Long-term improvement of limb reflux prevalence and severity after iliac vein stent placement

Seshadri Raju, MD, Michael Lucas, MS, Cooper Luke, MS, Hunter Peeples, MS, Taimur Saleem, MD, *and* Arjun Jayaraj, MD, *Jackson, Miss*

ABSTRACT

Background: The effect of iliac vein stenting on ipsilateral limb reflux is unknown and has remained a matter of speculation. It has been suggested that the propensity for reflux might worsen when proximal stenosis is corrected. This could allow for retrograde flow with coughing and the Valsalva maneuver, stressing the valve. We examined this hypothesis by an analysis of the long-term effects of iliac vein stenting on limb reflux using a single-center, retrospective analysis of prospectively collected data.

Methods: Reflux data from duplex ultrasound of 1387 limbs in 1228 patients who had undergone iliac vein stenting from 1997 to 2018 were analyzed. Of the 1387 limbs, 632 (46%) had had ipsilateral duplex ultrasound-determined valve reflux before stenting, and 747 limbs (54%) had not had reflux; data were missing for 8 limbs. Reflux status before and after stenting was available for seven individual segments for each limb in the database for analysis (total, 9653 segments). The stented patients were examined for reflux at least annually during the follow-up period (range, 1-26 years). Segmental reflux prevalence was detected using duplex ultrasound. We have referred to this as "duplex reflux" or simply "reflux." Reflux severity was graded using (1) a reflux segmental score, assigning one point each for refluxing segments in the limb; (2) air plethysmography (venous filling index [VFI_{90}]); and (3) ambulatory venous pressure (venous filling time [VFT]).

Results: Present duplex reflux was present in a combination of superficial, deep, and perforator segments. Reflux prevalence ranged from 7% of deep femoral segments to 51% at the popliteal segment. Post-stent reflux resolution varied from 21% at the femoral vein segment to 58% at the perforator segments. Reflux had completely resolved in 23% of the limbs. New-onset reflux was rare, with a median incidence of 7% for all segments at risk, with cumulative improvement (Kaplan-Meier curve) in reflux severity (segment score, VFI_{90}, and VFT) for most limbs. These metrics were unimproved, with residual reflux in only 18%, 11%, and 6% (segment score, VFI_{90}, and VFT, respectively) of the limbs at long-term follow-up.

Conclusions: Long-term follow-up of limbs after iliac vein stenting has shown that the associated ipsilateral reflux prevalence and severity will improve in most limbs over time. (J Vasc Surg Venous Lymphat Disord 2022;■:1-6.)

Keywords: Iliac vein stent; Valve reflux; Iliac vein stenosis

The pathology of chronic venous disease (CVD) is either obstruction or reflux, or both. Microcirculatory venous hypertension induced by these pathologies is thought to be the offending mechanism.[1] The treatment of reflux has been the focus of CVD treatment in the previous century. The focus has been shifting to the relief of obstruction with the advent of venous stent technology. In addition, it has been increasingly realized that obstruction is a common pathology in CVD, more so than previously thought.[2]

In a previous report of our stent experience, we noted that a significant fraction of patients who had undergone iliac vein stenting had not had reflux but only pure obstruction.[3] Thus, we speculated that stenting might make preexisting reflux worse because the obstruction might have limited the reverse flow of reflux, "protecting" the reflux from worsening. This, however, was not borne out by postoperative testing of the stented limbs.[4] Furthermore, the clinical outcomes after stenting were the same for patients with and without reflux.[5,6] It was surprising that patients with multisegment reflux (average score, 2.1), including those with axial reflux, had had excellent clinical outcomes that were sustained in the long term despite uncorrected residual reflux. Thus, in the present study, we have reported the long-term outcomes of reflux for patients who had undergone iliac vein stenting. The patients who had had no reflux at stenting were used as a case-control cohort.

From The RANE Center for Venous and Lymphatic Diseases.

Author conflict of interest: S.R.: venous stent design, U.S. patent intravascular ultrasound (diagnostic). M.L., C.L., H.P., T.S., and A.J. have no conflicts of interests.

Additional material for this article may be found online at www.jvsvenous.org.

Correspondence: Seshadri Raju, MD, The RANE Center for Venous and Lymphatic Diseases, 971 Lakeland Dr, Ste 401, Jackson, MS 39216 (e-mail: rajusybil@earthlink.net).

The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2213-333X

https://doi.org/10.1016/j.jvsv.2022.01.009

METHODS

Patients

A total of 3637 limbs in 3532 patients had undergone iliac vein stent placement at a tertiary venous center from 1997 to 2018 for nonocclusive iliac vein stenosis. Prospectively entered data were extracted from the electronic medical records for retrospective analysis.

Exclusions

Limbs in which the stents had become occluded (n = 103) were excluded. In addition, limbs that had undergone superficial, deep, or perforator venous intervention (n = 1512) before or after stent placement were excluded from the present analysis. Also, the limbs with missing pre- or postoperative reflux data (n = 635; 15%) were excluded. Because of the unexpected reflux outcomes after stenting, a diligent effort was made to curate the included limbs for analysis. Patients who had had specific pathology or had undergone interventions that could have influenced the reflux metrics were rigorously excluded. The included patients were "new" who had undergone stenting for the first time.

A total of 1387 limbs in 1228 patients had had reflux data available for analysis after the exclusions. Of the 1387 limbs, 632 (46%) had had duplex reflux before stent placement, and 747 (54%) had not had reflux for stenting; data were missing for 8 of the limbs. Functional tests of reflux (air plethysmography, ambulatory venous pressure) had been performed less frequently than duplex ultrasound, and the results were available for 1209 limbs.

Iliac vein stenting

The indications, technique, clinical follow-up, and stent surveillance protocols have been reported in detail previously.[7,8] Stent placement was determined by the presence of symptoms, not by the degree of stenosis. The median degree of stenosis treated was >50%. Iliac vein stenting in the context of treating acute deep vein thrombosis was excluded from the present analysis. Long-term follow-up included clinical examinations, stent surveillance, and reflux assessment at 6 weeks, 3 months, and 6 months and annually thereafter. The reflux data analyzed in the present study were from the last available follow-up examination.

Reflux assessment

Duplex ultrasound. The prevalence of reflux (yes vs no) was assessed using a color duplex ultrasound machine (Logiq 9; GE Healthcare, Wauwatosa, Wis). We have referred to these data as "duplex reflux" or simply "reflux." The patients were examined in the erect position using automated inflation-deflation cuffs to provoke reflux. Reflux was defined as reverse flow for >1 second for both superficial and deep veins. This threshold has been used in our practice since 1995 and was retained for continuity, although the recent Society for Vascular Surgery and American Venous Forum guidelines have included shorter reflux thresholds for superficial veins. Asymptomatic contralateral limbs were not assessed because of patient resistance (needle stick) and the denial of payor authorization.

Reflux severity was assessed using three different methods: (1) a reflux segment score; (2) air plethysmography (APG); and (3) ambulatory venous pressure (AMVP). The basic technologies underlying these methods differ, with various sensitivities, thresholds, and scales of resolution.[9]

Reflux segment score. Reflux was quantified using a reflux segment score, with one point awarded for reflux in each of seven segments: the great saphenous vein trunk in the thigh, small saphenous vein, femoral vein, deep femoral vein, popliteal vein, posterior tibial vein, and perforator.[9] Using the reflux segment score, a score of 0 indicates no reflux and a score of 7, the maximum presence of reflux across the segments.

Venous filling index. APG (ACI Medical, San Marcos, Calif) was also used to grade reflux as measured by the venous filling index (VFI_{90}). The protocol described by Christopoulos et al[10] was used. A $VFI_{90} \geq 2.3$ mL/second was considered to indicate reflux.

Ambulatory venous pressure. The AMVP was measured using a needle in the dorsal foot vein and a high frequency transducer and digital software (Biopac Systems, Goleta, Calif).[9] The resting pressure with the patient in the erect position was measured with the patient standing on the opposite leg. The AMVP changes with 10 tiptoe movements were recorded to determine the postexercise pressure. We used the venous filling time (VFT; ie, the time required for pressure recovery from the nadir back to baseline) because it is more sensitive than the percentage of decrease.[9] A VFT off <20 seconds was considered to indicate reflux.

ARTICLE HIGHLIGHTS

- **Type of Research:** A single-center, retrospective analysis of prospectively collected longitudinal data
- **Key Findings:** The reflux outcomes for 1387 limbs that had undergone stenting for iliac vein stenosis during a 26-year period were analyzed. Prestent reflux found using duplex ultrasound (n = 632 limbs) had improved or resolved for 44%, was unchanged for 37%, and had worsened for 19% during follow-up. The prevalence of duplex ultrasound-determined reflux (Kaplan-Meier curve) had declined from 100% to 42% of limbs at 14 years after stenting.
- **Take Home Message:** Long-term follow-up of limbs after iliac vein stenting showed that the incidence and severity of prestenting reflux improved in most limbs with time.

Table I. Valve segment duplex reflux in limbs[a] (stented limbs, n = 1379[b])

Valve segment	Prestent segment reflux	Reflux after stenting		
		Resolved	Unchanged	New onset
Great saphenous	273/632 (43)	97/273 (36)	176/273 (64)	136/1002 (14)
Popliteal	320/632 (51)	72/320 (23)	248/320 (78)	82/1033 (8)
Small saphenous	205/632 (32)	77/205 (38)	128/205 (62)	70/1076 (7)
Femoral	208/632 (33)	44/208 (21)	164/208 (79)	75/1143 (7)
Perforator	67/632 (11)	39/67 (58)	28/67 (42)	35/652 (5)
Posterior tibial	69/632 (11)	31/69 (45)	38/69 (55)	30/1269 (2)
Deep femoral	42/632 (7)	23/42 (55)	19/42 (45)	26/1315 (2)
Median, % (range)	32 (7-51)	38 (21-58)	62 (42-79)	7 (2-14)
Total	1184/4424 (27)	383/1184 (32)	801/1184 (68)	454/7490 (6)

Data presented as number/total (%) of refluxing limbs, unless noted otherwise.
[a]Seven named segments per limb for 9653 total segments.
[b]Eight limbs had missing duplex ultrasound data before or after stenting.

Statistical analysis

The χ^2 test and two-tailed t tests were used for the comparison of proportions and continuous variables, respectively. The survival proportions for the change in reflux in the cohorts were analyzed using Kaplan-Meir curves. The Kaplan-Meir curves were truncated when the standard error of the mean was >10%. Log-rank (Mantel-Cox) test was used to compare the Kaplan-Meir curves. Commercially available software, GraphPad Prism, version 9 (GraphPad Software Inc, San Diego, Calif), was used for the analyses. The results from the various tests are presented in Tables I to III and Figs 1 to 3 in context.

Permission

All the patients had provided written informed consent for the various tests and procedures. The institutional review board granted permission for the report of our de-identified analysis.

RESULTS

The demographics of the patients are presented in the Supplementary Table (online only). No significant differences were found in most categories, although more women had had prestent reflux. In addition, more patients had had CEAP (clinical, etiologic, anatomic, pathophysiologic) clinical class 5 and 6 in the limbs with prestent reflux.

The distribution of reflux and post-stent evolution for the various named segments (seven segments per limb) are presented in Table I. Prestent reflux involvement varied widely, ranging from a low of 7% for the deep femoral segment to a high of 51% for the popliteal vein segment. Perforator reflux showed the greatest resolution after stent placement. Finally, new-onset reflux after stenting was rare (median incidence, 7%). Reflux evolution stratified by the various measurement techniques after stent placement is shown in Table II. The proportions reported are the noncumulative raw data.

The determination of improvement in reflux severity using the listed methods was not possible for the limbs without prestent reflux, because the scores were normal from the beginning. Reflux severity, measured using the segmental score, had improved in 44% of limbs, worsened in 19%, and showed no change in 37%. The VFI_{90} and VFT had improved in 60% and 52% of the limbs, respectively. Complete resolution of duplex reflux had occurred in 148 limbs (23%) at the last follow-up examination in this group. The VFI_{90} and VFT had normalized in 98 (31%) and 29 (24%) limbs, respectively. Most of the listed post-stent changes for better or worse were statistically significant (before vs after stenting). The median scores for reflux severity (segmental score, VFI_{90}, and VFT) before and after stenting are shown in Table III. Overall, significant improvement was found in the various measures of reflux severity.

Most of the limbs with abnormal VFI_{90} and VFT values had had duplex reflux. However, no duplex reflux was found in 68 of 629 limbs (11%) with an abnormal VFI_{90} and 28 of 140) limbs (20%) with an abnormal VFT. The VFI_{90} and VFT scores had improved after stenting for most (69% and 54%, respectively) of these limbs.

The cumulative residual reflux (Kaplan-Meier curves) according to the various reflux grading tests is shown in Fig 1. The prevalence of duplex reflux had declined from 100% to 42% at 14 years after stenting. The reflux severity had declined from 100% for each test before stenting to 18% for the segmental score, 11% for the VFI_{90} score, and 6% for the VFT score at 14 years after stent placement. We found no differences between the nonthrombotic and post-thrombotic limbs in the Kaplan-Meier curves (log-rank test).

Table II. Limb reflux parameters after iliac vein stent placement (n = 1379 limbs; venous filling index [VFI_{90}] data available for 1209 limbs; venous filling time [VFT] data available for 307 limbs)

Reflux parameter[a]	Normal/abnormal threshold	Abnormal prevalence	Normalized	Improved	Normalized and improved	Unchanged	Worsened[b]
Duplex reflux (n = 1379; 100%)	Reflux (yes vs no)	632 (46)	148 (23)	131 (21)	279 (44)	232 (37)	121 (19)
Reflux segmental score (n = 1379; 100%)	>0 (range, 1-7)	632 (46)	148 (23)[c]	131 (21)[c]	279 (44)[c]	813 (59)	288 (21)[c]
APG/VFI_{90} (n = 1209; 88%)	≥2.3 mL/s	313 (26)	98 (31)[c]	428 (35)[c]	526 (44)[c]	65 (5)	618 (51)[c]
AMVP/VFT (n = 307; 22%)	≤19 seconds	120 (39)	29 (24)[c]	86 (28)[c]	115 (37)[c]	51 (17)	141 (46)[c]

AMVP, Ambulatory venous pressure; *APG*, air plethysmography.
[a]Cross-prevalence.
[b]Including new-onset reflux.
[c]$P < .0001$ (before vs after stenting).

The cumulative improvement in the various reflux measures over time is shown Fig 2. The limbs with improvements in reflux were indexed to the limbs at risk at the intervals shown, without censoring the limbs with improvement (unlike the Kaplan-Meier curves). Duplex valve competence had improved from 0 in the prestent reflux group to 23% at 20 years after stenting. The segmental score, VFT score, and VFI_{90} score had improved in 44%, 52%, and 60% of limbs compared with the prestent levels at 20 years after stenting. We found rapid improvement in the first year, followed by more gradual improvement at 8 years after stenting. Thereafter, the curves had flattened and had remained stable without obvious deterioration.

DISCUSSION

Reflux improvement. Long-term follow-up of patients after iliac vein stent placement showed significant improvement in reflux prevalence and severity. In the limbs with prestent reflux, the reflux had resolved in one or more segments (median, 38%; Table I), improving the reflux segment score. The functional tests of reflux showed improvement in 60% and 52% for VFI_{90} and VFT, respectively (Fig 2). Complete resolution of reflux resulting in a segmental score of 0 was present in 23% of limbs. The VFI_{90} and VFT had normalized in 31% and 24% of the limbs with prestent reflux, respectively. The limbs without preexisting reflux had largely (78%) maintained their reflux-free status after stent placement. New-onset reflux had developed in 22% of limbs, with the greatest incidence (12%) in the great saphenous vein. Because the limbs with improved reflux status after stent placement substantially outnumbered the limbs that showed reflux deterioration, the overall median values from before to after stenting showed significant improvement.

These qualitative and quantitative measures of reflux appear durable in the long term, with no signs of deterioration in the trajectory of the curve. In contrast, steady deterioration in valve function over time has been reported after valve repair procedures.[11] The improvement in reflux status after stent placement also explains the curious finding that the patients with stenting appeared to tolerate residual uncorrected reflux.[5]

Tools to measure reflux prevalence and grade its severity. Duplex ultrasound, with reflux defined by a valve closure time of <1 second, is a tool to measure the prevalence of reflux at valve sites but cannot be used to grade the severity of reflux itself, except in a binary fashion (yes vs no).[12] The VFI_{90} has generally been

Table III. Reflux severity before and after stent placement

Parameter	Reflux severity		
	Before stenting	After stenting	*P* value
Reflux segmental score (n = 632)	2 (1-7)	1 (0-7)	<.0001
APG/VFI_{90} (n = 313)	3.2 (2.3-13.9)	3 (0-20.2)	.01
AMVP/VFT (n = 120)	10 (0-19)	9.5 (0-61)	.001

AMVP, Ambulatory venous pressure; *APG*, air plethysmography; *VFI_{90}*, venous filling index; *VFT*, venous filling time.
Data presented as median (range).

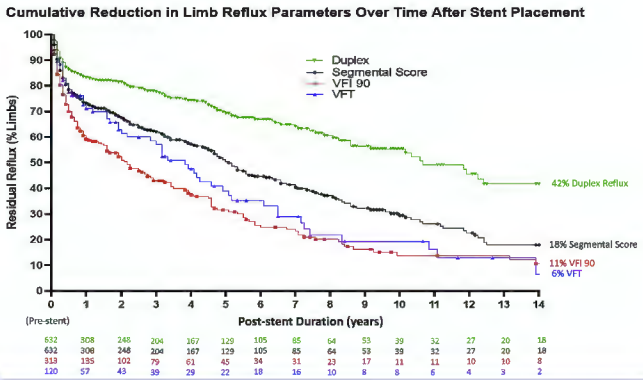

Fig 1. Kaplan-Meier curves showing prestent reflux prevalence and severity after iliac vein stenting. All limbs with an abnormal reflux or severity parameter were included. Limbs with an abnormal venous filling time (VFT) and venous filling index (VFI_{90}) in the absence of duplex reflux were also included. Residual reflux progressively declined after stent placement. Abnormal values persisted in 6% to 41% of limbs for the various parameters (see text for details).

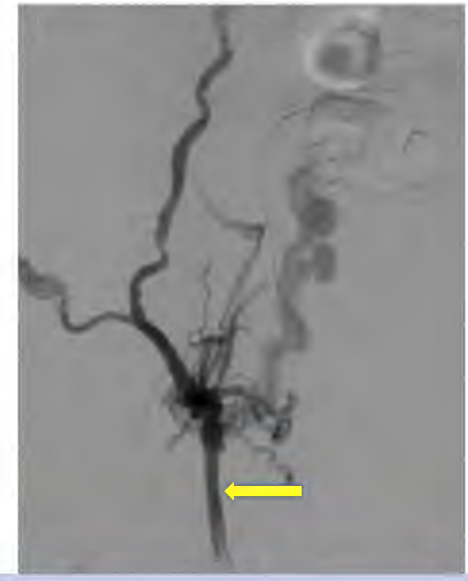

Fig 3. Great saphenous vein reflux (*arrow*) fed by primary branch collateral vessels in a limb with iliac vein obstruction.

regarded as a reliable index of reflux severity. The segment reflux score also appears to be a useful measure of reflux severity. In addition to the VFI_{90}, it appears to be more sensitive than the AMVP measurement.[9,13] The AMVP measurement has long been regarded as the ultimate global measure of reflux. The reflux segment score, VFI_{90}, and VFT are each based on different technologies. They differ from each other in the reflux threshold definition, metric scale used, and resolution. All three methods are inferior to duplex ultrasound for measuring the prevalence of reflux.

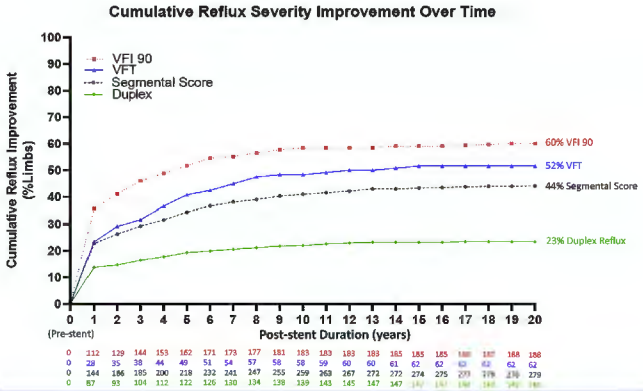

Fig 2. Proportion of limbs with reflux improvement after iliac vein stent placement. Reflux improvement was cumulative without censoring of improved limbs. The initial improvement was rapid during the first year of follow-up after stent placement, followed by more gradual improvement for ≤8 years of follow-up. The curves flattened thereafter without degradation (see text for details). *VFI_{90}*, Venous filling index; *VFT*, venous filling time.

Nonreflux calf pump dysfunction. The VFI_{90} and VFT were abnormal in a fraction of the limbs without reflux, which has been previously described.[14,15] Reflux has remained a major contributor to abnormal scores for these two tests. However, abnormalities of other factors such as compliance, capacitance, ejection and residual fractions and arterial inflow can also influence these measures. These APG measures have been shown to improve after stent placement.[16] Improvement in the VFI_{90} and VFT in the absence of reflux in the present analysis suggests that extra-reflux factors could be important in calf pump function.

Several speculative explanations are possible for the reflux improvement after stent placement. A reduction in the vein caliber below the stent will occur, likely from a reduction in pressure after stenting.[16] A subsequent reduction in the caliber of the valve station, resulting in a competent valve, can be hypothesized. A post-stent reduction in the venous pressure itself likely results in less load on the valve cusps during movement. The presence of prestent reflux in the great saphenous vein had resolved in 36% after stent placement. The primary branches of this vein are important collateral routes in iliac vein obstruction. The disappearance of reflux fed by high pressure collateral vessels into the dilated saphenous vein after stent placement is likely (Fig 3). The appearance of new saphenous vein reflux in stented limbs without preexisting reflux is consistent with the normal pattern of new-onset reflux in this vein with increasing age.[17,18] These findings touch on the relationship between obstruction and reflux in venous pathology. Venous hypertension has been postulated as an end mechanism; however, the pressure relationship between these pathologies remains poorly understood.[19]

CONCLUSIONS

The long-term follow-up data from our study for limbs that had undergone iliac vein stenting showed that reflux prevalence and severity will improve in most limbs with time.

Statistical consultation for data analysis was provided by Jennifer Stafford, PhD, Mississippi College, Clinton, Miss.

AUTHOR CONTRIBUTIONS

Conception and design: SR
Analysis and interpretation: SR, ML, CL, HP, TS, AJ
Data collection: ML, CL, HP
Writing the article: SR
Critical revision of the article: SR, ML, CL, HP, TS, AJ
Final approval of the article: SR, ML, CL, HP, TS, AJ
Statistical analysis: ML, CL, HP
Obtained funding: SR
Overall responsibility: SR

REFERENCES

1. Pascarella L, Schonbein GW, Bergan JJ. Microcirculation and venous ulcers: a review. Ann Vasc Surg 2005;19:921-7.
2. Neglen P, Thrasher TL, Raju S. Venous outflow obstruction: an underestimated contributor to chronic venous disease. J Vasc Surg 2003;38:879-85.
3. Raju S, Neglen P. High prevalence of nonthrombotic iliac vein lesions in chronic venous disease: a permissive role in pathogenicity. J Vasc Surg 2006;44:136-43; discussion: 144.
4. Neglen P, Hollis KC, Olivier J, Raju S. Stenting of the venous outflow in chronic venous disease: long-term stent-related outcome, clinical, and hemodynamic result. J Vasc Surg 2007;46:979-90.
5. Raju S, Darcey R, Neglen P. Unexpected major role for venous stenting in deep reflux disease. J Vasc Surg 2010;51:401-8; discussion: 408.
6. Raju S, Kirk OK, Jones TL. Endovenous management of venous leg ulcers. J Vasc Surg Venous Lymphat Disord 2013;1:165-72.
7. Jayaraj A Sr. Iliac-caval Obstruction. 9th ed. 2019. Elsevier.
8. Raju S. Treatment of iliac-caval outflow obstruction. Semin Vasc Surg 2015;28:47-53.
9. Raju S, Knepper J, May C, Knight A, Pace N, Jayaraj A. Ambulatory venous pressure, air plethysmography, and the role of calf venous pump in chronic venous disease. J Vasc Surg Venous Lymphat Disord 2019;7:428-40.
10. Christopoulos DG, Nicolaides A, Szendro G, Irvine AT, Bull ML, Eastcott HH. Air-plethysmography and the effect of elastic compression on venous hemodynamics of the leg. J Vasc Surg 1987;5:148-59.
11. Raju S, Fredericks RK, Neglen PN, Bass JD. Durability of venous valve reconstruction techniques for "primary" and postthrombotic reflux. J Vasc Surg 1996;23:357-66; discussion: 366-7.
12. Neglen P, Egger JF III, Olivier J, Raju S. Hemodynamic and clinical impact of ultrasound-derived venous reflux parameters. J Vasc Surg 2004;40:303-10.
13. Criado E, Farber MA, Marston WA, Daniel PF, Burnham CB, Keagy BA. The role of air plethysmography in the diagnosis of chronic venous insufficiency. J Vasc Surg 1998;27:660-70.
14. Raju S, Neglén P, Carr-White PA, Fredericks RK, Devidas M. Ambulatory venous hypertension: component analysis in 373 limbs. Vasc Endovasc Surg 1999;33:257-66.
15. Raju SWJM, Jones T. Quantifying saphenous reflux. J Vasc Surg Venous Lymphat Disord 2015;3:8-17.
16. Raju S, Kirk O, Davis M, Olivier J. Hemodynamics of "critical" venous stenosis and stent treatment. J Vasc Surg Venous Lymphat Disord 2014;2:52-9.
17. Maurins U, Hoffmann BH, Losch C, Jockel KH, Rabe E, Pannier F. Distribution and prevalence of reflux in the superficial and deep venous system in the general population—results from the Bonn Vein Study, Germany. J Vasc Surg 2008;48:680-7.
18. Robertson LA, Evans CJ, Lee AJ, Allan PL, Ruckley CV, Fowkes FG. Incidence and risk factors for venous reflux in the general population: Edinburgh Vein Study. Eur J Vasc Endovasc Surg 2014;48:208-14.
19. Raju S, Knight A, Lamanilao L, Pace N, Jones T. Peripheral venous hypertension in chronic venous disease. J Vasc Surg Venous Lymphat Disord 2019;7:706-14.

Submitted Jun 17, 2021; accepted Jan 21, 2022.

Additional material for this article may be found online at www.jvsvenous.org.

Supplementary Table (online only). Demographics of stented limbs (n = 1379)

Demographics	Limbs with prestent reflux	
	No (n = 747)	Yes (n = 632)
Age, years	57 (11-96)	60 (16-96)
Male/female ratio	1:6[a]	1:2
Left/right/bilateral ratio	4:2:1	3:2:1
NTS/PTS ratio	2:5	1:4
CEAP clinical class		
C0-C2[b]	52 (7)	29 (5)
C3	388 (52)	304 (48)
C4	250 (33)	193 (31)
C5	9 (1)	21 (3)[c]
C6	48 (7)	85 (13)[d]

CEAP, Clinical, etiologic, anatomic, pathophysiologic; *NTS*, non-thrombotic; *PTS*, post-thrombotic.
Data presented as median (range) or number (%), unless noted otherwise.
[a] $P < .0001$.
[b] With orthostatic venous pain (visual analog scale score, ≥5 of 10).
[c] $P < .01$.
[d] $P < .001$.