

Official Title: A Multicenter, Prospective, Observational Study of the Vflower Self-Expanding Nitinol Stent for Symptomatic Iliofemoral Vein Stenosis or Occlusion

NCT Number: To be assigned

Document Date: July 2, 2026

Protocol Version: V2.2

Protocol Signature Page

I will strictly adhere to Good Clinical Practice (GCP), faithfully fulfill my responsibilities as an investigator, and personally participate in or directly supervise this clinical trial. I have read and confirmed this protocol and agree to fulfill my responsibilities in accordance with applicable Chinese laws and regulations, the Declaration of Helsinki, GCP, and this study protocol. Any amendments to the protocol must be made with the consent of the coordinating center and the sponsor, and the amended protocol must be approved by the Ethics Committee prior to implementation, except where emergency measures are necessary to protect the safety, rights, and welfare of study subjects.

Study Site: Shanghai General Hospital

Principal Investigator (Printed Name): Zhiwei Zhang

Protocol Summary

- **Project Title:** A Multicenter, Real-World Study of Venous Stent System for the Treatment of Iliofemoral Vein Stenosis or Occlusion
- **Objective:** To evaluate the effectiveness and safety of the Vflower Venous Stent System in real-world clinical practice for the treatment of iliofemoral vein stenosis or occlusion via balloon angioplasty and stent implantation.
- **Study Design:** Multicenter, Real-World Study (integration of prospective and retrospective data)
- **Number of Study Centers:** 5
- **Total Sample Size:** Planned enrollment of 310 subjects (70 subjects each from Shanghai General Hospital, Changhai Hospital, Renji Hospital, and Shanghai Ninth People's Hospital; 30 subjects from Shanghai TCM-Integrated Hospital)
- **Inclusion Criteria:**
 1. Patients who have received the Vflower venous stent for observational/retrospective study;
 2. Age ≥ 18 years, any gender, not pregnant or lactating;
 3. Presence of symptoms and signs of chronic venous disease of the lower extremities;
 4. CEAP classification $\geq$ Class 3;
 5. Imaging confirmation (ultrasound/CTV/MRA/IVUS) of iliofemoral vein stenosis or occlusion (target vessel stenosis $\geq 75\%$);

6. Surgical plan determined by the attending physician, with confirmed use of the Vflower Venous Stent System and signed surgical informed consent;
 7. Ability to understand the study objectives, voluntary participation, signed informed consent, and willingness to undergo follow-up.
- **Exclusion Criteria:**
 1. Iliac vein occlusion extending into the inferior vena cava;
 2. Prior stent implantation in the target lesion;
 3. Fatal pulmonary embolism within 6 months prior to informed consent;
 4. Patients with organ failure (e.g., hepatic or renal);
 5. Known hypersensitivity to nitinol alloy materials or contrast agents;
 6. History of active bleeding, coagulopathy, or refusal of blood transfusion;
 7. Life expectancy <12 months (e.g., advanced malignancy);
 8. Pregnancy, lactation, or intention to become pregnant during the study period;
 9. Participation in other drug or medical device clinical trials without completion of the primary endpoint;
 10. Poor compliance with expected inability to complete scheduled follow-ups.
 - **Primary Endpoint:** Target lesion primary patency rate at 12 months post-procedure, defined as no thrombotic occlusion, no conversion to surgical or secondary endovascular intervention (excluding non-target lesion-related interventions), and in-stent stenosis $\leq 50\%$ (assessed by DSA/Doppler ultrasound/CTV).
 - **Secondary Endpoints:**
 1. Device success rate;
 2. Procedural and technical success rates;
 3. Changes in CEAP classification at 6 months, 12 months, and 2 years post-procedure;
 4. Changes in VCSS score at 6 months, 12 months, and 2 years post-procedure;
 5. Target lesion revascularization (TLR) rate at 6 months, 12 months, and 2 years;
 6. Target vessel revascularization (TVR) rate at 6 months, 12 months, and 2 years;
 7. Incidence of Major Adverse Events (MAE) within 30 days post-procedure or during hospitalization, including device/procedure-related death, device/procedure-related arteriovenous injury of the target vessel or lesion (requiring surgical/interventional treatment), clinically symptomatic pulmonary embolism (chest pain, hemoptysis, dyspnea, hypoxia), device/procedure-related major bleeding of the target vessel or lesion (requiring transfusion/surgical/interventional treatment), in-stent thrombotic occlusion, and device/procedure-related acute deep vein thrombosis;
 8. Adverse events at 6 months, 12 months, and 2 years post-procedure, regardless of relationship to the investigational device.
 - **Statistical Analysis:** Descriptive statistics: continuous variables will be summarized as mean, standard deviation, median, minimum, maximum, Q1, and Q3; categorical variables as counts and percentages. All statistical tests will be two-sided unless otherwise specified. A P-value <0.025 (one-sided) will be considered statistically significant.
 - **Study Duration:** 3 years

Abbreviations

- **CEAP:** Clinical-Etiologic-Anatomic-Pathophysiologic Classification System
- **CTV:** Computed Tomography Venography
- **MRA:** Magnetic Resonance Angiography
- **IVUS:** Intravascular Ultrasound
- **DSA:** Digital Subtraction Angiography
- **VCSS:** Venous Clinical Severity Score
- **MAE:** Major Adverse Event
- **CAD:** Coronary Artery Disease
- **COPD:** Chronic Obstructive Pulmonary Disease
- **DVT:** Deep Vein Thrombosis
- **PTS:** Post-Thrombotic Syndrome
- **IVCS:** Iliac Vein Compression Syndrome
- **PMT:** Percutaneous Mechanical Thrombectomy
- **WBC:** White Blood Cell
- **RBC:** Red Blood Cell
- **PLT:** Platelet
- **HB:** Hemoglobin
- **sCr:** Serum Creatinine
- **BUN:** Blood Urea Nitrogen
- **ALT:** Alanine Aminotransferase
- **AST:** Aspartate Aminotransferase
- **TBIL:** Total Bilirubin
- **DBIL:** Direct Bilirubin
- **IBIL:** Indirect Bilirubin
- **GLU:** Glucose
- **ALB:** Albumin
- **APTT:** Activated Partial Thromboplastin Time
- **PT:** Prothrombin Time
- **INR:** International Normalized Ratio
- **FIB:** Fibrinogen
- **TT:** Thrombin Time
- **D-Dimer:** D-Dimer
- **CRF:** Case Report Form
- **eCRF:** Electronic Case Report Form
- **EC:** Ethics Committee
- **EDC:** Electronic Data Capture
- **DMP:** Disease Management Program
- **DVP:** Data Validation Plan
- **CRC:** Clinical Research Coordinator
- **SAP:** Statistical Analysis Plan
- **FAS:** Full Analysis Set
- **PPS:** Per-Protocol Set
- **QD:** Quaque Die (Once Daily)

1. Background

Iliofemoral venous stenosis or occlusive disease represents the most prevalent condition in venous surgery, encompassing non-thrombotic iliac vein compression syndrome, deep vein thrombosis (DVT), and post-thrombotic syndrome (PTS). According to the China Cardiovascular Health and Disease Report 2020, the prevalence of lower extremity venous disease is 8.89%, affecting nearly 100 million individuals, with a 逐年 increasing trend. The prevalence of iliac vein compression syndrome in China ranges from 14% to 32%, also showing a 逐年 increase. These conditions significantly impair quality of life and impose substantial burdens on labor productivity and healthcare costs [1-2].

With rapid advancements in endovascular techniques, intervention has become the primary treatment for iliofemoral venous stenosis or occlusion. The pathophysiology, anatomy, biomechanics, and hemodynamics of iliofemoral venous disease are complex. Venous stents must possess the following characteristics: (1) Strong radial force to maintain long-term patency; (2) High flexibility to accommodate the tortuous anatomy of the iliac vein; (3) Precise positioning to ensure complete lesion coverage and sustained patency.

Leading global medical device companies, such as Bard and Boston Scientific, have introduced dedicated venous stents for iliac vein compression syndrome. These stents, typically laser-cut, offer excellent support and precise positioning [3-4]. A meta-analysis by Mahmood K. Razavi et al. [5] on stent placement for iliofemoral venous outflow obstruction included 37 studies with 2,869 patients (non-thrombotic: 1,122; acute thrombotic: 629; PTS: 1,118). One-year primary patency rates were 96%, 87%, and 79%, respectively. Clinical follow-up of similar devices indicates long-term patency rates exceeding 90%, confirming the safety and efficacy of venous stent implantation.

Domestically, several companies have developed iliac vein stents (e.g., Grency, ZYLOX Penguin), but gaps remain in design innovation and applicability. Addressing the complex biomechanical demands of the iliofemoral vein, Shanghai Lanmai Medical Technology Co., Ltd. developed the Vflower Venous Stent System. This device features an integrated design with variable mesh density, balancing radial force and flexibility. Its delivery system incorporates a reverse-thread compensation mechanism for precise deployment of braided stents. The biomimetic tapered design reduces chronic outward force, accommodating varying vessel diameters while providing sustained support to prevent restenosis. Shanghai Lanmai Medical Technology Co., Ltd. holds a Medical Device Production License, and the Vflower Venous Stent System has received NMPA marketing authorization. This study aims to verify the effectiveness and safety of the Vflower Venous Stent System in clinical practice.

References: [1] Javad Salimi, et al. Surg Open Sci. 2024, 19:131-140.

[2] Hao Qingzhi, et al. Chin J Clinicians (Electronic Edition). 2013, 7(24):11611-11613.

[3] J Stephen Jenkins. Prog Cardiovasc Dis. 2011, 54(1):70-6.

- [4] Thomas Powell, et al. J Vasc Surg Venous Lymphat Disord. 2023, 11(1):82-90.e2.
[5] Razavi MK, et al. Circ Cardiovasc Interv. 2015, 8(10):e002772.
-

2. Objectives

To evaluate the effectiveness and safety of the Vflower Venous Stent System in real-world clinical practice for the treatment of iliofemoral vein stenosis or occlusion via balloon angioplasty and stent implantation.

3. Subject Selection

Inclusion Criteria (All must be met)

1. Patients who have received the Vflower venous stent for observational/retrospective study;
2. Age ≥ 18 years, any gender, not pregnant or lactating;
3. Presence of symptoms and signs of chronic venous disease of the lower extremities;
4. CEAP classification $\geq$ Class 3;
5. Imaging confirmation (ultrasound/CTV/MRA/IVUS) of iliofemoral vein stenosis or occlusion (target vessel stenosis $\geq 75\%$);
6. Surgical plan determined by the attending physician, with confirmed use of the Vflower Venous Stent System and signed surgical informed consent;
7. Ability to understand the study objectives, voluntary participation, signed informed consent, and willingness to undergo follow-up.

Exclusion Criteria (Any one disqualifies)

1. Iliac vein occlusion extending into the inferior vena cava;
 2. Prior stent implantation in the target lesion;
 3. Fatal pulmonary embolism within 6 months prior to informed consent;
 4. Patients with organ failure (e.g., hepatic or renal);
 5. Known hypersensitivity to nitinol alloy materials or contrast agents;
 6. History of active bleeding, coagulopathy, or refusal of blood transfusion;
 7. Life expectancy < 12 months (e.g., advanced malignancy);
 8. Pregnancy, lactation, or intention to become pregnant during the study period;
 9. Participation in other drug or medical device clinical trials without completion of the primary endpoint;
 10. Poor compliance with expected inability to complete scheduled follow-ups.
-

4. Clinical Study Content

4.1 Study Design

This is a multicenter, real-world study integrating prospective observation and retrospective data.

The study will be conducted at 5 sites. Attending physicians will treat patients with iliofemoral venous stenosis or occlusion (including thrombotic conditions such as DVT and PTS, and non-thrombotic conditions such as IVCS) using the Vflower Venous Stent System manufactured by Shanghai Lanmai Medical Technology Co., Ltd. Investigators will solely observe the treatment outcomes.

A total of 310 subjects are planned for enrollment. An Electronic Data Capture (EDC) system will be used for subject registration.

Clinical follow-up will be conducted within 30 days post-procedure or prior to discharge, and at 6 months, 12 months, and 2 years. Vascular imaging (DSA/CTV/Doppler ultrasound) will be performed as clinically indicated.

4.2 Study Population

- **Retrospective Cohort:** Historical cases treated with the Vflower stent at participating centers from October 1, 2025, until the date of Ethics Committee approval, meeting inclusion/exclusion criteria.
 - **Prospective Cohort:** Newly enrolled subjects meeting inclusion/exclusion criteria following Ethics Committee approval.
-

5. Endpoints

Primary Endpoint

Target Lesion Primary Patency Rate at 12 Months Post-Procedure

Defined as: No thrombotic occlusion, no conversion to surgical or secondary endovascular intervention (excluding non-target lesion-related interventions), and in-stent stenosis $\leq 50\%$ (assessed by DSA/Doppler ultrasound/CTV).

Secondary Endpoints

1. **Device Success Rate:** Successful delivery, deployment, and retrieval of the delivery system, with no conversion to open surgery at procedure end or death within 24 hours.
2. **Procedural Success Rate:** Technical success with no MAE prior to discharge.
3. **Technical Success Rate:** Post-procedure angiography showing residual stenosis $\leq 50\%$ in the target lesion. Adjunctive intra-procedural interventions do not constitute technical failure.
4. **CEAP Classification Change at 6 Months, 12 Months, and 2 Years:** Improvement ≥ 1 class compared to baseline.
Timepoints: Pre-procedure, 6 months, 12 months, 2 years, and annually thereafter.
5. **VCSS Score Change at 6 Months, 12 Months, and 2 Years:** Improvement ≥ 2 points compared to baseline.
Timepoints: Pre-procedure, 6 months, 12 months, 2 years, and annually thereafter.
6. **Target Lesion Revascularization (TLR) Rate at 6 Months, 12 Months, and 2 Years:** Repeat intervention due to clinical indication or stenosis $\geq 50\%$ at the narrowest point of the target lesion.
Timepoints: 6 months, 12 months, 2 years, and annually thereafter.

7. **MAE Incidence Within 30 Days or During Hospitalization:** Includes device/procedure-related death, arteriovenous injury (requiring intervention), symptomatic PE, major bleeding (requiring transfusion/intervention), in-stent thrombosis, and acute DVT.
8. **Adverse Events at 6 Months, 12 Months, and 2 Years:** Any unfavorable medical event, regardless of device relationship.

Other Observational Parameters

1. **Demographics & Comorbidities:** Age, gender, smoking status, diabetes, hypertension, hyperlipidemia, renal insufficiency, CAD, COPD, malignancy, autoimmune disease, prior DVT.
 2. **Procedural Details:** Date, duration, contrast volume, venous access, target lesion extent/length/stenosis, treatment modality, blood loss.
 3. **Hospitalization:** Length of stay, costs.
 4. **Target Vessel/Lesion Management:** Presence of thrombus, debulking method (PMT device/model), balloon angioplasty/stent details (stent model), thrombus clearance rate, subsequent catheter-directed thrombolysis.
-

6. Adverse Event Monitoring

1. Definition

Any adverse medical event occurring within one month after iliac vein balloon angioplasty and stent implantation, regardless of relationship to the investigational device.

2. Classification and Management

2.1 Intra-procedural Adverse Events

(1) Vascular Access Complications

Definition: Vascular injury during puncture, including pseudoaneurysm, arteriovenous fistula, or vessel rupture.

Clinical Manifestations: Local hematoma, pulsatile mass, bruit, persistent bleeding.

(2) Stent Migration/Embolization

Definition: Stent displacement during delivery or post-deployment.

Clinical Manifestations: Angiographic malposition, migration, flow obstruction.

2.2 Early Post-procedural Adverse Events (Within 30 Days)

(3) In-Stent Thrombosis

Definition: Thrombus formation within the stent causing restenosis or occlusion.

Clinical Manifestations: Worsening limb swelling, pain, varicosities, imaging confirmation.

(4) Contrast-Related Adverse Reactions

Definition: Allergic reaction or renal impairment post-contrast administration.

Clinical Manifestations: Rash, pruritus, dyspnea, hypotension, elevated creatinine/BUN.

(5) Post-procedural Bleeding

Definition: Bleeding from puncture site or surgical site.

Clinical Manifestations: Hematoma, hypotension, tachycardia, pallor.

2.3 Late Post-procedural Adverse Events (>30 Days)

(6) Restenosis/Occlusion

Definition: Recurrent stenosis or occlusion post-implantation.

Clinical Manifestations: Limb swelling, pain, skin changes, imaging confirmation.

(7) Stent Fracture

Definition: Structural failure of the stent.

Clinical Manifestations: Imaging confirmation, symptom recurrence, abnormal flow.

(8) PMT-Related Complications (Thrombotic Patients)

Definition: Vascular injury or embolization from percutaneous mechanical thrombectomy.

Clinical Manifestations: Vascular injury, embolization, bleeding, pain.

(9) Catheter-Directed Thrombolysis-Related Complications (Thrombotic Patients)

Definition: Bleeding or allergy from thrombolytic therapy.

Clinical Manifestations: Bleeding, allergic reaction, thrombolysis failure, thrombus recurrence.

3. Severity Assessment

In this observational study, adverse events are diagnosed, managed, and documented by the attending physician. Investigators will solely collect documented AE data and will not participate in AE adjudication or management.