PROPOSAL APPLICATION FORM

Peripheral Arterial Disease (PAD) project registration form

Title of research project: **A**THE**R**ECTOMY AND OPEN REPA**I**R FOR COMMON FEMORAL ARTERY ATHERO**S**CLERO**T**IC LESI**ON**S. (The **ARISTON** Trial).

Short title (acronym) – if applicable: the ARISTON trial.

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Brief Project proposal

Peripheral artery disease represents a significant health care burden and is associated with high morbidity and mortality (1)(2). The prevalence of peripheral artery disease (PAD) is continuously rising due to prolonged life expectancy and increasing number of patients with type 2 diabetes mellitus. Thus, PAD is estimated to affect >200 million individuals worldwide and ≥30% of older patients. In addition, epidemiologic studies reveal that the 10-year mortality in patients with chronic claudication reaches up to 30%, whereas in critical limb threatening ischemia (CLTI), overall morbidity and mortality rates are substantially higher (3). Endovascular approaches for the treatment of peripheral artery disease (PAD) have developed tremendously in the past decade, emerging as the first choice for the treatment in a vast majority of patients with claudication and CLTI (4).

Lesions of the common femoral artery (CFA), however, still constitute a complex pathology for which surgical treatment is primarily recommended as the gold standard (5). In the search of less invasive strategies for the specific requirements of the CFA region, particularly tailored to the needs of elderly and multimorbid PAD patients, recent reports highlighted the feasibility of advanced endovascular therapy options, combining atherectomy devices as vessel preparation and adjunctive use of drug-coated balloon angioplasty (DCB) treatment (6-8). Such therapeutic options are increasingly gaining clinical importance, considering the burden of co-morbidities and high perioperative risk, especially in older patients, who are per se not optimal candidates for open surgery. Recently, atherectomy in combination with DCB exhibited low rates of stent placement in the CFA region in combination with acceptable target lesion revascularization (TLR) rates (6, 9). This is particularly promising since this strategy convoys with the leave nothing

behind notion, in a partially moving ‘no stent zone’, which needs to be preserved as a future access site and bypass landing zone.

Currently, the multi-center randomized PESTO-AFC trial (NCT02517827) aims at comparing endovascular versus surgical treatment of the CFA. However, the study is restricted to the use of directional atherectomy and DCB for the endovascular treatment of the CFA, whereas study recruitment and follow-up was slowed down due to the pandemic in the years 2020-2021.

Primary Objectives: To investigate the safety and effectiveness of the endovascular and surgical revascularization techniques for the treatment of consecutive patients with CFA lesions within a real-world registry. Patients will be included with claudication or rest pain due CFA stenosis or occlusion.

In addition, outcomes including improvement in terms of Rutherford category, target lesion revascularization, will be systematically analyzed in all patients.

Study design: multi-center, retrospective observational study.

Study period: 01.01.2015 – 31.12.2021

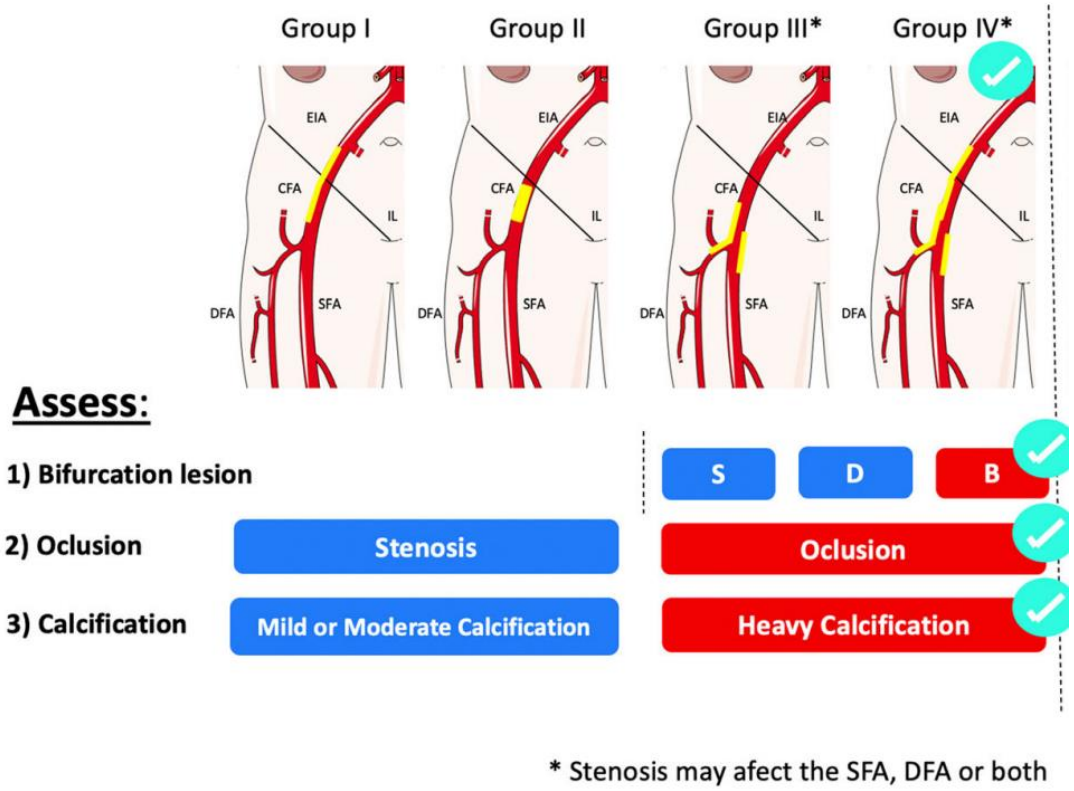
Study population: All comers >18 years with symptomatic PAD.

Requirements and inclusion criteria:

1. Waived informed consent.
2. Subject must be >18 years old.
3. Clinical diagnosis of symptomatic peripheral artery disease defined by Rutherford 2, 3 or 4.
4. Common femoral artery (CFA) stenosis (with or without inclusion of the femoral bifurcation) >70% (visual estimate) or occlusion; Additional lesion(s) in remaining non-target vessel(s), except ipsilateral iliac arteries, can be treated at the physician´s discretion.
5. Angiographic or CTA evaluation of CFA lesion based on the CFA occlusive disease classification available based on the novel CFA lesion classification, as recently proposed by Rabellino et al, which combines characteristics of the Azema (10) classification, simultaneously subcategorizing bifurcation lesions and assessing the presence of CTO and of mild/moderate versus severe calcification (11).
6. At least one vessel outflow (infrapopliteal arteries) to the foot (without stenosis >50%).
7. Endovascular Procedure: successful target lesion crossing of the guidewire (guidewire located intraluminally). Vessel preparation by all available types of lesion preparation by atherectomy in first line but also with intravascular lithotripsy and additional use of POBA, DCB, scoring balloon or combination treatment of the above-mentioned options is allowed.
8. Surgical revascularization techniques included patch endarterectomy or direct suture of the common femoral artery with or without involvement of the distal

portion of the external iliac artery and femoral bifurcation. Hybrid approach with stenting of the common iliac artery to optimize inflow in the CFA is allowed.

9. Ipsilateral treatment of significant iliac disease within or prior to the index session is mandatory. Ipsilateral femoropopliteal disease (only TASC A & B lesions) is allowed.
10. Clinical or if available duplex follow-up postoperatively available.



CFA occlusive disease classification, as described by Rabellino et al (11) for type I, II and subclassifying type III CFA lesions. In addition, information is provided on the presence of CTO and on lesion calcification.

Exclusion Criteria:

1. Evidence of thrombus within target vessel or thrombolysis within 72 hours prior to the index procedure.
2. In-Stent restenosis of the CFA.
3. Restenosis after surgical endarterectomy.
4. Ipsilateral femoropopliteal TASC C & D lesions.
5. Patients with CLTI and Rutherford 5 & 6 category.

Outcome measures (12 months of follow-up):

- Reintervention (TLR).
- Restenosis confirmed by ABI or by duplex sonography.
- Periprocedural and 30-day mortality.
- Endovascular (pseudoaneurysm or bleeding requiring surgery, symptomatic peripheral embolization with clinical impairment in the deep femoral artery or in the popliteal/tibial vessels) and surgical complications (wound complications (lymphorrhea, lymphocele) needed re-operations, VAC placement, persistent nerve irritation influencing quality of life).
- Length of hospital stay
- Clinical improvement defined as cumulative improvement of 1 class by Rutherford scale.
- Major adverse events during hospital stay.

Predefined subgroups:
Octogenarians >80yrs. of patients >70yrs. with significant comorbidities such as symptomatic heart failure, unstable coronary or carotid disease.

Statistical justification: Descriptive statistics. In addition, propensity matching will be assessed to adjust for any potential confounders using logistic regression models. Thus, matching will be performed, including variables such as sex, age, body-mass-index, Rutherford category, bypass graft length, number of BTK run-off vessels, atherogenic risk factors, concomitant coronary artery or cerebrovascular disease, ankle-brachial-index etc.

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