PROPOSAL APPLICATION FORM

Peripheral Arterial Disease (PAD) project registration form

Title of research project: Comparison of **EN**dovascular and **SU**rgical treatment options for patients presenting with Claudication or CLTI due to **PRO**sthetic femoropopliteal bypass occlusion.

Short title (acronym) – if applicable: ENSUPRO trial.

Chief Investigator responsible for project

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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).

Despite technical developments however, even advanced endovascular techniques may fail in terms of long-term patency in patients with extreme vessel calcification and long (>25cm) occlusive lesions. Such patients therefore undergo femoropopliteal bypass surgery, which is an established revascularization method, recommended for the treatment of >25cm long occlusive lesions by current guidelines (5). However, maintaning patency has always been difficult for failing prosthetic femoropopliteal bypass grafts especially in those with bypass occlusion (6).

Such patients with thrombotic bypass occlusion may present either with claudication or with CLTI, the latter in case of thromboembolic nature of the disease and poor run-off issues. The prognosis of such patients may be especially poor in terms both of limb salvage and all-cause mortality. Basically, several tratment options can be considered in such patients, including:

1. Local lysis,
2. Percutaneous or surgical mechanical thrombectomy or embolectomy,
3. Combination of (1) and (2) with additional PTA and if required stent implantation,
4. Combination of (1) and (2) with additional implantation of covered stent grafts,
5. Recanalization of the native artery or,
6. Re-do bypass surgery and patch angioplasty.

However, limited data are available for the comparative value of such treatment regimes in terms of safety (for example bleeding events), graft patency and procedurally related and long-term mortality. In this regard, thrombectomy in combination with lysis may be more effective than thrombectomy alone for removing thrombus burden; however lysis may leed to bleeding complications, than may result in major complications in some, particularly elderly patients. Thus, collecting data in this field of prosthetic bypass occlusion and performiming retrospective prospensity matching analysis for patient and lesion characteristics may shed more light to identify the optimal treatment regime for such individuals. This may be a first step, allowing hypothesis generation for future randomized trials in this field.

Primary Objectives: To investigate the safety and effectiveness of different endovascular and surgical revascularization techniques for the treatment of patients who present with CLTI due acute or subacute prosthetic bypass graft occlusion.

Based on the time duration between onset of symptoms and presentation limb ischemia is defined as *acute* in case of patient presentation within 2 weeks after symptom onset and *subacute or chronic* in case of presentation at 2 weeks and 3 months, respectively after symptom onset.

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

Study design: Multi-center, retrospective observational study.

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

Requirements:

1. Waived informed consent.
2. Acute or subacute occlusion of a prosthetic bypass graft.

Outcome measures (12 months of follow-up):

- Reintervention.
- Restenosis by ABI or if available by duplex sonography.
- Minor or major above ankle amputation.
- Clinical improvement defined as cumulative improvement of 1 class by Rutherford scale.
- Wound healing (WIfI threatened limb score if available).

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-brachia-index etc.

References:

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