Peripheral Arterial Disease (PAD) project registration form

Title of research project: Large-scale, multicenter study on the outcomes of surgical, hybrid and endovascular treatments of Acute Limb Ischemia

Short title (acronym) – if applicable: ALIVE (Acute Limb Ischemia Vascular Outcomes Evaluation)

Investigator responsible for project

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Background

Acute limb ischemia (ALI) of the lower extremities is one of the most common emergencies in vascular practice with potentially debilitating outcomes without timely intervention: up to 40% amputation and 15-20% mortality rates have been reported (1). With the establishment of catheter directed thrombolysis (CDT) as a viable alternative to surgical thrombectomy, a shift towards endovascular means has been observed over the past three decades (2, 3). However, there is a paucity in published data since the landmark thrombolysis trials of the ‘90s. This lack of data becomes especially important when considering the advent of specialized endovascular thrombectomy devices, with mostly industry-sponsored projects to back them up.

A recent observational study of French health insurance claims reported on the outcomes of 51,390 patients undergoing ALI treatment and found lower mortality and major amputation rates after one year of endovascular treatment compared to surgical procedures (4). The study is however limited by its design, whereby hybrid procedures were grouped together with the open surgical ones. Moreover, as expected in a study like this, granular data on treatment (device, access, anatomical extension of disease) are lacking.

In our own two center experience, we analyzed the outcomes after surgical, hybrid and endovascular revascularization for ALLI across 395 patients from two centers and concluded that endovascular treatment led to higher amputation-free survival rates compared to open surgical and hybrid treatments (5).

Objective

To investigate outcomes after surgical, hybrid and endovascular treatment of ALI focusing on long-term efficacy of the various endovascular thrombectomy devices and lysis in the modern setting.

Hypothesis

Our hypothesis is that endovascular ALI treatment provides lower rates of complications in the early postoperative period and shorter hospital stays. Moreover, we hypothesize that endovascular treatment is safer and more efficient compared to surgical and hybrid treatments in the the long term.

Methodology

We propose a multicenter, retrospective, comparative study of consecutive patients undergoing treatment for ALI. Inclusion criteria would be ALI presentation due to occlusion of native peripheral vessels, occlusion of bypass grafts, stents and stent-grafts. Patients with distal embolization during an open or endovascular procedure or vascular trauma would be excluded from the analysis due to fundamental differences in pathophysiology, presentation and treatment. Patients with popliteal artery occlusion or aortic aneurysm occlusion can be included and they will be separately analyzed.

Primary study endpoints would be the composite of major amputation and/or death (amputation-free survival; AFS). Secondary endpoints would be defined as technical success, major amputation, mortality, local complications (vascular access complications, wound infection, chylous leak), clinically driven target lesion revascularization (CD-TLR) and reintervention.

According to a priori sample size calculations for an expected incidence of approximately 25% loss of AFS in the surgical and hybrid group and 15% in the endovascular group, a minimum of 334 patients in each group must be obtained for a two-sided $\alpha=0.05$ and a strong power $(1-\beta)=0.9$, amounting to a total of 1,002 participants. Alternatively, 750 participants for 80% statistical power would also be adequate.

Data analysis

Tests for normality with the Shapiro-Wilk method will be undertaken and parametric as well as non-parametric tests will be used. Categorical variables will be compared by use of the χ^2 test or Fisher exact test for discrete values. Independent two-sample t-tests will be used for normally distributed continuous variables and the Wilcoxon rank-sum test for non-normally distributed continuous and ordinal variables.

Logistic regression multivariate analysis as well as proportional hazards modelling for time-to-event analysis will be employed.

We expect, according to historical data, that a major factor impacting the quality of the analyses will be variance in the cohort regarding key variables, especially Rutherford classification upon presentation, anatomical disease distribution and de-novo lesions vs. occluded grafts/stents/stent-grafts. To tackle this issue, propensity score matching while controlling for key variables will be undertaken between the three groups.

References:

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3. Ebben HP, Jongkind V, Wisselink W, Hoksbergen AWJ, Yeung KK. Catheter Directed Thrombolysis Protocols for Peripheral Arterial Occlusions: a Systematic Review. Eur J Vasc Endovasc Surg. 2019;57(5):667-75.
4. Espitia O, Del Giudice C, Hartung O, Herquelot E, Schmidt A, Sapoval M, et al. Editor's Choice -- Survival, Limb Salvage, and Management of Patients with Lower Limb Acute Ischaemia: A French National Retrospective Observational Study. Eur J Vasc Endovasc Surg. 2024;67(4):631-42.
5. Konstantinou N, Argyriou A, Dammer F, Bisdas T, Chlouverakis G, Torsello G, et al. Outcomes After Open Surgical, Hybrid, and Endovascular Revascularization for Acute Limb Ischemia. J Endovasc Ther. 2023:15266028231210232.