainly located in the vascular endothelial and stromal cells, while it is also expressed in activated monocytes, differentiated macrophages, erythroid precursors, fibroblasts, melanocytes and dendritic cells in smaller quantities.[42-45] CD105 is significantly expressed in tissues with increased neo-angiogenesis, as a result of inflammation or neoplasia.[45] In normal endothelium, CD105 is

expressed along β-glycane, which is part of the TGF-β receptor.[32] CD105 is an auxiliary co-receptor of TGF-β, which is a pleiotropic cytokine regulating the differentiation, migration and coagulation of cells.[32,46,47] TGF-β also promotes inflammation and the release of angiogenetic factors by the inflammatory cells.[48,49]

Despite the fact that existing literature supports that MMPs play a significant role in the development of AAA, the predictive role of MMPs for AAA is not well established.[50] Some studies have demonstrated the strong correlation between MMP9 and the aortic dilatation.[18] Other studies also so the predictive value of MMPs for the development of AAA, the presence of persisting endoleak or the successful exclusion of an AAA.[16,51] In our study, MMP9 was employed as an indirect biomarker of aortic wall destruction in order to evaluate the effect of the hydrostatic pressure and PPE on the aortic wall elastic and collagen fibers.

As expected the selected animal model of PPE infusion under hydrostatic pressure was technically successful, producing AAA in all the animals of the study group. The efficiency of this animal model is well described in the existing literature since its first conception by the team of Anidjar.[21,52] The study group demonstrated a gradual dilatation of the infrarenal aorta at T7, but that did not reach a statistically significant difference compared to the control group until T14.

Concentrations of CD105 followed the trend of aortic dilatation. Initially at T0, CD105 concentration of the study group was at similar levels with the control group and at T7 it rose without reaching statistical significance. At T14, CD105 of the study group rose significantly compared to the control group and the T0 and T7 concentrations of the study group. MMP9 demonstrated a slightly different trend.

At T0, MMP9 concentration was similar for both groups. At T7, MMP9 of the study group rose significantly, that is before the aortic diameter changed significantly. At T14, the aortic dilatation as well as the levels of both CD105 and MMP9 rose significantly.

From these results, it is evident that MMP9 follows the destruction of the aortic wall elements and the consequent dilatation of the aorta. This is an expected process as MMP9 as PPE infusion under pressure acts by overstretching the aortic wall while there is chemical degradation of elastin fibers. These two mechanisms are reflected on the serum concentration of MMP9 in the study group. Despite that at T7 the aortic diameter is still not significantly increased (although a clear trend exists), MMP9 concentration is already significantly higher than at T0. The process of aortic wall destruction is already commenced, but the result is still to be observed. Simultaneously, the control group does not demonstrate any of these changes; no increase in diameter nor in MMP9 concentration.

At T14 all variables peak and their values are significantly higher compared to the in-group values at T7 and compared to the values of the control group. As described, CD105 plays a major role in the neo-angiogenesis and therefore to the reconstruction of damaged tissue. At T14, while the inflammation still persists and aortic aneurysm is already established, the organism tries to employ CD105 (amongst other biomarkers) to assist in the reconstruction of the vessel. As a result, CD105 could potentially have a prognostic value for the reconstruction of the vessel wall, but it doesn't reflect the destruction of the aortic wall.

All future studies should also pay attention on the threshold and time point at which CD105 starts to have a predictive role for AAA expansion. We chose a weekly interval between different points in time (T) based on our previous knowledge of "delayed" AAA formation using this animal model and in order to (a) allow the rats some time to recuperate in-between two laparotomies and (b) to maintain the same model with previous research on similar biomarkers.

Our study comes with two limitations: there was no power analysis and the cohort of the study was limited. Both weaknesses derive from the fact that this was a pilot study in order to initially evaluate whether CD105 would demonstrate the qualities of a valid biomarker for AAA development. A larger study should be completed in order to confirm or not the role of CD105 as a prognostic biomarker for the development of AAA or for process of aortic wall repair. Translation of our finding into humans could also represent a hazardous task, despite the molecular similarities between human and animal C105.

CONCLUSIONS

CD105 could have a prognostic value for the reconstruction of the vessel after an aneurysm is formed, but it doesn't reflect the destruction of the aortic wall as MMP9 does or the rate of aortic expansion.

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Conflict of interest: None

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Endovascular repair of aorto-iliac aneurysmal disease with the Gore IBE device: midterm outcomes of a single center experience

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Abstract:

Introduction: Preservation of the internal iliac artery (IIA) perfusion during endovascular repair of isolated iliac or aorto-iliac aneurysms is important in order to avoid significant ischemic complications. The aim of the study is to evaluate the early results of endovascular treatment of patients with either single or bilateral iliac and aorto-iliac aneurysmal disease preserving the IIA blood flow with the use of the Gore IBE device.

Methods: A single center retrospective study including patients with unilateral or bilateral common iliac and/or aorto-iliac aneurysmal disease treated by endovascular means was undertaken. All patients were treated with IIA flow preservation with the Gore IBE device during the 2017-2019 period. Primary outcomes included technical success rate, mortality and 30 days target vessel patency, while secondary outcomes were procedure related morbidities, freedom from re-intervention and freedom from aneurysm exclusion events.

Results: From 2017 to 2019, 8 patients with aorto-iliac aneurysmatic disease (88.8%; 8/9 patients) and 1 with bilateral isolated iliac aneurysms (11.1%; 1/9) underwent endovascular repair. Technical success rate was 88.8%. One IIA branch thrombosis was detected at the completion angiography due to adverse artery angulation. Mortality rate was 0% and 30-days patency rate was 88.8%. The mean follow up period was 9,6 ± 8.1 months (range 1-24 months). Overall patency remained at 88.8%. No other thrombosis events occurred. Re-intervention rate was 0%. No procedure related complications such as buttock, bowel or spinal ischemia events occurred in any patient. The patient with the iliac branch intraoperative thrombosis was also asymptomatic. Freedom from endoleak type I/III IBE related was 100%.

Conclusion: The GORE EXCLUDER IBE device achieved good early and midterm results with high technical success and patency rates, along with low complication and reintervention rates.

Keywords: Iliac branch device, IBE, Aneurysm, Iliac, Endovascular

INTRODUCTION

Common iliac artery aneurysms (CIAAs) are defined as an artery of diameter > 18mm. As an isolated pathological vascular entity, CIAAs are quite rare with a prevalence of 0.03% of the general population and 3% of all kinds of aneurysms. Up to 40% of the patients with an abdominal aortic aneurysms (AAAs), present a concomitant CIAA.[1,2]

CIAAs may extend to the iliac bifurcation without an adequate proximal or distal neck, thus making their treatment quite challenging. Open surgical repair includes internal iliac artery (IIA) transposition, bypass or ligation, but exposes these patients to increased risk for postoperative morbidity.[3] On the other hand, endovascular approach has been adopted during the last decade showing good outcomes. Endovascular approach includes two main techniques: i. coverage/embolism of IIA ii. Preservation of IIA. Patients undergoing coverage or embolism of the IIA using coils or vascular plugs have been at higher risk of gluteal ischemia (16%-55%) and erectile dysfunction (10%-46%), or even worse complications such as bowel or spinal cord ischemia, especially when bilateral.[4,5] In a systematic review of the literature, Kouvelos et al.[6] reported that unilateral or bilateral IIA occlusion during EVAR seems to carry a substantial risk of significant ischemic complications in nearly one quarter of patients. Bilateral IIA occlusion was related to a significantly higher rate of buttock claudication.[6]

Preservation of the IIA perfusion by endovascular means included primarily the bell-bottom technique, the double-barrel "sandwich" technique, or surgeon modified devices through the off-label use of endografts. From 2006 the first dedicated devices for the treatment of CIAAs were introduced in the market. The *Iliac Branched Devices* consisting of one branched component, positioned in the CIA and extended

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with a covered stent in the IIA, thus achieving preservation of the antegrade blood flow in the IIA. Since then, several companies launched their devices to the market.

The aim of the study is to evaluate the early results of endovascular treatment of patients with both single or bilateral iliac and aorto-iliac aneurysmal disease preserving the IIA blood flow with the use of the IBE device.

METHODOLOGY

A single center retrospective study including patients with unilateral or bilateral common iliac and/or aorto-iliac aneurysmal disease treated by endovascular means was undertaken. All patients were treated with IIA flow preservation with the Gore (W.L. Gore & Associates, Flagstaff, AZ, USA) IBE device during the 2017-2019 period. This device has been introduced in the EU market in 2013 and in the US market in 2016. The IBE device consists of two dedicated components, both specifically designed for the iliac treatment: the Iliac Branch Component (IBC) and the Internal Iliac Component (IIC). The IBE device is designed to be used in conjunction with the Gore Excluder AAA Endoprosthesis and is composed of an expanded polytetrafluoroethylene (ePTFE) graft and a nitinol stent. Bilateral femoral access is required in most of the cases, while in some cases, brachial access can be of use. The details of the intervention have been previously described. [10,12]

Indications for the treatment of CIAA was a diameter of >20 mm isolated or associated with an AAA and anatomical characteristics that allowed the deployment of the device such as:

-CIA diameter > 17 mm in the proximal zone

-Non-aneurysmal length of the external iliac artery (EIA) > 10 mm with a diameter of 6.5 to 13.5 mm or with a diameter range of 6.5 to 25 mm in case an extension is used.

-Diameter of the IIA should be 6.5 to 13.5 mm with a distal sealing zone length of at least 10 mm.

-There is no limitation regarding the length of the CIA.

-A minimal distance of 165 mm between the lowest renal artery and the iliac bifurcation is required.

Sizing and planning were performed based on the pre-operative computed tomography angiography (CTA) using a 3Mensio workstation (Medical Imaging B.V., Bilthoven, the Netherlands) with dedicated reconstruction software. All of the procedures were performed in an adequately equipped operating room, using a moveable radiolucent surgical table and a mobile digital angiographic system (Ziehm Vision RFD 3D, Ziehm Imaging GmbH, Nuremberg, Germany).

Baseline and procedural characteristics

Demographic data, like age and pre-operative comorbidities [coronary artery disease CAD), chronic obstructive pulmonary disease (COPD), hypertension (HT), hypelipidemia (HL) and diabetes mellitus (DM)] were recorded. Anatomical details the aneurysmal disease was recorded. Procedural characteristics as the type of endograft used in combination with the IBE device, the type of the iliac stent graft, access site and eventual relining were captured. Other procedural details like the operation time, the radiation time and the amount of contrast used, were reported.

All patients underwent a follow up protocol including ultrasonographic examination before discharge and at 6 months and a CTA at 1 month, 12 months and yearly thereafter.

Outcomes and definitions

Primary outcomes constituted of technical success rate, mortality and 30 days target vessel patency, while secondary outcomes were procedure related morbidities as well as freedom from re-intervention and freedom from aneurysm exclusion events occurred during the study period.

Technical success was defined as successful implantation of the IBE in the target iliac vessels with preservation of antegrade flow into the IIA with aneurysm exclusion (no type Ib or III endoleak on the completion angiogram). Morbidities related to the procedure include buttock claudication, ischemic colitis and spinal cord ischemia. Aneurysm exclusion outcome events include rupture, endoleaks type I or III of the target vessels detected on completion angiography and subsequent imaging exams (Computed Tomography Angiography) during the follow up period.

Statistical analysis

Continuous data were expressed as mean ± standard deviation. Categorical data were expressed as absolute numbers and percentage of prevalence (%) in the study cohort. Statistical analysis was carried out using SPSS 19 (IBM, Armonk, NY).

RESULTS

Baseline and anatomic characteristics

From 2017 to 2019, 8 patients with aorto-iliac aneurysmatic disease (88.8%; 8/9 patients) and 1 with bilateral isolated iliac aneurysms (11.1%; 1/9) were treated electively by endovascular means (Table 1). All patients were males with a mean age of 70.2 ± 8 years. The most common comorbidities included HL (100%; 9/9 patients), HT (88.8%; 8/9 patients) and CAD (55.5%; 5/9 patients),

Seven patients had bilateral iliac aneurysms (77.7%; 7/9 patients), including the one with isolated iliac aneurysmal disease. In the group of patients with aortoiliac aneurysms, the mean maximum aortic aneurysm diameter was 61.3±2mm. The mean maximum right iliac aneurysm diameter was 33±10mm and the left 38.3±19mm.

Peri-operative and procedural details

All of the patients were treated under general anesthesia. In eight of them, a bifurcated GORE EXCLUDER (W. L. Gore and Associates, Flagstaff, Ariz) aortic endograft was combined to the IBE device; in one patient there was an infrarenal aortic aneurysm treated with the “chimney technique” (Table 2). A tubular thoracic endoprosthesis BOLTON-RELAY (Bolton Medical, Sunrise, Fla) was placed in a patient with a previous standard endovascular aortic repair (EVAR) and endoleak type Ia that required

a tubular graft to extend the proximal sealing at the level of the celiac artery and to establish splancic perfusion through the placement of three covered stents to the renals and superior mesenteric artery with the chimney technique. Moreover, an IBE device was placed to his left iliac, in order to treat his common iliac aneurysm and maintain flow in the IIA.

In 7/9 interventions, the IBE was introduced through femoral access (figure 1), while in two cases a brachial access was used due to internal iliac catheterization issues (adverse IIA angulation) (figure 2).

Patients	Gender	Age	Commorbodities	Aortoiliac Disease	Isolated CIAAs	Unilateral CIAAs	Bilateral CIAAs	AAA Dmax	RCIAA Dmax	LCIAA Dmax
1	MALE	55	DLP, HT, CAD, COPD	YES	NO	NO	YES	90	29,9	58,3
2	MALE	66	DLP, HT	YES	NO	NO	YES	69,7	38,3	35,6
3	MALE	66	DLP, HT, COPD	YES	NO	YES (L)	NO	60,8	19	40,4
4	MALE	73	DLP, COPD, LUNG Ca	YES	NO	YES (R)	NO	56	56	18,4
5	MALE	65	DLP, HT, CAD	YES	NO	NO	YES	50,1	33,9	20,8
6	MALE	76	DLP, HT, DM, CAD	YES	NO	NO	YES	52,8	27,4	29,1
7	MALE	82	DLP, HT, CAD	YES	NO	NO	YES	95,2	35,9	35,1
8	MALE	69	DLP, HT, CAD, DM, COPD	YES	NO	NO	YES	53,7	34,3	27,2
9	MALE	80	DLP, HT, DM, COPD	NO	YES	NO	YES	23,7	22,3	80,3
AVG (Std Dev)		70,2±8,45						61,3±21,6	33±10,7	38,3±19,6

AVG (Std Dev): Average (Standard Deviation), DLP: Dyslipidemia, HT: Hypertension, CAD: Coronary Artery Disease, COPD: Chronic obstructive pulmonary disease, DM: Diabetes Mellitus, Lung Ca: Lung Carcinoma, CIAA: Common Iliac Artery Aneurysm, Dmax: Maximum Diameter, RCIAA: Right CIAA, LCIAA: Left CIAA

Table 1. Demographics of the patients included in the study and morphological characteristics of the aorto-iliac and isolated iliac aneurysms

Patients	Graft	Access	Iliac Stent	Relining	Anesthesia	Operation Time (mins)	Radiation Time (mins)	Contrast	LOS	Complications	FU
1	EXCLUDER, IBE	Brachial	Viabahn, 13x5	NO	GENERAL	220	40	200	4	NO	24
2	EXCLUDER, IBE	Femoral	GORE IBC, 16x10	NO	GENERAL	200	45,38	130	4	NO	12
3	EXCLUDER, IBE	Femoral	Viabahn 13x5	NO	GENERAL	420	137,30	300	6	NO	18
4	EXCLUDER, IBE	Femoral	GORE IBC, 16x10	NO	GENERAL	145	30	100	4	NO	6
5	EXCLUDER, IBE	Femoral	GORE IBC, 16x12	NO	GENERAL	120	29,16	80	3	NO	1
6	EXCLUDER, IBE	Femoral	GORE IBC, 16x12	NO	GENERAL	180	45	150	4	NO	12
7	RELAY, IBE	Brachial	Viabahn 13x5	YES	GENERAL	360	102	180	10	NO	12
8	EXCLUDER, IBE	Femoral	GORE IBC, 16x14	NO	GENERAL	240	9,32	170	4	NO	1
9	EXCLUDER, IBE	Femoral	GORE IBC, 16x14	NO	GENERAL	180	7,02	120	7	NO	1
AVG (Std Dev)						229,4±99	54,25±32,43	158,8±65,4	5,1±2,2		9,6±8,1

AVG (Std Dev): Average (Standard Deviation), IBE: Internal Iliac extension, IBC: Iliac Branch Component, LOS: Length of Stay, FU: Follow Up

Table 2. Procedural details

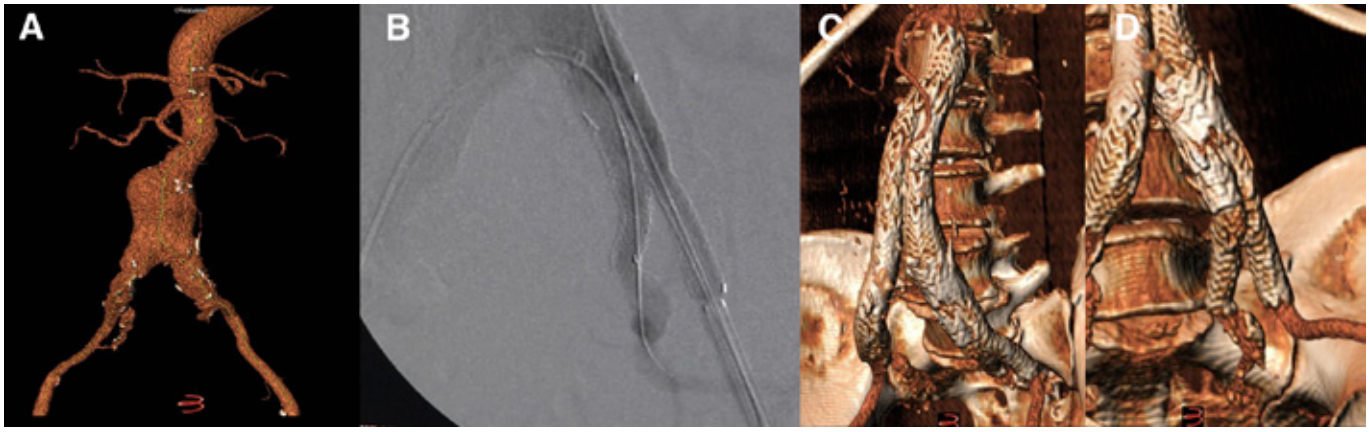

Figure 1. Bilateral aorto-iliac aneurysm. A: Pre-operative 3D reconstruction and center lumen line of the aneurysm, B: Deployment of the Internal Iliac Component through contralateral femoral access, C: Post-operative image of the bifurcated aortic endograft combined with the IBE device on the left ilac, D: Anteroposterior view of the IBE device

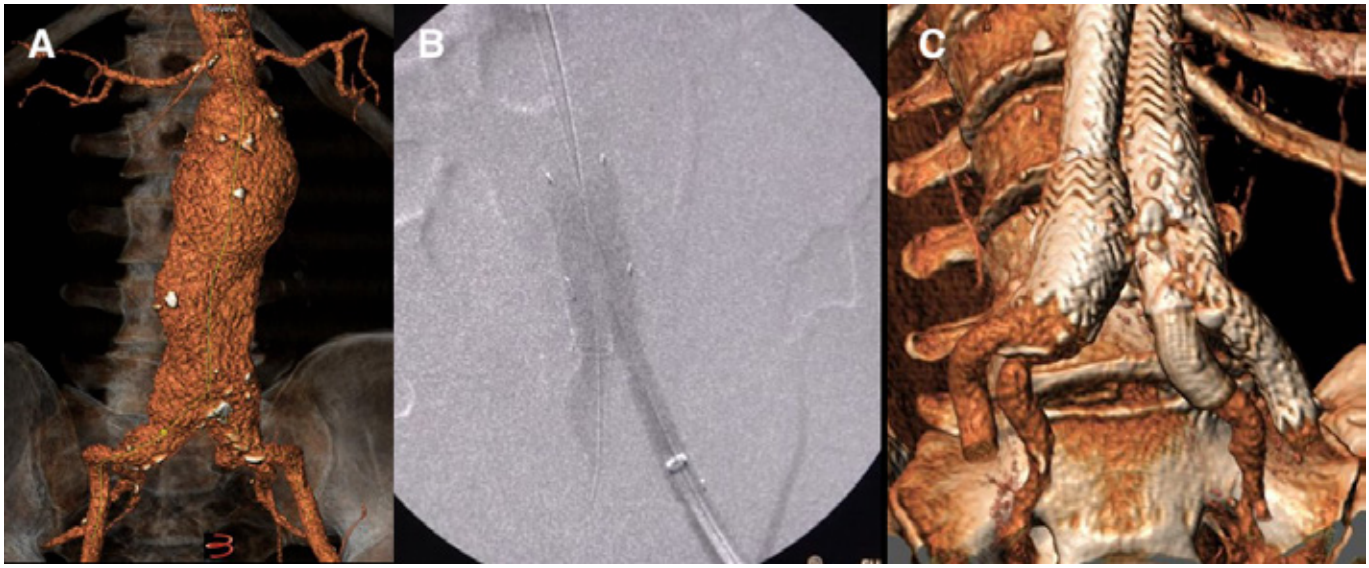

Figure 2. Bilateral aorto-iliac aneurysm treated with "Bell bottom" technique on the right side and an IBE device on the left side. B: Cannulation of the left internal iliac artery through left brachial access, C: Post-operative image of the bifurcated aortic endograft combined with the IBE device on the left ilac

In most cases (6/9; 67%) the GORE IIC available diameter of 16mm) was used to establish blood flow in the IIA. In 3 cases, a Viabahn self-expandable covered stent was combined to the IBE device. The choice of the stent graft was based on the access site in two cases, since a longer shaft is needed when brachial access is used (available Viabahn shaft of 120mm, instead of the IBC shaft of 63mm) and the smaller IIA diameter in the third one. (available diameter of 13mm).

Relining with an additional balloon expandable bare metal stent was undertaken only in one patient due to severe angulation of the IIA treated.

The median procedure time was calculated at 229 minutes (range 120-420 minutes) while the median radiation exposure time was 54 minutes (range 7-137.3 minutes). The median contrast volume used was 158ml (range 80-300ml). Patients were discharged after a median hospitalization time of 5 days (range 3-10 days).

The technical success rate was 88.8% (8/9 successful stent placements). One IIA branch thrombosis was detected at the completion angiography. It concerned a Viabahn self-expanding stent occluded due to adverse IIA angulation. Mortality rate was 0%. The 30-days patency rate was 88.8% as no other target arteries occluded and antegrade flow was preserved (Table 3).

Technical Success	88,8%
30days Patency	88,8%
Morbidity	0
Mortality Aneurysm Exclusion Events	11,2%
Reintervention Rate	0

Table 3: Primary and secondary outcomes

The mean follow up period was 9,6 ± 8.1 months (range 1-24 months). Overall patency during the follow up period remained at 88.8% as no other thrombosis events occurred. The re-intervention rate was 0% during follow up period. No procedure related complications such as buttock, bowel or spinal ischemia events occurred in any patient. The patient with the iliac branch intraoperative thrombosis did also show no clinical symptoms. Freedom from endoleak type I/III IBE related was 100%. There was only one endoleak type Ib, but on the contralateral side of a patient that was treated with the "bell-bottom" technique. The 30 days follow up examination revealed a patent IBE on one side and the endoleak Ib on the contralateral side. The patient with this endoleak was treated with the "coil and cover" technique, by occluding the internal iliac artery with coils and extending further to the external iliac artery. After 6 months, the iliac extension was occluded (the patient presented with acute limb ischemia) due to adverse limb tortuosity and a femoral-femoral by pass re-established blood flow among the patient's lower limbs. No other events were recorded during the follow up period.

DISCUSSION

The occlusion or preservation of IIA blood flow during an EVAR has been in the center of interest during last years. Major complications from the occlusion of IIA are buttock claudication, bowel and spinal cord ischemia. The main IIA occlusion techniques are IIA coverage with stenting with or without coiling. Those interventions were correlated to a significant percentage of ischemic complications. Verzini et al.[7] reported a morbidity up to 22% after IIA occlusion. In a recent systematic review of the literature, Kouvelos et al.[6] demonstrated that pooled 30-day buttock claudication rate was 29.2% in patients undergoing IIA occlusion (uni- or bilateral), compared to patients with IIA preservation (4.1%).

Both the American and European Vascular Societies' most recent guidelines, strongly recommend the preservation of blood flow to at least one internal iliac artery [(Society of

Vascular Surgery, Level 1A) and (European Society of Vascular Surgery, Class I, Level B)].[14,15] The bell-bottom technique is a treatment option for common iliac arteries with up to 24 mm of diameter. Although apparently effective in the short-term, long-term durability has been questionable with reported type 1b endoleak rates varying from 3.4-7.8% and high reintervention rates.[8] Other techniques, like parallel graft "sandwich" technique and IBD have been proven to be safe and valid approaches, with less anatomical restrictions. Nevertheless, while there is scarce data on ST's outcomes and durability, IBD placement has been established as an effective and durable procedure.[9] Our experience, even if preliminary, has shown that implantation of an IBD such as the GORE EXCLUDER IBE device, leads to high procedural success, low re-intervention rates, and high short and mid-term patency. The technical success rate was 88.8% and overall patency rate remained excellent during the follow up period. Along this line, a Dutch retrospective cohort analysis of IBE implantation in 46 patients with iliac aneurysmal disease, presented a procedural success rate of 93.4% and early patency rates (after 6 months of follow up period) of 94%. Similar results were reported by Maldonado et al.[11], with successful placement of IBE in 97,9% of the patients showing patency rates of 97.5% at 6 months. In a multicenter study in the United States, Schneider et al.[12], showed a procedural success rate of 95.2% and patency rate of 95.1%. Midterm outcomes of this study reported also high patency rate (93.6%) up to 24 months of follow up.[13]

In the present series, no ischemic complications occurred (buttock claudication, ischemic colitis or spinal cord ischemic). The patient with the IIA branch occluded was completely asymptomatic. Reintervention rate in the target arteries treated was null. There was one intentional IIA occlusion in a patient with bilateral CIA aneurysms, but on the contralateral side from the IBE. The aneurysm initially treated with the "Bell bottom" technique, required IIA coiling and overstenting, due to an endoleak type Ib found at 30 days CTA. In this case there were no clinical ischemic symptoms after the re-intervention. In a multicenter study in the United States, reintervention rate was 2.1% at the IDE group for thrombotic events and 5% for non-thrombotic events at 6 months, while 3.4% and 4.1% of patients treated of type II endoleaks at 12 months and 24 months, respectively.[13] The Dutch large series published by van Sterkenburg et al,[10] reported a new-onset buttock claudication ipsilateral to the IBE device in 4.6% of the patients postoperatively, that disappeared during follow up. Schneider et al, reported loss of patency of the IIA of 4.9%.[12] Similarly, based on data from a large European registry, the PELVIS registry, Donas et al showed that midterm experience with placement of IBDs is associated with a low incidence of secondary procedures (overall postoperative reintervention rate of 8.9%)[16] and even in more complex treatment options (f/bEVAR) the use of IBDs can achieve equally good results and have become the standard of care.[17]

In the present study, most of the iliac branch devices were delivered through femoral access. In two of the patients, brachial access was used, because of adverse iliac anatomy with severe tortuosity and kinking of the common iliac arteries. Brachial access can become an alternative access in the patients with relative contra-indication due to anatomy. However, an alternative covered stent may be required in such cases, with a longer shaft than the dedicated IBE's IIC. In the present series a 13mmx5mm Viabahn (W. L. Gore & Associates, Flagstaff, Ariz) stent graft was used in both cases.

The Gore (W.L. Gore & Associates, Flagstaff, AZ, USA) IBE device, is not the only iliac branched device exists in the market. Another FDA-approved iliac branched device is Cook (Cook, Bloomington, IN, USA) IBD, with slightly different characteristics between the two. Gore IBE is a lower profile endoprosthesis with a 16 Fr introducer sheath suitable for narrower common femoral arteries than the Cook IBD that requires a 20 Fr sheath. The use of Cook IBD is limited by the need for a smaller internal iliac diameter (6-11 mm) and a narrower external iliac artery (EIA: 8-11mm), compared to the IBE (IIA diameter: 6.5-13.5 and EIA: 6.5-25mm). In case of patients with severe iliac tortuosity, the Gore IBE branched iliac stent graft is more conformable than the Cook IBD as it does not modify with the indices of tortuosity nor the post-endovascular aneurysm repair lengths of the iliac axes, as Della Schiava et al.[18] have shown in their recent study. The key for a successful iliac branched device implantation is the proper device selection that best suits the patients' anatomical criteria.

The main limitation of the study is its retrospective nature, the small number of patients and the relatively short follow up period. No data on erectile dysfunction were recorded.

CONCLUSION

The GORE EXCLUDER IBE device achieved good early and midterm results with high technical success and patency rates, along with low complication and re-intervention rates.

Conflict of interest: None

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INVITED COMMENTARY

The GORE iliac branch device: a new kid on the block

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Preservation of at least one hypogastric artery is a common practice in the endovascular repair of aorto-iliac aneurysmal (AIA) disease, as this has been recommended from both the European and the Society of Vascular Surgery guidelines.[1,2] At present, there are several devices in the market, which are dedicated to treat solely by endovascular means aneurysms involving the common iliac artery. The main concept behind all these devices is the delivery of a bridging stent-graft through a contralateral or a trans-brachial approach and through a small iliac side branch in the hypogastric artery.

Until the introduction of the new GORE® Excluder® Iliac Branch Endoprosthesis (IBE, W.L. Gore & Associates, Flagstaff, AZ, USA), the most frequently used CE-certified off-the-shelf iliac-branch devices were the Zenith® Branch Endovascular Graft- Iliac Bifurcation (ZBIS, COOK Medical, Limerick, Ireland) and the E-iliac stent-graft (Jotec, Hechingen, Germany). The effectiveness of both endografts has been confirmed in several studies.[3-5] Thus, the added value of an additional iliac-side branch device remains questionable.

Considering the features of each device in details, we can recognize that all three have their pros and cons. The ZBIS device has been implanted in the largest number of patients worldwide.[3] Currently, the PeLVIS investigators from 9 European centers showed favorable outcomes, with a low rate of late graft occlusion and aneurysm-related death in a real world setting.[4] Of note, no significant differences in clinical outcomes were observed in patients receiving hypogastric balloon-expandable vs self-expandable stent-graft or endovascular relining.[4] However, the main limitations of the ZBIS device are: (1) the single proximal of 12mm which is disadvantageous for isolated common iliac artery aneurysms, (2) the distal diameter which varies between 10 and 12 mm, which is problematic for larger external iliac artery and (3) finally, the stiffness of the device, which may lead to kinking in angulated iliac arteries. Of note, the ZBIS device is not indicated for aneurysms of the hypogastric artery.

The self-expanding E-liac® stent-graft system consists also of a bifurcated graft including a main iliac limb with an additional reinforced stump for the internal iliac artery side branch.[5] Its tip-to-tip design with asymmetric stents provides flexibility and clear visibility during implantation whereas compression springs ensure the connection of the bridging stent at the side branch. The E-iliac registry enrolled 45 patients at 11 European sites and confirmed high clinical success rate, low rates of device-related re-interventions and excellent patency rate.[5] Compared to the ZBIS device, the E-liac® is available in more configurations with the proximal diameter ranging between 14 and 18mm and the distal diameter 10-14mm.[5] This is advantageous in cases of larger diameters of common iliac artery (CIA) in isolated CIA aneurysms or large external iliac artery (EIA). The CIA segment length can be 41, 53 or 65 mm and can be simplify the endovascular repair of aneurysmal distal seal post endovascular aortic aneurysm repair (EVAR) considering that the majority of EVAR limbs are up to 14mm in diameter. Again, this device is not indicated for aneurysms of the hypogastric artery.

The GORE Excluder IBE consists of two modular components: the iliac branch component (IBC) and the internal iliac component (IIC). *Schneider et al.*[6] showed in the framework of the IBE 12-04 study that the IBE device is effective at treating CIAs and AIAs, maintaining blood flow into the hypogastric artery with excellent patency rates. The device has unique characteristics, which expands the indications of IBE in more demanding anatomies. The proximal diameter of 23 mm allows endovascular repair of isolated CIA aneurysms with minimum iliac diameter of 17 mm at the proximal implantation zone. Moreover, the unique flexibility of the PTFE-covered endoskeleton of the GORE devices makes it unique for severely elongated distal landing zones, whereas the distal diameter allows external iliac artery treatment diameter range of 6.5 - 25 mm. Finally, the device is the only one which is indicated also for aneurysms of the internal iliac artery (IIA) with treatment diameter range of 6.5 - 13.5 mm. In this context, the combined use of Viabahn stent-grafts with the dedicated internal iliac component allows treatment of aneurysms involving even the first branches of the hypogastric artery.

In this context, *Batzalexis et al.*[7] reported on the mid-term outcomes of the GORE Excluder IBE device regarding the endovascular repair of aorto-iliac aneurysmal disease and they have to be congratulated for their encouraging outcomes. This is single center experience in a real-world setting with demanding anatomies; thus, this explains the patency rate of 89%, which were lower than the IBE 12-04 study. Moreover,

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once the device was successfully implanted without any 30-day events, no further events during the follow-up occurred. The freedom from type I/III endoleak was 100%.

In summary, the GORE Excluder IBE device is a new kid on the block, which seems to be a necessary tool expanding even more our ability to treat challenging aortoiliac anatomies. The first studies showed excellent short and mid-term performance, whereas data about the long-term performance (> 5 years) still remain mandatory.

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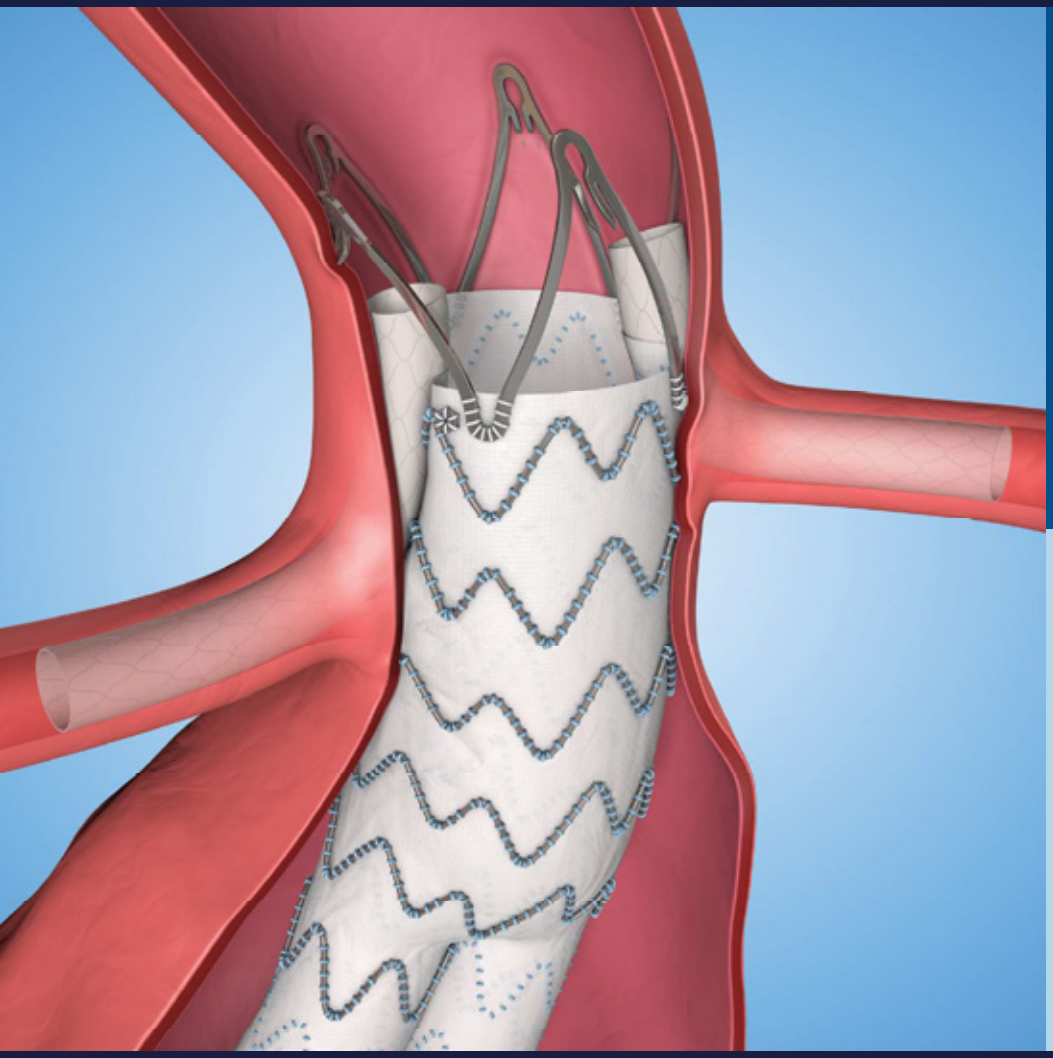

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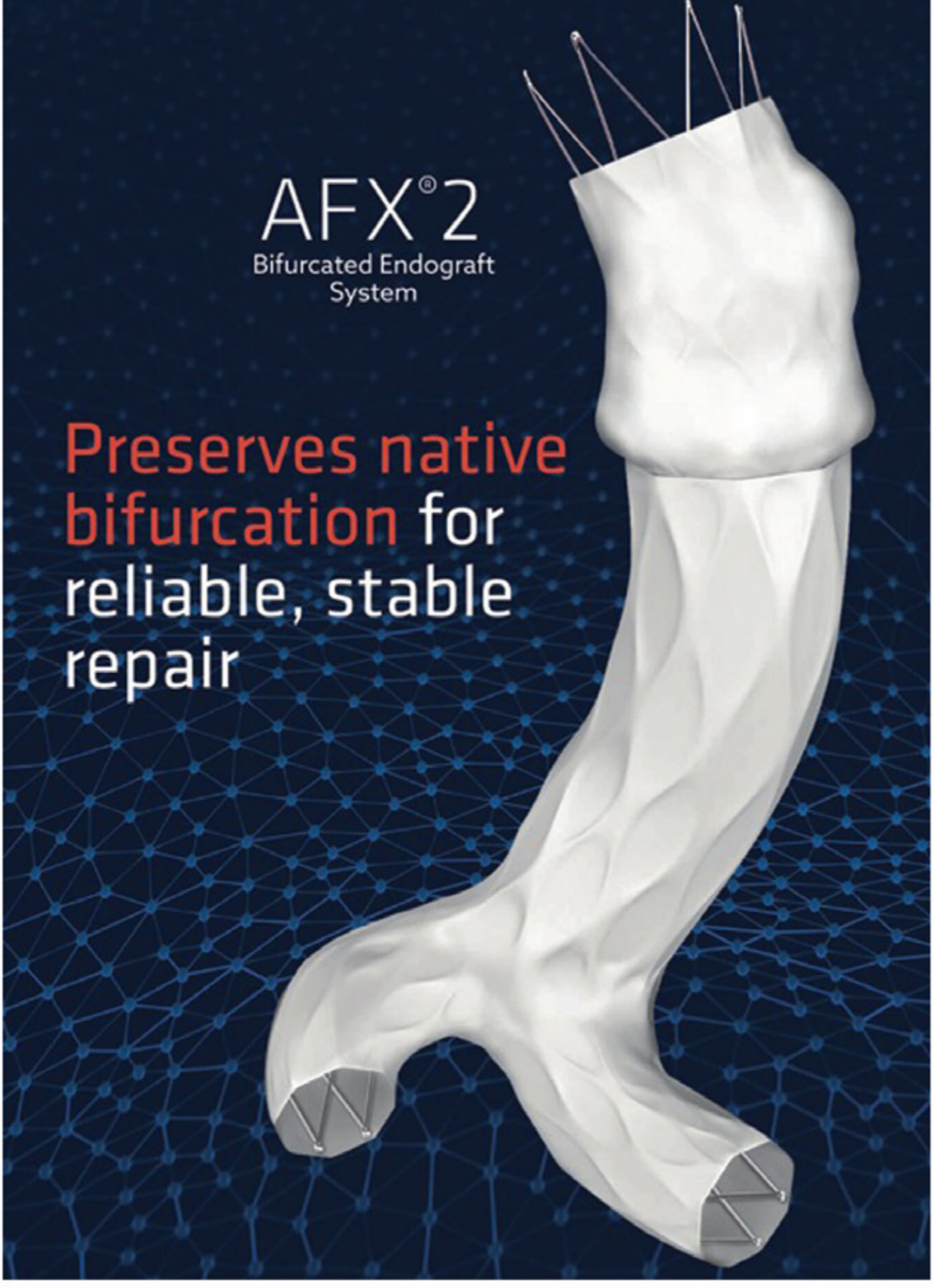

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Applied statistics in vascular surgery Part VII: Plots with dots

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Abstract:

Data visualization is of paramount importance while working with numerous data, as it can easily summarize the available evidence. In this article, we present the use of basic plots with dots, which allow the reader to see basic characteristics of the working dataset in a glimpse.

INTRODUCTION

Plots in medical statistics are a very comprehensive method of representing data graphically[1]. Two basic plots, ***dot plot*** and ***scatterplot***, with their extensions, make use of a very common symbol (the dot) to illustrate data in a convenient and easily "digested" way.

DOT PLOT

When dealing with small data set, ***dot plot*** (or ***strip plot*** or ***dot chart***) may be a quite useful and quick way to assess the distribution of mainly univariate variables. It is similar to a bar graph in a way that the height of each "bar" equals to the number of observations in this category. However, in dot plot, instead of bars, there is a stack of dots, with one dot placed above the other. The number of the dots is relative to the number of observations in this category[2]. Illustration of a dot plot includes drawing a horizontal line (x axis) with categories written beneath it, while the number of dots represents the frequency of observation in each category (Figure 1). The dot plot is simple to read, while it is useful for tracing certain data trends or groupings, highlight clusters and gaps and easily identify outliers. In their extensions, the "***Wilkinson Dot Plot***", uses a perpendicular to the scale local displacement to prevent the dots from overlapping, while in the "***Cleveland dots plot***" several different categories of the data can be visualized with dots in the same plot.

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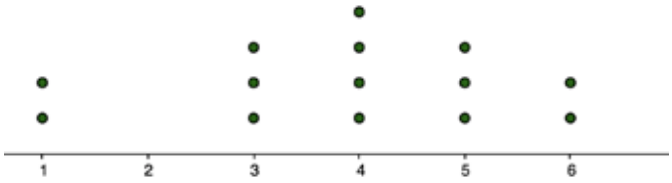

Figure 1. A simple form of dot plot with distribution of observations in six categories (1-6)

SCATTERPLOT

A more extended plot with dots, is ***scatter plot*** (or ***scatter chart*** or ***scatter graph***). In this graphical illustration, dots are placed on the horizontal and vertical axis, in a way that the position of a dot represents values for two different numeric variables, one in x and the other in y axis (Figure 2). This plot is mainly used to capture relationships between two variables. Correlation between two variables, as long as outliers can be easily depicted with the use of scatterplot[2,3]. More specifically, an independent and a dependent variable can be plotted with dots, and a positive or negative, strong or weak, linear or nonlinear or other relationship can be illustrated. This association, can be additionally shown with the addition of a line of best fit in this type of plot. Making a scatterplot can be done by using data in a way that values in one column represent values of dependent and values of another column represent values of independent variable. Each row will then form a single dot in the scatterplot with coordinates according to the column values. Notably, the researcher must be aware that correlation does not imply causation, when studying a scatterplot[2]. One other form of scatterplot, which is useful to illustrate time trends is the "***connected scatterplot***". In a more sophisticated version, a ***3D scatterplot*** can be used to illustrate multiple variables in multiple axes with the use of advanced software. Although very useful, one limitation of the scatterplot is overplotting. In that case, dots overlap in the plot and this complicates the recognition of trends and correlations.

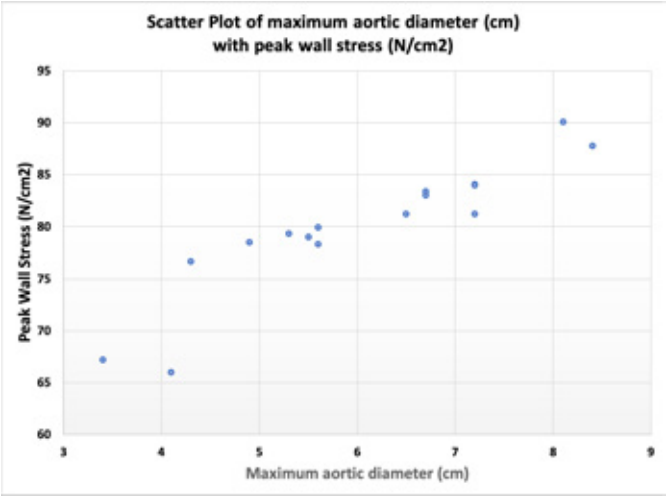

Figure 2. Scatterplot showing the distribution of patients according to maximum aortic diameter (cm) and peak wall stress (N/cm^2)

BUBBLE PLOT

When we need to combine data coming from independent and dependent variables in a single plot, scatterplot is a good solution. Additionally, it may be also useful in case we need to illustrate another variable (group) in our scatterplot. In that case, we need to paint the dots with different colors or shapes, based on the number of different categories of the grouping variable. In the special issue, where the third variable is continuous (numeric), changing of the dot's size can be quite useful. This form is called "***bubble plot***"[4], and the size of the dot (or bubble in this case) is proportional to the size of the grouping variable (Figure 3). Although very useful, a special caution is needed when dealing with negative or zero values of the grouping variable. A good solution is to use full circles for positive, and empty circles for negative values, while use a symbol like "×" to indicate that the size of the bubble represents the absolute value of a negative data value.

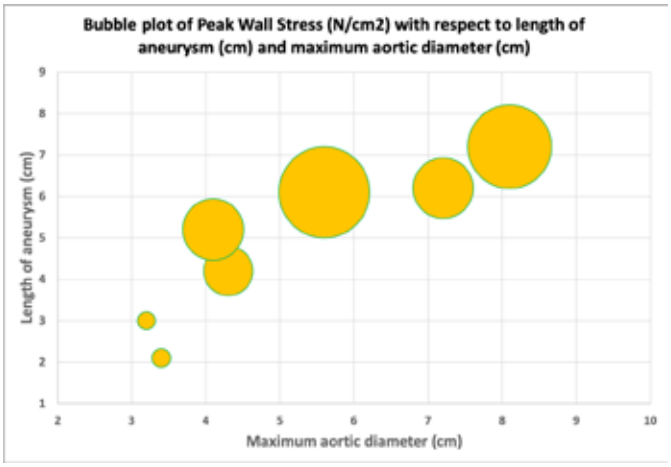

Figure 3. Bubble plot showing peak wall stress (N/cm^2) of patients with respect to maximum aortic diameter (cm) and length of aneurysm (cm); the size of the circles is proportional to the values of peak wall stress (N/cm^2)

CONCLUSION

Plots with dots are a quick and very effective way to present many forms of scientific data in a coherent manner, so that the it can be easily and conveniently read and understood.

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Gradual elastic suture approximation (shoelace technique) for closure of large fasciotomy wounds following delayed lower extremity revascularisation: a report of a rather forgotten technique

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Abstract:

Fasciotomy wounds following delayed revascularization of the lower extremity can be really hard to manage, may get complicated with infection, elongate hospitalization, and significantly increase morbidity and healthcare costs. Gradual elastic suture approximation (the shoelace technique) is a rather simple, effective, and inexpensive technique to gradually approximate the skin edges as swelling resolves. This results in a fine linear scar, without the need for skin grafting. We report a case of severe compartment syndrome following delayed revascularization of Rutherford IIB acute limp ischemia where the shoelace technique was successfully applied. This brief technical note is supported with technical tips, illustrations of the application process, and images of the wounds at all stages.

INTRODUCTION

The use of decompressive fasciotomy to prevent compartment syndrome following delayed revascularization is crucial for the management of a threatened extremity.[1] However, the high exudate fasciotomy wounds, the significant muscle and subcutaneous edema, and associated skin contracture can be really hard to manage.[2] In addition, fasciotomy wounds may get complicated with infection, elongating hospitalization, and significantly increasing morbidity and healthcare costs.[3] This can be really distressing for the patient, and reduce quality of life in the long-term.[4] A plethora of devices and techniques has been developed to tackle the issue of delayed closure of fasciotomy wounds.[5] The above is indicative of the fact that no technique has shown a clear superiority and no consensus has been reached about the best surgical management.

The shoelace technique has been described in 1980s and its' use, for the closure of fasciotomy wounds, has since been reported in several surgical specialties to manage difficult wound in need of split-skin grafting or flap cover.[5] The gradual approximation is done via application of elastic vessel loops or rubber bands that are cheap and readily available in all institutions and operating theatres. Unfortunately, despite its simplicity, vascular surgeons are not always aware of how to apply the gradual elastic suture approximation, and/or are reluctant to use it.

We report a case of severe compartment syndrome following delayed revascularization of Rutherford IIB acute limp ischemia where this technique was successfully applied and provide a brief technical note of how we do it.

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CASE REPORT

A 62 year old male patient was transferred to our department from a small rural hospital with acute left lower limb ischemia. The patient had a history of left ilio-femoral bypass with PTFE graft for occlusive disease some 20 years ago. The left leg was profoundly ischemic, with rest pain, and neurological deficit of the entire foot including sensory loss and foot drop indicating acute ischemia of at least stage IIb. A CT angiography confirmed the clinical findings; the ilio-femoral bypass had acutely occluded due to disease progression causing outflow issues. Specifically, the common femoral artery (CFA) and profound femoral artery (PFA) had significant atherosclerotic stenosis, and the distal superficial femoral artery (SFA) also had chronic occlusion. The popliteal and below knee arteries were patent. Limb viability was threatened and prompt revascularization was necessary. Via a femoral cut-down we performed a PTFE patch angioplasty of the CFA and extensive profundo-plasty. Furthermore, the transposition technique was performed, creating a wide common orifice between the SFA and PFA.

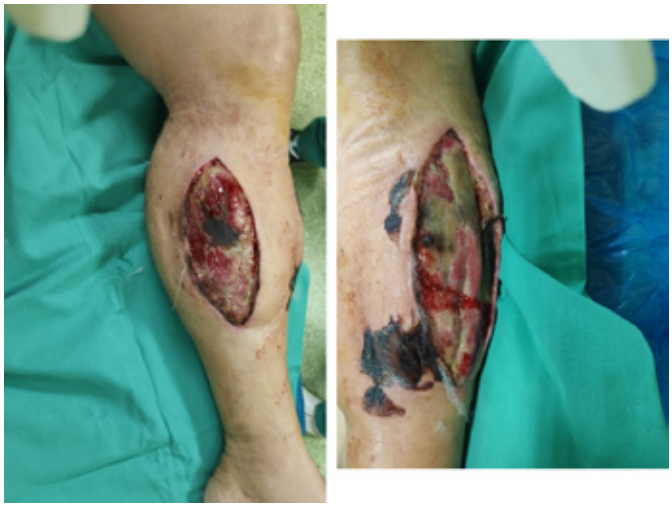

Image 1. Severe revascularization syndrome with edema and necrosis of the calf muscles and skin

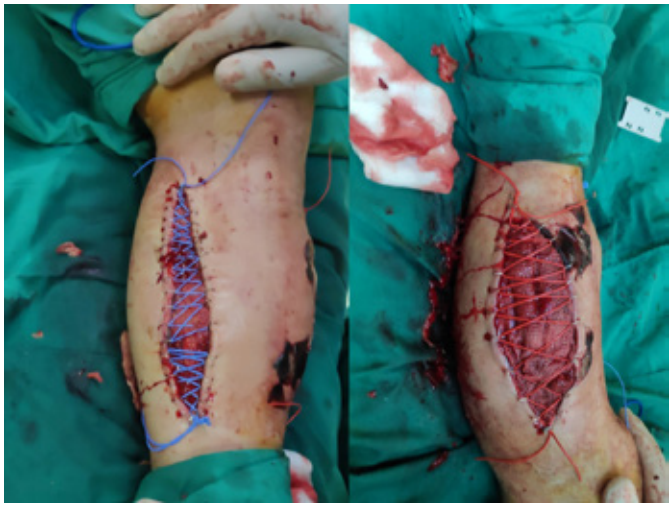

Image 2. Wounds after the application of gradual elastic suture approximation (shoelace technique)

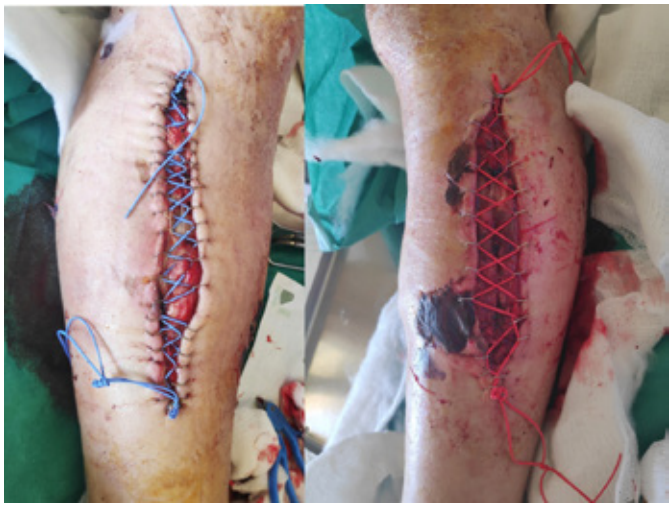

Image 3. On day 3, both fasciotomy wounds had significantly shrunk

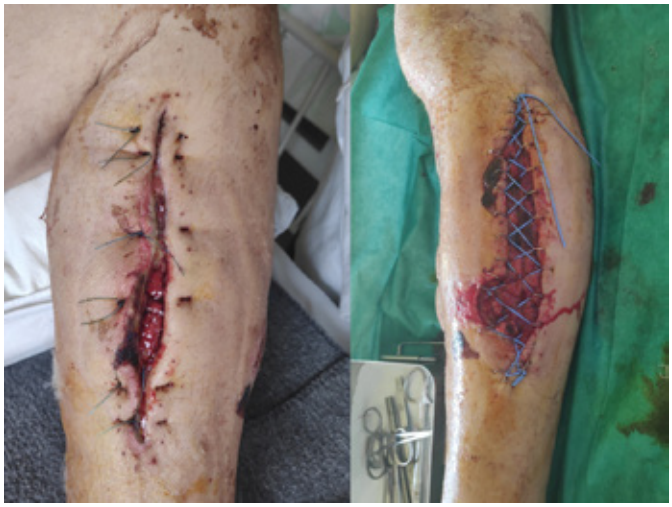

Image 4. The wounds at 2-weeks follow-up

The inflow was successfully corrected via ilio-femoral graft thrombectomy. An angiogram was performed and the distal SFA occlusion was opened with angioplasty using a 5mm drug-eluting balloon. By the end of the procedure, the patient had palpable dorsalis pedis and, anticipating a significant revascularization syndrome, we decided to perform dual incision fasciotomy of the leg to decompress all four muscular compartments.

The patient suffered severe revascularization syndrome with edema and necrosis of the calf muscles and skin (Image 1) and persistent foot drop. The CPK reached a high of 20,000 U/L. The patient neurological deficit gradually improved. On the second post-operative day, a decision was taken to surgically remove the skin and the muscle that were affected and apply gradual elastic suture approximation (shoelace technique) (Image 2). The results of the shoelace technique were excellent and on day 3 both fasciotomy wounds had significantly shrunk (Image 3). On day 7, the approximation was good enough to apply skin sutures and partly close the wounds. Overall, the result was excellent as shown by the photos taken at 2-weeks follow-up (Image 4).

Technical note

These are the steps we normally take when performing the shoelace technique for closure of fasciotomy wounds:

1. The operation should be performed under standard aseptic conditions. Local or general anesthesia may be used.
2. All necrotic tissue should be removed from the skin and the underlying tissues. We highly recommend muscle de-bulking that will permit easier and more effective elastic suture approximation
3. The skin edges may be mobilized from the underlying fascia to permit more effective traction.
4. We normally start at the proximal apex and continue toward the middle of the wound. A double surgical knot is formed to tie the ends of the elastic band (Medi-Loops - vessel loops) and form a closed loop. The knot is attached to the skin at the apex of the wound with metal clips, ap-

plied with a surgical stapler (Figure 1). The loop is then attached to one side of the incision with clips vertical to the edge of the incision and passed over the open wound to be attached on the opposite side. This is a sequence that resembles a zigzag from the proximal to the distal regions with 1cm steps between the metal clips. If the fasciotomy is lengthy, an additional elastic band will be needed. It is best to similarly start from the distal apex and progress towards the middle where the two elastic bands will meet (Figure 2).

5. The wound is then dressed with Vaseline gauze and elastic bandages are applied.
6. The dressing should be changed daily and the elastic band gradually tightened by pulling and attaching the knot at new anchoring point.
7. When the wound has shrunk enough to permit safe closure, the elastic band can be removed and the incision sutured (Figure 3).

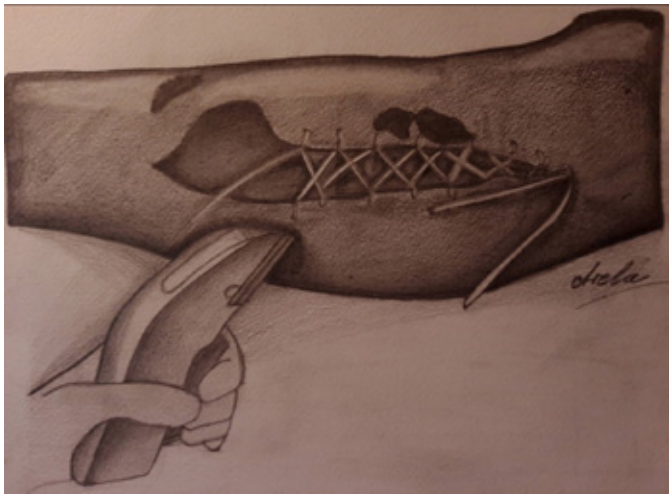

Figure 1. Illustration of the application of the shoelace gradual elastic suture approximation. Sketched by AL

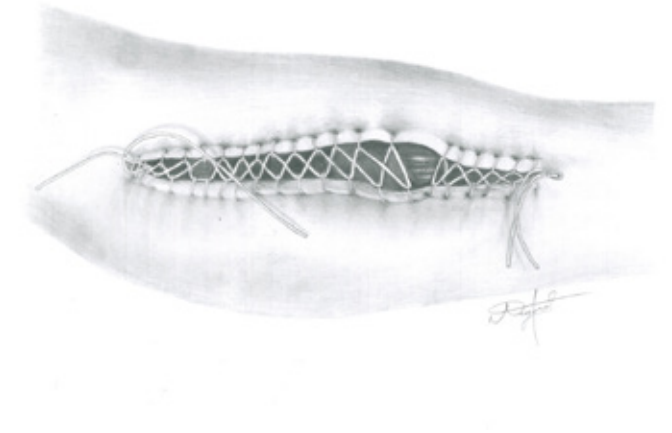

Figure 2: The application starts from the wound apexes and progresses towards the middle where the two elastic bands will meet. Sketched by AN

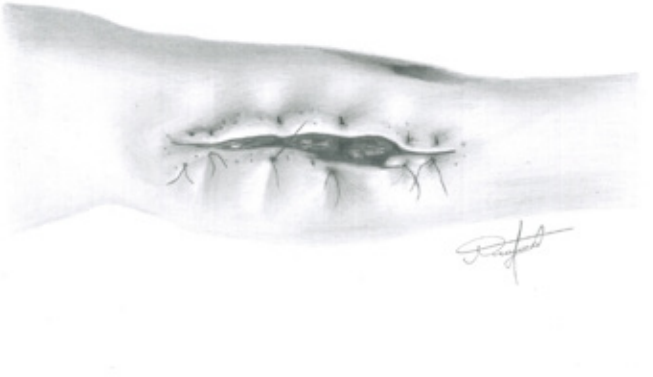

Figure 3. When the wound has shrunk enough to permit safe closure, the elastic band can be removed and the incision sutured. Sketched by AN

We normally tighten the vessel loops by applying a new anchoring point at the apex of the wound twice weekly. Ideally, as in our case, the wound will shrink considerably within 1-2 weeks and then standard suture approximation can be applied.

Alternatively, sterile rubber bands may be used instead of vessels loops. The rubber bands are applied in a similar fashion. In wounds that have high exudate and/or are complicated with infection a combination of vacuum-assisted closure (VAC) and the shoelace technique can be used.

It should be noted that we try to limit the length of the skin incision to permit easier closure. However, we always elongate the incision of the fascia under the skin. By using scissors, it is possible to extend the fasciotomy and leave the overlying skin intact.

DISCUSSION

A recent meta-analysis included 23 studies comparing split-thickness skin graft (STSG), gradual suture approximation (including shoelace technique, intracutaneous, Ty-Raps, and subcuticular prolene sutures), dynamic dermatotraction (7 different commercial devices), and VAC.[5] Gradual suture approximation had success rate of 92.4% and complication rate of 14.83%. This is similar to the success rate of the dynamic dermatotraction devices (92.7%) that involves significant costs which can be US$500–US$1000 per device and also presents a higher complication rate (18.4%). VAC had the lowest success rate of 78.1% and the lowest rate of complications 2.49% also involving a cost of US$96.51 per day. Finally, STSG is the operative alternative when the above methods fail. It should be noted that this is major surgery under general anesthesia that may involve additional complications at the graft donor site, infection, graft failures, and poor cosmesis.

The shoelace technique is a rather simple, effective, and inexpensive technique to gradually approximate the skin edges as swelling resolves.[6,7] This results in a fine linear scar, without the need for skin grafting.[6,8] It should be noted that staples may detach and/or the vessel loops may break be-

cause of point loading from tightening and limb mobilization; in this case, staples and vessel loops need to be checked and repositioned. Skin edge ischemia and necrosis may rarely occur, again due to point loading at the staple sites. The elastic suture approximation has the advantage of gradual wound closure. This is really important because it allows time for antibiotics to be administered, high wound exudate to be evacuated, and for the infection to settle down. In cases of ongoing severe infection and tissue necrosis, the gradual tightening can be delayed or even abandoned.

In conclusion, the presented case demonstrates that even in severe compartment syndrome with extreme muscle necrosis, tissue edema, and skin contracture the timely and knowledgeable application of the shoelace technique can provide effective wound closure and help the patient avoid additional surgery and costly interventions. Finally, the presented technical note and illustrations may be of practical value to the vascular surgeons who deal with fasciotomy wounds in their everyday practice.

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Conflict of interest: None

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Endovascular repair of a failed EVAS using the Altura endograft

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Abstract:

Although endovascular aneurysm sealing (EVAS) for abdominal aortic aneurysm repair has shown encouraging early outcomes, the long-term effectiveness and durability of the technique have been doubted, especially after the initial 2 years of follow-up. EVAS, novel endografts and further endovascular means have been used to for the need of re-intervention in complications after EVAS. We report a case of a 67-year-old male patient, who was initially treated for an infra-renal aortic aneurysm using the Nellix device (EVAS). Endograft migration was detected at 2-year follow-up and the Altura endograft was used because of its design (two D-shape stents) to achieve successful proximal stability, fixation and sealing. At 12 months after re-intervention, no proximal endoleak or migration is detected. Altura endograft may be a safe approach in cases that a re-intervention is needed after a failed EVAS.

INTRODUCTION

Observational studies, showed encouraging early outcomes regarding the use of endovascular aneurysm sealing (EVAS) with the Nellix device (Endologix, CA, USA).[1] The acceptable procedure-related mortality and low early post-operative complication and re-intervention rate further supported EVAS application for the management of abdominal aortic aneurysms (AAAs).[1,2] Early results maintained a highly acceptable freedom from endoleak and rupture, however, mid-term and late complications as device migration, type 1A endoleak, and aneurysm sac expansion have been recorded during follow-up.[3]

EVAS is characterized by obliteration of the aneurysmal sac by polymer-filled endobags, while maintaining the normal flow with two balloon expandable stent grafts.[4] The low profile Altura Endograft System (Lombard Medical, OX, UK) consists also of two stent grafts which have a double "D-shaped" stent design, using, though, suprarenal fixation.[5] The analogous double stent conformation of both devices would permit the application of Altura into a failed EVAS to achieve proximal sealing. Herein, we report a case of a 67-year-old male, presenting with a proximal migration after EVAS, 2-year after the initial treatment, who was treated with an Altura endograft in order to restore proximal stability, fixation and potentially sealing. This report has been approved by the Ethics Committee of the Hospital.

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CASE REPORT

A 67-year old male with a medical history of tobacco use, hypertension, dyslipidemia and chronic obstructive pulmonary disease presented to the outpatient clinic due to an incidentally diagnosed AAA. Computed tomography angiography (CTA) revealed an infrarenal AAA with a maximum diameter at 54.5 mm. Mean neck diameter was 22 mm and neck length was estimated at 30mm. No extreme angulations (8°) were detected and sac thrombus did not exceed the 1/4 of the aneurysm sac volume. Considering patient's medical history and aneurysm anatomy, an endovascular approach using the Nellix device was decided. The presence of multiple lumbar arteries was also a relative indication for the choice of EVAS for the prevention of type II endoleak.

In January 2017, under general anesthesia, the patient underwent an endovascular aneurysm repair using a Nellix device (N10-180 right stent and N10-170 left one). The left stent was extending down to the external iliac artery to achieve optimal distal sealing. No embolization of internal iliac artery was needed. Completion angiography confirmed renal artery and right internal iliac artery patency while no endoleak was detected. The patient was discharged the 2nd post-operative day in a good general condition. During the first month follow-up, no migration or endoleak was detected in CTA while the aneurysm sac was stable (Figure 1). Similarly, 6-month follow-up was uneventful. The aneurysm was assessed using duplex ultrasonography and no endoleak was detected.

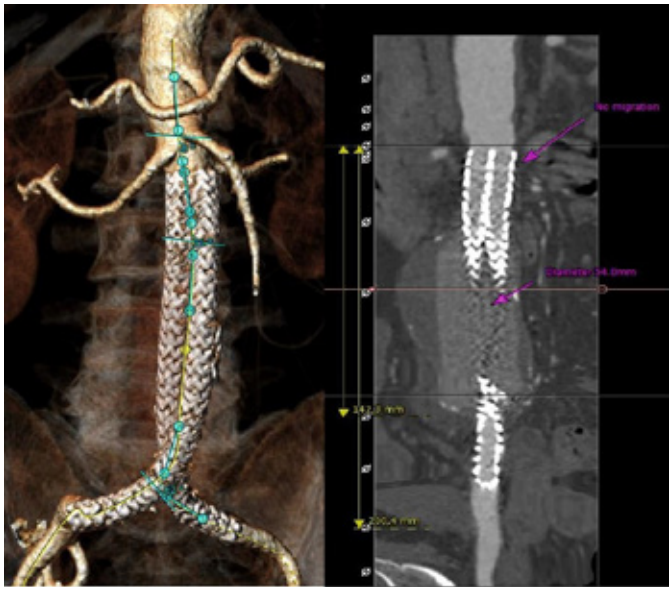

Figure 1. Early follow-up did not detect any graft migration or endoleak (Panel A). Sac diameter remained stable (Panel B).

At 1st year follow-up, a CTA was performed. Once more, no endoleak was recorded; however, a graft migration of more than 1cm was identified (Figure 2). The left stent migrated caudally 13mm while the right one, 18mm. Aneurysm diameter was estimated at 52.4mm. A conservative approach was decided at that time. A year later, a new CTA revealed a more excessive graft migration of 20mm at the left stent (Figure 3). After an extensive discussion with the patient regarding the risk of proximal endoleak and the need for re-intervention, the option of the Nellix explantation did not seem attractive to the patient. Thus, an endovascular approach for the treatment of the failed EVAS was decided. The special configuration of the endograft did not permit the use of a standard bifurcated device. At that time, a novel type of a low profile endograft, Altura, consisting of two D-shape stents, seemed a rational approach to treat Nellix migration; offering at the same time a proximal suprarenal fixation.

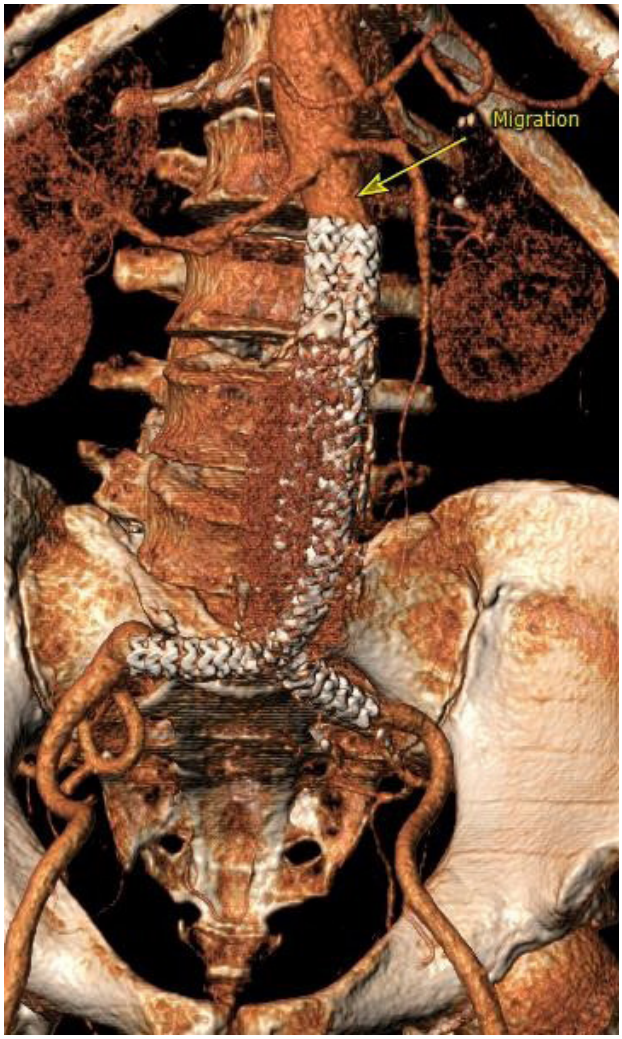

Figure 2. At 12-month follow-up, the CTA revealed a proximal migration of both Nellix stents. No endoleak was detected and a conservative management was decided.

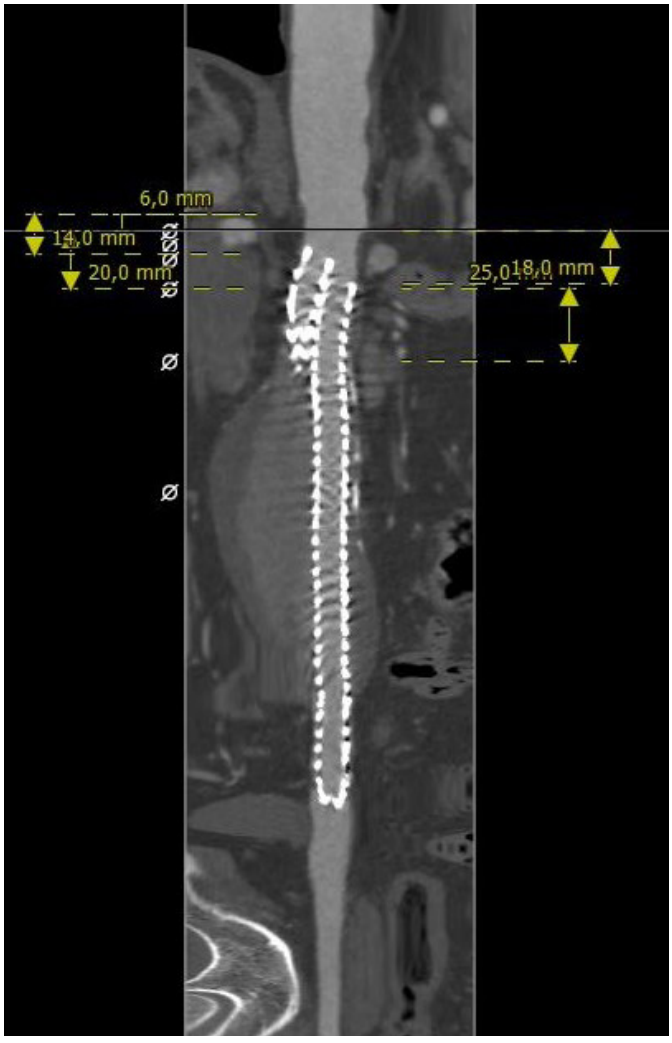

Figure 3. A year later, the CTA recorded an even more pronounced migration and loss of proximal sealing. The indication for surgery was set.

Using the percutaneous approach to overcome an inguinal re-incision, Nellix stents were catheterized. The Altura stents were placed infra-renally into the previous stents (both stents 24*90mm). The suspicion of a left in-stents stenosis was treated using bilateral balloon expandable stents using the kissing stent technique (Valeo, Bard, USA, both 10*36mm). The left Altura stent was extended using a self-expanding covered stent down to the iliac bifurcation to achieve optimal sealing (Viabahn, W. L. Gore & Associates, DE, USA, 13*10mm). Completion angiography revealed no endoleak while both renal arteries and the right internal iliac artery remained patient. The patient was discharged the 1st post-operative day in a good general condition. Follow-up 6 months post-operatively revealed no further complication, with complete sac exclusion and adequate proximal and distal sealing (Figure 4).

Figure 4. Altura with the double D-shaped stent grafts offered proximally an adequate sealing with supra-renal fixation.

DISCUSSION

Endovascular treatment of AAA has an initial survival advantage over open repair, but more frequent complications which increase cost and long-term aneurysm-related mortality.[6] EVAR-1 long-term follow-up revealed that, at beyond 8-year follow-up, open-repair has significantly lower mortality while the increased aneurysm-related mortality in EVAR was mainly addressed to secondary aneurysm rupture.[7] EVAR seems to have an inferior late survival compared with open repair while lifelong surveillance and re-interventions are mandatory to preserve survival and the durability of the procedure.[6,7] Open surgical conversion after failed EVAR due to type I or II endoleak, migration, sac expansion and rupture, results in significant morbidity and mortality.[8]

Endovascular re-intervention for failed EVAR have become a more popular approach during the last decade. The most frequent indications for secondary intervention are endoleak type I, II or III, stent graft migration and thrombosis.[9] Endovascular means are applied in more than 80% of cases with null early morbidity and mortality.[9] Outcomes after EVAR re-interventions are highly acceptable, except secondary interventions due to rupture or infection, which are associated to high post-operatively mortality.[9] The endovascular management of post-EVAR complications seems safe and effective, without significant impact on EVAR survival.

While the early outcomes of EVAS were encouraging, the mid and long-term durability has raised significant doubts. An important risk for loss of proximal sealing due to the absence of any active fixation mechanism was considered the mean reason for the high rates of endoleak type Ia and migration.[10] Mid-term follow-up (≥24 months) in EVAS cases reported a high rate of stent graft failure.[11,12] In this case, the migration was already detected during the 1st year follow-up; however it was even more prominent at 2 years; arising the need for further intervention. Patient's close follow-up with CTAs has probably played an important role in the prevention of more important complications as endoleak, sac expansion or even rupture. A meticulous long-term surveillance with CTA may be mandatory in EVAS patients.

Altura endograft is a novel low profile device with good early outcomes. During the 1st year of follow-up, no aneurysm ruptures, surgical conversions, or AAA-related deaths were recorded.[5] However, further clinical investigation is needed to evaluate the role of the device in the treatment of AAA during long-term follow up.[5] For the moment, no literature data are available for the use of Altura in failed EVAS and this is the first case reported. Altura offers a rational endovascular approach for migrated Nellix devices, as the double stent construction fits identically in the Nellix device and offers the suprarenal fixation that does not exists in EVAS. In this case, Altura performed sufficiently at least during the early follow-up.

CONCLUSION

Altura was a safe approach in this case of failed EVAS. Re-interventions after failed EVAR may be adequately managed using percutaneous approach and further novel endovascular means.

Acknowledgement: None

Conflict of interest: None

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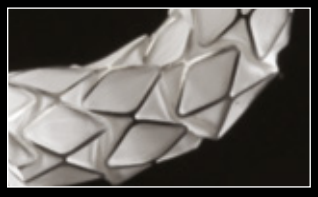

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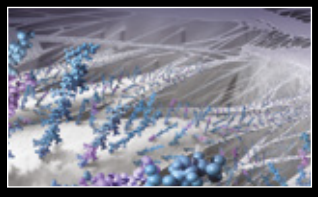

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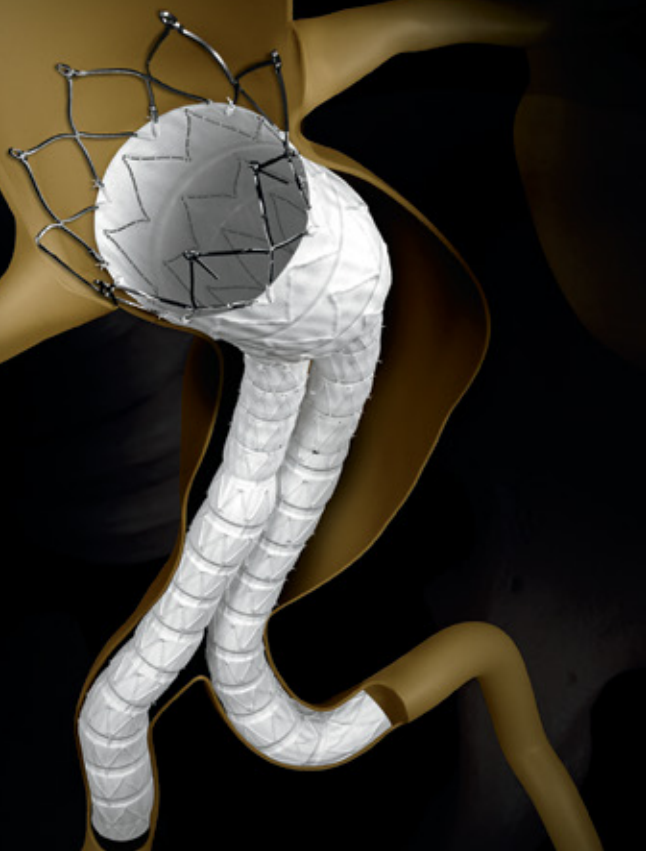

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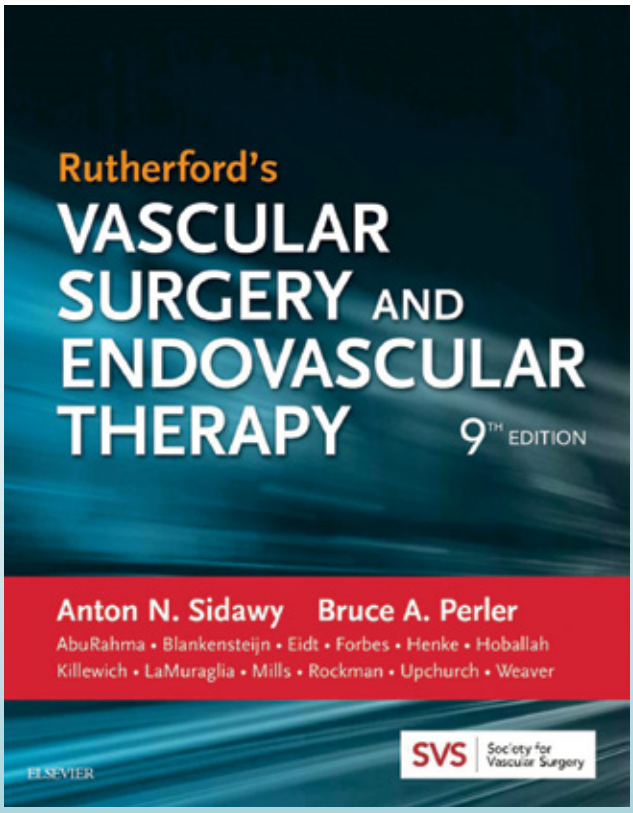

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