Supplementary file

5. Characteristics of ongoing studies

BEST

Study name	Best Endovenous Treatment, Including STenting, Versus Non-endovenous Treatment in Chronic Proximal Deep Venous Disease (BEST)
Methods	Patients are being randomised between deep venous stenting or best medical therapy. Allocation: randomised. Intervention model: parallel assignment. Masking: Double (Investigator, Outcomes Assessor) Primary purpose: treatment.
Participants	Estimated enrolment participants: 328 Age: 18-100 years. Male and female participants are eligible. Inclusion criteria: Adult patients with chronic venous disease secondary to chronic proximal thrombotic or nonthrombotic stenosis or occlusion Disease in iliac and/or caval deep venous system(s) CEAP clinical C3, C4, C5, C6 or symptoms of venous claudication Anatomically suitable for endovenous reconstruction Exclusion criteria: Contraindications to stenting (e.g. anatomically unsuitable, contrast allergy) Contraindications to prolonged anticoagulation Existing diagnosis of profound pro-thrombotic states (Beh et's, anti-phospholipid syndrome) Caval occlusion at or proximal to the level of the renal veins Open / hybrid open-endovascular deep venous intervention Pregnancy Inability to provide consent Need to intervene caudal to common femoral vein confluence to achieve inflow Participants that have tested positive for coronavirus within the last 3

	months
Interventions	Intervention: endovascular reconstruction, which encompasses balloon venoplasty and venous stenting plus BMT. A dedicated venous stent will be used, the brand of which the individual interventionist will decide. Control: BMT. Compression stockings encompass a range of therapies used to provide an externally applied graduated-pressure up the length of the limb aiming to improve venous function and decrease lower limb swelling. For the purpose of this trial Class II and Class III graduated compression stockings should be used, with the aim of providing Class III if tolerated. Antithrombotic agents include, but are not limited to: warfarin, apixaban, rivaroxaban, aspirin, and clopidogrel.
Outcomes	Primary: VCSS at 6 months Secondary: Re-intervention, number of participants requiring an additional procedure. [Time Frame: 6 weeks, 3 months, 6 months, 12 months] Stent patency, dichotomous outcome, number of participants with a patent stent at last follow-up. [Time Frame: 6 weeks, 3 months, 6 months, 12 months] Cost-effectiveness of deep venous reconstruction [Time Frame: 12 months] Disease-specific QoL measure. [Time Frame: 6 weeks, 6 months, 12 months] Villalta score [Time Frame: 6 weeks, 6 months, 12 months] Ginsberg score, dichotomous outcome (Yes / No) [Time Frame: 6 weeks, 6 months, 12 months] Venous ulceration, dichotomous outcome [Time Frame: 6 weeks, 6 months, 12 months] QoL SF-36 [Time Frame: 6 weeks, 6 months, 12 months] QoL EQ-5D-5L [Time Frame: 6 weeks, 6 months, 12 months] Walking distance [Time Frame: 6 weeks, 6 months, 12 months]
Starting date	3 September 2022
Contact information	Alun Davies Imperial College Healthcare NHS Trust Recruiting London, UK, United Kingdom, W68RF 0208 3311 7320 BESTtrial@imperial.ac.uk
Notes	This study is in recruiting phase Sponsor: Imperial College London ClinicalTrials.gov identifier: NCT05622500

C-TRACT

Study name	Chronic Venous Thrombosis: Relief With Adjunctive Catheter-Directed Therapy - The C-TRACT Trial
Methods	This is an NIH-funded, Phase III, multicentre, randomised, open-label, assessor-blinded, parallel two-arm, controlled clinical trial. The purpose of this study is to determine if the use of image-guided, endovascular therapy (EVT) is an effective strategy with which to reduce PTS disease severity and improve QoL in patients with established disabling iliac-obstructive PTS. Allocation: Randomised. Intervention Model: Parallel Assignment. Masking: Single (Outcomes Assessor). Primary Purpose: Treatment. Masking Description: Clinical assessments for PTS will be obtained at baseline (pre-randomisation) and at the 6, 12, 18 and 24-month follow-up visits. Examining clinicians will complete PTS training to ensure accuracy across all Clinical Centres. The examiners for PTS must be blinded to the subjects' treatment allocation. Subjects will be reminded not reveal to clinic staff which therapy they received (EVT or No-EVT). Subjects should be examined in the afternoon (the later the better) to allow the symptoms and signs of PTS to manifest. The assessment is performed as follows: ● The subject should be asked to rate the 5 symptoms on the Villalta PTS scale for each leg, record his/her ratings on the chronic renal failure. ● The subject's legs should be unclothed and he/she should be seated facing the blinded clinician (nurse or physician). The 5 signs of PTS and VCSS measures will be recorded by the blinded clinician. Leg ulcers (if present) will be assessed and measured.

Participants	Estimated enrolment participants: 374. Age: 18 Years and older. Male and female participants are eligible. Inclusion Criteria: 1. Disabling (moderate-to-severe) PTS, defined by a) presence of chronic venous disease > 3 months duration in a leg with history of DVT; and b) either a VCSS > 8 or a Villalta score > 10 or an open venous ulcer); and 2. Ipsilateral iliac vein obstruction documented within 3 months prior to screening by either: occlusion or >50% stenosis of the iliac vein on venogram, CT venogram, MR venogram, or IVUS or Air plethysmography showing deep venous obstruction of the ipsilateral leg (reduced venous outflow fraction), and ultrasound showing echogenic material in the ipsilateral iliac vein and non-phasic continuous Doppler flow in the ipsilateral CFV in the presence of normal phasic Doppler flow in the contralateral CFV. Exclusion Criteria: 1. Age less than 18 years 2. Acute ipsilateral proximal DVT episode within the last 3 months, or acute contralateral DVT for which thrombolytic therapy is planned 3. Lack of suitable inflow into the ipsilateral common femoral vein per the treating physician 4. Documented obstruction (occlusion or > 50% diameter stenosis) of an IVC filter 5. Chronic arterial limb ischemia (ankle-brachial index < 0.5) 6. Presence of open venous ulcer > 50 cm^2 area, or suspicion for active ulcer infection in the ipsilateral leg 7. Inability to tolerate endovascular procedure due to acute illness, or general health 8. Severe allergy to iodinated contrast refractory to steroid premedication 9. Known allergy to stent or catheter components 10. Haemoglobin < 8.0 g/dl, uncorrectable INR > 3.5, or platelet count < 50,000/ml 11. Severe renal impairment (estimated GFR < 30 ml/min) 12. Disseminated intravascular coagulation or other major bleeding diathesis 13. Pregnancy (positive pregnancy test) 14. Life-expectancy < 6 months or chronically non-ambulatory for reasons other than PTS

	15. Inability to provide informed consent or to comply with study assessments Note - patients who initially meet an exclusion criterion can be re-screened at a later date, and may be enrolled if all eligibility criteria are met at that time

Interventions	All subjects (EVT and No-EVT Arms) will receive optimal PTS care. At each Clinical Centre, this will be supervised by a physician experienced in managing PTS. experimental: endovascular therapy (including stent device). Subjects randomised to EVT will receive the following: 1. Imaging-guided iliac vein stent placement, and 2. Endovenous ablation of refluxing saphenous vein(s), if the patient has truncal reflux and is still symptomatic. 3. Optimal PTS therapy: medical and compression, lifestyle interventions and venous ulcer care. Ultrasound-guided puncture of vein, fluoroscopic monitoring of catheter/guidewire manipulations, and baseline venogram of CFV through infrarenal IVC. Iliac vein should be pre-dilated to at least 12 mm. Bare, self-expanding stents made of elgiloy or nitinol legally marketed in the USA for any indication and that are at least 12 mm in diameter should be used to recanalise the entire diseased segment of vein. The use of devices > 14 mm is highly recommended for the iliac vein and dilated to at least 14 mm, unless compelling patient factors dictates dilatation to a smaller diameter. Balloon angioplasty of inflow veins. After successful iliac vein recanalization, patients who continue to be symptomatic beyond 2 weeks follow-up and who have valvular reflux in GSV, accessory GSV, anterolateral thigh circumflex, and/or SSV should be offered endovenous ablation. Any FDA-approved method may be used including radiofrequency or laser ablation, sclerotherapy or pharmacomechanical ablation. Control group: non-endovascular therapy. All subjects will receive optimal PTS care as noted above.

Outcomes	Primary outcome: PTS Severity over 6 month follow-up. At 6 months post-randomisation, VCSS will be obtained and PTS severity will be evaluated. Secondary outcome: not provided.
Starting date	Starting date: May 7, 2018. Estimated Primary Completion Date: December 31, 2021.
Contact information	Angela Oliver, RN, BSN, MS; 314-747-8951; olivera@wustl.edu; USA
Notes	This study is in recruiting phase. Collaborators: Ontario Clinical Oncology Group (OCOG) - McMaster University VasCore - Massachusetts General Hospital Mid America Heart Institute - St. Luke's Hospital Principal Investigator: Suresh Vedantham, MD; Clinical Coordinating Center at Washington University School of Medicine, USA 1UG3HL138325-01 (USA NIH Grant/Contract) ClinicalTrials.gov Identifier: NCT03250247

IRCT201108035625N3

Study name	Traditional medical treatment versus interventional approach in acute iliofemoral vein thrombosis.
Methods	Single centre not blinded randomised controlled clinical trial to compare conventional medical therapy (heparin followed by warfarin) with multimodality therapy (lytic therapy with or without angioplasty and stenting) in patients with acute iliofemoral thrombosis.

Participants	Consecutive patients, male and female, without limit of age, with acute extensive iliofemoral venous thrombosis are included.
Interventions	Thrombolytic agent is streptokinase and concomitantly, heparin is administered and continued until therapeutic anticoagulation with warfarin is accomplished. In addition to regional lytic therapy due to lesion situation angioplasty and stenting are performed.
Outcomes	Primary: Venous patency. One, six and twelve months follow-up. Secondary: Symptom changes. One, six and twelve months follow-up.
Starting date	Starting date: August 6, 2011. Estimated Primary Completion Date: June 5, 2013
Contact information	Dr. Yaser Jenab MD, Assistant professor of cardiology, Tehran Heart Center, North Kargar and Jalal Al Ahmad cross Tehran, Tehran; Islamic Republic of Iran Postal code 1411713138 / +98 21 88029600 / +98 91 23375795 / +98 21 88029600 jenab@razi.tums.ac.ir Dr. Neda Ghaffari-Marandi MD, Researcher, Tehran Heart Center, North Kargar and Jalal Al Ahmad cross Tehran, Tehran; Islamic Republic of Iran Postal code 1411713138, Phone +98 21 8802 9600, Fax +98 21 8802 9256 ghaffari_15255@yahoo.com

Notes	Recruitment complete. IRCT registration number: IRCT201108035625N3

NCT04250025

Study name	Angioplasty-stenting vs optimal medical treatment on post-thrombotic syndrome reduction (endoPTS)
Methods	Patients are being randomised between deep venous stenting or conservative management. Allocation: randomised. Intervention model: parallel assignment. Masking: single blind (outcomes assessor). Primary purpose: treatment.
Participants	Estimated enrolment participants: 120 Age: 18 years and older. Male and female participants are eligible. Inclusion criteria: Patient age ≥ 18 years' old Patient with disabling PTS defined as a Villalta score ≥ 10, more than 6 months after unilateral proximal deep vein thrombosis (first or recurrent episode) involving at least iliac vein. A contralateral distal or superficial vein thrombosis was not considered as bilateral thrombosis. Rationale for main inclusion criteria: Patients would be screened more than 6 months after the index DVT event to be sure that symptoms were related to chronic phase of PTS and not to the acute DVT event. Although endovascular therapy has actually matured to propose a systematic evaluation, the procedure remains experimental with potential risks. Therefore, the study must focus on patients with advanced PTS and iliofemoral obstruction, since this population appears to have the greatest attempted benefit. Exclusion criteria: Index DVT without iliac thrombosis Bilateral proximal deep vein thrombosis or Inferior vena cava thrombosis Lower limb arteriopathy defined as ante-brachial index < 0.5

	Vena cava filter Venous ulcers ≥ 50 cm² Life expectancy < 6 months Contraindication to anticoagulant treatment by direct oral anticoagulant Contraindication to the use of low-dose aspirin (100 mg) Use of dual antiplatelet agents aspirin/clopidogrel Use of Prasugrel or Ticagrelor Previous venous recanalization of the same leg Impossible to follow-up Contraindication to contrast iodine Renal insufficiency (Cockroft < 30 mL/min, (less than 3 months old)) Subject in exclusion period from another study, Pregnant or breastfeeding women Subject under administrative or judicial control Subject under legal protection Subject hospitalized for psychiatric care
Interventions	Intervention: immediate venous angioplasty stenting plus medical treatment, i.e. elastic compression and anticoagulation Control: standard treatment for 6 months i.e elastic compression and anticoagulation if needed
Outcomes	Primary: comparison of percentage of patients with corrected PTS (Villalta < 5 i.e. absence of PTS) at 6 months after randomization in control group and 6 months after intervention in experimental group. Secondary: not provided.
Starting date	Start Date: 1 September 2019. Estimated completion date: 1 December 2022
Contact information	Gilles Gilles Pernod, MD PH, GPernod@chu-grenoble.fr Grenoble-Alps University Hospital (CHUGA), Grenoble, Cs 10217, France, 38043
Notes	This study is in recruiting phase Sponsor: University Hospital, Grenoble ClinicalTrials.gov identifier: NCT04250025

NCT05744843

Study name	Structured Exercise Versus Endovascular Reconstruction in Post Thrombotic Syndrome (SEvERe-PTS)
Methods	Patients are being randomised between deep venous stenting or cardiovascular and lower limb strengthening exercise.

	Allocation: randomised. Intervention model: parallel assignment. Masking: none (Open Label). Primary purpose: treatment.
Participants	Estimated enrolment participants: 54 Age: 18 years and older. Male and female participants are eligible. Inclusion criteria: Patients with symptomatic chronic venous outflow obstruction secondary to PTS or other cause affecting the IVC or iliofemoral vein(s) for greater than 12 months duration and clinical indication for Deep Venous Stenting. Exclusion criteria: Deep Vein Thrombosis or Pulmonary Embolism within the last 12 months Significant or untreated left sided heart disease Significant or untreated respiratory disease Significant renal diseaseSignificant liver disease Significant Musculoskeletal or Neurological disease Active cancer Life expectancy of less than 2 years or non-ambulatory status Current or Planned pregnancy within the study period Any other contraindication to exercise Any impairment preventing the provision of informed consent and compliance with study protocol Healthy Volunteers in the control group with presence of any arterial or venous disease
Interventions	Intervention: deep venous stenting Control: exercise, i.e. cardiovascular and lower limb strengthening exercise programme
Outcomes	Primary: Villalta score. [Time Frame: 0 (baseline, prior to intervention, 2 weeks post intervention, on average week 8-12 of the study, and at study completion, 6 months] Secondary: VO2 max - maximal oxygen consumption [Time Frame: 0, 2 weeks, 8-12 weeks] Six minute walk test [Time Frame: 0, 2 weeks, 8-12 weeks] Incline walk test [Time Frame: 0, 2 weeks, 8-12 weeks] Calf ejection fraction by plethysmography [Time Frame: 0, 2 weeks, 8-12 weeks] VEINES-QoL/Sym [Time Frame: 0, 2 weeks, 8-12 weeks, 6 months] Maximal calf isometric contract strength as measured by isometric dynamometry [Time Frame: 0, 2 weeks, 8-12 weeks]

	Deep venous flow velocity [Time Frame: 0, 2 weeks, 8-12 weeks]
Starting date	April 2023
Contact information	Ehsanul K Choudhury, MRCS St. Thomas' Hospital, Guy's and St. Thomas' NHS Foundation Trust London, United Kingdom, SE1 7EH +44 20 7188 7188 ext 53821 ehsanul.choudhury@gstt.nhs.uk
Notes	This study is not yet recruiting Sponsor: Guy's and St Thomas' NHS Foundation Trust ClinicalTrials.gov identifier: NCT05744843

STEVECO

Study name	Stent versus conservative treatment in patients with deep venous obstruction.
Methods	Patients are being randomised between deep venous stenting or conservative management. Allocation: randomised. Intervention model: parallel assignment. Masking: single blind (outcomes assessor). Primary purpose: treatment.

Participants	Estimated enrolment participants: 130 Age: 18 Years and older. Male and female participants are eligible. Inclusion criteria: ● Age > 18 years ● Meet criteria for PTS or ● Patients with May-Thurner syndrome on additional imaging ● Life expectancy of more than one year ● Deep venous thrombosis > 1 year ● Signed informed consent Exclusion criteria: ● Previous intervention of central veins (inferior vena cava, iliac veins, common femoral vein) on the affected limb ● Known pregnancy ● Inability to answer Dutch QoL questionnaires or limited communication in Dutch (written and spoken) ● Contra-indication for prolonged anticoagulant treatment ● Recent, < 1 year, deep venous thrombosis or pulmonary embolism ● Known contrast allergy ● Known dialysis or renal insufficiency needing additional preparation for injection of contrast
Interventions	Intervention: patients will receive deep venous stenting in the iliaco-femoral region. Control: conservative management of complaints.
Outcomes	Primary: quality of life score at 12 months. Secondary: not provided.

Starting date	Starting date: March 9, 2017. Estimated Primary Completion Date: June 2018
Contact information	Timme van Vuuren, MD, +31433871558, timme.van.vuuren@mumc.nl; Cees Wittens, MD, PhD, Prof, c.wittens@mumc.nl, Netherlands
Notes	This study was terminated because recruiting the required number of participants within a reasonable timeframe was impossible. The last update was posted on 8 April 2022. There are no results available. Sponsor: Maastricht University Medical Center, Netherlands ClinicalTrials.gov Identifier: NCT03026049

Footnotes

CFV: common femoral vein

CT: computed tomography

DVT: deep venous thrombosis

EVT: endovascular therapy

FDA: Food and Drug Administration, USA agency

GFR: glomerular filtration rate

GSF: great saphenous vein

INR: international normalized ratio

IRCT: Iranian registry of clinical trials

IVC: inferior vena cava

IVUS: intravascular ultrasound

MR: magnetic resonance

PTS: post-thrombotic syndrome

QoL: quality of life

SSV: small saphenous vein

VCSS: venous clinical severity score; higher scores indicate more severe disease

Villalta score: grades the severity of each of five symptoms (pain, cramps, heaviness, pruritus, and paraesthesia) and six signs (oedema, skin induration, hyperpigmentation, venous ectasia, redness, and pain during calf compression). The maximum summative score is 33; higher scores indicate more severe disease.