The PORTuguese Registry of Supera supported femoral-popliteal revascularization

SupPORT registry

Study protocol – V1

Date: April 1st 2023.

Primary endpoints (at hospitalization, 30 days, 6 months, 1 year)

1. Limb salvage (freedom from major amputation).
2. Target lesion revascularization (TLR)
3. Freedom from major adverse limb events (MALE – Major Amputation, any index limb revascularization)

Secondary endpoints (at hospitalization, 30 days, 6 months, 1 year)

1. Freedom from Major adverse cardiovascular events (5-point endpoint: Stroke, myocardial infarction/Acute coronary syndrome, Any limb revascularization, Decompensated Congestive Heart Failure, Cardiovascular death[1])
2. All-cause death / Cardiovascular death
3. Primary Patency(defined by Duplex Ultrassound Scan [DUS][2]) Primary-Assisted Patency, Secondary Patency
4. Ankle-Brachial Index (ABI)
5. Rutherford-Becker classification

Inclusion Criteria

Clinical

- Evidence of symptomatic obstructive peripheral arterial disease
- Individuals aged 18 and older
- All-comer patients undergoing endovascular lower-limb revascularization with Supera® stent implantation in the superficial femoral (SFA) or popliteal arteries
- Patient or legal representative understand the SupPORT registry procedures, and have voluntarily provided informed written consent regarding their participation.
- Participant is willing to remain in the SupPORT Registry for at least 1 year.

Angiographic

- Target lesion is a primary atherosclerotic lesion or a restenosis occurring in a non-stented of the SFA or the popliteal artery, distancing at least ≥ 1 cm from any previously implanted vascular stent.
- Target lesion causes a ≥50% arterial obstruction (visually confirmed on digital subtraction angiography).

Exclusion criteria

- Any contraindication for peri-interventional or post-interventional anti-thrombotic therapy (including, but not restricted to Non-fractioned heparina, low-molecular weight heparina [LMWH],

Clopidogrel, Ticagrelol, Ticlopidine, Acetylsalicylic acid, dipiridamol, direct thrombin [factor II] or factor Xa inhibitors, vitamin-K antagonists).

- Participation in other research study that may influence obtained results.
- Pregnant or breastfeeding women, or expected pregnancy to occur during the study period.
- Treatment of intrastent restenosis/occlusion of previous peripheral vascular stent.
- Non-corrected hemodynamically significant obstructive arterial disease of the ipsilateral inflow arteries (aorta, iliac arteries)

Procedure Protocol – Endovascular revascularization

- Participating centers are invited to maintain local practice standards, used in endovascular peripheral arterial revascularization. Pre-implant ballooning and peri-interventional anti-thrombotic therapy will be captured by the database. Intra-procedural and peri-procedural adjuncts are allowed, and will be recorded.

Follow-up Protocol

- Minimum follow-up will include a clinical assessment up to 30-days post-intervention, at 6 months, and at 1 year. Routine ABI is mandatory. Routine DUS is recommended.
- Post-interventional anti-thrombotic therapy will be captured by the database, and will follow international recommendations, but also local practice standards and will be at the discretion of the assisting-physician.

Data collection and storage

- Data will be inserted at each center by the Investigation team on an electronic platform, created and managed by Infortucano.
- Principal Investigators will have access to the enrolled center's participant data.
- **System components**

1. Registry Database

All data regarding each participant's records will be anonymously collected in a Central Database, where it will be stored. There are no limits to the number of participating centers.

2. Web Application – SupPORT Registry

a. Registry - The application will run on internet browser, with individual user authentication required for each Principal investigator. This application will allow the recording of the data and follow-up data by each participating center.

b. Information extraction - Inserted data by each center/investigator will be only accessible to each center/investigator during the study period. The Registry administrator will have access privileges to all participants' data. The application will provide general tables/graphics with generic information throughout the study period, accessible to all investigators (number or participants per center, overall inclusion, to be defined). All inserted data will be exportable to CSV files, allowing import to Microsoft Excel or SPSS software.

c. Technological architecture - All components are developed Microsoft.NET platform. The web application will be developed on ASP.NET 3.5/4.0. The Database Management System (DBMS) will be Microsoft SQL Server 2012/2019. The used Web Server will be Microsoft IIS 7.0.

d. Storage - The Central System and DBMS will be lodged in Safe Cloud Microsoft Azure Servers (InforTucano). The application address will be www.rnsupport.com. Cloud Microsoft Azure Server Characteristics:

- Physical Location: Western Europe (The Netherlands)
- Data backups with differential archives of the previous 15 days
- Availability - 99,9 %
- Anti-virus ESET File Security for Windows Server
- Double-Firewall (Windows Server e Microsoft Azure Firewall)
- Test version: http://test.infortucano.pt/RegistoSupPORT
    - User: admin
    - Pwd: admin123

Statistical analysis

Statistical analysis: Continuous variables with a normal distribution will be described as mean and standard deviation. Continuous variables are presented as median and interquartile range (IQR) if skewed and will be tested among groups using the Mann-Whitney U-Test for independent samples. Related variables will be compared with the Wilcoxon Signed Rank Test. Categorical variables will be presented as count and percentage and will be compared using the Pearson's $\chi 2$ test or the Fisher´s exact test in cases of low number of events. Life-table based analyses will be used for endpoint assessment. Kaplan-Meier curves will be created, and differences tested according to the log rank test. For association between baseline characteristics endpoints, a multivariable logistic regression model (including time as a co-variate) or a Cox hazards proportion model will be created including variables with α-value ≤ 0.10 on univariate analysis, if appropriate. Stepwise backward elimination of variables with a P-value >.050 will be also used during multivariable modelling. Confidence-intervals of 95% (95%CI) will be used and statistical significance will be considered for $\alpha < .05$. All statistical analyses will be performed using Statistical Package for Social Sciences 21.0 (IBM Inc, Chicago, Ill, USA).

Variable List

1. **Identifiers**

    1. Registry number ID (Code)

2. **Demographic**
    1. Age
    2. Gender
    3. Weight
    4. American Society of Anesthesiology Classification

3. **Comorbidities**
    1. Diabetes Mellitus
    2. Renal function – Seric Creatinine
    3. Hemodialysis status
    4. Smoking habits (current, previous, non-smoker).
    5. Smoking - Pack/year units
    6. Hypertension
    7. Cerebrovascular disease
    8. Coronary ischemic disease
    9. Congestive Heart Failure
    10. Previous Contralateral Major Amputation
    11. Baseline antithrombotic medication (pre-admission)
    12. Baseline statin therapy (pre-admission, none/low/high intensity)[3].

4. **Peripheral arterial disease**
    1. Lower Limb laterality
    2. Rutherford-Becker classification
    3. Trophic lesion severity – according to WIFi classification[4]
    4. Calcaneal involvement by trophic lesion
    5. Trophic lestion infection (according to WIFI classification)
    6. Ankle-Brachial index, baseline
    7. Any previous intervention of the superficial femoral (SFA) or popliteal artery ? Descriptive.

5. **Index lesion classification**
    1. GLASS classification – all sectors of index limb.[5]
        i. Femoral-popliteal
        ii. Infrapopliteal
        iii. Below-the-ankle
        iv. Global Classification (I to III)
    2. Lesion length (Short - <25cm / Long >25cm)
    3. Calcification (Peripheral Artery Calcification Scoring System)[6]

6. **Intervention**
    1. Date
    2. Systemic heparinization (UI/kg) (dose)
    3. Pre-dilation – maximum balloon diameter
    4. Use of other adjuvants in lesion preparation (Descriptive
    5. Supera implant – diameter
    6. Supera implant – total stent length implanted

7. Supera implant – Compressed)/Nominal/Elongated) (overall stent assessment – if length < or > than 10% of the nominal length, then stent is considered compressed or elongated, respectively)
8. Supera implant – nº of stents used (1, >1)
9. SUPERA location (SFA- proximal, SFA- distal/proximal popliteal artery; distal popliteal artery)
10. Adjuvant inflow intervention (at time of Supera implant, before, or after during index hospitalization, yes/no and descriptive)
11. Adjuvant below-the-knee intervention (at time of Supera implant, before, or after during index hospitalization, yes/no and descriptive)
12. Technical success (Stenosis ≤30% or pressure gradient ≤10mmHg)
13. Direct inline flow to flow obtained? (yes/no)
14. Below-the-knee runoff vessels (1/2/3)
15. Unexpected procedural events (descriptive) (may include non-treated non-flow-limiting dissection – grade A or B according to the NHLBI classification, other adjuvant interventions following Supera implant).
16. Adverse intraprocedural events – descriptive (thromboembolic – stent thrombosis, distal embolization, catheter aspiration thrombectomy, thrombolysis, conversion to open surgery, arterial rupture, conversion to covered stent, others.

17. **Post-procedural data – early (during index admission),**
18. Complications? –
    1. Stent thrombosis
    2. Residual stenosis in Supera-stented segment
    3. Hematome/Pseudoaneurysm
    4. Acute myocardial infarct / Stroke
    5. Renal impairement /hemodialysis
17. Mortality
    1. Related or not with procedure?
    2. Cause of death
19. ABI – post-procedural
20. Major amputation?
21. Discharge date

7. Follow-up data (30 day assessment, 6 month, 12 month

1. Follow-up evaluation
    i. Date
    ii. ABI
    iii. Duplex ultrasound performed? (Yes/no)
        1. Permeability? Stenosis (PSV ratio ≥2.5 indicates ≥50% stenosis)
    iv. Lesion healing (yes/no/ favourable)
    v. Rutherford-Becker classification
2. Major amputation?
    i. If yes - Date
3. Target Lesion Revascularization (TLR)
    i. If yes - Date
4. MALE (Major Adverse Limb Event
    i. If yes - Date
5. Major Adverse Cardiovascular Event
    i. If yes - Date
6. Death
    i. If yes – Date
    ii. Cause of death

Bibliographic references

1. Bosco E; Hsueh L, McConeghy KW; et al. Major adverse cardiovascular event defnitions used in observational analysis of administrative databases: a systematic review. BMC Med Res Methodol (2021) 21:241.https://doi.org/10.1186/s12874-021-01440-5
2. Gao M, Hua Y, Zhao X, Jia L, Yang J, Liu B. Optimal Ultrasound Criteria for Grading Stenosis of the Superficial Femoral Artery. Ultrasound Med Biol. 2018 Feb;44(2):350-358. doi: 10.1016/j.ultrasmedbio.2017.10.001. Epub 2017 Nov 14.
3. 2018 AHA/ACC/AACVPR/AAPA/ ABC/ACPM/ADA/AGS/APhA/ ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: Executive Summary, JACC VOL. 73, NO. 24, 2019 https://doi.org/10.1016/j.jacc.2018.11.002
4. Mills, J.L; Conte M.S.; Armstrong D.G.; Pomposelli F.B.; Schanzer A.; Sidway A.N.; et al. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: Risk stratification based on Wound, Ischemia, and foot Infection (WIfI). J Vasc Surg 2014; 59:220-34.
5. Conte M.S.; Bradbury A.W.; Kolh P.; White J.V.; Dick F.; Fitridge R.; Mills J.L.; et al. Global Vascular Guidelines on the Management of Chronic Limb-Threatening Ischemia. Eur J Vasc Endovasc Surg 2019, 58:S1-S109.
6. Rocha-Singh K.J.; Zeller T.; Jaff M.R. Peripheral arterial calcification: prevalence, mechanism, detection, and clinical implications. Catheter Cardiovasc Interv. 2014; 83(6):E212-20. doi: 10.1002/ccd.25387. Epub 2014 Feb 10.

Key words

Supera, Vasculomimetic, Stent, Chronic limb-threatening ischemia, Chronic limb ischemia, Superficial femoral artery, Popliteal artery.

Conditions

Lower limb ischemia, peripheral arterial disease, chronic limb-threatening ischemia, chronic limb ischemia, atherosclerosis femoral artery, superficial/popliteal femoral artery stenosis/occlusion/disease