DOI:10.14753/SE.2023.2747

SEMMELWEIS EGYETEM

DOKTORI ISKOLA

Ph.D. értekezések

2747.

SARKADI HUNOR SÁNDOR

Klinikai és kísérletes angiológiai kutatások
című program

Programvezető: Dr. Sótonyi Péter, egyetemi tanár

Témavezető: Dr. Dósa Edit, egyetemi docens

DOI:10.14753/SE.2023.2747

ARTERIAL PSEUDOANEURYSM FORMATION AND FEMOROPOPLITEAL STENT FRACTURE AND IN-STENT RESTENOSIS

Ph.D. Thesis

Hunor Sándor Sarkadi, M.D.

Doctoral School of Clinical Medicine

Semmelweis University

Supervisor: Edit Dósa, M.D., Ph.D.

Official Reviewers: Kristóf Hirschberg, M.D., Ph.D.

Dávid Korda, M.D., Ph.D.

Head of the Complex Examination Committee:

György Reusz, M.D., D.Sc.

Members of the Complex Examination Committee:

András Folyovich, M.D., Ph.D.

Gábor Varga, M.D., D.Sc.

Budapest

2022

DOI:10.14753/SE.2023.2747

Table of contents

List of abbreviations 4
1. Introduction 6
1.1. Local complications 6
1.1.1. Punctured vessel-related early complication – arterial pseudoaneurysm 6
1.1.1.1. Incidence of arterial pseudoaneurysm 7
1.1.1.2. Etiology of arterial pseudoaneurysm 8
1.1.1.3. Symptoms of arterial pseudoaneurysm 8
1.1.1.4. Diagnosis of arterial pseudoaneurysm 8
1.1.1.5. Treatment of arterial pseudoaneurysm 9
1.1.1.6. Prevention of punctured vessel-related complications 10
1.1.2. Intervention (site)-related late complication – femoropopliteal stent fracture 10
1.1.2.1. Incidence of femoropopliteal stent fracture 11
1.1.2.2. Predisposing factors for femoropopliteal stent fracture 11
1.1.2.3. Diagnosis of femoropopliteal stent fracture 11
1.1.2.4. Possible consequences of femoropopliteal stent fracture 12
1.1.2.5. Treatment of femoropopliteal stent fracture 12
1.1.3. Intervention (site)-related late complication – femoropopliteal in-stent restenosis 12
1.1.3.1. Incidence of femoropopliteal in-stent restenosis 12
1.1.3.2. Pathophysiology of femoropopliteal in-stent restenosis 13
1.1.3.3. Predisposing factors for femoropopliteal in-stent restenosis 14
1.1.3.4. Symptoms of femoropopliteal in-stent restenosis 14
1.1.3.5. Diagnosis of femoropopliteal in-stent restenosis 14
1.1.3.6. Treatment of femoropopliteal in-stent restenosis 15
2. Objectives 17
2.1. Study I (Incidence of and predisposing factors for arterial pseudoaneurysm formation) 17
2.2. Study II (Safety, clinical outcome, and fracture rate of femoropopliteal stenting using 4F compatible delivery system) 17

DOI:10.14753/SE.2023.2747

3. Results 18
3.1. Study I (Incidence of and predisposing factors for arterial pseudoaneurysm formation) 18
3.1.1. Background information for interpreting the results 18
3.1.2. The results obtained 19
3.2. Study II (Safety, clinical outcome, and fracture rate of femoropopliteal stenting using 4F compatible delivery system) 34
3.2.1. Background information for interpreting the results 34
3.2.2. The results obtained 36
4. Discussion 43
4.1. Study I (Incidence of and predisposing factors for arterial pseudoaneurysm formation) 43
4.2. Study II (Safety, clinical outcome, and fracture rate of femoropopliteal stenting using 4F compatible delivery system) 45
5. Conclusions 48
5.1. Study I (Incidence of and predisposing factors for arterial pseudoaneurysm formation) 48
5.2. Study II (Safety, clinical outcome, and fracture rate of femoropopliteal stenting using 4F compatible delivery system) 48
6. Summary 49
7. References 50
8. Bibliography of the candidate’s publications 65
9. Acknowledgements 67

DOI:10.14753/SE.2023.2747

List of abbreviations

ABI:	ankle-brachial index
ASA:	acetylsalicylic acid
BA:	brachial artery
BAV:	balloon aortic valvuloplasty
BMI:	body mass index
CA:	catheter ablation
CFA:	common femoral artery
CI:	confidence interval
CIE:	clinical intracardiac electrophysiological
CLI:	critical limb ischemia
CT:	computed tomography
CTA:	computed tomography angiography
DSA:	digital subtraction angiography
EIA:	external iliac artery
4-EVER:	4F Endovascular Treatment Approach
Hb:	hemoglobin
HCT:	hematocrit
INR:	international normalized ratio
IQR:	interquartile range
ISR:	in-stent restenosis
MR:	magnetic resonance
NOAC:	novel oral anticoagulant
OR:	odds ratio
PA:	popliteal artery
PEACE I:	Patency Evaluation After Implantation of the 4-French Pulsar-18 Self-Expanding Nitinol Stent in Femoropopliteal Lesions
PSA:	pseudoaneurysm
PTA:	percutaneous transluminal angioplasty
RA:	radial artery
RBC:	red blood cell

DOI:10.14753/SE.2023.2747

SD: standard deviation
SF: stent fracture
SFA: superficial femoral artery
TASC: TransAtlantic Inter-Society Consensus
TAVI: transcatheter aortic valve implantation
UA: ulnar artery
UGC: ultrasound-guided compression
UGTI: ultrasound-guided thrombin injection
VCD: vascular closure device
WBC: white blood cell

DOI:10.14753/SE.2023.2747

1. Introduction

Minimally invasive endovascular techniques are becoming increasingly popular around the world. Despite being minimally invasive, they can cause systemic (e.g., contrast-induced responses, such as allergy and nephropathy), as well as local complications. (1–3)

1.1. Local complications

Access site-related complications, punctured vessel-related complications, and intervention (site)-related complications are the three types of local complications. (4) Nerve damage, infection, and abscess formation are access site-related complications. (5) There are two sorts of complications associated with punctured vessels: hemorrhagic and non-hemorrhagic. Hemorrhagic complications include vessel perforation-induced bleeding and hematoma, which may or may not require transfusion, while the two most common non-hemorrhagic complications are pseudoaneurysm (PSA) and arteriovenous-fistula. (5) Vessel perforation with bleeding distant from the access site, arterial dissection, and thrombosis/embolism leading to organ or limb ischemia should be noted among the intervention (site)-related complications. (5–7)

Most of the local complications listed here occur during or immediately after the procedure, but some complications (particularly those related to the site of intervention: stent fracture [SF] and in-stent restenosis [ISR]) can develop years later.

As arterial PSA formation, femoropopliteal SF, and femoropopliteal ISR were the main subjects of my research, these are described in detail in the Introduction section.

1.1.1. Punctured vessel-related early complication – arterial pseudoaneurysm

Arterial PSA is a pulsating mass formed as a result of vessel wall injury. It consists of a neck and a sac. However, unlike a true aneurysm, its wall is made up of tunica adventitia and surrounding tissue. (8, 9) (Figure 1) In general, iatrogenic PSA is more common on the arterial side, (10) but may rarely occur on the venous side. (11)

DOI:10.14753/SE.2023.2747

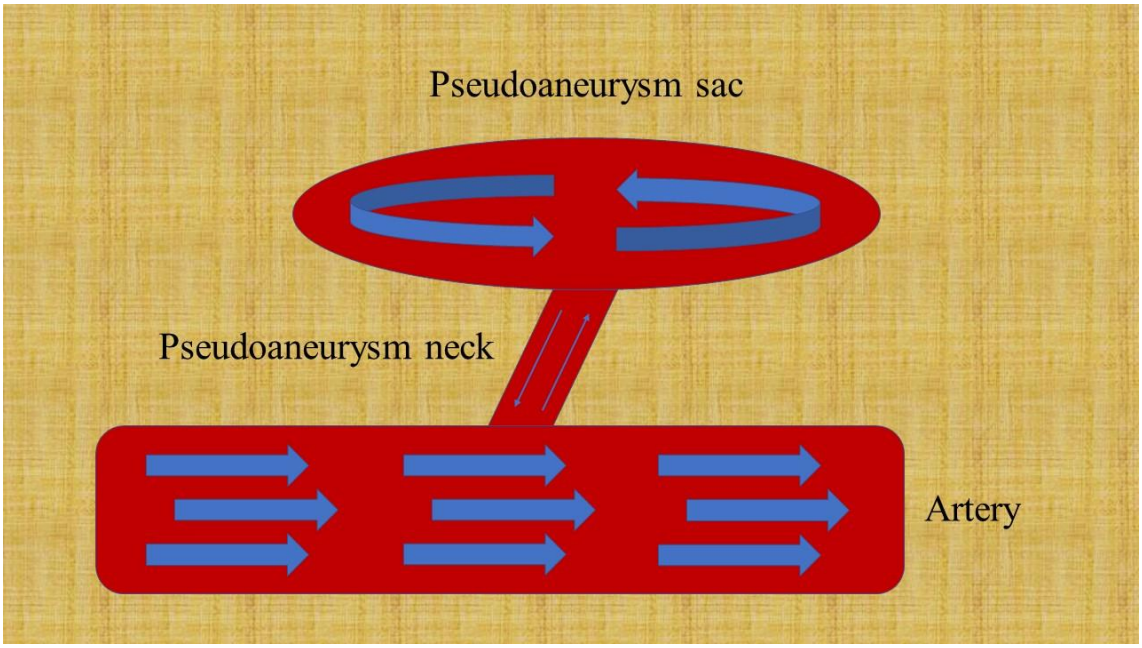


Figure 1. Schematic representation of an arterial pseudoaneurysm (The image was made by Hunor Sándor Sarkadi.)

1.1.1.1. Incidence of arterial pseudoaneurysm

PSA development is second in the line of complications in those undergoing arterial intervention. (5) Its prevalence is between 0.05% and 6%. (1, 5–7, 12) Radial and ulnar artery PSA are rare; their incidence is below 0.1%, (13–16) whereas the prevalence of PSA in the brachial artery is as high as 1.1%–1.3%. (17, 18) Although complications of radial and ulnar punctures are less common, (13–16, 18, 19) the femoral approach is still often used to this day, especially when working through a large sheath (e.g., transcatheter aortic valve implantation [TAVI], balloon aortic valvuloplasty [BAV], and aortic stent graft implantation) or when performing a lower limb intervention. (20) According to published data, the femoral artery PSA rate ranges from 0.05% to 2% for diagnostic catheterizations and from 2% to 6% for therapeutic treatments. (12, 21) In patients with non-coronary artery cardiac interventions (e.g., intracardiac electrophysiological procedures and TAVI), the incidence of femoral artery PSA was found to be 0.3%–5.9%. (22–25)

1.1.1.2. Etiology of arterial pseudoaneurysm

The etiology of PSA is multifactorial. Female gender, older age (>65 years), obesity, the presence of hypertension, arterial disease, chronic kidney failure, previous arterial intervention, poor puncture technique, the site of the puncture, the size of the inserted sheath, severe vascular calcification, the complexity and length of the procedure, the antiplatelet and anticoagulant therapy applied, and inadequate compression following arterial puncture have been shown to play a role in PSA formation. (5, 17–19, 26)

1.1.1.3. Symptoms of arterial pseudoaneurysm

Patients with PSA can be either asymptomatic or symptomatic. PSA is most indicated by pain and swelling at the site of the puncture. (5) However, due to its compressive effect on nerves and vessels, it can also cause neuropathy, venous thrombosis, claudication, and possibly critical limb ischemia (CLI). (27–31) Although extremely rare, local ischemia of the skin may lead to necrosis and infection. (5) The most catastrophic symptom of PSA may be fatal bleeding from rupture of the sac. (5)

1.1.1.4. Diagnosis of arterial pseudoaneurysm

Physical examination may reveal thrill or bruit, skin changes, marked tenderness, or a pulsatile mass at the site of arterial puncture. (12, 17–19) Ultrasound scanning in gray-scale, color, and Doppler modes is the best way to detect PSA. (28) On gray-scale images, a PSA is a pulsatile, anechoic, saccular lesion with varying echogenicity depending on the presence of a thrombus in the sac. (30) On color mode images, the PSA sac shows a bidirectional, turbulent, swirling blood flow pattern called the “yin-yang” sign. (28) (Figure 2) On Doppler mode images, a characteristic “to-and-fro” pattern can be detected in the communicating neck between the punctured artery (feeding artery) and the PSA sac. (27) If the visibility of ultrasound is uncertain for some reason (e.g., swelling or obesity) or the PSA has a complex morphology, better imaging is expected from computed tomography angiography (CTA), or less frequently from magnetic resonance (MR) imaging. (27–31) Today, digital subtraction angiography (DSA) is limited to cases aimed at treating PSAs endovascularly. (32)

DOI:10.14753/SE.2023.2747

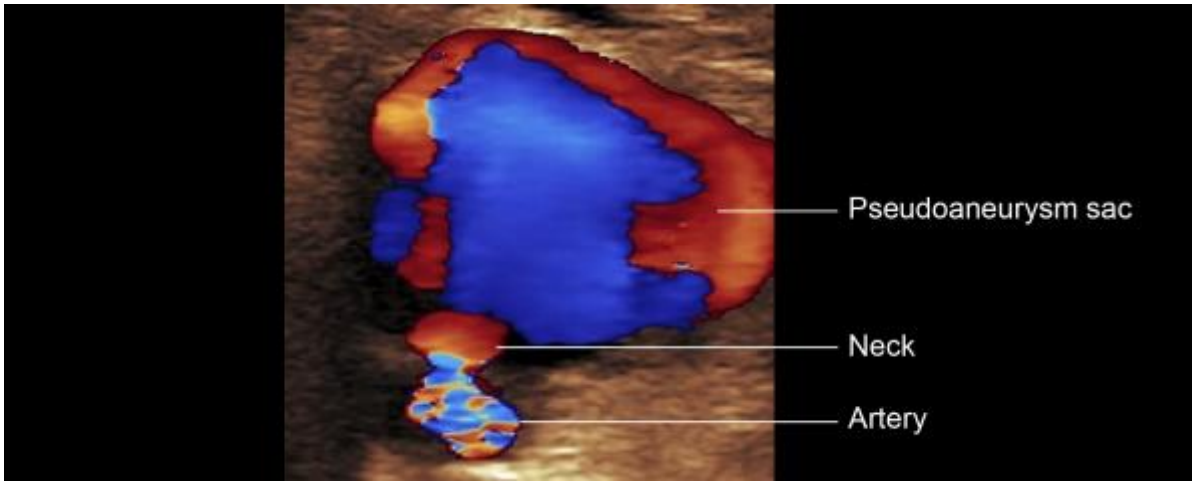


Figure 2. Ultrasound image of an arterial pseudoaneurysm in color mode (The ultrasound image was made by Hunor Sándor Sarkadi.)

1.1.1.5. Treatment of arterial pseudoaneurysm

Despite the fact that PSAs can thrombose spontaneously, most patients require some kind of treatment, such as pressure bandage replacement, ultrasound-guided compression (UGC), ultrasound-guided thrombin injection (UGTI), and endovascular or open surgical repair. (5–7, 12, 27–36) Mechanical compression with replacement of the pressure bandage or UGC is usually the first-line treatment of choice in patients whose coagulation status is normal, when the PSA is detected within a week of the procedure, the PSA sac is superficial, simplex, and small (<20 mm), and the PSA neck is long and narrow. (12, 20) The compression pressure should preferably be applied to the neck of the PSA or the site of the vessel wall damage (for 6 hours for radial and ulnar artery PSAs, for 8 hours for brachial artery PSAs, and for 12 hours for femoral artery PSAs). (31, 37) The UGC should not last longer than 15–30 minutes and should not be repeated more than three times. (12, 20, 37) In other cases, UGTI or endovascular or open surgical repair may be preferred. During UGTI, thrombin is injected under ultrasound guidance into the PSA sac as close to the neck as possible. (29) Endovascular and open surgical repair is reserved for cases where other techniques are contraindicated or have failed. (1, 3, 5, 33–36) Of the endovascular options, covered stent implantation, transcutaneous or transarterial coiling, the use of vascular plugs, vascular closure devices (VCDs), or fibrin adhesives, and balloon occlusion are usually the methods of

choice. (5, 32–36) Open surgical repair can be done by direct suturing of the arterial defect, by patch plasty, and by inserting an interpositum or bypass graft. (1)

1.1.1.6. Prevention of punctured vessel-related complications

In addition to proper patient selection, there are several ways to reduce the number of punctured vessel-related complications, such as choosing vascular access where the incidence of PSA is low, performing the puncture with ultrasound guidance, inserting a smaller diameter sheath, controlling the blood pressure, administering only as many antiplatelet and anticoagulant drugs as needed, and using VCDs. (38–43)

For example, until a few years ago, femoropopliteal arterial interventions with bare metal stents were carried out only through a 6F sheath. In the case of a 6F sheath, the incidence of punctured vessel-related complications varies between studies, but can be as high as 20%, depending on the definition and criteria used. (38) Not so long ago, however, self-expanding femoropopliteal bare metal stents that could also be delivered through 4F sheaths were introduced. Two large, prospective multicenter trials (4F Endovascular Treatment Approach [4-EVER] and Patency Evaluation After Implantation of the 4-French Pulsar-18 Self-Expanding Nitinol Stent in Femoropopliteal Lesions [PEACE I]) investigated the safety and efficacy of 4F stent implantation in patients with symptomatic femoropopliteal steno-occlusive disease. (44, 45) The punctured vessel-related complication rates were 3.3% in the 4-EVER trial and 2% in the PEACE I study, and all the complications could be managed by non-surgical treatments. (44, 45) These rates are lower than most of the published rates on 6F devices. (38) In addition, femoropopliteal arterial interventions with 4F-sheath-compatible bare metal stents can be accomplished with similar 12-month patency and revascularization rates as their 6F counterparts. (44, 45)

1.1.2. Intervention (site)-related late complication – femoropopliteal stent fracture

Allie et al. proposed a four-type classification system for the fracture of nitinol stents in peripheral arteries, (46) which was later expanded to five types by Jaff et al. (47) In the case of type I, only one strut is fractured. Type II refers to multiple strut fractures occurring at different locations on the stent. Type III is a complete transverse fracture without stent displacement. Type IV is a complete transverse fracture with stent

displacement, while type V is a spiral fracture leading to complete disintegration of the stent. (47) (Figure 3)

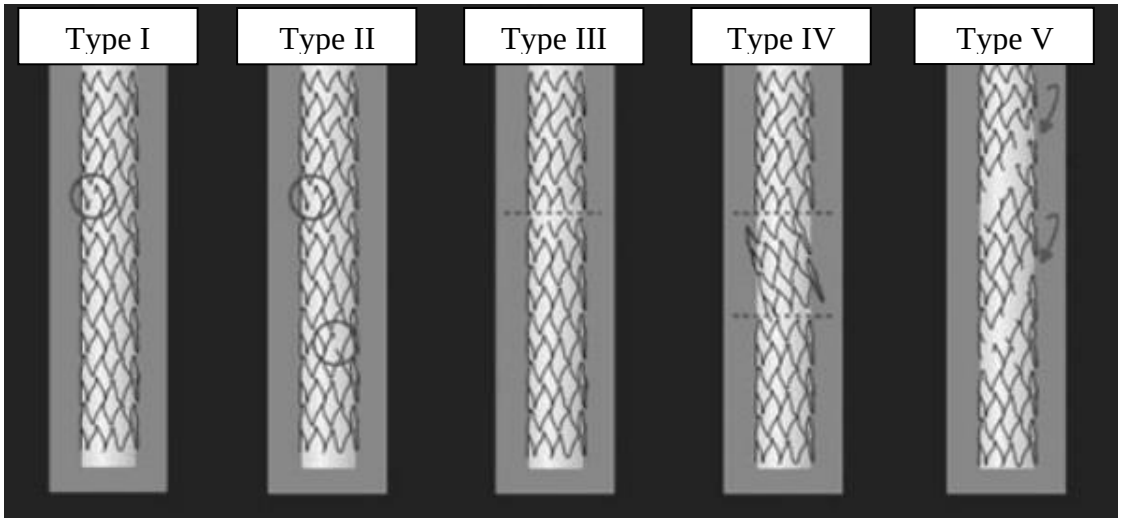


Figure 3. Types of stent fracture (47)

1.1.2.1. Incidence of femoropopliteal stent fracture

Although SF is not uncommon in the carotid, innominate, subclavian, vertebral, renal, and iliac arteries (with a cumulative incidence of 8% to 33%, depending on location), (48, 49) it is mostly detected in the femoropopliteal arteries (0.9%–76%), where longer self-expanding stents are usually implanted. (48, 50)

1.1.2.2. Predisposing factors for femoropopliteal stent fracture

Patient- (e.g., hypertension, chronic kidney disease), lesion- (e.g., location, etiology, plaque components [calcification], stenosis grade, and length), balloon/stent- (e.g., material, type, design, conformity, diameter, and length), and procedure-related parameters (e.g., malposition, distortion, and residual stenosis) have been shown to influence SF. (48, 50–56) Moreover, the popliteal region is critical in that vessels must adapt to movement-induced mechanical forces (e.g., axial compression and bending). (57–60)

1.1.2.3. Diagnosis of femoropopliteal stent fracture

The most commonly used imaging method to detect SF is high magnification fluoroscopic examination (plain X-ray or cine-loop) from at least three projections

(posteroanterior and left and right oblique). (51, 56, 61, 62) Conventional B-mode ultrasound can usually only diagnose SFs with displacement (types IV and V). (63) Intravascular ultrasound is a good option for identifying almost all types of SFs, but due to its invasiveness, it is rarely—in conjunction with endovascular treatment—performed for this purpose. (64–66) Computed tomography (CT) also provides an opportunity to assess SFs. However, in connection with CT scans, the blooming effect should not be forgotten, which makes strut fractures difficult to detect even with CT. (67)

1.1.2.4. Possible consequences of femoropopliteal stent fracture

Usually, the consequences of SF rather than SF alone are responsible for the symptoms. SF alone can be attributed to symptoms in only 1%–2% of cases. (49, 68) SFs may result in stent thrombosis, ISR, vessel perforation, and PSA development. In addition, it can be a source of distal embolization. (48)

1.1.2.5. Treatment of femoropopliteal stent fracture

There is no clear recommendation for therapy for SFs. Many consider SF benign, accompanied by a negligible incidence rate of target vessel-related adverse events, and, therefore, advocate only the continuation of antiplatelet therapy. (69) However, if an SF-related complication occurs, invasive therapy usually becomes necessary. Given the variety of possible complications and their invasive therapeutic methods, these are not explained in more detail.

1.1.3. Intervention (site)-related late complication – femoropopliteal in-stent restenosis

ISR is defined as a decrease in luminal diameter within the stent and/or at the proximal and/or distal edges of the stent. (70)

1.1.3.1. Incidence of femoropopliteal in-stent restenosis

Femoropopliteal ISRs can be expected from a few weeks to 2 years after revascularization, with a peak between 9 and 15 months. (71) After 2 years, the probability of occurrence of ISR is lower. (72, 73) The primary patency rate of self-expanding nitinol stents has been reported to be 92%, 86.2%, 79.1%, 75.1%, 62.2%,

and 33% at 6 months, 1 year, 2 years, 3 years, 5 years, and 7 years, respectively. (74–76)

1.1.3.2. Pathophysiology of femoropopliteal in-stent restenosis

ISR is a complex process that involves several overlapping mechanisms. (77) Elastic recoil of the vessel wall (vasoconstriction due to endothelial disruption) is caused by overstretching; it develops from minutes to hours after intervention, but due to the rigid scaffolding of the stents, the role of the elastic recoil is minimal in ISR. (77) ISR can be partitioned into early (days to weeks) and late (weeks to months) phases. (77) The early phase starts with relocation of the axially transmitted plaque, reorganization of the thrombus, and an acute inflammatory response to the vessel wall injury. (77, 78) Reorganization of the thrombus is a process provoked by damage/denudation of the endothelium and medial dissection due to stent implantation. (78) Consequently, platelets are exposed to subintimal molecules, causing their adherence and aggregation, which contribute to the inflammatory reaction. (77, 78) The first step in the inflammatory reaction is an increase in the migration of leukocytes into the vessel wall. The increased migration of leukocytes (predominantly monocyte-derived macrophages) into the arterial wall followed by the continued secretion of cytokines, mitogens, adhesion molecules, and chemoattractants by platelets, monocytes, and smooth muscle cells promotes further leukocyte enrollment and infiltration. (77) The key episode of the late phase is the phenotypic alteration of medial smooth muscle cells pursued by their recruitment and successive proliferation in the intimal layer. (77) Subsequently, extracellular matrix and collagen are synthesized by smooth muscle cells, leading to neointima formation, which is the main cause of ISR. (78)

Neointimal hyperplasia can also be affected by the atherosclerotic process, resulting in a neointimal atherosclerotic change (neoatherosclerosis), which has been shown to contribute to late ISR, occurring usually beyond 5 years. (79–81) Neoatherosclerotic lesions are marked by infiltration and aggregation of lipid-laden foamy macrophages, owing to the inability to sustain a completely functional endothelial surface within the stent. (81, 82) Neoatherosclerotic lesions may also contain calcifications. (81)

1.1.3.3. Predisposing factors for femoropopliteal in-stent restenosis

Known predictors of ISR in patients treated for femoropopliteal steno-occlusive disease include the following: atherosclerotic risk factors, anemia, long-segment stenosis (>100 mm), baseline occlusion, poor runoff, excessive stent oversizing (stent to reference vessel diameter ratio greater than 1.4:1), stent undersizing (although it is more predictive for stent thrombosis than restenosis with a stent to reference vessel diameter ratio less than 1.1:1), long stent, stent placement into the popliteal 3 segment, SF, and high-grade residual stenosis. (22, 51, 83–91)

1.1.3.4. Symptoms of femoropopliteal in-stent restenosis

The symptoms of femoropopliteal ISR are the same as those of peripheral arterial disease. There are several classification systems. (92) The Fontaine classification system grades the clinical presentation of patients to four stages, (92) while the Rutherford classification system grades it to six categories. (93) The Fontaine stages are: I, asymptomatic, incomplete blood vessel obstruction; II, mild claudication pain in limb (IIA, claudication at a distance > 200 m and IIB, claudication at a distance < 200 m); III, rest pain, mostly in the feet; and IV, necrosis and/or gangrene of the limb. (92) The Rutherford categories are: 0, asymptomatic (no hemodynamically significant occlusive disease); 1, mild claudication; 2, moderate claudication; 3, severe claudication; 4, ischemic rest pain; 5, minor tissue loss (nonhealing ulcer, focal gangrene with diffuse pedal ischemia); and 6, major tissue loss (extending above transmetatarsal level, functional foot no longer salvageable). (93)

1.1.3.5. Diagnosis of femoropopliteal in-stent restenosis

Pulse palpation and ankle-brachial index (ABI) measurements are usually supplemented with duplex scanning because ABI has not been proven to be an accurate method to assess ISR (a 15% decrease in ABI was only weakly correlated with clinically significant ISR). (70) In the majority of cases, the location, percentage, morphology, and length of the ISR can be well assessed by ultrasound. (94) If reintervention is deliberated, the duplex scan with a suspicion of significant ISR has to be confirmed by other imaging modalities (CTA or DSA). (94) Unfortunately, conventional MR sequences are not suitable for detecting either vascular calcification or ISR. (94) A

major advantage of DSA over CTA is that establishment of the diagnosis can be combined with therapy. Based on the angiographic appearance, Tosaka et al. (95) classified femoropopliteal ISRs into three categories. Class I (focal ISR) includes lesions ≤50 mm in length located in the body of the stent, at the proximal or distal edge of the stent, or both; class II (diffuse ISR) includes lesions >50 mm in length located in the body of the stent, at the proximal or distal edge of the stent, or both; class III includes total stent occlusions. (95) This classification also has a prognostic value, as the recurrent ISR and occlusion rates at 2 years after percutaneous transluminal angioplasty (PTA) were higher in patients with class III lesions (84.9% and 64.6%, respectively), compared to patients with class I (49.9% and 15.9%, respectively) or class II lesions (53.3% and 18.9%, respectively). (95)

1.1.3.6. Treatment of femoropopliteal in-stent restenosis

Currently, the Society for Vascular Surgery does not endorse prophylactic intervention for ISR in the absence of symptoms, in contrast to vein bypass graft stenosis. (70, 94) Therapy for femoropopliteal ISRs may be pharmacological and/or invasive. (94)

Cilostazol is the only pharmacological treatment that has been noted to decrease the risk of ISR. (70) Cilostazol is a phosphodiesterase inhibitor. Selective inhibition of phosphodiesterase type III causes accumulation of cyclic adenosine monophosphate, which initiates a cascade of events, such as upregulation of the oncogene p53. In turn, p53 blocks cell cycle progression and induces apoptosis in vascular smooth muscle cells, leading to an antiproliferative effect. (96) Thus, the administration of cilostazol may be beneficial in the first 2 years after femoropopliteal stenting. (96, 97)

No standard invasive therapy exists for patients with femoropopliteal ISR. Endovascular options include PTA with plain, cutting, and drug-eluting balloons, stenting with bare metal, drug-eluting, and covered stents, and less frequently atherectomy, cryoplasty, and intravascular brachytherapy. (70) Plain balloon angioplasty is quite feasible; however, it is followed by a high rate of recurrence, suggesting that recoil of hyperplastic lesions occurs frequently. (95) Despite the fact that cutting balloons offer the theoretical advantage of less vessel wall trauma because of controlled incisions by balloon-mounted microtomes, given the uniform rubbery texture of ISR lesions, there has been no demonstrable benefit of cutting balloons over

plain balloons in the recurrent ISR rate, ABI, or maximum walking capacity. (98) The surface of drug-eluting balloons and stents are coated with a thin layer of antiproliferative drug combined with an excipient or spacer substance, which facilitates drug transfer to the vessel wall. As antiproliferative agents, rapamycin and paclitaxel have both been used for femoropopliteal applications. Drug-eluting devices have shown a clinical advantage in terms of patency and freedom from reintervention in several randomized clinical trials, compared to standard PTA and stent implantation. (99–104) Covered stents, like drug-eluting devices, can achieve better patency rates for femoropopliteal ISRs than plain balloons and bare metal stents. (70) In the treatment of ISRs, open surgery (e.g., femoropopliteal bypass grafting) is usually considered only if ISR develops repeatedly and within a short period of time after multiple endovascular interventions, or if the femoropopliteal arterial segment is occluded along its entire length. (70, 87, 105)

DOI:10.14753/SE.2023.2747

2. Objectives

2.1. Study I (Incidence of and predisposing factors for arterial pseudoaneurysm formation – Institutional Review Board Approval No. 176/2020**)**

Since most publications are limited to case series and studies with a small sample size, we aimed:

1) to determine the incidence of arterial PSA development in a large patient population in a high-volume, multidisciplinary, tertiary center; and

2) to identify risk factors for arterial PSA development in a large patient population in a high-volume, multidisciplinary, tertiary center.

2.2. Study II (Safety, clinical outcome, and fracture rate of femoropopliteal stenting using 4F compatible delivery system – Institutional Review Board Approval No. 138/2013**)**

With the exception of the 4-EVER and PEACE I trials, no comprehensive data have been published on 4F stents in patients with femoropopliteal steno-occlusive disease. Therefore, the purpose of this study was:

1) to determine the safety of femoropopliteal stenting using a 4F compatible delivery system;

2) to determine the clinical outcome of femoropopliteal stenting using a 4F compatible delivery system; and

3) to determine the fracture rate of femoropopliteal stenting using a 4F compatible delivery system.

DOI:10.14753/SE.2023.2747

3. Results

3.1. Study I (Incidence of and predisposing factors for arterial pseudoaneurysm formation)

3.1.1. Background information for interpreting the results

All electronic medical records for PSA development were examined at Semmelweis University Heart and Vascular Center in 30,196 patients who underwent any type of radiological or cardiac endovascular procedure (including electrophysiological interventions) requiring arterial puncture. The study covered the period from January 2016 to May 2020. Furthermore, PSAs resulting from procedures where arterial puncture was unintended were also collected. However, PSAs associated with aortic stent graft implantation by vascular surgeons were not included in the study.

Endovascular and electrophysiological procedures were conducted by vascular interventional radiologists, invasive cardiologists, or electrophysiologists in a standard manner. The patient received at least 5,000 IU heparin intra-arterially for each therapeutic intervention, and many cardiological procedures required the administration of weight-based heparin, eptifibatide, prasugrel, or alteplase. If the patient was not already on single (acetylsalicylic acid [ASA], 100 mg/day or clopidogrel, 75 mg/day orally) or dual antiplatelet medication, an oral or intravenous loading dose (ASA, 250–500 mg and/or clopidogrel, 300–600 mg) was given immediately after the intervention.

Following the procedures, the access site was managed as follows: a compression assist device (TR Band; SCW Medicath Ltd., Shenzhen, China or Radial Compression Hemostasis Device; Fervid Medical Technology Co., Guangdong, China) was applied over the puncture site for 2–4 hours in the case of radial and ulnar arteries, while in the case of the brachial artery, standard therapy was manual compression followed by pressure bandaging for 4–6 hours. Hemostasis was achieved in individuals with femoral artery puncture by manual compression followed by pressure bandaging for 6–8 hours, or by using a VCD (Angio-Seal; Terumo Corp., Tokyo, Japan, Exoseal; Cordis Corp., Hialeah, FL, USA, or Perclose ProGlide; Abbott Laboratories, Chicago, IL, USA).

Color Doppler ultrasound scanning was performed by a licensed vascular technician or radiologist in the presence of pain, swelling, skin changes, and/or bruit at

the site of sheath removal or any other abnormality. The size of the PSA sac, its number of compartments, the width and length of the PSA neck, and the distance between the top of the PSA sac and the skin surface were all measured in each patient.

Patients with PSA received pressure bandage, UGC, UGTI, or open surgical repair. (1, 5–7, 12) Replacement of the pressure bandage or UGC was attempted in patients whose coagulation status was normal, PSA was identified within a week of the procedure, the PSA sac was superficial, simplex, and tiny (<20 mm), and the PSA neck was long and narrow. (12, 20) UGTI or open surgical repair was used in other cases. When the PSA created local mass effect issues, was infected, had a short (<4 mm) and wide neck, or other minimally invasive procedures failed, open surgical repair was required. (20, 106) UGC and UGTI were carried out as described by Fellmeth et al. in 1991 and Cope and Zeit et al. in 1986. (106, 107) In the instance of UGTI, 500–1,000 U/mL bovine thrombin (Tisseel tissue adhesive; Baxter Healthcare Corp., Largo, FL, USA) was injected into the PSA sac. A simple suture of the arterial defect, patch plasty, or interposition grafting were all options for open surgical treatment. One day after treatment, color Doppler ultrasonography examination was carried out to assess the success of the pressure bandage replacement, UGC, and UGTI. After that, imaging was only performed if there were any relevant complaints or symptoms.

For statistical analysis, R version 4.0.0 (released on April 24, 2020) was used (R Core Team [2020]; R: A language and environment for statistical computing; R Foundation for Statistical Computing, Vienna, Austria).

3.1.2. The results obtained

In total, 134 PSAs were found in 134 subjects during the study period. Invasive vascular radiological procedures produced 53 PSAs (53/6,555 [0.8%]), invasive coronary artery procedures produced 31 PSAs (31/18,038 [0.2%]), and invasive non-coronary artery cardiac procedures produced 25 PSAs (25/5,603 [0.4%]). In addition, 25 PSA cases were caused by inadvertent artery puncture during procedures. The incidence of PSA was found to be significantly different between the vascular radiological and coronary artery groups (P<0.001 – chi-squared test), between the vascular radiological and non-coronary artery cardiac groups (P=0.038 – chi-squared test), and between the coronary artery and non-coronary artery cardiac groups (P=0.001 – chi-squared test). Thirty-four

DOI:10.14753/SE.2023.2747

PSAs (25.4%) were identified on the upper extremity arteries, while 100 (74.6%) arose from the lower extremity arteries. (Figures 4 and 5)

DOI:10.14753/SE.2023.2747

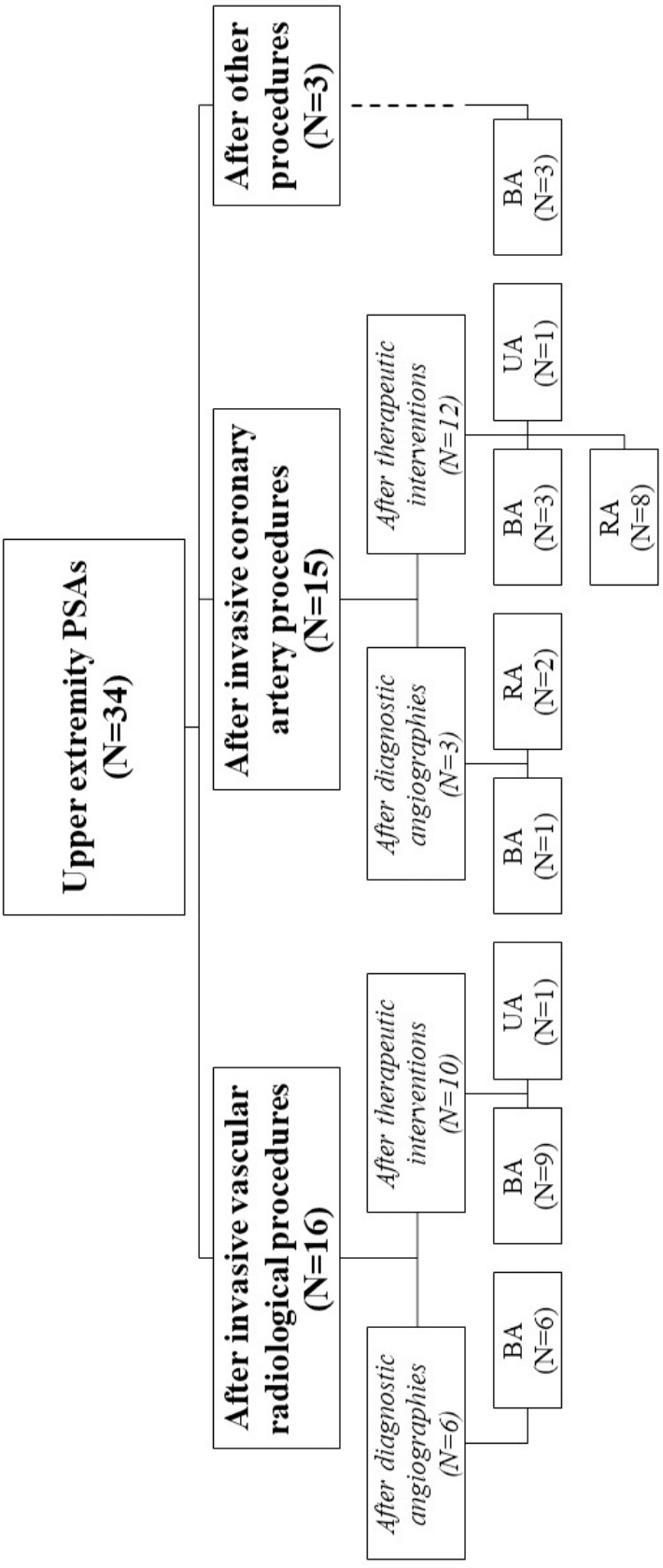


Figure 4. Upper extremity pseudoaneurysms

BA, Brachial artery; *PSA*, pseudoaneurysm; *RA*, radial artery; *UA*, ulnar artery.

DOI:10.14753/SE.2023.2747

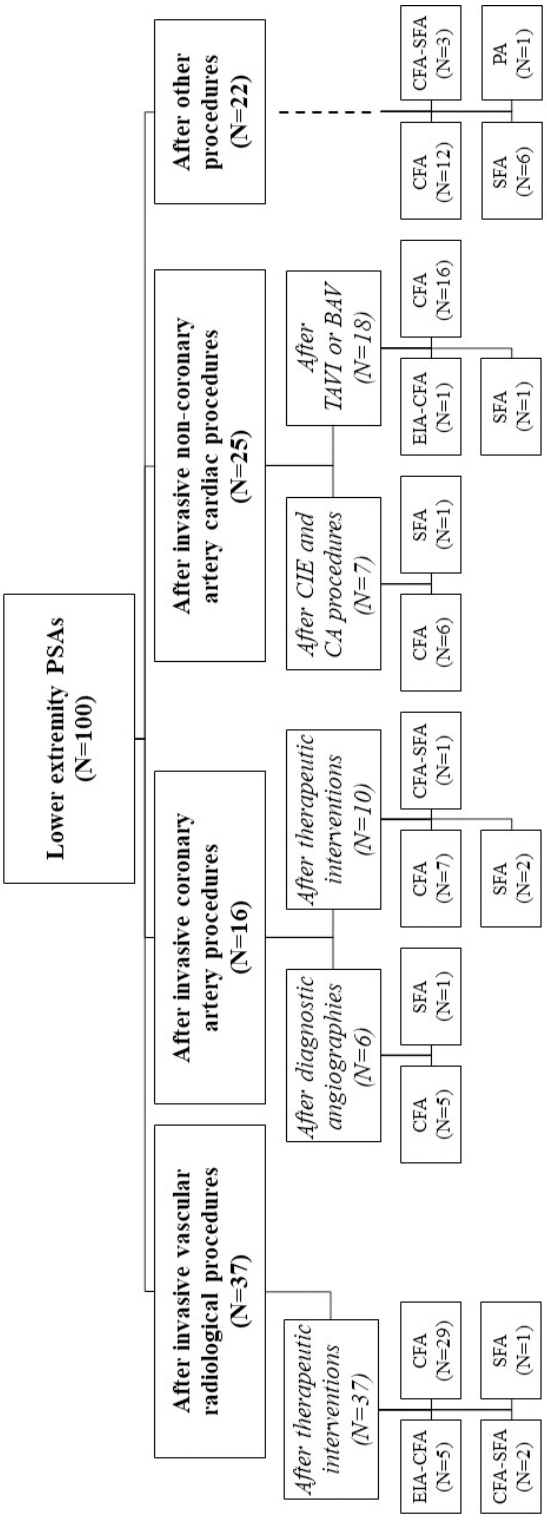


Figure 5. Lower extremity pseudoaneurysms

BAV, Balloon aortic valvuloplasty; *CA*, catheter ablation; *CFA*, common femoral artery; *CIE*, clinical intracardiac electrophysiological; *EIA*, external iliac artery; *PA*, popliteal artery; *PSA*, pseudoaneurysm; *SFA*, superficial femoral artery; *TAVI*, transcatheter aortic valve implantation.

The mean (± standard deviation [SD]) age of the 134 patients (women, N=72; men, N=62) was 69.5 (±15.2) years. Twenty-eight patients (20.9%) were obese (body mass index [BMI] >30 kg/m^2), 76 (56.7%) were smokers, 123 (91.8%) had hypertension, 51 (38.1%) had dyslipidemia, 37 (27.6%) had diabetes mellitus, and 37 (27.6%) had chronic kidney disease. The medication regimens of the patients are provided in Table 1.

Table 1. Medication regimens of patients with a pseudoaneurysm

Medications	Patients with an upper extremity PSA (N=34)	Patients with a lower extremity PSA (N=100)
ASA monotherapy, N (%)	1 (2.9)	14 (14)
Clopidogrel monotherapy, N (%)	2 (5.9)	6 (6)
Dual antiplatelet therapy, N (%)	11 (32.4)	24 (24)
Cilostazol therapy, N (%)	1 (2.9)	0 (0)
Dual antiplatelet therapy + cilostazol therapy, N (%)	0 (0)	2 (2)
Conventional anticoagulant therapy, N (%)	5 (14.7)	15 (15)
Mono antiplatelet therapy + conventional anticoagulant therapy, N (%)	7 (20.6)	13 (13)
Dual antiplatelet therapy + conventional anticoagulant therapy, N (%)	5 (14.7)	1 (1)
NOAC therapy, N (%)	0 (0)	16 (16)
Mono antiplatelet therapy + NOAC therapy, N (%)	0 (0)	8 (8)
Dual antiplatelet therapy + NOAC therapy, N (%)	1 (2.9)	3 (3)

ASA, Acetylsalicylic acid; *NOAC*, novel oral anticoagulant; *PSA*, pseudoaneurysm.

Upper extremity pseudoaneurysms

Sixteen (47.1%) of 34 upper extremity PSAs were observed after invasive vascular radiological procedures, 15 (44.1%) after invasive coronary artery procedures, and three (8.8%) were due to procedures in which the arterial puncture was unintended. These procedures included the placement of a peripheral intravenous catheter (N=2) and cannulation of a fistula for dialysis (N=1). In four patients (4/31 [12.9%]), an antegrade puncture resulted in PSA. The brachial artery was the site of the antegrade puncture, and all four patients underwent hemodialysis fistula angioplasty.

Localization and sheath-related parameters are shown in Figure 4 and Table 2. VCD was not used in any of the patients.

Table 2. Localization and sheath-related parameters of patients with an upper extremity pseudoaneurysm

Localization, sheath-related parameters	Patients with an upper extremity PSA (N=34)
Localization	
Brachial artery, N (%)	22 (64.7)[a]
Radial artery, N (%)	10 (29.4)[b]
Ulnar artery, N (%)	2 (5.9)[c]
Sheath size[d]	
4F, N (%)	4/31 (12.9)
5F, N (%)	7/31 (22.6)
6F, N (%)	17/31 (54.8)
7F, N (%)	2/31 (6.5)
8F, N (%)	1/31 (3.2)
Sheath replacement, N (%)	11/31 (35.5)
Time spent by the sheath in the artery (minutes), mean (SD)	31.3 (24.4)

PSA, Pseudoaneurysm; *SD*, standard deviation.

[a] 22/1,897 (1.2%)—all brachial artery punctures.

[b] 10/20,478 (0.05%)—all radial artery punctures.

[c] 2/1,818 (0.1%)—all ulnar artery punctures.

[d] The largest sheath size used was counted for each patient.

The PSA sac had a mean (±SD) diameter of 22.4 (±14.5) mm and a mean (±SD) length of 13.1 (±8.8) mm. The PSA neck measured 2.6 (±0.8) mm in width and 7.3 (±7.2) mm in length. Two patients (5.9%) had PSA with more than one compartment. The top of the PSA sac was 6.2 (±3.9) mm from the skin surface on average (±SD).

Eleven PSAs (32.4%) were treated with replacement of the pressure bandage, four (11.8%) with UGC, 13 (38.2%) with UGTI, and six (17.6%) with open surgical repair (simple suture of the arterial defect, N=6). In three cases (8.8%), the PSA was not successfully eliminated in the first try. In two cases, the replacement of the pressure bandage, in one case, the UGTI failed. For those in whom replacing the pressure bandage did not result in the elimination of PSA, UGTI was used as a last resort, while the third patient received interposition grafting. The primary success rate for replacing the pressure bandage was 81.8%, with UGC at 100%, UGTI at 92.3%, and open surgical repair at 100%. No complications were reported during PSA treatments.

Lower extremity pseudoaneurysms

PSAs were found in 37 (37%) of 100 lower extremity patients after invasive vascular radiological procedures, 16 (16%) after invasive coronary artery procedures, 25 (25%) after invasive non-coronary artery cardiac procedures, and 22 (22%) after procedures that resulted in an unintended arterial puncture. Procedures in the latter group included electrophysiological therapies for arrhythmias (N=20), cannulation of a deep vein for catheter-directed thrombolysis (N=1), and insertion of a central venous catheter for therapeutic plasma exchange (N=1). The prevalence of femoral artery PSA was 0.4% (99/22,202) in the whole patient group, while it was 2.9% (18/630) in a subgroup of patients with BAV or TAVI. In TAVI, both femoral arteries were punctured; therefore, the PSA prevalence for the punctured artery was 1.2% (14/1,126) in the case of TAVI. The femoral artery PSA prevalence for the punctured artery was 0.4% (81/21,009) for the other procedures. In 11 patients (11/78 [14.1%]), PSA occurred after an antegrade puncture. The intended site of the antegrade puncture was the common femoral artery in all patients.

Localization, sheath- and VCD-related parameters can be seen in Figure 5 and Table 3. The prevalence of PSA for the punctured artery with and without VCD use was 37/3,555 (1%) and 97/27,204 (0.4%), respectively (odds ratio [OR], 2.94; 95% confidence interval [CI], 1.95–4.34; P<0.001 – chi-squared test).

Table 3. Localization, sheath- and vascular closure device-related parameters of patients with a lower extremity pseudoaneurysm

Localization, sheath- and VCD-related parameters	Patients with a lower extremity PSA (N=100)
Localization	
Transition between the EIA and the CFA, N (%)	6 (6)
CFA, N (%)	75 (75)
Transition between the CFA and the SFA, N (%)	6 (6)
SFA, N (%)	12 (12)
Popliteal artery, N (%)	1 (1)
Sheath size[a]	
4F, N (%)	1/78 (1.3)
5F, N (%)	11/78 (14.1)
6F, N (%)	55/78 (70.5)
8F, N (%)	2/78 (2.6)
9F, N (%)	2/78 (2.6)
12F, N (%)	1/78 (1.3)
14F, N (%)	1/78 (1.3)
16F, N (%)	5/78 (6.4)
Sheath replacement, N (%)	19/78 (24.4)
Time spent by the sheath in the artery (minutes), mean (SD)	55.4 (34.7)
PSA development despite the use of a VCD, N (%)	37 (37)

VCD type	
Angio-Seal, N (%)	30/37 (81.1)[b]
Perclose ProGlide, N (%)	6/37 (16.2)[c]
Exoseal, N (%)	1/37 (2.7)[d]

CFA, Common femoral artery; *EIA*, external iliac artery; *PSA*, pseudoaneurysm; *SD*, standard deviation; *SFA*, superficial femoral artery; *VCD*, vascular closure device.

[a] The largest sheath size used was counted for each patient.

[b] 30/2,894 (1%)—all Angio-Seal cases.

[c] 6/563 (1.1%)—all Perclose ProGlide cases.

[d] 1/98 (1%)—all Exoseal cases.

The PSA sac had a mean (±SD) diameter of 27 (±16.1) mm and a mean (±SD) length of 19 (±11.4) mm. The PSA neck measured 3.3 (±1.3) mm in width and 10.8 (±7.1) mm in length. Thirty patients (30%) had PSA with more than one compartment. The top of the PSA sac was 13.2 (±7.8) mm from the skin surface on average (±SD).

Fourteen PSAs (14%) were treated with replacement of the pressure bandage, one (1%) with UGC, 73 (73%) with UGTI, and 12 (12%) with open surgical repair (simple suture of the arterial defect, N=8; patch plasty, N=2; interposition grafting, N=2). In 16 cases (16%), the PSA was not successfully eliminated in the first try. In six cases, the replacement of the pressure bandage, in 10 cases, the UGTI failed. The final solution for those whose PSA did not disappear after the first attempt was either UGTI (N=3) or simple suture of the arterial defect (N=13). The primary success rate for replacing the pressure bandage was 57.1%, with UGC at 100%, UGTI at 86.3%, and open surgical repair at 100%. No complications were reported during PSA treatments.

Comparison of patients with and without pseudoaneurysm

A control group of 134 patients was created to reveal predictors of PSA formation. Controls were randomly selected in a 1:1 fashion matched according to age, gender, and the type of procedure, either from the study population (for patients with PSA in whom the arterial puncture was intended, N=109) or from our medical record archiving system (for patients with PSA in whom the arterial puncture was unintended, N=25). (Table 4)

Table 4. Characteristics of the pseudoaneurysm and the control group

Parameters	Patients with PSA (N=134)	Control group (N=134)	P-value
Demographic parameters			
Age (years) Mean (SD) Median (IQR)	 69.5 (15.2) 72.5 (15.8)	 69.5 (15.2) 72.5 (15.8)	1.000
Female sex, N (%)	72 (53.7)	72 (53.7)	1.000
Atherosclerotic risk factors			
BMI >30 kg/m^2, N (%)	28 (20.9)	25 (18.7)	0.759
Smoking, N (%)	76 (56.7)	77 (57.5)	1.000
Hypertension, N (%)	123 (91.8)	115 (85.8)	0.175
Dyslipidemia, N (%)	51 (38.1)	45 (33.6)	0.446
Diabetes mellitus, N (%)	37 (27.6)	39 (29.1)	0.892
Chronic kidney disease, N (%)	37 (27.6)	40 (29.9)	0.787
Preprocedural blood test parameters			
White blood cells (G/L) Mean (SD) Median (IQR)	 8.47 (3.45) 8.05 (3.25)	 7.87 (3.55) 7.39 (3.54)	0.160
Red blood cells (T/L)			<0.001

Mean (SD) Median (IQR)	4.13 (0.80) 4.01 (1.12)	4.59 (0.51) 4.60 (0.65)	
Hematocrit (L/L) Mean (SD) Median (IQR)	 0.37 (0.06) 0.37 (0.08)	 0.41 (0.05) 0.42 (0.05)	 <0.001
Hemoglobin (g/dL) Mean (SD) Median (IQR)	 122 (22.4) 122 (32.0)	 138 (15.2) 139 (19.5)	 <0.001
Platelets (G/L) Mean (SD) Median (IQR)	 227 (86.4) 206 (99.0)	 233 (72.6) 222 (90.3)	 0.546
Prothrombin activity (%) Mean (SD) Median (IQR)	 81.7 (18.7) 83.0 (25.5)	 89.9 (14.3) 92.0 (7.8)	 <0.001
International normalized ratio (IU) Mean (SD) Median (IQR)	 1.19 (0.25) 1.14 (0.24)	 1.10 (0.17) 1.06 (0.08)	 <0.001
Creatinine (μmol/L) Mean (SD) Median (IQR)	 129.0 (144.0) 89.0 (48.5)	 90.2 (59.9) 77.5 (26.5)	 0.005
Procedure types			
Vascular radiological, N (%)	53 (39.6)	53 (39.6)	1.000
Coronary artery, N (%)	31 (23.1)	31 (23.1)	1.000
Non-coronary	25 (18.7)	25 (18.7)	1.000

artery cardiac, N (%)			
Others, N (%)	25 (18.7)	25 (18.7)	1.000
Access site			
Upper extremity, N (%)	34 (25.4)	30 (22.4)	0.667
Sheath size			
>8F, N (%)	9 (6.7)	11 (8.2)	0.816
Closure device, N (%)	37 (27.6)	14 (10.4)	<0.001

BMI, Body mass index; *IQR*, interquartile range; *PSA*, pseudoaneurysm; *SD*, standard deviation.

P-values are based on the chi-squared test for categorical variables and Welch's *t*-test for continuous variables.

A logistic regression model was used to determine which parameters had a significant effect on PSA formation and how strong that effect was. To avoid the multicollinearity problem caused by the high correlation between red blood cell (RBC) count, hematocrit (HCT), and hemoglobin (Hb) values, three final models were developed. White blood cell, RBC (or HCT or Hb), and platelet counts; international normalized ratio (INR) and creatinine levels; BMI >30 kg/m^2; atherosclerotic risk factors/comorbidities; puncture site; and sheath size were all included in the models. The effect of RBC count (OR, 0.33; at average INR value), HCT value (OR, 0.87; at average INR value), Hb value (OR, 0.96; at average INR value), INR (OR, 12.97; at average RBC count), the RBC count—INR interaction (OR, 22.28) (or the HCT value—INR interaction [OR, 1.35] or the Hb value—INR interaction [OR, 1.08]), and the RBC count—VCD use interaction (OR, 3.27) (or the HCT value—VCD use interaction [OR, 1.17] or the Hb value—VCD use interaction [OR, 1.05]) on PSA formation was significant. (Table 5) Figure 6 depicts the single effect of RBC count, HCT, Hb, and INR levels on PSA formation. Neither other laboratory parameters, nor atherosclerotic risk factors and comorbidities, site of the puncture, and size of the sheath used showed correlation with the development of PSA.

DOI:10.14753/SE.2023.2747

Table 5. Predictors of pseudoaneurysm formation

Parameters	OR	95% CI	P-value
BMI >30 kg/m^2	1.19	0.56–2.53	0.626
Smoking	1.06	0.60–1.88	0.835
Hypertension	1.94	0.77–4.93	0.153
Dyslipidemia	1.37	0.78–2.44	0.276
Diabetes mellitus	0.73	0.39–1.38	0.332
Chronic kidney disease	0.76	0.41–1.44	0.403
WBC count	1.06	0.97–1.16	0.190
RBC count	0.33	0.21–0.52	<0.001
HCT value	0.87	0.82–0.91	<0.001
Hb value	0.96	0.94–0.97	<0.001
Platelet count	1.00	0.10–1.00	0.857
INR	12.97	2.58–65.30	<0.001
Creatinine level	1.00	0.10–1.01	0.059
Upper extremity access	1.12	0.58–2.16	0.727
>8F sheath	1.01	0.35–2.95	0.985
Closer device	3.58	1.71–7.47	<0.001
RBC count—INR interaction	22.28	2.91–170.61	0.003
HCT value—INR interaction	1.35	1.07–1.71	0.014
Hb value—INR interaction	1.08	1.01–1.16	0.036
RBC count—closer device use interaction	3.27	1.09–9.80	0.036
HCT value—closer device use	1.17	1.02–1.34	0.022

interaction			
Hb value—closer device use interaction	1.05	1.01–1.09	0.012

BMI, Body mass index; *CI*, confidence interval; *Hb*, hemoglobin; *HCT*, hematocrit; *INR*, international normalized ratio; *OR*, odds ratio; *RBC*, red blood cell; *WBC*, white blood cell.

For statistical analysis, ANOVA and likelihood-ratio tests were calculated (using package car [version 3.0.8] with the function Anova).

DOI:10.14753/SE.2023.2747

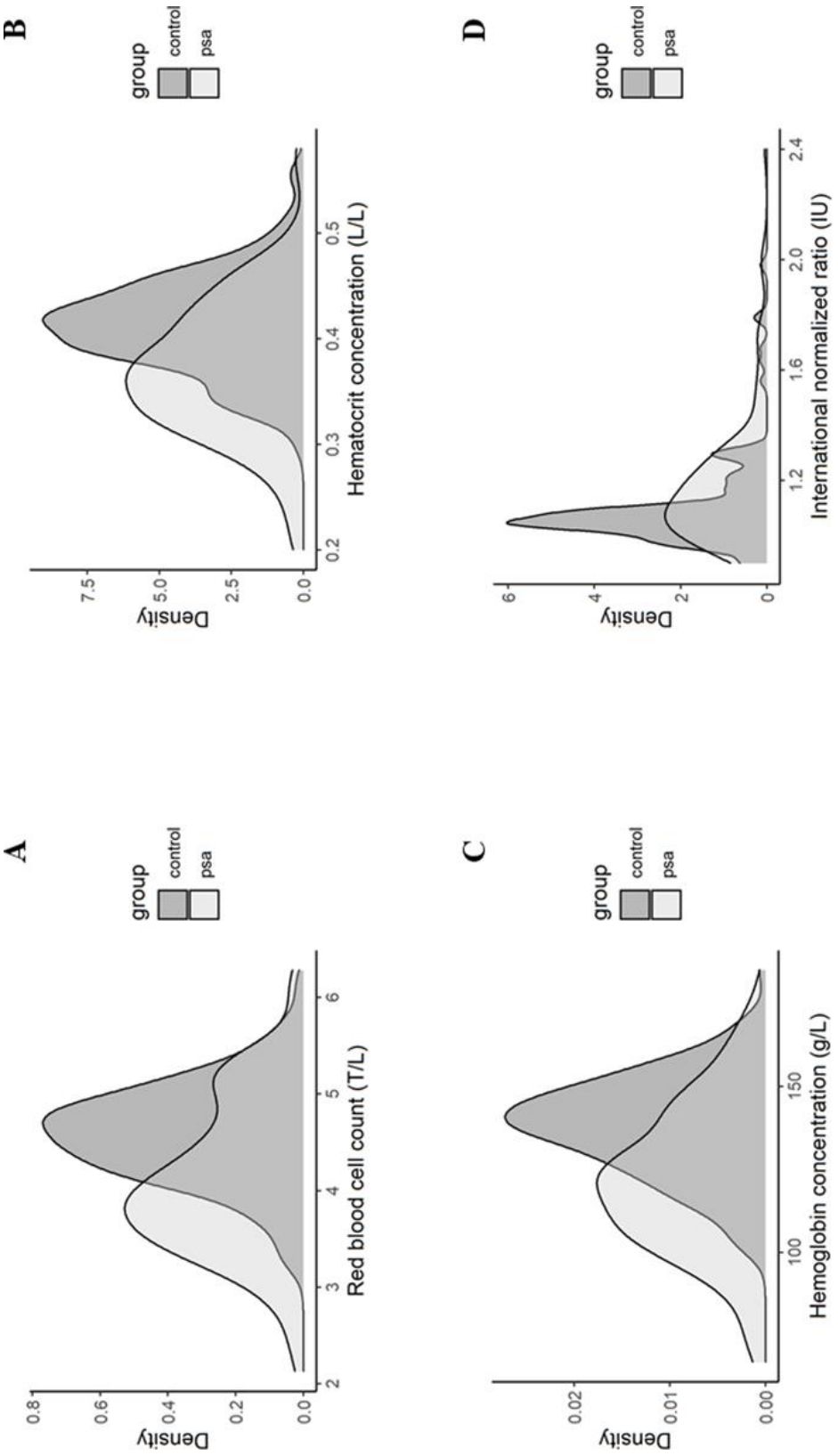


Figure 6. The single effect of red blood cells (A), hematocrit (B), hemoglobin (C), and international normalized ratio (D) on pseudoaneurysm development

Kernel density plots of distributions.

3.2. Study II (Safety, clinical outcome, and fracture rate of femoropopliteal stenting using 4F compatible delivery system)

3.2.1. Background information for interpreting the results

Between January 2010 and December 2011, 441 patients underwent femoropopliteal endovascular intervention. In this retrospective study, only 112 consecutive patients with severe claudication (Rutherford–Becker score = 3) or chronic CLI (Rutherford–Becker score = 4–6) who received stenting with a 4F compatible delivery device were examined. (93) The indication for stent implantation was suboptimal PTA due to unfavorable morphology of the lesion (severe calcification and complete occlusion) or failed angioplasty (residual stenosis ≥30% and flow-limiting dissection). Vascular interventional radiologists performed all of the stentings. At each intervention, the patient received at least 5,000 IU heparin intra-arterially. If the patient was not already on single (ASA, 100 mg/day orally or clopidogrel, 75 mg/day orally) or dual antiplatelet therapy, an oral or intravenous loading dose was given immediately following the procedure (ASA, 250–500 mg and/or clopidogrel, 300–600 mg). Hemostasis after femoral artery puncture was achieved by manual compression, followed by pressure bandage placement for 6–8 hours. The procedures were performed at the Heart and Vascular Center and at the Department of Radiology and Oncotherapy of Semmelweis University.

Follow-up visits were due 4 weeks, 3–6 months, and 12 months after the procedure, and then once a year. These dates were changed in the event of a symptom/complaint or any invasive arterial therapy. Symptoms were evaluated, femoropopliteal and foot pulses were palpated, and ABI was measured during follow-up exams. Patients with worsening symptoms, an impalpable popliteal pulse, and an ABI of less than 0.5 were suspected of having a significant ISR. Ultrasonography, CTA, and DSA were used to confirm the presence of ISR. Patency rates were classified as primary (patients without ISR; stents remained patent without further intervention), primary assisted (patients with significant ISR; patients required additional intervention to preserve stent patency), and secondary (patients with stent occlusion; stent patency needed to be re-established by another intervention). (108) Target lesion revascularization was defined as any repeat percutaneous intervention of the target

lesion (including 5 mm proximal and distal to the stent) or surgical bypass of the target vessel performed for restenosis or other complication involving the target lesion, whereas target vessel revascularization meant any repeat percutaneous intervention or surgical bypass of any segment of the target vessel. (109)

Patients were asked to return for an extra follow-up visit in 2013, during which a fluoroscopic SF evaluation was performed in addition to the above-mentioned tests. The high magnification fluoroscopic examinations were performed in an angiography suite (AXIOM Artis FA; Siemens Medical Solutions AG Corp., Erlangen, Germany) with the following parameters: 7.5 frames per second, 100–125 kV, and 550–800 mA (Heart and Vascular Center); or in an examination room with an X-ray system using a digital flat panel (Carestream DRX-1 System; Carestream Health Inc., Rochester, NY, USA) with the following parameters: 60–70 kV, 63 mA with a grid (Department of Radiology and Oncotherapy). To visualize the implanted stents, three cine loops with a length of three cardiac cycles (Heart and Vascular Center) or digital X-rays (Department of Radiology and Oncotherapy) were recorded in posteroanterior, and right and left anterior oblique 30–45° projections. The postprocessing was accomplished on a Leonardo workstation (Syngo 2003; Siemens Medical Solutions AG Corp., Erlangen, Germany) (Heart and Vascular Center) or on a PACS workstation (IMPAX 6.5.2; Agfa HealthCare NV Corp., Mortsel, Belgium) (Department of Radiology and Oncotherapy). Two experienced interventional radiologists assessed the fluoroscopic images in agreement. The Cardiovascular Institute of the South created a nitinol stent fracture classification, which was used to define SFs (Houma, LA, USA). (46) Type I = single strut fracture, type II = multiple strut fractures at different sites in the stent, type III = multiple strut fractures resulting in complete transverse stent fracture, and type IV = complete transverse fracture with stent separation.

Statistical analysis was performed with SPSS 21.0 software (IBM, Armonk, NY, USA).

3.2.2. The results obtained

Patient data

Because 10 patients were lost to follow-up, they were not included in the analysis. The remaining 102 patients (women, N=40; men, N=62) had a mean (±SD) age of 66.4 (±10.1) years. Severe claudication was the reason for femoropopliteal revascularization in 63 patients (61.8%) and chronic CLI in 39 patients (38.2%). At the time of intervention, none of the patients had significant ipsilateral iliac or common femoral artery stenosis. Atherosclerotic risk factors included obesity (BMI >30 kg/m^2) in 44 patients (43.1%), smoking in 89 (87.3%), hypertension in 96 (94.1%), dyslipidemia in 41 (40.2%), diabetes mellitus in 42 (41.2%), and chronic kidney disease in 16 (15.7%). Twenty-seven patients (26.5%) had coronary artery bypass grafting and/or percutaneous coronary intervention, 23 (22.5%) had supra-aortic surgical and/or endosurgical reconstruction, and 21 (20.6%) had lower extremity open and/or percutaneous revascularization, according to the medical history.

Lesion, procedure, and stent characteristics

A total of 114 lesions were treated. In 87 cases (76.3%), the lesions were *de novo* stenoses, and in 27 cases (23.7%), the lesions were restenoses after previous PTA. Sixty-four (56.1%) of the lesions treated were stenoses, whereas 50 (43.9%) were total occlusions. In 49 cases (43%), the lesions were long and in 35 cases (30.7%), they were heavily calcified. Long lesions were those that were longer than 100 mm, while heavily calcified lesions were those with calcification apparent on fluoroscopy more than 75% of the length of the stenotic or occluded segment. The side distribution of the lesions was almost equal (left, N=58; right, N=56). Lesions were located in the superficial femoral artery in 36 cases (31.6%), in the femoropopliteal transitional zone in 47 (41.2%), and in the popliteal artery in 31 (27.2%). According to the TransAtlantic Inter-Society Consensus (TASC) classification, (110) the lesions were TASC–A, TASC–B, TASC–C, and TASC–D in 35 (30.7%), 34 (29.8%), 30 (26.3%), and 15 cases (13.2%), respectively. (Table 6)

DOI:10.14753/SE.2023.2747

Table 6. Lesion characteristics

Variables	Lesions (N=114)
Underlying pathology	
Atherosclerosis, N (%)	87 (76.3)
Restenosis, N (%)	27 (23.7)
Stenosis grade (%), mean (SD)	91.5 (8.8)
Total occlusion, N (%)	50 (43.9)
Length (mm), mean (SD)	80.9 (64.1)
Length ≥100 mm, N (%)	49 (43)
Calcification, N (%)	57 (50)
Heavy calcification, N (%)	35 (30.7)
Location	
Proximal SFA, N (%)	2 (1.8)
Proximal–mid SFA, N (%)	6 (5.3)
Mid SFA, N (%)	7 (6.1)
Mid–distal SFA, N (%)	6 (5.3)
Distal SFA, N (%)	7 (6.1)
Entire SFA, N (%)	8 (7)
Femoropopliteal transitional zone, N (%)	47 (41.2)
P1–2 segments, N (%)	15 (13.2)
P1–3 or P2–3 segments, N (%)	16 (14)

P, Popliteal; *SD*, standard deviation; *SFA*, superficial femoral artery.

In 79 cases, the procedures were performed with an ipsilateral antegrade approach and in 31 cases, with a contralateral crossover approach. Due to failed recanalization through the femoral artery in two patients, an ipsilateral retrograde approach (one through the popliteal artery and the other through the dorsalis pedis artery) was required. A total of 119 stents were implanted. All patients received self-expanding nitinol stents (Astron Pulsar, N=42; Pulsar-18, N=77; Biotronik AG, Bülach, Switzerland). Forty-six (38.7%) of the deployed stents were long and 10 (8.4%) were implanted in a partially overlapping position. (Table 7) Stents with a length of 120 mm

or more were considered long. In 17 patients (16.7%), below the knee interventions were also performed.

Table 7. Stent characteristics

Variables	Stents (N=119)
Type	
4F Astron Pulsar, N (%)	42 (35.3)
4F Pulsar-18, N (%)	77 (64.7)
Length (mm), mean (SD)	92.2 (53.0)
Length ≥120 mm, N (%)	46 (38.7)
Overlapping stents, N (%)	10 (8.4)

Early postprocedural period (within 30 days)

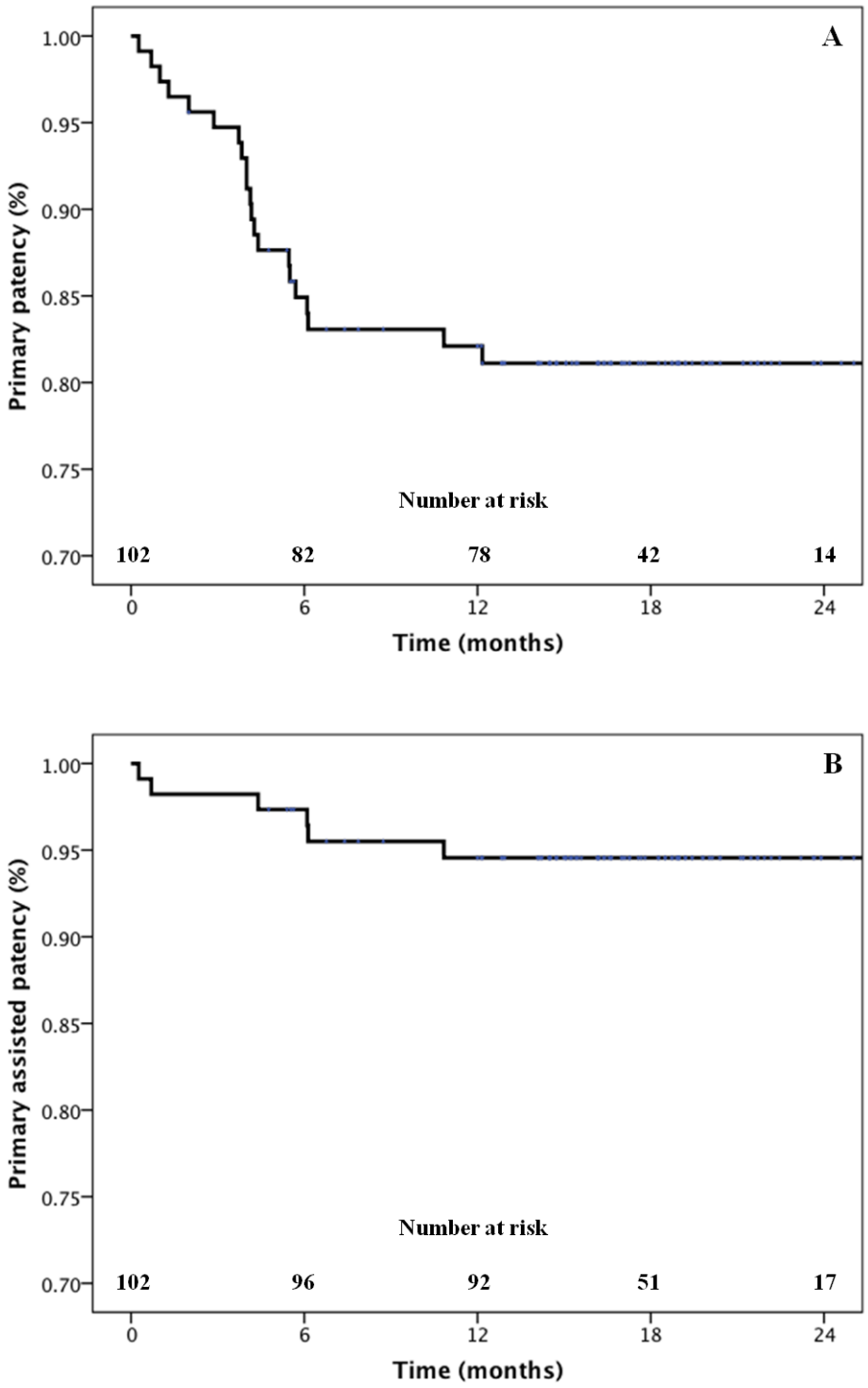
The technical success rate, which was defined as <30% residual stenosis without dissection or extravasation, was 100%. Two patients (2%) developed PSA at the femoral puncture site, and both were treated with UGTI. The 30-day all-cause mortality rate was zero. Minor amputations were performed on five individuals (4.9%) (interphalangeal, N=2; ray, N=2; and transmetatarsal, N=1). All patients mentioned improvement or resolution of the preprocedural symptoms.

Follow-up period

The mean (±SD) follow-up time was 25.3 (±6.2) months. Eleven patients (10.8%) died during the follow-up period (acute myocardial infarction, N=4; stroke, N=2; and malignancy, N=5). Significant (≥70%) ISR was observed in 21 patients (20.6%). Target lesion revascularization was carried out in 15 patients (14.7%; PTA, N=13 and stenting, N=2), while target vessel revascularization was performed in six patients (5.9%; PTA, N=3; stenting, N=1; and open surgery, N=2). Major amputation was necessary in nine patients (8.8%; below the knee, N=5 and above the knee, N=4). Indications for amputation were acute ischemia in four cases and chronic ischemia in five cases. All stents were patent in the below the knee amputation group, while all stents were blocked in the above the knee amputation group. The primary, primary assisted, and secondary

DOI:10.14753/SE.2023.2747

patency rates were 83.1%, 97.2%, 86.2%, respectively, at 6 months and 80.4%, 94.3%, 85.4%, respectively, at 12 months. (Figure 7)



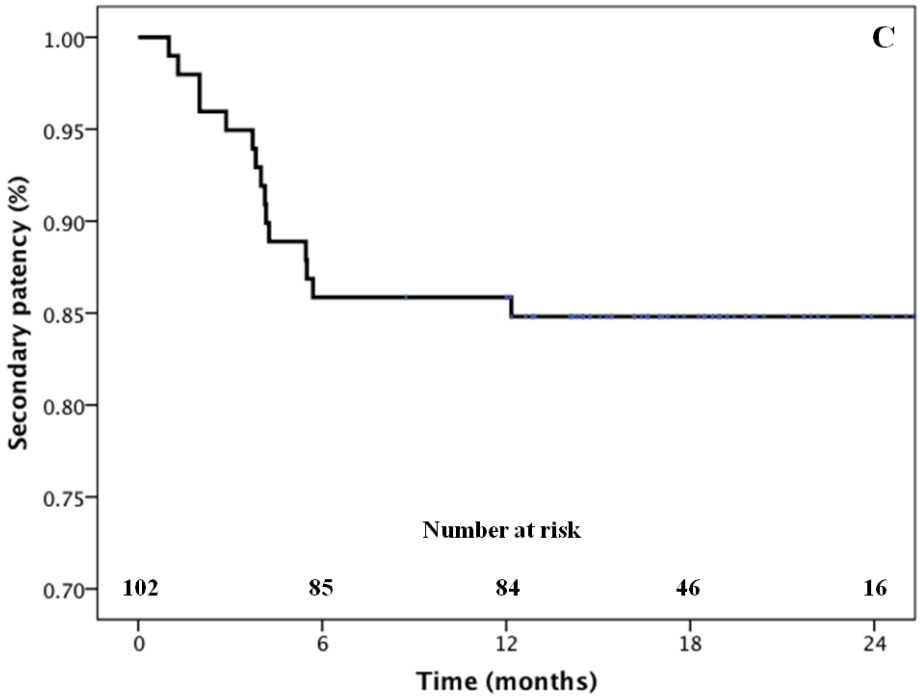


Figure 7. Primary (A), primary assisted (B), and secondary patency rates (C)

Kaplan–Meier curves.

The mean (±SD) Rutherford–Becker classification improved from 3.9 (±1.1) before the procedure to 2.1 (±1.4) at the most recent follow-up (P<0.001 – Mann–Whitney *U* test). The mean (±SD) resting ABI improved from 0.5 (±0.1) before the procedure to 0.8 (±0.2) at the most recent follow-up (P<0.001 – Student *t*-test).

Stent fracture

Patients who died or underwent above the knee amputation and who had stents that were placed during the follow-up were excluded from the analysis of SF. A total of 104 stents were analyzed. In 87 patients, 27 SFs (26%) were found: type I in nine cases, type II in eight cases, type III in five cases, and type IV in five cases. (Figure 8) In 83% of the stents, the fracture was localized to their middle part. The number of patients with ISR (occurring at any time throughout the follow-up) was significantly higher in the fractured group than in the non-fractured group (N=15 versus N=2; P<0.001 – chi-squared test) at the time of the fluoroscopic study.

DOI:10.14753/SE.2023.2747

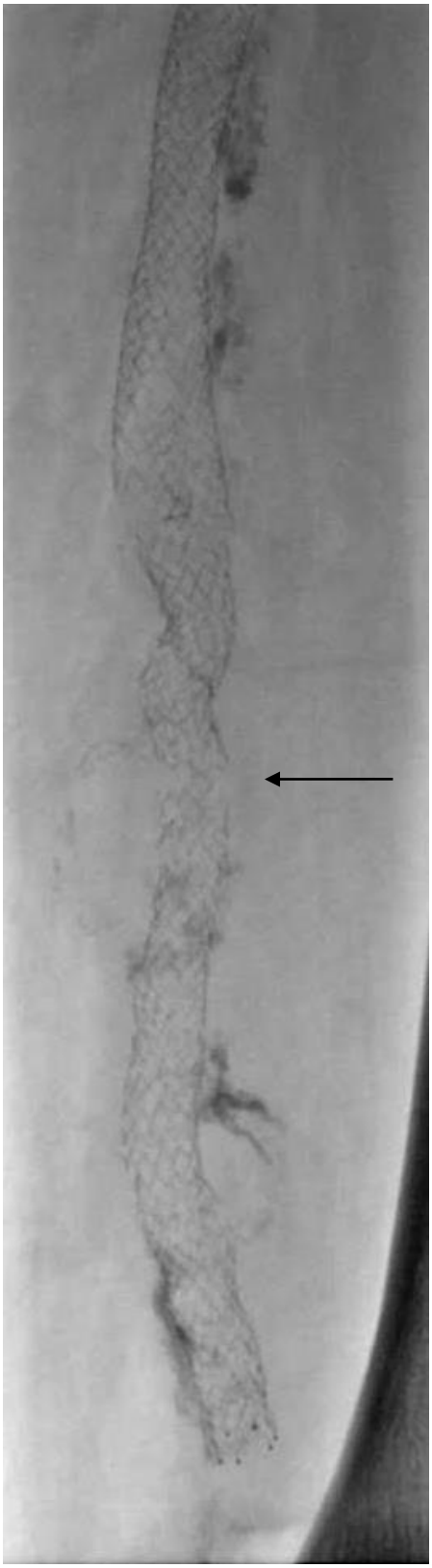


Figure 8. Fluoroscopic image of a type IV stent fracture (Right anterior oblique view; the fluoroscopic image was made by Hunor Sándor Sarkadi.)
The arrow points to a complete transverse fracture with subsequent stent separation.

Predictors of in-stent restenosis and stent fracture

The following parameters were evaluated: female sex, age ≥70 years, obesity, smoking, hypertension, dyslipidemia, diabetes mellitus, chronic kidney disease, total occlusion, long lesion, calcified lesion, heavily calcified lesion, TASC lesions, proximal superficial femoral artery stent, proximal–mid superficial femoral artery stent, mid superficial femoral artery stent, mid–distal superficial femoral artery stent, distal superficial femoral artery stent, femoropopliteal transitional zone stent, P1–2 stent, P1–3 or P2–3 stent, long stent, overlapping stents, Astron Pulsar stent, and Pulsar-18 stent. Univariate logistic regression analysis revealed that stents placed in P1–2 location were associated with an increased incidence of ISR (OR, 3.83; 95% CI, 1.10–13.31; P=0.030). Calcified, especially heavily calcified lesions were found to be predictive of SF (OR, 19.64; 95% CI, 4.31–89.47; P<0.001 and OR, 116.07; 95% CI, 22.57–597.03; P<0.001, respectively).

DOI:10.14753/SE.2023.2747

4. Discussion

4.1. Study I (Incidence of and predisposing factors for arterial pseudoaneurysm formation)

PSA was significantly more common in vascular radiological procedures than in coronary artery procedures, which can be explained by a higher percentage of therapeutic interventions (4,180/6,555 [63.8%] versus 7,709/18,038 [42.7%], respectively) and more frequent use of brachial and femoral access in the vascular radiological group (4,181/6,555 [63.8%] versus 1,419/18,038 [7.9%], respectively). In therapeutic interventions, compared to diagnostic angiographies, sheaths are generally larger in caliber, device changes are more frequent, and more time is required to perform them; all of these factors are known to predispose patients to PSA development. (5–7, 12) The reason for the difference in PSA incidence between the coronary artery and non-coronary artery cardiac groups may be the same (therapeutic interventions, 7,709/18,038 [42.7%] versus 5,603/5,603 [100%]; brachial and femoral access, 1,419/18,038 [7.9%] versus 1,430/5,603 [25.5%]). The higher PSA incidence of vascular radiological procedures, compared to non-coronary artery cardiac interventions, could be due to the fact that the majority of vascular radiological procedures are used to treat atherosclerotic steno-occlusive disease, which means that the punctured arteries of this patient population are more calcified and thus more prone to PSA formation.

In the upper limb, the radial and brachial arteries are the most common puncture sites, but the ulnar artery is also increasingly used. (13, 17–19, 111) Radial and ulnar punctures have a lower major complication rate than brachial and femoral punctures. (13–15, 18, 19, 111) Two complications related to radial and ulnar puncture, namely spasm and occlusion, should be highlighted, (13–15, 111) but they rarely cause clinical symptoms as the hand has a dual arterial blood supply. The incidence of radial and ulnar PSA is low, less than 0.1%. (13–15, 111) Major complications associated with the brachial approach include local thrombus formation, PSA, and nerve compression by hematoma and/or PSA. (17, 18) In a study by Yusuke et al., (17) the prevalence of PSA and nerve compression by PSA was significantly higher in brachial (1.1% and 2.2 %, respectively) than in femoral access (0.4% and 0%, respectively). In another study

comparing three puncture sites (radial, brachial, and femoral), the brachial puncture site had the highest risk of developing a large hematoma (0.7%, 4.4%, and 1.5%, respectively) or PSA (0%, 1.3%, and 0%, respectively). (18) Our results are consistent with literature data, as the order of PSA incidence in the upper limb was as follows: 1) brachial artery (1.2%), 2) ulnar artery (0.1%), and 3) radial artery (0.05%).

The femoral access is still extensively used, especially when a large sheath is required (e.g., at BAV, TAVI operations). Furthermore, the common femoral artery is used for the majority of lower extremity procedures. (16) The incidence of femoral PSA is 0.05%–2% after peripheral artery or coronary artery diagnostic catheterizations (21) and 2%–6% after therapeutic interventions. (12) In patients with non-coronary artery cardiac interventions, such as intracardiac electrophysiological procedures or TAVI, the prevalence of femoral PSA was 0.3%–0.9% (22, 23) and 1.6%–5.9%, (24, 25) respectively. The incidence of femoral PSA was 0.4% in our patient population, while it was 2.9% in a subset of patients who underwent BAV or TAVI.

VCDs are most commonly used to close femoral punctures. The use of VCD reduces the time to hemostasis, thus facilitating early patient mobilization, eliminating discomfort caused by prolonged bed rest, and shortening hospital stay length. (112) Although VCDs reduce the overall number of puncture-related complications, they slightly increase the risk of PSA formation. (39, 112, 113) The exact mechanism by which the use of VCD leads to the development of PSA is unknown. Presumably, it is not the VCD itself, but the choice of the wrong type and size or its incorrect use that results in PSA.

Replacement of the pressure bandage is still commonly used for PSA therapy, with efficacy ranging from 23.2% to 98.1%. (114–117) The primary success rate of mechanical compression in the upper limb (81.8%) was higher than in the lower limb (57.1%) in our study, which could be due to the treated arteries being closer to the skin surface in the upper limb than in the lower limb. Less invasive procedures, such as UGC and UGTI, have gradually supplanted traditional open surgical repair of PSAs. (31) UGTI has a higher success rate (89%–100%) than UGC (57%–99%), especially if the PSA is large and/or if the patient is anticoagulated. (9) For UGTI, we showed a primary success rate of 92.3% for the upper limb and 86.3% for the lower limb, while for UGC, we observed a primary success rate of 100% for both the upper and lower limbs. Other

minimally invasive techniques, such as Angio-Seal or Perclose ProGlide, have only been tried on a few patients. (32)

Anemia has been linked to an increased frequency of perioperative complications in individuals undergoing cardiac and non-cardiac surgery. (118–120) Low RBC counts, as well as low HCT and Hb levels, were revealed to be prognostic factors for PSA development in our study. RBCs have an important rheological effect, interacting with endothelial cells, platelets, and fibrin(ogen) both directly and indirectly. Their aggregation and deformability cause laminar shearing with platelet margination. (121, 122) HCT, like RBCs, has been shown to promote the transport of platelets to the site of vessel wall injury, thereby enhancing their interaction with the endothelium. (121, 123) In anemia, the reduced effect of RBCs and HCT on platelets may increase the risk of post-puncture PSA development. The relationship between intracellular Hb and PSA occurrence is unclear and is probably related to anemia.

PSA development was significantly influenced by the INR level. Higher INR values have long been associated with bleeding complications. (124) Popma et al. (125) conducted a meta-analysis and found that patients undergoing coronary artery intervention with an INR >3 had a three-fold higher risk of bleeding events than those with an INR ≤3. High INR values have been linked to the development of PSA (5, 126) and the requirement for reintervention after UGTI (114). High INR values are thought to cause PSA formation through the delayed coagulation cascade.

The study had three primary limitations: 1) it was a single-center, retrospective study, 2) the patient population was heterogeneous due to the large number of cases, and 3) after the interventions, a duplex scan was only performed if the patient had a symptom or complaint corresponding to the punctured extremity.

4.2. Study II (Safety, clinical outcome, and fracture rate of femoropopliteal stenting using 4F compatible delivery system)

In our study, access site complications were found in 2% of the patients. At 12 months, there was an 80.4% overall primary patency rate and 85.3% freedom from target lesion revascularization. After an average follow-up of 25.3 months, the incidence of SFs was 26%.

Each year, the number of peripheral vascular procedures rises. Aside from major complications, arterial puncture-related complications include bleeding, hematoma, PSA, arteriovenous fistula, arterial occlusion, femoral neuropathy, and infection, all of which are linked to increased morbidity, mortality, and cost. (38, 39) A larger sheath increases the risk of complications at the access site. (38) Up until a few years ago, only 6F or larger sheaths were used for femoropopliteal stenting. The reported incidence of puncture site complications during interventions through 6F sheaths varies between studies, but could be as high as 20%, (38) depending upon the definition and criteria used. Recently, self-expanding femoropopliteal stents that are deliverable through 4F sheaths have been introduced. Two large prospective multicenter trials (4-EVER and PEACE I) have been carried out to examine the safety and efficacy of implantation of 4F stents in patients with symptomatic femoropopliteal occlusive disease. (44, 45) The access-related complication rates were 3.3% in the 4-EVER trial and 2% in our study, and all of the complications could be managed by non-surgical treatments. (44) These rates are lower than most of the published rates on 6F devices. (38)

Regarding effectiveness of the procedures, the overall 12-month primary patency rate was 81.4% in the 4-EVER trial, 79.5% in the PEACE I trial, and 80.4% in our study, while the freedom from target lesion revascularization at 12 months was 89.3%, 81%, and 85.3%, respectively. (44, 45) The slightly worse results in the PEACE I trial can be explained by the fact that the percentage of patients with TASC–D lesions and total occlusions was higher (32.2% and 56.7%, respectively) compared to the 4-EVER trial (0% and 20.8%, respectively) and the current study (13.2% and 43.9%, respectively). (44, 45) Moreover, the treated lesions were longer in the PEACE I trial (111.5±71.4 mm) than they were in the 4-EVER trial (71.0±45.9 mm) and the current study (80.9±64.1 mm). (44, 45) Two other smaller 4F studies should be mentioned; in one of them, only patients with TASC–D lesions were enrolled, while only those having long segment femoropopliteal stenosis (≥120 mm) were enrolled in the other. (127, 128) The 12-month patency and revascularization rates of these two studies are similar to the rates of the PEACE I trial. (45, 127, 128) More importantly, these results are not worse than the reported 12-month outcomes with 6F stents. (73, 129–134)

Neointimal hyperplasia is the major cause of ISR. Patient-specific characteristics (e.g., ubiquitous comorbidities and insufficient antiplatelet therapy), as well as many

lesion-, stent-, and procedure-related factors (e.g., stent type, stent design, stent configuration, stent diameter, stent length, incomplete stent apposition, incomplete stent expansion, and overlapping stents) are known to precipitate ISR. (135) Femoropopliteal ISR occurs with a frequency of 19%–37% in lesions less than 150 mm in length after 12 months. (73, 136) In our study, the incidence of ISR was 20.6% and stents in P1–2 location were found to be associated with ISR. Certain dynamic forces, such as bending the artery during knee flexion, produce persistent deformation of the stent, which negatively affects the dynamics of blood flow in the vessel and leads to ISR, according to Early and Kelly. (137)

SFs have been extensively investigated in many vascular territories and were noted to be one of the most common in the femoropopliteal arteries, with a prevalence of 2%–65%. (48) Here, a 26% SF rate was reported after an average follow-up of 25.3 months. A literature search for the SF rates of 4F Astron Pulsar and Pulsar-18 stents revealed only one study (the 4-EVER trial). (44) Although, the SF rate was 4.2% in this trial, the percentage of patients with TASC–D lesions, total occlusions, calcified lesions, and long stents was significantly lower compared to our study. (44) Femoropopliteal stents are almost continuously exposed to mechanical forces, which can themselves result in “stress” fractures, especially when stents are placed behind the knee. Patient-, lesion-, stent-, and procedure-related parameters may further increase the risk of SF. (50) Calcified lesions were found to be predictive of SF in our study. Calcification due to changes in the regional wall stiffness and creating excessive focal pressure on certain parts of the stent has already been demonstrated to play a role in the development of SF. (48)

The study had two primary limitations: 1) it was a single-center, retrospective study, and 2) the SF analysis was performed in two separate centers in two slightly different ways.

DOI:10.14753/SE.2023.2747

5. Conclusions

5.1. Study I (Incidence of and predisposing factors for arterial pseudoaneurysm formation)

1) The incidence of PSA was 0.8% after radiological procedures, 0.2% after coronary artery procedures, and 0.4% after non-coronary artery cardiac procedures.

2) The effects of VCD use ($P<0.001$), RBC count ($P<0.001$), HCT value ($P<0.001$), Hb value ($P<0.001$), INR ($P<0.001$), RBC count—INR interaction ($P=0.003$), and RBC count—VCD use interaction ($P=0.036$) on PSA formation were significant.

In conclusion, the prevalence of PSA was highest after radiological procedures. Patients in whom the puncture site is closed with a VCD require increased observation. Preprocedural laboratory findings are useful for the identification of patients at high risk of PSA formation.

5.2. Study II (Safety, clinical outcome, and fracture rate of femoropopliteal stenting using 4F compatible delivery system)

1) The peri- and postprocedural complication rate for femoropopliteal stenting with a 4F sheath compatible delivery system was low at 2%.

2) The 30-day major amputation and all-cause mortality rates were zero. The primary, primary assisted, and secondary patency rates were 80.4%, 94.3%, 85.4%, respectively, at 12 months.

3) Over a mean (±SD) follow-up of 25.3 (±6.2) months, the incidence of SF was 26%.

In conclusion, the complication rate of femoropopliteal stenting using a 4F compatible delivery system is low, the 12-month patency rate is good, and the SF rate is acceptable.

DOI:10.14753/SE.2023.2747

6. Summary

PSA formation is one of the most common punctured vessel-related complications. There are several ways to reduce the number of such complications (e.g., by inserting a smaller diameter sheath). We aimed to evaluate factors for PSA development and to determine the safety, clinical outcome, and fracture rate of femoropopliteal stenting using a 4F compatible delivery system. The studies were carried out retrospectively.

Single PSAs were found in 134 patients: 53 PSAs occurred after radiological procedures (53/6,555 [0.8%]), 31 after coronary artery procedures (31/18,038 [0.2%]), 25 after non-coronary artery cardiac procedures (25/5,603 [0.4%]), and 25 due to procedures in which the arterial puncture was unintended. Thirty-four PSAs (25.4%) were localized to the upper extremity arteries, while 100 (74.6%) arose from the lower extremity arteries. The PSA prevalence was 0.05% (10/20,478) in the radial artery, 0.1% (2/1,818) in the ulnar artery, 1.2% (22/1,897) in the brachial artery, and 0.4% (99/22,202) in the femoral artery. The prevalence of PSA for the punctured artery with and without VCD use was 37/3,555 (1%) and 97/27,204 (0.4%), respectively ($P<0.001$). The effects of the RBC count ($P<0.001$), HCT value ($P<0.001$), Hb value ($P<0.001$), INR ($P<0.001$), RBC count—INR interaction ($P=0.003$), and RBC count—VCD use interaction ($P=0.036$) on PSA formation were significant.

In total, 114 femoropopliteal lesions (TASC C–D, N=45; ≥100 mm, N=49; heavily calcified, N=35) were treated with 119 stents (Astron Pulsar, N=42; Pulsar-18, N=77; ≥120 mm, N=46). The technical and clinical success rates were 100%. Two puncture-related complications were noted. Eleven patients died and nine patients underwent major amputation (above the knee, N=4). The primary, primary assisted, and secondary patency rates were 80.4%, 94.3%, 85.4%, respectively, at 12 months. The prevalence of SF was 26% (types III and IV, 10%) after an average follow-up of 25.3 months.

Patients in whom the puncture site is closed with a VCD require increased observation. Preprocedural laboratory findings are useful for the identification of patients at high risk of PSA development. The complication rate of femoropopliteal stenting using a 4F compatible delivery system is low, the 12-month patency rate is good, and the SF rate is acceptable.

7. References

1. Mayer J, Tacher V, Novelli L, Djabbari M, You K, Chiaradia M, Deux JF, Kobeiter H. (2015) Post-procedure bleeding in interventional radiology. Diagn Interv Imaging, 96: 833–840.

2. Al Adas Z, Lodewyk K, Robinson D, Qureshi S, Kabbani LS, Sullivan B, Shepard AD, Weaver MR, Nypaver TJ. (2019) Contrast-induced nephropathy after peripheral vascular intervention: Long-term renal outcome and risk factors for progressive renal dysfunction. J Vasc Surg, 69: 913–920.

3. Piazza M, Squizzato F, Milan L, Miccoli T, Grego F, Antonello M; Global Registry for Endovascular Aortic Treatment (GREAT) investigators. (2019) Incidence and Predictors of Neurological Complications Following Thoracic Endovascular Aneurysm Repair in the Global Registry for Endovascular Aortic Treatment. Eur J Vasc Endovasc Surg, 58: 512–519.

4. Venermo M, Sprynger M, Desormais I, Björck M, Brodmann M, Cohnert T, De Carlo M, Espinola-Klein C, Kownator S, Mazzolai L, Naylor R, Vlachopoulos C, Ricco JB, Aboyans V. (2019) Editor's Choice - Follow-up of Patients After Revascularisation for Peripheral Arterial Diseases: A Consensus Document From the European Society of Cardiology Working Group on Aorta and Peripheral Vascular Diseases and the European Society for Vascular Surgery. Eur J Vasc Endovasc Surg, 58: 641–653.

5. Delf J, Ramachandran S, Mustafa S, Saeed A, Kandiyil N. (2019) Factors associated with pseudoaneurysm development and necessity for reintervention: a single centre study. Br J Radiol, 92: 20180893.

6. Minici R, Paone S, Talarico M, Zappia L, Abdalla K, Petullà M, Laganà D. (2020) Percutaneous treatment of vascular access-site complications: a ten years' experience in two centres. CVIR Endovasc, 3: 29.

7. Eleshra A, Kim D, Park HS, Lee T. (2019) Access site pseudoaneurysms after endovascular intervention for peripheral arterial diseases. Ann Surg Treat Res, 96: 305–312.

8. Brilakis E. Manual of Percutaneous Coronary Interventions: A Step-by-Step Approach. Elsevier Inc., Amsterdam, 2020: 471–484.

9. Stolt M, Braun-Dullaeus R, Herold J. (2018) Do not underestimate the femoral pseudoaneurysm. Vasa, 47: 177–185.

10. Ahmad F, Turner SA, Torrie P, Gibson M. (2008) Iatrogenic femoral artery pseudoaneurysms--a review of current methods of diagnosis and treatment. Clin Radiol, 63: 1310–1316.

11. Isoda R, Morita I, Yoshida M. (2020) Iatrogenic femoral vein pseudoaneurysm. J Vasc Surg Cases Innov Tech, 6: 285–287.

12. Webber GW, Jang J, Gustavson S, Olin JW. (2007) Contemporary management of postcatheterization pseudoaneurysms. Circulation, 115: 2666–2674.

13. Polytarchou K, Triantafyllou K, Antypa E, Kappos K. (2016) Ulnar pseudoaneurysm after transulnar coronary angiogram treated with percutaneous ultrasound-guided thrombin injection. Int J Cardiol, 222: 404–406.

14. Gallinoro E, Natale F, D'Elia S, Golino P, Cimmino G. (2019) Radial pseudoaneurysm in elderly: a rare event with undefinied therapeutical approach. A case report and literature review. Monaldi Arch Chest Dis, 89.

15. Tosti R, Özkan S, Schainfeld RM, Eberlin KR. (2017) Radial Artery Pseudoaneurysm. J Hand Surg Am, 42: 295.e1–295.e6.

16. Jeon SH, Kang HG, Kim HJ, Seo MW, Shin BS. (2019) Femoral artery pseudoaneurysm after carotid artery stenting: Two case reports. Medicine (Baltimore), 98: e15309.

17. Tamanaha Y, Sakakura K, Taniguchi Y, Yamamoto K, Tsukui T, Seguchi M, Wada H, Momomura SI, Fujita H. (2019) Comparison of Postcatheterization Pseudoaneurysm between Brachial Access and Femoral Access. Int Heart J, 60: 1030–1036.

18. Otsuka M, Shiode N, Nakao Y, Ikegami Y, Kobayashi Y, Takeuchi A, Harima A, Higaki T, Oi K, Dai K, Kawase T, Nakama Y, Suenari K, Nishioka K, Sakai K, Shimatani Y, Masaoka Y, Inoue I. (2018) Comparison of radial, brachial, and femoral accesses using hemostatic devices for percutaneous coronary intervention. Cardiovasc Interv Ther, 33: 62–69.

19. Basu D, Singh PM, Tiwari A, Goudra B. (2017) Meta-analysis comparing radial versus femoral approach in patients 75 years and older undergoing percutaneous coronary procedures. Indian Heart J, 69: 580–588.

20. Madia C. (2019) Management trends for postcatheterization femoral artery pseudoaneurysms. JAAPA, 32: 15–18.
21. Hessel SJ, Adams DF, Abrams HL. (1981) Complications of angiography. Radiology, 138: 273–281.
22. Gupta A, Perera T, Ganesan A, Sullivan T, Lau DH, Roberts-Thomson KC, Brooks AG, Sanders P. (2013) Complications of catheter ablation of atrial fibrillation: a systematic review. Circ Arrhythm Electrophysiol, 6: 1082–1088.
23. Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J, Kim YH, Klein G, Natale A, Packer D, Skanes A, Ambrogi F, Biganzoli E. (2010) Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. Circ Arrhythm Electrophysiol, 3: 32–38.
24. Hayashida K, Lefèvre T, Chevalier B, Hovasse T, Romano M, Garot P, Mylotte D, Uribe J, Farge A, Donzeau-Gouge P, Bouvier E, Cormier B, Morice MC. (2011) Transfemoral aortic valve implantation new criteria to predict vascular complications. JACC Cardiovasc Interv, 4: 851–858.
25. Toggweiler S, Leipsic J, Binder RK, Freeman M, Barbanti M, Heijmen RH, Wood DA, Webb JG. (2013) Management of vascular access in transcatheter aortic valve replacement: part 2: Vascular complications. JACC Cardiovasc Interv, 6: 767–776.
26. Erol F, Arslan Ş, Yüksel İÖ, Üreyen ÇM, Serdar S, İnci S, Şenocak H. (2015) Determinants of iatrogenic femoral pseudoaneurysm after cardiac catheterization or percutaneous coronary intervention via the femoral artery. Turk Kardiyol Dern Ars, 43: 513–519.
27. Jargiełło T, Sobstyl J, Światłowski Ł, Kuczyńska M, Kuklik E, Sojka M, Drelich-Zbroja A, Pech M, Powerski M. (2018) Ultrasound-guided thrombin injection in the management of pseudoaneurysm after percutaneous arterial access. J Ultrason, 18: 85–89.
28. Chun EJ. (2018) Ultrasonographic evaluation of complications related to transfemoral arterial procedures. Ultrasonography, 37: 164–173.
29. Yoo T, Starr JE, Go MR, Vaccaro PS, Satiani B, Haurani MJ. (2017) Ultrasound-Guided Thrombin Injection Is a Safe and Effective Treatment for Femoral Artery Pseudoaneurysm in the Morbidly Obese. Vasc Endovascular Surg, 51: 368–372.

30. Kuma S, Morisaki K, Kodama A, Guntani A, Fukunaga R, Soga Y, Shirai S, Ishida M, Okazaki J, Mii S. (2015) Ultrasound-guided percutaneous thrombin injection for post-catheterization pseudoaneurysm. Circ J, 79: 1277–1281.

31. Kontopodis N, Tsetis D, Tavlas E, Dedes A, Ioannou CV. (2016) Ultrasound Guided Compression Versus Ultrasound Guided Thrombin Injection for the Treatment of Post-Catheterization Femoral Pseudoaneurysms: Systematic Review and Meta-Analysis of Comparative Studies. Eur J Vasc Endovasc Surg, 51: 815–823.

32. Robken J, Shammas NW. (2016) Novel Technique to Treat Common Femoral Artery Pseudoaneurysm using Angio-Seal Closure Device. Int J Angiol, 25: 266–270.

33. Loh EJ, Allen R. (2019) Endovascular treatment of refractory iatrogenic femoral artery pseudoaneurysm using Amplatzer vascular plugs following unsuccessful retrograde Angio-Seal deployment. Indian J Radiol Imaging, 29: 211–214.

34. Ocke Reis PE, Roever L, Ocke Reis IF, de Azambuja Fontes F, Rotolo Nascimento M, Nunes Dos Santos L, de Almeida Sandri P. (2016) Endovascular Stent Grafting of a Deep Femoral Artery Pseudoaneurysm. EJVES Short Rep, 33: 5–8.

35. Kobeiter H, Lapeyre M, Becquemin JP, Mathieu D, Melliere D, Desgranges P. (2002) Percutaneous coil embolization of postcatheterization arterial femoral pseudoaneurysms. J Vasc Surg, 36: 127–131.

36. Chang HY, Liu ZG, Li YL, Liu B, Wang WJ, Wang W, Wang YZ. (2021) Endovascular stenting and coil embolization for management of radiation-induced pseudoaneurysms of the peripheral arteries. J Int Med Res, 49: 300060520984933.

37. Stone PA, Campbell JE, AbuRahma AF. (2014) Femoral pseudoaneurysms after percutaneous access. J Vasc Surg, 60: 1359–1366.

38. Merriweather N, Sulzbach-Hoke LM. (2012) Managing risk of complications at femoral vascular access sites in percutaneous coronary intervention. Crit Care Nurse, 32: 16–29.

39. Koreny M, Riedmüller E, Nikfardjam M, Siostrzonek P, Müllner M. (2004) Arterial puncture closing devices compared with standard manual compression after cardiac catheterization: systematic review and meta-analysis. JAMA, 291: 350–357.

40. Fukuda K, Okazaki S, Shiozaki M, Okai I, Nishino A, Tamura H, Inoue K, Sumiyoshi M, Daida H, Minamino T. (2021) Ultrasound-guided puncture reduces bleeding-associated complications, regardless of calcified plaque, after endovascular

treatment of femoropopliteal lesions, especially using the antegrade procedure: A single-center study. PLoS One, 16: e0248416.

41. Lisowska A, Knapp M, Usowicz-Szaryńska M, Kozieradzka A, Musial WJ, Dobrzycki S. (2011) Iatrogenic femoral pseudoaneurysms - a simple solution of inconvenient problem? Adv Med Sci, 56: 215–221.

42. Sulzbach-Hoke LM, Ratcliffe SJ, Kimmel SE, Kolansky DM, Polomano R. (2010) Predictors of complications following sheath removal with percutaneous coronary intervention. J Cardiovasc Nurs, 25: E1–8.

43. Stone PA, Martinez M, Thompson SN, Masinter D, Campbell JE, Campbell Ii JR, AbuRahma AF. (2016) Ten-Year Experience of Vascular Surgeon Management of Iatrogenic Pseudoaneurysms: Do Anticoagulant and/or Antiplatelet Medications Matter? Ann Vasc Surg, 30: 45–51.

44. Bosiers M, Deloose K, Callaert J, Keirse K, Verbist J, Hendriks J, Lauwers P, D'Archambeau O, Scheinert D, Torsello G, Peeters P. (2013) 4-French-compatible endovascular material is safe and effective in the treatment of femoropopliteal occlusive disease: results of the 4-EVER trial. J Endovasc Ther, 20: 746–756.

45. Lichtenberg M, Kolks O, Hailer B, Stahlhoff WF, Tiefenbacher C, Nolte-Ernsting C, Arjumand J, Wittenberg G. (2014) PEACE I all-comers registry: patency evaluation after implantation of the 4-French Pulsar-18 self-expanding nitinol stent in femoropopliteal lesions. J Endovasc Ther, 21: 373–380.

46. Allie DE, Hebert CJ, Walker CM. (2004) Nitinol Stent Fractures in the SFA. Endovasc Today, 1: 22–34.

47. Jaff M, Dake M, Pompa J, Ansel G, Yoder T. (2007) Standardized evaluation and reporting of stent fractures in clinical trials of noncoronary devices. Catheter Cardiovasc Interv, 70: 460–462.

48. Rits J, van Herwaarden JA, Jahrome AK, Krievins D, Moll FL. (2008) The incidence of arterial stent fractures with exclusion of coronary, aortic, and non-arterial settings. Eur J Vasc Endovasc Surg, 36: 339–345.

49. Adlakha S, Sheikh M, Wu J, Burket MW, Pandya U, Colyer W, Eltahawy E, Cooper CJ. (2010) Stent fracture in the coronary and peripheral arteries. J Interv Cardiol, 23: 411–419.

50. Neil N. (2013) Stent fracture in the superficial femoral and proximal popliteal arteries: literature summary and economic impacts. Perspect Vasc Surg Endovasc Ther, 25: 20–27.

51. Scheinert D, Scheinert S, Sax J, Piorkowski C, Bräunlich S, Ulrich M, Biamino G, Schmidt A. (2005) Prevalence and clinical impact of stent fractures after femoropopliteal stenting. J Am Coll Cardiol, 45: 312–315.

52. Iida O, Nanto S, Uematsu M, Morozumi T, Kotani J, Awata M, Onishi T, Ito N, Sera F, Minamiguchi H, Akahori H, Nagata S. (2006) Effect of exercise on frequency of stent fracture in the superficial femoral artery. Am J Cardiol, 98: 272–274.

53. Iida O, Nanto S, Uematsu M, Ikeoka K, Okamoto S, Nagata S. (2009) Influence of stent fracture on the long-term patency in the femoro-popliteal artery: experience of 4 years. JACC Cardiovasc Interv, 2: 665–671.

54. Davaine JM, Quérat J, Guyomarch B, Brennan MÁ, Costargent A, Chaillou P, Patra P, Gouëffic Y. (2013) Incidence and the clinical impact of stent fractures after primary stenting for TASC C and D femoropopliteal lesions at 1 year. Eur J Vasc Endovasc Surg, 46:201–212.

55. Lin Y, Tang X, Fu W, Kovach R, George JC, Guo D. (2015) Stent fractures after superficial femoral artery stenting: risk factors and impact on patency. J Endovasc Ther, 22: 319–326.

56. Daher MA, Lopez GE, Duarte PV. (2020) Stents in the femoropopliteal territory: prevalence of fractures and their consequences. Rev Col Bras Cir, 47: e20202481.

57. Poulson W, Kamenskiy A, Seas A, Deegan P, Lomneth C, MacTaggart J. (2018) Limb flexion-induced axial compression and bending in human femoropopliteal artery segments. J Vasc Surg, 67: 607–613.

58. Sato K, Emura S, Tomiyoshi H, Morita S. (2019) Morphologic Changes of the Femoropopliteal Arterial Segment with Knee Flexion after Endovascular Therapy. Ann Vasc Dis, 12: 210–215.

59. Nikanorov A, Smouse HB, Osman K, Bialas M, Shrivastava S, Schwartz LB. (2008) Fracture of self-expanding nitinol stents stressed in vitro under simulated intravascular conditions. J Vasc Surg, 48: 435–440.

60. Ansari F, Pack LK, Brooks SS, Morrison TM. (2013) Design considerations for studies of the biomechanical environment of the femoropopliteal arteries. J Vasc Surg, 58:804–813.

61. Hüttl AB, Hüttl A, Vértes M, Nguyen DT, Bérczi Á, Hüttl K, Dósa E. (2019) The presence of long and heavily calcified lesions predisposes for fracture in patients undergoing stenting of the first part of the subclavian artery. J Vasc Surg, 70: 1146–1154.e1.

62. Dósa E, Nemes B, Bérczi V, Novák PK, Paukovits TM, Sarkadi H, Hüttl K. (2014) High frequency of brachiocephalic trunk stent fractures does not impair clinical outcome. J Vasc Surg, 59: 781–785.

63. Metzger PB, Volpato MG, Folino MC, Rossi FH, Gomes Petisco AC, Saleh MH, Izukawa NM, Kambara AM. (2015) Outcomes after implantation of superflexible nitinol stents in the superficial femoral artery. Rev Bras Cardiol Invasiva, 23: 220–225.

64. Hernández Hernández F, Jurado Román A, García Tejada J, Velázquez Martín M, Albarrán González-Trevilla A, Tascón Pérez JC. (2013) Intravascular diagnosis of stent fractures: beyond X-ray imaging. Rev Esp Cardiol (Engl Ed), 66: 751–753.

65. Hitchner E, Zayed M, Varu V, Lee G, Aalami O, Zhou W. (2015) A prospective evaluation of using IVUS during percutaneous superficial femoral artery interventions. Ann Vasc Surg, 29: 28–33.

66. Doi H, Maehara A, Mintz GS, Tsujita K, Kubo T, Castellanos C, Liu J, Yang J, Oviedo C, Aoki J, Franklin-Bond T, Dasgupta N, Lansky AJ, Dangas GD, Stone GW, Moses JW, Mehran R, Leon MB. (2009) Classification and potential mechanisms of intravascular ultrasound patterns of stent fracture. Am J Cardiol, 103: 818–823.

67. Mahnken AH. (2012) CT Imaging of Coronary Stents: Past, Present, and Future. ISRN Cardiol, 2012: 139823.

68. Park KW, Park JJ, Chae IH, Seo JB, Yang HM, Lee HY, Kang HJ, Cho YS, Yeon TJ, Chung WY, Koo BK, Choi DJ, Oh BH, Park YB, Kim HS. (2011) Clinical characteristics of coronary drug-eluting stent fracture: insights from a two-center des registry. J Korean Med Sci, 26: 53–58.

69. Lee SE, Jeong MH, Kim IS, Ko JS, Lee MG, Kang WY, Kim SH, Sim DS, Park KH, Yoon NS, Yoon HJ, Kim KH, Hong YJ, Park HW, Kim JH, Ahn YK, Cho JG,

Park JC, Kang JC. (2009) Clinical outcomes and optimal treatment for stent fracture after drug-eluting stent implantation. J Cardiol, 53: 422–428.

70. Ho KJ, Owens CD. (2017) Diagnosis, classification, and treatment of femoropopliteal artery in-stent restenosis. J Vasc Surg, 65: 545–557.

71. Hellings WE, Moll FL, de Vries JP, de Bruin P, de Kleijn DP, Pasterkamp G. (2008) Histological characterization of restenotic carotid plaques in relation to recurrence interval and clinical presentation: a cohort study. Stroke, 39: 1029–1032.

72. Dake MD, Ansel GM, Jaff MR, Ohki T, Saxon RR, Smouse HB, Zeller T, Roubin GS, Burket MW, Khatib Y, Snyder SA, Ragheb AO, White JK, Machan LS; Zilver PTX Investigators. (2011) Paclitaxel-eluting stents show superiority to balloon angioplasty and bare metal stents in femoropopliteal disease: twelve-month Zilver PTX randomized study results. Circ Cardiovasc Interv, 4:495–504.

73. Laird JR, Katzen BT, Scheinert D, Lammer J, Carpenter J, Buchbinder M, Dave R, Ansel G, Lansky A, Cristea E, Collins TJ, Goldstein J, Jaff MR; RESILIENT Investigators. (2010) Nitinol stent implantation versus balloon angioplasty for lesions in the superficial femoral artery and proximal popliteal artery: twelve-month results from the RESILIENT randomized trial. Circ Cardiovasc Interv, 3: 267–276.

74. Zeller T. (2007) Current state of endovascular treatment of femoro-popliteal artery disease. Vasc Med, 12: 223–234.

75. Schönefeld E, Torsello G, Osada N, Herten M, Bisdas T, Donas KP. (2013) Long-term outcome of femoropopliteal stenting. Results of a prospective study. J Cardiovasc Surg (Torino), 54: 617–623.

76. Stavroulakis K, Torsello G, Manal A, Schwindt A, Hericks C, Stachmann A, Schönefeld E, Bisdas T. (2016) Results of primary stent therapy for femoropopliteal peripheral arterial disease at 7 years. J Vasc Surg, 64: 1696–1702.

77. Mitra AK, Agrawal DK. (2006) In stent restenosis: bane of the stent era. J Clin Pathol, 59: 232–239.

78. Bennett MR. (2003) In-stent stenosis: pathology and implications for the development of drug eluting stents. Heart, 89: 218–224.

79. Buccheri D, Piraino D, Andolina G, Cortese B. (2016) Understanding and managing in-stent restenosis: a review of clinical data, from pathogenesis to treatment. J Thorac Dis, 8: E1150–E1162.

80. Nakazawa G, Otsuka F, Nakano M, Vorpahl M, Yazdani SK, Ladich E, Kolodgie FD, Finn AV, Virmani R. (2011) The pathology of neoatherosclerosis in human coronary implants bare-metal and drug-eluting stents. J Am Coll Cardiol, 57: 1314–1322.

81. Otsuka F, Byrne RA, Yahagi K, Mori H, Ladich E, Fowler DR, Kutys R, Xhepa E, Kastrati A, Virmani R, Joner M. (2015) Neoatherosclerosis: overview of histopathologic findings and implications for intravascular imaging assessment. Eur Heart J, 36: 2147–2159.

82. Park SJ, Kang SJ, Virmani R, Nakano M, Ueda Y. (2012) In-stent neoatherosclerosis: a final common pathway of late stent failure. J Am Coll Cardiol, 59: 2051–2057.

83. Soga Y, Tomoi Y, Sato K, Iida O, Yokoi H. (2013) Clinical outcome after endovascular treatment for isolated common femoral and popliteal artery disease. Cardiovasc Interv Ther, 28: 250–257.

84. Mehran R, Dangas G, Abizaid AS, Mintz GS, Lansky AJ, Satler LF, Pichard AD, Kent KM, Stone GW, Leon MB. (1999) Angiographic patterns of in-stent restenosis: classification and implications for long-term outcome. Circulation, 100: 1872–1878.

85. Zhao HQ, Nikanorov A, Virmani R, Jones R, Pacheco E, Schwartz LB. (2009) Late stent expansion and neointimal proliferation of oversized Nitinol stents in peripheral arteries. Cardiovasc Intervent Radiol, 32: 720–726.

86. Saguner AM, Traupe T, Räber L, Hess N, Banz Y, Saguner AR, Diehm N, Hess OM. (2012) Oversizing and restenosis with self-expanding stents in iliofemoral arteries. Cardiovasc Intervent Radiol, 35: 906–913.

87. Gray BH, Sullivan TM, Childs MB, Young JR, Olin JW. (1997) High incidence of restenosis/reocclusion of stents in the percutaneous treatment of long-segment superficial femoral artery disease after suboptimal angioplasty. J Vasc Surg, 25: 74–83.

88. Ihnat DM, Duong ST, Taylor ZC, Leon LR, Mills JL Sr, Goshima KR, Echeverri JA, Arslan B. (2008) Contemporary outcomes after superficial femoral artery angioplasty and stenting: the influence of TASC classification and runoff score. J Vasc Surg, 47: 967–974.

89. Spiliopoulos S, Kitrou P, Galanakis N, Papadimatos P, Katsanos K, Konstantos C, Palialexis K, Reppas L, Kehagias E, Karnabatidis D, Brountzos E, Tsetis D. (2018)

Incidence and Endovascular Treatment of Isolated Atherosclerotic Popliteal Artery Disease: Outcomes from the IPAD Multicenter Study. Cardiovasc Intervent Radiol, 41: 1481–1487.

90. Cui C, Huang X, Liu X, Li W, Lu X, Lu M, Jiang M, Yin M. (2017) Endovascular treatment of atherosclerotic popliteal artery disease based on dynamic angiography findings. J Vasc Surg, 65: 82–90.

91. Özpak B, Çayır MÇ. (2020) Drug-eluting balloon treatment in femoropopliteal in-stent restenosis of different lengths. Turk Gogus Kalp Damar Cerrahisi Derg, 28: 460–466.

92. Hardman RL, Jazaeri O, Yi J, Smith M, Gupta R. (2014) Overview of classification systems in peripheral artery disease. Semin Intervent Radiol, 31: 378–388.

93. Rutherford RB, Baker JD, Ernst C, Johnston KW, Porter JM, Ahn S, Jones DN. (1997) Recommended standards for reports dealing with lower extremity ischemia: revised version. J Vasc Surg, 26: 517–538.

94. Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, Collet JP, Czerny M, De Carlo M, Debus S, Espinola-Klein C, Kahan T, Kownator S, Mazzolai L, Naylor AR, Roffi M, Röther J, Sprynger M, Tendera M, Tepe G, Venermo M, Vlachopoulos C, Desormais I; ESC Scientific Document Group. (2018) 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries. Endorsed by: the European Stroke Organization (ESO), the Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J, 39: 763–816.

95. Tosaka A, Soga Y, Iida O, Ishihara T, Hirano K, Suzuki K, Yokoi H, Nanto S, Nobuyoshi M. (2012) Classification and clinical impact of restenosis after femoropopliteal stenting. J Am Coll Cardiol, 59: 16–23.

96. Iida O, Yokoi H, Soga Y, Inoue N, Suzuki K, Yokoi Y, Kawasaki D, Zen K, Urasawa K, Shintani Y, Miyamoto A, Hirano K, Miyashita Y, Tsuchiya T, Shinozaki N, Nakamura M, Isshiki T, Hamasaki T, Nanto S; STOP-IC investigators. (2013) Cilostazol reduces angiographic restenosis after endovascular therapy for

femoropopliteal lesions in the Sufficient Treatment of Peripheral Intervention by Cilostazol study. Circulation, 127: 2307–2315.

97. Nanto K, Iida O, Takahara M, Soga Y, Suzuki K, Hirano K, Kawasaki D, Shintani Y, Suematsu N, Yamaoka T, Uematsu M. (2015) Effect of Cilostazol Following Endovascular Intervention for Peripheral Artery Disease. Angiology, 66: 774–778.

98. Dick P, Sabeti S, Mlekusch W, Schlager O, Amighi J, Haumer M, Cejna M, Minar E, Schillinger M. (2008) Conventional balloon angioplasty versus peripheral cutting balloon angioplasty for treatment of femoropopliteal artery in-stent restenosis: initial experience. Radiology, 248: 297–302.

99. Tepe G, Laird J, Schneider P, Brodmann M, Krishnan P, Micari A, Metzger C, Scheinert D, Zeller T, Cohen DJ, Snead DB, Alexander B, Landini M, Jaff MR; IN.PACT SFA Trial Investigators. (2015) Drug-coated balloon versus standard percutaneous transluminal angioplasty for the treatment of superficial femoral and popliteal peripheral artery disease: 12-month results from the IN.PACT SFA randomized trial. Circulation, 131: 495–502.

100. Rosenfield K, Jaff MR, White CJ, Rocha-Singh K, Mena-Hurtado C, Metzger DC, Brodmann M, Pilger E, Zeller T, Krishnan P, Gammon R, Müller-Hülsbeck S, Nehler MR, Benenati JF, Scheinert D; LEVANT 2 Investigators. (2015) Trial of a Paclitaxel-Coated Balloon for Femoropopliteal Artery Disease. N Engl J Med, 373: 145–153.

101. Iida O, Soga Y, Urasawa K, Saito S, Jaff MR, Wang H, Ookubo H, Yokoi H; MDT-2113 SFA Japan Investigators. (2019) Drug-coated balloon versus uncoated percutaneous transluminal angioplasty for the treatment of atherosclerotic lesions in the superficial femoral and proximal popliteal artery: 2-year results of the MDT-2113 SFA Japan randomized trial. Catheter Cardiovasc Interv, 93: 664–672.

102. Schroeder H, Werner M, Meyer DR, Reimer P, Krüger K, Jaff MR, Brodmann M; ILLUMENATE EU RCT Investigators. (2017) Low-Dose Paclitaxel-Coated Versus Uncoated Percutaneous Transluminal Balloon Angioplasty for Femoropopliteal Peripheral Artery Disease: One-Year Results of the ILLUMENATE European Randomized Clinical Trial (Randomized Trial of a Novel Paclitaxel-Coated Percutaneous Angioplasty Balloon). Circulation, 135: 2227–2236.

103. Steiner S, Willfort-Ehringer A, Sievert H, Geist V, Lichtenberg M, Del Giudice C, Sauguet A, Diaz-Cartelle J, Marx C, Ströbel A, Schult I, Scheinert D; RANGER SFA

Investigators. (2018) 12-Month Results From the First-in-Human Randomized Study of the Ranger Paclitaxel-Coated Balloon for Femoropopliteal Treatment. JACC Cardiovasc Interv, 11: 934–941.

104. Tepe G, Gögebakan Ö, Redlich U, Tautenhahn J, Ricke J, Halloul Z, Meyer DR, Waliszewski M, Schnorr B, Zeller T, Müller-Hülsbeck S, Ott I, Albrecht T. (2017) Angiographic and Clinical Outcomes After Treatment of Femoro-Popliteal Lesions with a Novel Paclitaxel-Matrix-Coated Balloon Catheter. Cardiovasc Intervent Radiol, 40: 1535–1544.

105. Vartanian SM, Conte MS. (2015) Surgical intervention for peripheral arterial disease. Circ Res, 116: 1614–1628.

106. Fellmeth BD, Roberts AC, Bookstein JJ, Freischlag JA, Forsythe JR, Buckner NK, Hye RJ. (1991) Postangiographic femoral artery injuries: nonsurgical repair with US-guided compression. Radiology, 178: 671–675.

107. Cope C, Zeit R. (1986) Coagulation of aneurysms by direct percutaneous thrombin injection. AJR Am J Roentgenol, 147: 383–387.

108. Baum S, Pentecost MJ. Abrams' Angiography Interventional Radiology. Lippincott Williams & Wilkins, Philadelphia, 2005: 305.

109. Gouëffic Y, Della Schiava N, Thaveau F, Rosset E, Favre JP, Salomon du Mont L, Alsac JM, Hassen-Khodja R, Reix T, Allaire E, Ducasse E, Soler R, Guyomarc'h B, Nasr B. (2017) Stenting or Surgery for De Novo Common Femoral Artery Stenosis. JACC Cardiovasc Interv, 10: 1344–1354.

110. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG; TASC II Working Group. (2007) Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). J Vasc Surg, 45 Suppl S: S5–67.

111. Fernandez R, Zaky F, Ekmejian A, Curtis E, Lee A. (2018) Safety and efficacy of ulnar artery approach for percutaneous cardiac catheterization: Systematic review and meta-analysis. Catheter Cardiovasc Interv, 91: 1273–1280.

112. Noori VJ, Eldrup-Jørgensen J. (2018) A systematic review of vascular closure devices for femoral artery puncture sites. J Vasc Surg, 68: 887–899.

113. Smilowitz NR, Kirtane AJ, Guiry M, Gray WA, Dolcimascolo P, Querijero M, Echeverry C, Kalcheva N, Flores B, Singh VP, Rabbani L, Kodali S, Collins MB, Leon MB, Moses JW, Weisz G. (2012) Practices and complications of vascular closure

devices and manual compression in patients undergoing elective transfemoral coronary procedures. Am J Cardiol, 110: 177–182.

114. Dzijan-Horn M, Langwieser N, Groha P, Bradaric C, Linhardt M, Böttiger C, Byrne RA, Steppich B, Koppara T, Gödel J, Hadamitzky M, Ott I, von Beckerath N, Kastrati A, Laugwitz KL, Ibrahim T. (2014) Safety and efficacy of a potential treatment algorithm by using manual compression repair and ultrasound-guided thrombin injection for the management of iatrogenic femoral artery pseudoaneurysm in a large patient cohort. Circ Cardiovasc Interv, 7: 207–215.

115. Paschalidis M, Theiss W, Kölling K, Busch R, Schömig A. (2006) Randomised comparison of manual compression repair versus ultrasound guided compression repair of postcatheterisation femoral pseudoaneurysms. Heart, 92: 251–252.

116. Wong SC, Laule M, Turi Z, Sanad W, Crowley J, Degen H, Bennett K, Coleman JE, Bergman G. (2017) A multicenter randomized trial comparing the effectiveness and safety of a novel vascular closure device to manual compression in anticoagulated patients undergoing percutaneous transfemoral procedures: The CELT ACD trial. Catheter Cardiovasc Interv, 90: 756–765.

117. Pawlaczyk K, Gabriel M, Nowak M, Krasiński Z, Juszkat R, Stanisić M, Jawień AA, Oszkinis G. (2007) The value of different forms of compression therapy in the treatment of iatrogenic femoral pseudoaneurysms. Acta Angiologica, 13: 75–84.

118. Dunkelgrun M, Hoeks SE, Welten GM, Vidakovic R, Winkel TA, Schouten O, van Domburg RT, Bax JJ, Kuijper R, Chonchol M, Verhagen HJ, Poldermans D. (2008) Anemia as an independent predictor of perioperative and long-term cardiovascular outcome in patients scheduled for elective vascular surgery. Am J Cardiol, 101: 1196–1200.

119. Gupta PK, Sundaram A, Mactaggart JN, Johanning JM, Gupta H, Fang X, Forse RA, Balters M, Longo GM, Sugimoto JT, Lynch TG, Pipinos II. (2013) Preoperative anemia is an independent predictor of postoperative mortality and adverse cardiac events in elderly patients undergoing elective vascular operations. Ann Surg, 258: 1096–1102.

120. Nuis RJ, Sinning JM, Rodés-Cabau J, Gotzmann M, van Garsse L, Kefer J, Bosmans J, Yong G, Dager AE, Revilla-Orodea A, Urena M, Nickenig G, Werner N, Maessen J, Astarci P, Perez S, Benitez LM, Amat-Santos IJ, López J, Dumont E, van

Mieghem N, van Gelder T, van Domburg RT, de Jaegere PP. (2013) Prevalence, factors associated with, and prognostic effects of preoperative anemia on short- and long-term mortality in patients undergoing transcatheter aortic valve implantation. Circ Cardiovasc Interv, 6: 625–634.

121. Litvinov RI, Weisel JW. (2017) Role of red blood cells in haemostasis and thrombosis. ISBT Sci Ser, 12: 176–183.

122. Roeloffzen WW, Kluin-Nelemans HC, Bosman L, de Wolf JT. (2010) Effects of red blood cells on hemostasis. Transfusion, 50: 1536–1544.

123. Goldsmith HL, Bell DN, Braovac S, Steinberg A, McIntosh F. (1995) Physical and chemical effects of red cells in the shear-induced aggregation of human platelets. Biophys J, 69: 1584–1595.

124. Nguyen J, Nguyen T. (2013) Percutaneous coronary intervention in patients with active bleeding or high bleeding risk. Anadolu Kardiyol Derg, 2: 165–170.

125. Popma JJ, Ohman EM, Weitz J, Lincoff AM, Harrington RA, Berger P. (2001) Antithrombotic therapy in patients undergoing percutaneous coronary intervention. Chest, 119: 321S–336S.

126. Ikedaa S, Manabeb T, Sugawarab S, Soneb M, Ishikawaa M, Katoa T. (2016) Spontaneous Rupture of a Deep Femoral Pseudoaneurysm Mimicking Lymphedema After Radical Hysterectomy in a Woman Who Was Receiving Warfarin. J Med Cases, 7: 299–302.

127. Lichtenberg M, Stahlhoff W, Boese D. (2013) Superficial femoral artery TASC D Registry: twelve-month effectiveness analysis of the Pulsar-18 SE nitinol stent in patients with critical limb ischemia. J Cardiovasc Surg (Torino), 54: 433–439.

128. Baumann F, Do DD, Willenberg T, Baumgartner I, Diehm N. (2012) Treatment for long-segment femoro-popliteal obstructions: initial experience with a 4-F compatible self-expanding nitinol stent and review of the literature. J Cardiovasc Surg (Torino), 53: 475–480.

129. Bosiers M, Torsello G, Gissler HM, Ruef J, Müller-Hülsbeck S, Jahnke T, Peeters P, Daenens K, Lammer J, Schroë H, Mathias K, Koppensteiner R, Vermassen F, Scheinert D. (2009) Nitinol stent implantation in long superficial femoral artery lesions: 12-month results of the DURABILITY I study. J Endovasc Ther, 16: 261–269.

130. Schulte KL, Müller-Hülsbeck S, Cao P, Becquemin JP, Langhoff R, Charalambous N, Desgranges P, Kobeiter H, Midulla M, Vladimir Borovicanin V, Paunovic D, Beregi JP. (2010) MISAGO 1: first-in-man clinical trial with Misago nitinol stent. EuroIntervention, 5: 687–691.

131. Dake MD, Scheinert D, Tepe G, Tessarek J, Fanelli F, Bosiers M, Ruhlmann C, Kavteladze Z, Lottes AE, Ragheb AO, Zeller T; Zilver PTX Single-Arm Study Investigators. (2011) Nitinol stents with polymer-free paclitaxel coating for lesions in the superficial femoral and popliteal arteries above the knee: twelve-month safety and effectiveness results from the Zilver PTX single-arm clinical study. J Endovasc Ther, 18: 613–623.

132. Bosiers M, Deloose K, Callaert J, Moreels N, Keirse K, Verbist J, Peeters P. (2011) Results of the Protégé EverFlex 200-mm-long nitinol stent (ev3) in TASC C and D femoropopliteal lesions. J Vasc Surg, 54: 1042–1050.

133. Schulte KL, Kralj I, Gissler HM, Bagnaschino LA, Buschmann I, Pernès JM, Haage P, Goverde P, Beregi JP, Válka M, Boudny J, Geibel T, Velkoborsky M, Zähringer M, Paetzel C, Fanelli F, Müller-Hülsbeck S, Zeller T, Langhoff R. (2012) MISAGO 2: one-year outcomes after implantation of the Misago self-expanding nitinol stent in the superficial femoral and popliteal arteries of 744 patients. J Endovasc Ther, 19: 774–784.

134. Matsumura JS, Yamanouchi D, Goldstein JA, Pollock CW, Bosiers M, Schultz GA, Scheinert D, Rocha-Singh KJ. (2013) The United States StuDy for EvalUating EndovasculaR TreAtments of Lesions in the Superficial Femoral Artery and Proximal Popliteal By usIng the Protégé EverfLex NitInol STent SYstem II (DURABILITY II). J Vasc Surg, 58: 73–83.e1.

135. Razzouk L, Aggarwal S, Gorgani F, Babaev A. (2013) In-stent restenosis in the superficial femoral artery. Ann Vasc Surg, 27: 510–524.

136. Schillinger M, Sabeti S, Loewe C, Dick P, Amighi J, Mlekusch W, Schlager O, Cejna M, Lammer J, Minar E. (2006) Balloon angioplasty versus implantation of nitinol stents in the superficial femoral artery. N Engl J Med, 354: 1879–88.

137. Early M, Kelly DJ. (2011) The consequences of the mechanical environment of peripheral arteries for nitinol stenting. Med Biol Eng Comput, 49: 1279–1288.

DOI:10.14753/SE.2023.2747

8. Bibliography of the candidate's publications

8.1. Peer reviewed articles with relevance to the current work

1. Sarkadi H, Gőre J, Veres DS, Szegedi N, Molnár L, Gellér L, Bérczi V, Dósa E. (2021) Incidence of and predisposing factors for pseudoaneurysm formation in a high-volume cardiovascular center. PLoS One, 16: e0256317. **IF: 3.240**

2. Sarkadi H, Bérczi V, Kollár A, Kiss D, Jakabfi P, Végh EM, Nemes B, Merkely B, Hüttl K, Dósa E. (2015) Safety, clinical outcome, and fracture rate of femoropopliteal stenting using a 4F compatible delivery system. Eur J Vasc Endovasc Surg, 49: 199–204. **IF: 2.912**

8.2. Other peer-reviewed articles

1. Bérczi Á, Kaposi NP, **Sarkadi H**, Péter Cs, Bérczi V, Dósa E. (2021) Vascular procedures during the COVID-19 pandemic in a high volume Eastern European interventional radiology department. IMAGING, 13: 138–141. **IF: -**

2. Dósa E, Nemes B, Bérczi V, Novák PK, Paukovits TM, **Sarkadi H**, Hüttl K. (2014) High frequency of brachiocephalic trunk stent fractures does not impair clinical outcome. J Vasc Surg, 59: 781–785. **IF: 3.021**

3. Fehérvári M, **Sarkadi H**, Krepuska M, Sótonyi P, Acsády G, Entz L, Lakatos P, Szeberin Z. (2013) Bone mineral density is associated with site-specific atherosclerosis in patients with severe peripheral artery disease. Calcif Tissue Int, 93: 55–61. **IF: 2.748**

4. Szeberin Z, Fehérvári M, Krepuska M, Apor A, Rimely E, **Sarkadi H**, Széplaki G, Prohászka Z, Kalabay L, Acsády G. (2011) Serum fetuin-A levels inversely correlate with the severity of arterial calcification in patients with chronic lower extremity atherosclerosis without renal disease. Int Angiol, 30: 474–450. **IF: 1.652**

5. Krepuska M, Szeberin Z, Sótonyi P, **Sarkadi H**, Fehérvári M, Apor A, Rimely E, Prohászka Z, Acsády G. (2011) Serum level of soluble Hsp70 is associated with vascular calcification. Cell Stress Chaperones, 16: 257–265. **IF: 3.013**

6. Szeberin Z, Fehérvári M, Krepuska M, Apor A, Rimely E, **Sarkadi H**, Bíró G, Sótonyi P, Széplaki G, Szabolcs Z, Prohászka Z, Kalabay L, Acsády G. (2011) Fetuin-A serum levels in patients with aortic aneurysms of Marfan syndrome and atherosclerosis. Eur J Clin Invest, 41: 176–182. **IF: 3.018**

DOI:10.14753/SE.2023.2747

9. Acknowledgements

My research was carried out at the Heart and Vascular Center and at the Department of Radiology and Oncotherapy of Semmelweis University. My thesis is based on two studies with the help and support of many colleagues, only a few of whom can be highlighted here.

First of all, I would like to express my sincere thanks to my supervisor, Dr. Edit Dósa, who is an Associate Professor at Semmelweis University, without whom this Ph.D. thesis could not have been finished. During my doctoral work, I received constant guidance and support from her, and I could turn to her for advice whenever I needed it.

I am particularly grateful to Professor Béla Merkely, who is the Head of the Heart and Vascular Center and Rector of Semmelweis University, for giving me the opportunity to carry out this work.

I would like to express my special thanks to the co-authors of the published articles, the TDK students who participated in the research, and the residents who contributed to the publication of our research results in prestigious international journals.

Last but not least, I would like to thank with great respect my family and friends for being a constant source of inspiration.