Evaluation of Supracardiac Venous Angioplasty and Stenting on Orthostatic Intolerance and Orthostatic Hypotension - The STANDUP 2 Study

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Background

Nearly a century ago, Bradbury and Eggleston provided the first documented description of postural orthostatic hypotension [1]. It is now widely recognized and is thought to affect approximately 16% to 30% of adults aged 65 years or older [2]. Orthostatic hypotension (OH), defined as a reduction of systolic blood pressure of at least 20 mmHg or diastolic blood pressure of at least 10 mmHg within 3 minutes of standing [3], is a form of orthostatic intolerance (OI), which is characterized by the inability to tolerate the upright posture due to symptoms such as dizziness or syncope that are relieved by recumbency [3]. OH is associated with a significantly increased risk of all-cause mortality, incident coronary heart disease, heart failure, and stroke [4]. It is also associated with an increased risk of atrial fibrillation [5], venous thromboembolism [6], and chronic kidney disease [7]. Current pharmacological treatments such as midodrine, fludrocortisone, droxidopa, and pyridostigmine are suboptimal in terms of symptom relief and often limited by serious side effects [3], including severe supine hypertension [8], adverse urological effects [9], hypokalemia, metabolic alkalosis [10], congestive heart failure [11], headaches, nausea, palpitations [12], fatigue, and muscle weakness [13].

Systemic arterial pressure is maintained via a complex orchestration of physical, chemical, and biological processes [14]. We propose that supracardiac venous outflow impairment disrupts this regulation and contributes to orthostatic hypotension and orthostatic intolerance (OI). The scientific rationale for this involves several interconnected mechanisms:

- **Baroreflex and Metabolite Clearance:** The body's primary defense against OH is the baroreflex mechanism. Baroreceptors in the carotid sinus and aortic arch detect blood pressure changes, transmitting information to the brainstem via the glossopharyngeal and vagus nerves. The nucleus tractus solitarii process this input, and the caudal and rostral ventrolateral medulla modulate sympathetic outflow to adjust heart rate and vascular tone [15]. Efficiency depends on proper metabolite clearance, governed by the Fick principle [16], where metabolite removal rate is proportional to the arterial-venous concentration difference and organ blood flow. Impairment in venous outflow can disrupt this tightly coordinated mechanism, exacerbating OH.
- **Venous Return and Cardiac Output Dynamics:** Venous return is a critical determinant of cardiac output. Gravity in the upright position causes pooling of more than 500 ml of blood in the venous capacitance vessels and splanchnic circulation, leading to a decrease in venous return and a drop in cardiac output of nearly 20% [3]. This produces a remarkable decrease in mean arterial pressure at the level of the head [17]. Cerebral autoregulation is less able to maintain stable perfusion during sudden hypotension compared to sudden hypertension [18]. Under normal circumstances, this is counteracted by multiple mechanisms for a smooth, asymptomatic postural transition. Venous return is defined as the difference between mean systemic venous pressure and resistance to venous return [VR = Pmsv - Rv] [19]. Venous valvular stenoses impede venous return proportionally to the number and degree of stenosed

valves, consequently decreasing cardiac output.

- **Vestibulo-Sympathetic Reflex and Sympathetic Anticipation Failure:** The vestibulo-sympathetic reflex integrates vestibular inputs from the inner ear with sympathetic nervous system activity to anticipate and counteract postural changes, such as standing [20]. In OH patients with supracardiac venous outflow obstruction, venous congestion leads to poor metabolite clearance in key sympathetic pathways, including the rostral ventrolateral medulla and sympathetic preganglionic neurons [15]. This impairs anticipatory sympathetic activation prior to standing, resulting in delayed or insufficient vasoconstriction and heart rate adjustments. Consequently, patients experience exaggerated drops in blood pressure upon postural change.
- **Static Venous Tone:** We suspect that venous tone in OH patients is somewhat static, failing to dynamically adjust to postural demands. This manifests as excessive venous constriction in the supine position (contributing to supine hypertension) and inadequate constriction while standing (exacerbating hypotension) [21]. Venous outflow obstruction may perpetuate this dysregulation by maintaining chronic congestion, preventing adaptive venoconstriction. Improving venous outflow via angioplasty or stenting could restore dynamic venous tone, alleviating both supine hypertension and standing hypotension [19].
- **Glymphatic Clearance, Venous Engorgement, and the Fick Principle:** A key underpinning mechanism contributing to the pathophysiology of orthostatic hypotension in the context of venous outflow obstruction is the disruption of the glymphatic system, a brain-wide perivascular network that clears metabolic waste. The glymphatic system, which is most active during sleep, relies on the active bulk flow of cerebrospinal fluid (CSF) into the brain along periarterial spaces, followed by the outflow of interstitial fluid and metabolic waste products along perivenous spaces. Glymphatic clearance is crucial for removing neurotoxic proteins and metabolites, including those that influence autonomic function. Cerebral venous outflow obstruction leads to increased intracranial pressure and venous congestion, which directly impacts the perivenous outflow component of the glymphatic system [19]. This venous engorgement can constrict the perivenous spaces, impeding the drainage of interstitial fluid. According to the Fick principle, the rate of metabolite removal is directly proportional to the blood flow [16]. When venous outflow is compromised, blood flow through the brain's microcirculation is slowed, reducing the efficiency of metabolite clearance from critical brainstem centers like the rostral ventrolateral medulla, which regulates sympathetic outflow [15]. This accumulation of metabolites can impair neuronal function, leading to a blunted or delayed sympathetic response to postural changes, a phenomenon we refer to as "sympathetic anticipation failure". Therefore, supracardiac venous angioplasty or stenting, by improving venous outflow, may restore proper glymphatic clearance and metabolite exchange [19], thereby re-sensitizing autonomic centers and improving orthostatic tolerance.

We conclude that improving venous outflow through supracardiac venous angioplasty or stenting may ameliorate OH and OI, at least to a tolerable degree.

Methods

Intervention

The procedure follows standard sterile techniques and includes the following steps, with RHC integration:

- **Access**: Vascular access is achieved using sterile Seldinger technique. Common sites include

common femoral veins, basilic veins, or internal/external jugular veins. Sheath sizes range from 5F to 9F. Arterial access for diagnostic angiography may be used if needed.

- **Arteriography**: Performed on bilateral common carotid, internal carotid, subclavian, and vertebral arteries with specified views (cervical, cranial, thoracic). Features such as stenosis, occlusion, collateral circulation are assessed, stagnation, reflux and venous phase anomalies are captured
- **Venography**: Performed on bilateral internal jugular and subclavian veins with cervical, cranial, and thoracic views. (Includes detailed assessment of catheter position, reflux, time to contrast clearance, structural anomalies [e.g., thrombosis, aneurysm, diverticulum, atresia], collaterals [mild/moderate/severe], venous structural anomalies, flow direction in the superior ophthalmic vein [antegrade/retrograde], and visualization of the middle meningeal vein [yes/no]. Occipital sinus presence [yes/no] is also noted.)
- **Intravascular Ultrasound (IVUS)**: Advanced into key venous structures (superior sagittal sinus, torcula, bilateral transverse/sigmoid sinuses, internal jugular veins, brachiocephalic veins). (Each vein is segmented into three parts for structural data capture, including smoke, organized thrombus, extrinsic compression, and vascular compression.)
- **Right Heart Catheterization (RHC)**: Integrated into the procedure to evaluate hemodynamic changes pre- and post-stenting. A Swan-Ganz catheter is advanced via venous access to measure:
  - Right atrial (RA) pressure
  - Right ventricular (RV) pressure (systolic/diastolic)
  - Pulmonary artery (PA) pressure (systolic/diastolic/mean)
  - Pulmonary capillary wedge pressure (PCWP)
  - Oxygen saturation (%)
  - Cardiac output (L/min) via thermodilution or Fick method
  - Cardiac index (L/min/m²)
  - Internal jugular vein (IJV) temperature (°C)
  - Central Vein temperature (°C)

  Measurements are taken before and immediately after stenting to assess improvements in cardiac output and repeated at 6 months to determine long term improvement. Waveforms and pressures are recorded for physiological analysis, including respiratory variation (poor/some/moderate/excellent) at relevant catheter stations.
- **Venous Angioplasty**: Performed based on IVUS/angiography. Balloons: Recommended 4-9 mm for intracranial stenoses; 10-14 mm for extracranial stenoses. Inflation: Recommended nominal for 10 seconds.
- **Venous Stenting**: Stents (Abre Stents are the only recommended ones). Sizing via angiography and IVUS. Post-stenting angioplasty with balloons (recommended armada or dorado). Follow-up imaging: Venogram and IVUS.
- **Hemostasis and Closure**: Manual compression or closure devices for access sites.

Medication De-Escalation Protocol

Following intervention, this is the preferred sequence of medication discontinuation: droxidopa (Northera) → pyridostigmine (Mestinon) → fludrocortisone (Florinef) → midodrine. On each day, if the patient is taking the next drug in sequence, stop it completely; if not, proceed to the next drug on the list. Continue orthostatic vitals (supine, seated, standing) and symptom checks (dizziness, presyncope, fatigue). If patient cannot tolerate the medication discontinuation, we will transition to a slower outpatient taper as clinically indicated.

Midodrine Equivalents (ME) Overview

Midodrine Equivalents (ME) provide a standardized way to compare the burden of different blood pressure–raising medications. Each drug's usual maximum daily dose is defined as 100 ME, and lower doses are expressed as proportional values (e.g., midodrine 15 mg/day ≈ 50 ME since 30 mg/day = 100 ME). A patient's total ME is the sum of all agents taken.

ME expresses daily OH medication burden on a common 0–100 scale per agent (100 ME = the drug's usual maximum daily dose). Totals are the sum across agents. The table below lists the conversion factor and the midodrine equivalents for common daily doses.

Medication	Max Daily Dose	Conversion (ME per mg)	Common Daily Doses → ME (≈)
Midodrine	30 mg/day	3.3333	5→17 • 10→33 • 15→50 • 20→67 • 30→100
Fludrocortisone	0.3 mg/day	333.3333	0.1→33 • 0.15→50 • 0.2→67 • 0.25→83 • 0.3→100
Droxidopa	1800 mg/day	0.055556	300→17 • 600→33 • 900→50 • 1200→67 • 1800→100
Pyridostigmine	180 mg/day	0.55556	60→33 • 90→50 • 120→67 • 150→83 • • 180→100

Note: ME assumes proportional dose–effect within usual ranges; clinical response varies. Clinical judgment should be used for tapering and re-initiation.

This protocol aims to minimize side effects while leveraging improved venous outflow.

Endpoints

Primary

1. Reduction in total prescribed midodrine-equivalence post-intervention.
2. Improvement in orthostatic blood pressure drop (supine to standing) post-intervention.

Secondary

1. Improvement in OHQ score post-intervention.

Safety Monitoring

Post-Procedure: Vitals q15min x2, then q30min x1 (total 1 hour). Access site and neurological checks. Follow-ups: Recommended 2-4 weeks, ~3 months, ~6 months, ~1 year and ~2 years.

- Reporting Adverse Events (AEs): The management of adverse events (AEs) and serious adverse events (SAEs) during and after interventional procedures involves a structured, proactive approach to ensure patient safety and mitigate risks. Once an AE is identified, the immediate priority is to stabilize the patient and address the complication based on its severity. For minor events, supportive measures such as observation or symptomatic treatment may suffice, while major complications may require urgent therapeutic interventions, such as additional procedures, escalation of care, or surgical consultation. The current escalation protocols are dictated by the cath lab and are critical and ensure that all team members are trained to recognize complications early and initiate appropriate responses. For example, in cases of bleeding or vascular injury, measures such as hemostatic agents, transfusions, or endovascular repair can be employed promptly. Post-procedurally, patients are closely monitored for early signs of complications. This includes regular clinical assessments, imaging when necessary, and laboratory evaluations (e.g., coagulation profiles). Clear discharge instructions are provided for outpatient cases, detailing symptoms that may indicate complications (e.g., swelling, pain, fever) and emergency contact information for the care team. Serious AEs are documented and reported according to institutional protocols. Root cause analysis is conducted for SAEs to identify contributing factors—whether technical, procedural, or systemic—and develop strategies to prevent recurrence. Recommendations from these reviews may lead to updates in procedural protocols, enhanced training programs, and improved patient pathways to strengthen overall safety of the procedure.

Funding

- Research Assistant - Provided by Interventional Neuro Associates
- Mentoring - Provided by St. Francis Research Center
- Principal and co investigators will volunteer their time

Scientific Benefit

This study will provide insights into venous outflow's role in OH/OI, including vestibulo-sympathetic mechanisms and venous tone. It evaluates RHC-guided interventions and medication de-escalation, potentially reducing pharmacological dependence and advancing VOODO (Venous Outflow Obstruction Disorders) understanding.

Subject Recruitment and Selection

Patients with OH/OI, recruited from neurology, primary care, cardiology. Aim: 200 participants over a 24-month period.

Location

St. Francis Hospital and Heart Center, 100 Port Washington Blvd, Roslyn, NY 11576.

Research Design

Prospective: Single-arm, unblinded registry trial.

- **Inclusion Criteria:**
  1. Age ≥18 years
  2. Diagnosed OH as defined above, or OI defined by a score greater than 3 on the orthostatic hypotension questionnaire (OHQ)
  3. Patient/surrogate/healthcare proxy able to provide informed consent
- **Exclusion Criteria:**
  - Pregnancy/breastfeeding
  - Active infection
  - Coagulopathy
- **Statistical Analysis:** Paired t-tests for pre/post measures; repeated measures ANOVA for QoL. Sample size: 200 for 97.8% power ($p<0.05$).
- **Potential Risks:**
  - **Intracranial Hemorrhage (Bleeding in the Brain):**
    - *What It Is:* This is when blood leaks inside your skull, maybe because a tiny blood vessel gets nicked while we're guiding the catheter or because of medicines we use to keep your blood from clotting too much. It is a rare complication of venous intervention.
    - *How It Might Feel:* You could suddenly get a very bad headache, feel confused, have trouble speaking, notice weakness or numbness on one side of your body, see seizures (shaking you can't control), or even pass out.
    - *How Serious:* This is very serious; it could harm your brain permanently or, in the worst case, be life-threatening if we don't stop it fast.
    - *How Long:* It could start right away during or after the procedure. If it's not treated quickly, the effects might last a long time or not go away at all.
    - *What We Will Do:* If we suspect bleeding in the brain, we will do a brain scan (like a CT) right away to find it, and we might need to do emergency surgery or give you medicines to stop the bleeding. We have brain surgeons ready to help, and we will tell you and your family immediately if this happens so you know what's going on and what we are doing to fix it.
  - **Intraspinal Hemorrhage (Bleeding in the Spinal Canal):**
    - *What It Is:* This is when blood collects around your spinal cord, possibly from a poke during the procedure or from pressure changes in your veins affecting your spine. Incidence is rare in catheter-based procedures.
    - *How It Might Feel:* You might feel sharp or intense back pain, numbness or tingling in your legs or arms, weakness that makes it hard to move, or trouble walking. In rare cases, it could make you unable to move parts of your body.
    - *How Serious:* This can range from uncomfortable to very serious, depending on how much blood there is and where it presses on your spine.

* *How Long:* It could start soon after the procedure and might last days, weeks, or longer if it's bad and not treated.
* *What We Will Do:* We'll pick entry points far from your spine to avoid this, check how you're moving and feeling every hour for the first hour after, and use a scan if you have symptoms. If we find bleeding, we might give you medicines to reduce swelling or do surgery to remove the blood. We will call in a spine expert, and we will let you know right away if we think this is happening, explaining every step we take to help you.

– **Stroke:**

* *What It Is:* A stroke happens if a blood clot or piece of debris blocks an artery in your brain during the procedure, stopping oxygen from reaching part of your brain tissue. This could come from the catheter or stent, with a risk of 1-3% in venous stenting.
* *How It Might Feel:* You might suddenly feel weak or numb in your face, arm, or leg (usually on one side), have trouble talking or understanding others, lose vision in one or both eyes, or feel dizzy and unsteady.
* *How Serious:* It could be noticeable but temporary, or it could cause lasting problems like trouble moving or thinking clearly, depending on how big an area of your brain is affected.
* *How Long:* It might start during or right after the procedure. Some effects could go away in hours, but others might stay for a long time or not go away.
* *What We Will Do:* We will give you medicine during the procedure to thin your blood and prevent clots, use X-rays to watch your brain's blood flow, and act fast if a clot forms, either with drugs to dissolve it or a tool to pull it out. We will check your vitals every 15 minutes after to catch this early, and if it happens, we will tell you and your family right away, starting treatment and keeping you updated.

– **Venous Infarction (Brain Tissue Damage from Blocked Veins):**

* *What It Is:* This is when a vein gets blocked, maybe by a clot in the stent, so blood can't drain out of part of your brain properly, causing swelling or damage there. Risk is estimated at 1-2% post-stenting.
* *How It Might Feel:* You could get a headache, feel confused, have blurry or double vision, or notice weakness in your body, kind of like a stroke but from a vein problem.
* *How Serious:* It could make you uncomfortable or, if it gets worse, cause serious brain swelling or bleeding that needs urgent care.
* *How Long:* It might show up hours or days after the procedure and could be short-lived or last a long time if not fixed.
* *What We Will Do:* After the procedure, we will take pictures (with a venogram or IVUS) to make sure the vein is open, give you medicines (like aspirin) to stop clots, and use drugs or surgery if swelling starts. We will let you know right away if we see this, set up more scans to check it, and explain what we are doing to make it better.

– **Renal Failure (Kidney Damage):**

* *What It Is:* The dye we use to see your veins on X-ray can sometimes hurt your kidneys, especially if they're already weak from things like diabetes or not drinking enough water. Contrast-induced nephropathy occurs in 3-7% of cases.

* *How It Might Feel:* You might pee less than usual, see swelling in your legs or hands, feel tired, or get nauseous a day or two after the procedure.
* *How Serious:* It could be a small problem that gets better on its own, or it could make your kidneys stop working well, needing special treatment like dialysis in rare cases.
* *How Long:* It might last a few days or weeks, but if it's really bad, it could affect your kidneys for a long time.
* *What We Will Do:* We will test your kidney function with a blood draw before the procedure, give you fluids through an IV to protect your kidneys, and use as little dye as we can. If your kidneys start having trouble, we will get a kidney doctor to help, adjust your care, and tell you what is happening and how we will support you.

– **Contrast Allergy:**

* *What It Is:* Your body might react to the dye we use, which has iodine in it, causing anything from a mild rash to a dangerous allergic attack called anaphylaxis. Severe reactions occur in <0.1% of cases.
* *How It Might Feel:* A mild reaction could mean itchy skin, a rash, or hives showing up soon after the dye goes in. A big reaction might make it hard to breathe, swell your throat, or speed up your heart, which would feel scary and urgent.
* *How Serious:* It could be just annoying or, if it's a big reaction, life-threatening without quick help.
* *How Long:* Mild stuff might last a few hours and fade; a serious reaction needs treatment right away but usually gets better fast with care.
* *What We Will Do:* We will ask if you have ever had allergies, especially to dye or shellfish, and might give you medicines (like steroids) ahead of time if you are at risk. We've got emergency drugs and equipment ready in the room, and if you start reacting, we will treat you instantly and let you know what's going on while we help.

– **Groin Hematoma (Bleeding at the Access Site):**

* *What It Is:* Blood can pool under your skin where we put the catheter in your groin, making a bruise or lump because of bleeding from the vein or artery there. Occurs in 5-10% of femoral access cases.
* *How It Might Feel:* You might see a dark spot or feel a sore, swollen area in your groin, maybe tender when you touch it or move.
* *How Serious:* Usually it's just bothersome, but if it gets big, it could press on things nearby and hurt more or need fixing.
* *How Long:* It could show up right after and last days to weeks; small ones heal up, bigger ones take longer or need help.
* *What We Will Do:* We will use an ultrasound to guide where we poke, press on it or use a special device to close it after, and check it often (every 15 minutes for an hour). If it is growing, we will use ice, more pressure, or surgery if it is bad, and we will keep you posted on what we see and do.

– **Pseudoaneurysm (False Aneurysm at Access Site):**

* *What It Is:* This is when blood leaks out of the artery in your groin but gets trapped in a

pocket next to it, making a lump that pulses because it's still connected to your blood flow. Incidence is 0.5-2% post-catheterization.

* *How It Might Feel:* You might feel a throbbing or beating lump in your groin, some pain, or swelling that doesn't go away like a regular bruise would.
* *How Serious:* It is usually manageable but could burst or cause clots if we do not fix it, making it a medium worry.
* *How Long:* It might stick around until we treat it, possibly showing up hours or days later and lasting weeks if ignored.
* *What We Will Do:* We will check with an ultrasound if your groin looks odd after the procedure, and fix it by pressing on it with ultrasound help or surgery if needed. We will tell you if we think this is happening and what we will do next.

– **Permanent or Long-Term Post-Procedural Pain at Intervention Sites:**

* *What It Is:* You might have lasting pain where we went in (like your groin) or where the stent sits, maybe from irritated nerves, scar tissue, or inflammation that doesn't settle down. Chronic pain occurs in 1-3% of cases.
* *How It Might Feel:* It could be a steady ache, a burning feeling, or sharp twinges, especially when you move or press on it, lasting past 3 months.
* *How Serious:* It might be a nuisance or make daily stuff harder, but it's not usually dangerous, just tough to live with.
* *How Long:* It could go on for months or even years if it turns into a chronic thing.
* *What We Will Do:* We will numb the area during the procedure, and give you pain medicines if it keeps up. We will talk with you about how it feels and adjust your plan to make you more comfortable.

– **Mortality (Death):**

* *What It Is:* This is the worst thing that could happen, where a really bad problem like a huge brain bleed, stroke, or allergic shock can't be fixed, and you don't survive despite our best efforts. Mortality risk is <0.5% in venous stenting.
* *How It Might Feel:* It would come after something big, like passing out, not being able to breathe, or your heart stopping; you wouldn't feel it long because it's so fast.
* *How Serious:* This is as serious as it gets; it means losing your life.
* *How Long:* It would happen suddenly and be permanent.
* *What We Will Do:* We will check your health carefully before to make sure you are okay for this, watch you super closely during and after (vitals every 15 minutes), and have a full emergency team ready with all the tools to save you. If anything starts going wrong, we will act right away and tell your family everything we are doing to try to help you.

– **Other Possible Risks:**

* *Infection:* Germs could get in where the catheter goes, making your skin red, warm, swollen, or giving you a fever. Risk is 1-2%. We'll keep everything clean, watch the spot, and give you antibiotics if it looks infected, letting you know what to look out for.
* *Radiation Exposure:* The X-rays we use give off a little radiation, like what you'd get

from a few plane flights. We'll keep it as short as possible and cover you with shields, and there's no immediate feeling from it; we'll explain it if you're curious.

* *Thrombosis (Clot Formation):* A clot could form in your vein or on the stent, maybe making your neck or arm swell or feel heavy. Stent thrombosis occurs in 3-5% of cases. We will give you blood thinners, check the vein's flow after, and tell you if we see a clot, fixing it with medicine or more procedures if needed.

- **Potential Benefits:**
  - **Symptom Improvement:**
    * The procedure might make your headaches less painful or happen less often, clear up some of that fuzzy thinking (brain fog), or quiet down the ringing or buzzing in your ears (tinnitus). For example, some people with vein problems like yours have felt their tinnitus get softer or less bothersome after similar treatments. You might find it easier to focus at work, enjoy quiet moments, or sleep without that pounding in your head.
    * *How We'll Check:* We'll use questionnaires, like the Headache Impact Test (HIT-6), Brain Fog Scale (BFS), and Tinnitus Handicap Inventory (THI), before the procedure, then at 2 to 4 weeks, 4 weeks to 8 weeks, and 3 to 6 months after, with optional remote collection in the interval period, to see if your symptoms change. We'll share your results with you so you know how you're doing.
  - **Better Quality of Life:**
    * If your symptoms get better, you could feel more like yourself, maybe have more energy to do things you love, like spending time with friends or family, without headaches or fog slowing you down. Your mood might lift, you could sleep better, or daily tasks might not feel so hard. Even small changes could make a big difference in how you feel overall.
    * *How We'll Check:* The SF-36 survey will ask about your energy, mood, pain, and daily activities before and after the procedure, with monthly remote options. We'll look at these answers to see if your life feels better, and we'll go over them with you at the end.
  - **Reduced Medication Use:**
    * If the procedure helps, you might not need as many pills, like painkillers for headaches, drugs to stay awake through brain fog, or anything you take for tinnitus. That could mean fewer side effects (like stomach upset from pain meds) or less hassle keeping up with prescriptions.
    * *How We'll Check:* We'll ask you what medicines you're taking at the start, 2 to 4 weeks, and 3 to 6 months, with monthly checks if you opt in remotely, and see if that list shrinks. We'll talk with you about any changes and how they feel.
  - **Helping Others:**
    * Even if you don't feel a big difference, your part in this study will teach us more about whether fixing these veins can help people with symptoms like yours. That could lead to better treatments down the road, not just for you, but for others too.
    * *How We'll Check:* Your answers and procedure results will go into our study data. We'll write up what we learn and share it with you and the medical world, so your effort counts no matter what.
- **Protection of Subjects:**

- **De-identification & Data Security:** All data are de-identified at collection using a unique study ID; the linkage file is stored separately. Data are stored on encrypted servers (encryption at rest and in transit), with role-based access and audit logs. Retention is 5 years, then purge/archival per institutional policy.
- **Minimal Necessary PHI:** Only the minimum PHI required for study conduct is accessed; exports for analysis use de-identified datasets.
- **Informed Consent Process:** Consent obtained by trained study staff with ample time for questions/answers; teach-back is used to confirm understanding; language-appropriate forms and interpreter services are offered; participation is voluntary and can be withdrawn at any time without impact on clinical care.
- **DSMB Oversight:** The team will review safety/efficacy data *quarterly or per every 30 subjects enrolled*, whichever comes first; convene ad hoc meeting with the St. Francis Research stewardship for serious/unanticipated problems; may recommend protocol modification, pause, or termination.
- **Adverse Event Monitoring & Reporting:** Bedside clinical monitoring plus protocol AE/SAE capture with prompt reporting to the IRB/DSMB per institutional timelines; clear pathways for medical management and follow-up.
- **Risk Minimization:** Standardized procedural techniques, lowest reasonable contrast/radiation, renal protection when indicated, and immediate escalation pathways for complications.
- **Confidentiality & Sharing:** Any data sharing uses de-identified datasets; external sharing requires IRB/DSMB approval and data-use agreements.

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