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A meta-analysis of the medium- to long-term outcomes in patients with chronic deep venous disease treated with dedicated venous stents

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ABSTRACT

Objective: This review summarizes the safety profile, stent patency, and clinical effectiveness of dedicated venous stents for the treatment of chronic deep venous disease. The approaches to stenting and post-procedural management of different vascular units are also explored.

Methods: The MEDLINE and Embase databases were searched for pertinent literature published from January 2010 to January 2023. Outcomes related to post-stenting symptoms and health-related quality of life were described narratively. A meta analysis was conducted to evaluate stent patency, ulcer healing, bleeding, and 30-day stent thrombosis, and these outcomes were presented as proportion event rates.

Results: Seventeen studies were identified comprising of 2218 patients. 62.7% of individuals had post-thrombotic stenosis or occlusion. The majority of patients (78.6%) were noted to have complete occlusions of their deep veins before stenting. Eleven different dedicated venous stents were deployed. At 12 months, the primary patency rate was 83% (95% confidence interval [CI]: 76%-90%), the primary-assisted patency rate was 90% (95% CI: 85%-96%), and the secondary patency rate was 95% (95% CI: 92%-98%). A significant improvement in health-related quality of life was demonstrated after intervention. In total, 68.8% (95% CI: 52.0%-83.7%) of ulcers healed at the last follow-up. The remaining symptomatic changes were described narratively; improvements in pain, venous claudication, and edema after stenting were observed. Seventeen deaths occurred, but none were linked to the stenting procedures. A total of 159 cases (7.2% of patients) of in-stent stenosis were observed, whereas 110 stents (5.0% of patients) were occluded. The incidence of major and minor bleeding was 1.7% (95% CI: 1.0%-2.5%) and 3.2% (95% CI: 1.3%-5.6%), respectively, more commonly seen in patients undergoing hybrid intervention.

Conclusions: Deep venous stenting using dedicated venous stents is a safe technique to treat chronic deep venous stenosis and/or occlusion. Within the limitations of this study, deep venous stenting is associated with good patency rates and symptomatic improvement. (J Vasc Surg Venous Lymphat Disord 2024;12:101722.)

Keywords: Dedicated venous stents; Deep vein thrombosis; Non-thrombotic iliac vein lesions; Post-thrombotic syndrome; Stenting; Venous disease

Chronic deep venous obstruction can occur after deep vein thrombosis (DVT) when a vein fails to recanalize due to incomplete clot lysis, resulting in damage to the venous architecture.[1] It is estimated that clinically significant post-thrombotic changes can develop in up to half of patients with DVT, with the greatest risk after proximal (iliofemoral or iliocaval) disease.[2] Alternatively, external compression from a nonthrombotic iliac vein lesion (NIVL) can also directly cause obstruction or predispose patients to DVT.[1] The most pertinent example is May-Thurner syndrome, where the left common iliac vein is compressed by the right common iliac artery. Current data estimate that up to 5% of DVTs are attributable to NIVLs, whereas up to a third of patients with NIVL demonstrate chronic deep venous changes.[3]

Patients with chronic deep venous obstruction present with limb heaviness, swelling, and claudication.[1,4] In addition, notable dermatological manifestations include hemosiderosis, lipodermatosclerosis, and ulceration in severe cases.[1,4] The mainstay of management has consisted of compression therapy and anticoagulation.[5] Patients with severe chronic venous disease (ulceration) or those who have symptoms that affect their daily living can be treated with venoplasty and deep venous stenting.[5]

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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

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https://doi.org/10.1016/j.jvsv.2023.101722

Initially, repurposed arterial stents were deployed in the venous system; however, these lack the specific radial force, flexibility, or deployment accuracy required for deep veins.[6] Consequently, a number of self-expanding nitinol-dedicated venous stents have entered clinical practice to complement the specific features of the venous system.

Research on the clinical effectiveness and side-effect profile of dedicated venous stents has demonstrated that these devices are generally safe and demonstrate good patency in the short term; however, this research has included patients treated with arterial stents.[7-9] In addition, published systematic reviews have not explored the medium- to long-term patency outcomes. This review focuses on the medium- to long-term patency and clinical outcomes in patients with chronic deep venous disease who are exclusively treated with dedicated venous stents.

METHODS

Search strategy. The MEDLINE and Embase databases were accessed using the Ovid platform.[10] Searches were performed by A.S.B. and T.K. and focused on studies published from January 2010 to January 2023, published in English only. The search strategy is attached as a Supplementary Table I (online only). Duplicate studies were automatically filtered out by the Ovid platform, and any remaining records were manually removed thereafter. Initially, study titles and abstracts were appraised by A.S.B. and T.K., and disagreements were adjudicated by G.K. and A.J.H. After this, the full texts of relevant studies were reviewed by A.S.B. and T.K. to determine their eligibility for inclusion in the review.

Inclusion and exclusion criteria. All observational studies and randomized controlled trials that investigated the management of chronic deep venous disease using dedicated venous stents qualified for inclusion. Studies were included if the iliofemoral region was treated, with or without caval involvement. At least 10 stented patients with a minimum of 6 months of follow-up were mandatory. In addition, the studies had to report post-stenting patency at 6 months or greater and/or the severity of chronic venous disease, using the Venous Clinical Severity Score (VCSS),[11] revised VCSS (rVCSS),[12] or the Villalta scale.[13] Studies were excluded if the primary stenting procedures employed arterial stents, if patients were only treated for acute DVT, or if >10% of the patients were not adults (<18 years old). In addition, systematic reviews, abstracts, and case reports were excluded but explored for additional studies.

Outcomes. Two primary outcomes were assessed in this systematic review: (1) clinical changes after stenting, measured using at least one clinical severity score: VCSS, rVCSS, or the Villalta scale; and (2) post-stenting patency categorized into primary patency, primary-assisted patency, and secondary patency. Primary patency was defined as stent patency in the absence of reintervention. Primary-assisted patency was defined as recanalization of a non-occluded stent through additional intervention. Secondary patency was defined as recanalization of an occluded stent through additional intervention. Current published data on patency outcomes predominantly extend to a period of 36 months after stenting. We have accordingly defined short-term patency as <12 months, medium-term patency as 12 to 24 months, and long-term patency as >24 months. The secondary outcomes were ulcer healing; post-stenting pain, edema, and venous claudication; complications (including but not limited to in-stent thrombosis, major and minor bleeding, and access-site complications); and health-related quality of life (HRQoL) as measured using the ChronIc Venous dIsease quality of life Questionnaire-20 (CIVIQ-20)[14] or VEnous INsufficiency Epidemiological and Economic Study—Quality of Life (VEINES-QoL)[15] instrument.

Assessment of the risk of bias and outcomes. Each study was appraised using six domains from the Risk Of Bias In Non-randomised Studies—of Interventions (ROBINS-I) tool[16]: (1) selection of participants into the study, (2) classification of interventions, (3) deviations from intended interventions, (4) missing data, (5) measurement of outcomes, and (6) selection of reported results. The ratings from each domain were consolidated into an overall risk of bias, scored as low, moderate, serious, or critical. In addition, the quality of evidence used in the meta-analysis was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool.[17] Funnel plots were used to examine bias in the patency analysis.

Data analysis and reporting. The study characteristics, procedural characteristics, and clinical outcomes were presented narratively due to variation in the availability and reporting of data. Differences in the methodology used to collect data on HRQoL, pain, claudication, edema, and complications precluded the pooling of data hence these outcomes were also reported narratively as mean or median values for continuous outcomes and counts for categorical outcomes.

Patency data were obtained from manuscript bodies or from the Kaplain-Meier curves when accompanied by numbers at risk and synthesized into proportions. These were then analyzed using the metaprop command in R (version 4.2.2; R Foundation for Statistical Computing)[18] and presented as forest plots.

In addition, the incidence of major and minor bleeding, 30-day stent thrombosis, and the incidence of ulcer healing were extracted, analyzed, and presented as proportion event rates. Additional subgroup analysis was

Table. Study and patient population characteristics

Author	Year	Number of patients	Limbs treated	Vessels involved	Procedures used in patients
Hong et al[20]	2022	n = 255 (females = 137) Mean age: [a]experimental group = 58.4 ± 9.9, [a]control group = 57.5 ± 9.5	255	Iliac vein: 255	Endovenous stenting using either the Venastent or the Zilver Vena stent
Lichtenberg et al[21]	2021	n = 67 (females = 34) Mean age: 46.7 ± 18.1 Malignancy: n = 12	67	Iliofemoral segment: 67	Endovenous stenting using the BLUEFLOW stent
Morris et al[29]	2022	n = 207 (females = 137) Median age: 42 Thrombophilia: n = 62	207	Iliac vein: 207	Endovenous stenting using one of the Vici Venous stent, Abre stent, Venovo stent, or the Zilver Vena stent
Murphy et al[30]	2022	n = 167 (females = 115) Mean age: DNM Thrombophilia: n = 22	167	[b]CIV: 154 EIV: 122 CFV: 71	Endovenous stenting using the Abre stent
Piao et al[31]	2022	n = 102 (females = 54) Mean age: endovascular group = 41.8 ± 16.5, hybrid group = 42.5 ± 13.0	108	IVC + CIV + EIV + CFV: 10 CIV + EIV + CFV: 90 EIV + CFV: 8	Endovenous stenting using various dedicated venous stents or hybrid intervention (endovascular stenting with endophlebectomy of the CFV and arteriovenous fistula creation)
Powell et al[32]	2023	n = 125 (females = 79) Median age: 60 (range 28-88)	125	DNM	Endovenous stenting using the Venovo stent
Razavi et al[33]	2022	n = 200 (females = 120) Mean age: 52.9 ± 16.3 Malignancy: n = 21	200	[b]CIV: 176 EIV: 166 CFV: 63	Endovenous stenting using the Vici Venous stent
Salem et al[34]	2021	n = 58 (females = 27) Mean age: 43.84 (range 25-60)	58	CIV: 5 CIV + EIV: 30 CIV + EIV + CFV: 16 EIV + CFV: 7	Endovenous stenting using the Zilver Vena stent
Lichtenberg et al[35]	2020	n = 79 (females = 44) Mean age: 57 ± 16 Malignancy: n = 9	82	CIV = 71 EIV = 7 CFV = 1	Endovenous stenting using the Venovo stent
Black et al[36]	2018	n = 88 (females = 60) Median age: 42 (range 13-83) Thrombophilia: n = 29	101	[b]IVC = 31 CIV = 101 EIV = 101 CFV = 63	Endovenous stenting primarily using the Vici Venous stent
Lichtenberg et al[22]	2019	n = 48 (females = 30) Mean age: 57 ± DNM standard deviation Malignancy: n = 1	48	CIV = 27 CIV + EIV = 16 CIV + EIV + CFV = 5	Endovenous stenting primarily using the Sinus-Obliquus stent
van Vuuren et al[23]	2018	n = 200 (females = 132) Mean age: 43.2 ± 14.5	200	IVC + CIV = 11 IVC + CIV + EIV = 6 IVC + CIV + EIV + CFV = 15 CIV = 60 CFV = 11 EIV + CIV = 35 CIV + EIV + CFV = 55 CIV + EIV + CFV + PFV = 7	Endovenous stenting primarily using the Sinus-Venous stent

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Table. Continued.

Author	Year	Number of patients	Limbs treated	Vessels involved	Procedures used in patients
Stuck et al[24]	2018	n = 93 (females = 56) Mean age: 45 ± 15.0 Malignancy: n = 13 Thrombophilia: n = 21	93	DNM	Endovenous stenting using various dedicated venous stents
Lichtenberg et al[25]	2018	n = 75 (females = 37) Median age: 57 (range 19-84) Malignancy: n = 11 Thrombophilia: n = 4	82	CIV = 34 CIV + EIV = 19 CIV + EIV + CFV = 9 EIV = 11 CFV = 2 EIV + CFV = 7	Endovenous stenting using the Vici Venous stent
de Wolf et al[26]	2015	n = 75 (females = 49) Median age: 45 (range 18–77)	75	[c]CIV = 2 CIV + EIV = 5 CIV + EIV + CFV above the SFJ = 29 EIV + CFV above the SFJ = 4	Endovenous stenting using the Sinus-Venous stent
van Vuuren et al[27]	2017	n = 369 (females = 257) Mean age: 43 ± 14	417	[d]IVC + CIV = 6 IVC + CIV + EIV + CFV = 10 CIV = 52 CIV + EIV = 33 CIV + EIV + CFV = 33 CIV + EIV + CFV + PFV = 2 CFV = 6	Endovenous stenting using various dedicated venous stents or hybrid intervention (endovascular stenting with endophlebectomy and arteriovenous fistula creation)
Stuck et al[28]	2017	n = 10 (females = 9) Mean age: 36 ± 12 Thrombophilia: n = 3	10	DNM	Endovenous stenting using the Sinus-XL Flex stent

CFV, Common femoral vein; *CIV*, common iliac vein, *DNM*, does not mention; *EIV*, external iliac vein; *IVC*, inferior vena cava; *NIVL*, nonthrombotic iliac vein lesion; *PFV*, profunda femoral vein; *PTS*, post-thrombotic syndrome; *SFJ*, saphenofemoral junction.
[a]Patients treated with Venastent, control group = patients treated with the Zilver Vena stent.
[b]More than one vein involved.
[c]Pertains to number of patients in the PTS subgroup. No data available for the NIVL subgroup.
[d]Disease location not stated in some patients.

conducted, with outcomes stratified by disease etiology (post-thrombotic syndrome [PTS] vs NIVL). Two-sided *P* values of <.05 were considered statistically significant. Heterogeneity between the studies was assessed using the I^2 test. A value of ≥50% represented substantial heterogeneity[19] hence a random-effects model was employed.

RESULTS

Literature search results

The initial literature search revealed 649 studies. After the review of titles and abstracts, 17 eligible studies[20-36] were included (Supplementary Fig 1, online only, and Table). A requisite for this review was that interventions could only involve dedicated venous stents hence a number of studies identified in a previous systematic review[7] were no longer eligible due to a minority of their procedures involving repurposed arterial stents.[26,37-42] Lichtenberg et al[35] investigated outcomes in a cohort of patients treated with the Venovo stent; data on short-[43] and long-term[35] outcomes were published however only the latter[35] were used for this systematic review to prevent duplication of results. Similarly, the VIRTUS trial published three papers[33,44,45] however the most recent publication[33] that pertained to the whole cohort of patients was included.

Study characteristics

A single study used a randomized controlled approach to compare two different dedicated venous stents.[20] The remaining literature was of an observational design; 12 studies[22,23,25-29,31,32,34-36] were carried out retrospectively, whereas 4 studies[21,24,30,33] were undertaken prospectively. A total of 2218 patients were included, of whom 62.1% were female (Table). In the literature, patients' ages were summarized using median or mean; the median age of patients ranged from 42 to 60 years, whereas the mean age ranged from 36 to 58.4 years. A total of 67 (3.02%) patients had a history of malignancy, and 141 (6.36%) patients had thrombophilia.

Overall, 2295 limbs were stented. Post-thrombotic stenosis or occlusion was the most common indication for intervention, comprising 62.7% of cases. Only 7

studies[20,21,25,26,34-36] mentioned whether lesions were stenotic or occlusive, and of these, 78.6% of patients demonstrated complete occlusion of their deep veins before intervention, whereas 10 studies[22-24,27-33] did not provide information on this. In addition, the study by Murphy et al[30] included patients with NIVL and PTS however it only detailed the degree of obstruction for the latter group.

Assessment of the risk of bias and outcomes

The ROBINS-I tool demonstrated that the majority of studies contained a moderate risk of bias. Some studies[24,26,38,39,41,43] did not specify the severity of chronic venous disease in their inclusion criteria using an objective instrument such as the VCSS scale, the rVCSS scale, or the Villalta scale.[20,21,23,24,26,28,31,32,34,35] Retrospective studies can be at risk of selection bias; hence, studies of this design were classified as having moderate bias.[22,23,25-29,31,32,34-36] If follow-up data were available for <90% of patients at the final follow-up, studies were judged to have a moderate risk of bias.[21,31-33,36] The risk of bias in measurement of outcomes was scored as moderate in the majority of studies, as assessors were not blinded to the intervention of patients when measuring symptom changes.[21-36] With the exception of two studies,[30,33] bias in selection of the reported results was graded as moderate as study protocols were unavailable hence the planned statistical analyses could not be reviewed. The GRADE assessment demonstrated "very low" quality of evidence in the meta-analyses.

The funnel plots of the primary patency and secondary patency analysis (Supplementary Fig 2, online only) demonstrated an asymmetrical scatter of points around the weighted mean. This was likely a consequence of publication bias and small study bias, whereby, due to the high meta-variability, smaller studies tended to be either over- or underpublished. In addition, it also reflected heterogeneity between studies attributable to differences in the demographics and disease characteristics of the different study populations.

Procedural characteristics and medical management

Eleven studies[21-27,29,31,35,36] used magnetic resonance venography for preoperative imaging, whereas 12 studies[21,22,24,25,28-33,35,36] reported the use of intraprocedural intravascular ultrasound (IVUS) imaging. Eleven dedicated venous stents were identified (Supplementary Table II, online only), with the Vici Venous stent (Boston Scientific) being most commonly deployed (n = 470). The deep venous system was most frequently accessed from the femoral vein alone,[20,22,25-27,29-31] or an alternative approach was used where the femoral vein or popliteal vein was punctured.[24,32] Nonetheless, in some cases, the superficial venous system of the lower limb[34] or the jugular vein[33,36] was punctured. Predilation was performed in 2075 patients, whereas 1727 patients received venoplasty after stent deployment. Two studies[21,28] did not report if venoplasty occurred. Technical success of the primary procedure was achieved in 99.6% of cases (95% confidence interval [CI]: 99.4%-99.9%).

Seven cases[27] were noted to have a stent extension into the profunda femoral vein or the femoral vein. With the exception of five studies[20,23,24,28,32] (n = 683), which did not provide information on the distal landing site, the remaining patients (n = 1528) were all treated with stents implanted above the profunda femoral vein.

Some patients received a hybrid intervention in conjunction with stenting. A total of 190 patients were treated with a arteriovenous fistula (AVF) and endophlebectomy,[23,27,31,36] whereas three patients received an AVF only[22,27] and four patients required endophlebectomy only.[27] Morris et al[29] reported that selected individuals were managed with AVF formation and endophlebectomy but did not disclose the number of procedures performed.

A direct oral anticoagulant (DOAC) was the long-term antithrombotic agent of choice in two studies (293 patients),[20,22] while 519 patients were treated with a regimen of bridging low-molecular-weight heparin followed by long-term vitamin K antagonist (VKA) (Supplementary Table II, online only).[23,25-27,29] In some centers,[22,30,35] either a DOAC or VKA was offered (294 patients). In two studies, 325 patients received lifelong aspirin with the addition of a DOAC for individuals at risk of in-stent thrombosis.[32,33] Alternatively, Salem et al[34] offered their patients (n = 58) a combination of clopidogrel and a DOAC. The length of treatment generally ranged from 6 to 12 months for patients with PTS and 3 to 6 months for patients with NIVL. Three studies[21,31,36] did not specify the antithrombotic agent offered to patients, whereas the length of treatment was absent from one study.[28]

Clinical symptom scores

Three studies[26,32,33] measured symptom changes for the overall study population using the VCSS scale only, five studies[20-22,25,35] used the rVCSS scale only, three studies[29,34,36] used the Villalta scale only, and five studies[23,24,27,28,30] employed both the Villalta scale and VCSS or rVCSS (Supplementary Table III, online only). Three studies[24,26,30] stratified symptom changes by disease etiology (PTS vs NIVL), whereas Morris et al[28] separated the scores according to the stent design (open cell vs closed cell). One study[31] did not report symptom changes using the VCSS or the Villalta scale.

The VCSS or rVCSS was measured from 1 to 24 months after intervention (Supplementary Table III, online only). The majority of studies (n = 10) noted a sustained improvement in symptoms,[20-24,26-28,30,33] or an initial improvement followed by no regression in symptoms[25,32] after stenting. However, in one study,[35] an

increase in the rVCSS score was observed from 12 months (4.1 ± 3.1) to 24 months (4.2 ± 2.8). Where available, all post-stenting VCSS/rVCSS scores were significantly lower than baseline.[21-28,32,35] Powell et al[32] observed the greatest improvement in symptoms at 12 months (57% reduction).

The Villalta score was assessed from 6 to 24 months after stenting (Supplementary Table III, online only). All studies reported a sustained improvement in symptoms[23,24,27-30] or an initial improvement followed by no decline in symptoms.[27,36] When reported, Villalta scores were significantly lower after intervention.[23,24,27-29] The largest reduction in the Villalta score was recorded by Murphy et al[30] (63% reduction).

Ulcer healing

Ulcer healing was reported in 10 studies.[20-22,25-27,30,32,35,36] Significant heterogeneity (I^2: 63.83%, P = .003) was observed between the studies; hence, a random-effects model was used. With the exception of three studies,[21,26,32] over two-thirds of ulcers healed at the latest follow-up in the various studies. The overall ulcer healing rate was 68.8% (95% CI: 52.0%-83.7%). Not all studies stratified ulcer healing by etiology. However, when this was reported, 32.3% (95% CI: 0.2%-78.1%; I^2: 72.78%, P = .012) of ulcers healed in patients with PTS[21,26,35,36] and 57.5% (95% CI: 4.7%-100%; I^2: 70.01%, P = .019) of ulcers healed in patients with NIVL.[20,21,26,35]

Pain

Three studies[20,21,32] assessed pain at baseline and follow-up (Supplementary Table IV, online only). Hong et al[20] used the rVCSS scale to identify the change in the frequency of pain from baseline to 12 months. Similarly, Lichtenberg et al[21] also employed the rVCSS scale but reported that the mean pain score (range: 0-3) significantly reduced at 12 months after intervention. In contrast, Powell et al[32] used the visual analog scale to identify that pain was significantly lower at 6 months after stenting, but symptoms regressed at the subsequent review at 12 months. In the Venovo study by Lichtenberg et al,[35] an improvement in the rVCSS pain score was observed; however, a baseline value was not reported.

Venous claudication

Venous claudication was reviewed before and after stenting in two studies,[23,26] consisting of 275 patients (Supplementary Table IV, online only). A definition was provided by de Wolf et al[26] as "the onset or worsening of pain and/or heaviness during exercise, which subsides during rest, especially when sitting or lying down" however it was unclear how the other study defined this symptom. A significant improvement was observed in both studies. In addition, Murphy et al[30] observed that 32.9% (55 of 167) of patients had claudication at baseline but did not provide data on follow-up.

Edema

The reporting of edema was identified in one study. Lichtenberg et al[25] demonstrated a reduction in the incidence of edema after intervention; however, it is unclear if this reduction was statistically significant (Supplementary Table IV, online only).

Health-related quality of life

Health-related quality of life was assessed in three studies.[30,32,33] Murphy et al[30] reported follow-up scores separately for patients with PTS and NIVL; a sustained improvement was noted for both groups from 6 to 12 months after intervention, with a larger increase observed in the NIVL group (Supplementary Table V, online only). The CIVIQ-20 instrument was employed by the other studies.[32,33] A reduction in the burden of chronic venous insufficiency was captured in both patient cohorts, with Powell et al[32] demonstrating a significant improvement.

Stent patency

Patency was typically evaluated by duplex ultrasound imaging[21-26,28-36] or in some cases by venography;[20,21,29-31] however, there was considerable heterogeneity in formal definitions and assessment protocols. Sixteen studies[22-27,36-38,40-45] reported patency outcomes (Supplementary Table VI, online only) from 3 months[26] to 60 months after intervention.[34] With the exception of one study,[35] higher primary- and secondary-patency rates were observed in patients with NIVL when compared with patients with PTS.

The overall 12-month primary, primary-assisted, and secondary patency were 83% (95% CI: 76%-90%), 90% (95% CI: 85%-96%), and 95% (95% CI: 92%-98%), respectively (Figs 1-3). The 12-month patency rate reported by Stuck et al[28] included patients with acute DVT; hence, it was not used for this analysis. Patency rates at 24 and 36 months are outlined in Supplementary Table VII, online only.

For patients with NIVL disease, the 12-month primary, primary-assisted, and secondary patency were 99% (95% CI: 98%-100%), 98% (95% CI: 96%-100%), and 100% (95% CI: 98%-100%), respectively. For patients with PTS, the 12-month primary, primary-assisted, and secondary patency were 79% (95% CI: 72%-85%), 87% (95% CI: 80%-93%), and 92% (95% CI: 87%-96%), respectively.

χ^2 tests revealed a significant difference in primary, primary-assisted, and secondary patency ($P < .05$) in the 12-month patency between the NIVL and PTS subgroups.

Complications

30-day stent thrombosis. Ten studies[20-22,25,30-33,35,36] provided data on in-stent thrombosis within 30 days of intervention. The incidence of this complications was

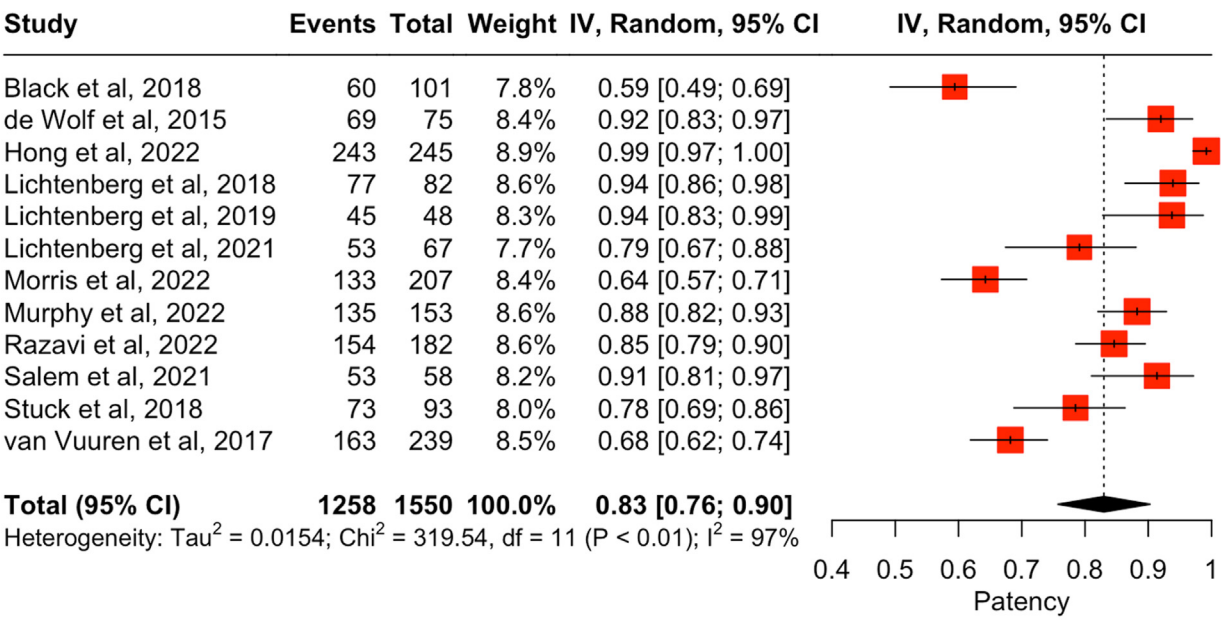

Fig 1. Forest plot of primary patency at 12 months for the overall study population. Events and total values represent limbs. *CI*, Confidence interval; *IV*, inverse variance.

1.7% (95% CI: 0.2%-4.3%) among the 1206 patients included in the analysis. In-stent thrombosis was more common in patients with PTS[21,25,30,31,33,35,36] (incidence = 2.8%; 95% CI: 0.1%-8.0%; I^2: 86.34%, $P < .001$) in comparison with patients with NIVL[20,21,25,30,33,35] (incidence = 0.1%; 95% CI: 0%-1.0%; I^2: 0%, $P = .549$). It was not possible to identify the disease etiology in two studies.[22,32]

Major bleeding. Major bleeding was mentioned in 10 studies.[20-25,27,30,31,35] The incidence of major bleeding was 1.7% (95% CI: 1.0%-2.5%) among 1455 patients. Patients who underwent endovascular intervention only had a lower incidence of major bleeding (incidence = 0.9%; 95% CI: 0.3%-1.5%; I^2: 0%, $P = .652$) compared with patients receiving hybrid intervention (incidence = 1.7%; 95% CI: 0.0%-5.9%; I^2: 0%, $P = .226$). In addition, one episode of major bleeding was reported by Powell et al,[32] although it was not stated whether this patient belonged to the dedicated venous stent subgroup.

Minor bleeding. Minor bleeding was reported in eight studies.[22-27,30,35] The incidence of minor bleeding was 3.2% (95% CI: 1.3%-5.6%) among 1106 patients. Minor bleeding was more common in patients treated with hybrid intervention (incidence = 13.1%; 95% CI: 7.8%-19.4%; I^2: 0%, $P = .192$) in comparison with those treated with endovascular intervention (incidence = 2.5%; 95%

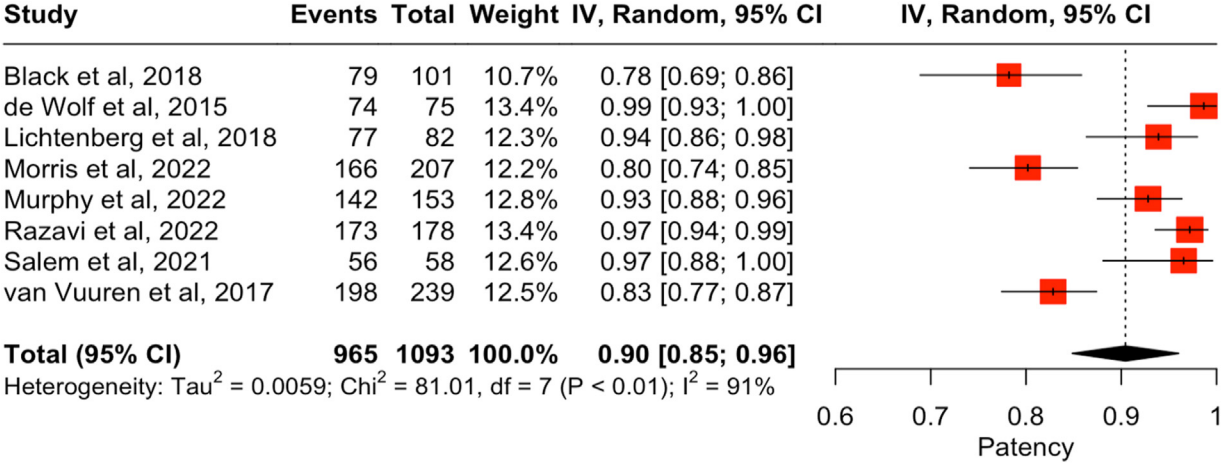

Fig 2. Forest plot of primary-assisted patency at 12 months for the overall study population. Events and total values represent limbs. *CI*, Confidence interval; *IV*, inverse variance.

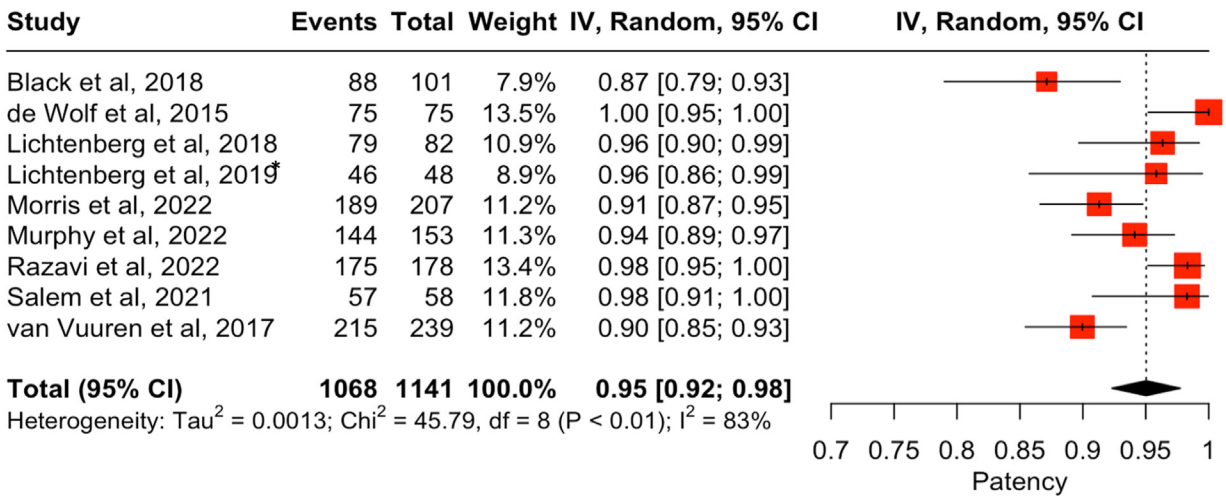

Fig 3. Forest plot of secondary patency at 12 months for the overall study population. Events and total values represent limbs. *CI*, Confidence interval; *IV*, inverse variance.

CI: 1.0%-4.6%; I^2: 61.26%, $P = .012$). Four episodes of minor bleeding were mentioned by Powell et al;[32] however, it is unclear if these patients were treated with dedicated venous stents.

Other complications. The remaining complications were organized into puncture site, stenting related, venous thromboembolism related, and death. Overall, 17 deaths occurred, although none were linked to the stenting procedure. There were 46 cases of wound infection, with 87% of these occurring in hybrid procedures. Similarly, 35 cases of lymphorrhea were observed, all present in patients receiving hybrid intervention. There were 159 cases of in-stent stenosis[21-24,26,27,29,30,34,35] and 110 cases of in-stent occlusion.[23-25,27] Stuck et al[28] also described three cases of in-stent stenosis but did not clarify if these occurred in patients with chronic deep venous disease. Fifteen stents were noted to have fractured,[27,29,33] of which fourteen[27,33] were Vici Venous stents and the remaining stent was not specified. Twelve of the fractured stents crossed the inguinal ligament. There were 18 stent-malfunction events[27] (kinking, implosion, and angulation). Moreover, eight cases of stent migration were observed;[23,26,33] however, none of these displaced into the heart. DVTs in the native vessels were observed to occur in 15 cases (bilateral = 1,[33] ipsilateral = 10,[20,27,33] and contralateral = 4[23,27,33]). In addition, five patients[20,30,33] experienced pulmonary emboli during follow-up.

DISCUSSION

Before the advent of dedicated venous stents, the deep venous system was treated using repurposed self-expanding arterial stents[6] hence contemporaneous large-scale systematic reviews[8,46-48] mainly included patients treated with these devices. Nonetheless, arterial stents had a disposition to foreshorten during deployment due to their braided design hence were inherent in issues related to accurate deployment and stent migration. In addition, when treating NIVLs, a low radial force at the periphery of these devices necessitated extension of the stents into the inferior vena cava to prevent stent collapse however this precipitated contralateral lower-limb DVT due to jailing of the contralateral outflow tract.[49] As a result, various dedicated venous stents have been developed to better complement the anatomical challenges related to the deep venous system. The increasing prevalence of dedicated venous stenting is reflected in this review, having identified 11 different devices used in 2218 patients. In addition, contrary to previous literature,[7,8] this review exclusively consists of patient treated with dedicated venous stents.

The analysis demonstrates that the 36-month primary patency, primary-assisted patency, and secondary patency rates are 59%, 80%, and 86%, respectively. Although the primary patency is lower, it demonstrates the need for regular surveillance and early intervention for recurrent stenosis to maintain long-term patency.[50,51] The results also indicate that dedicated venous stents engender superior medium- to long-term outcomes compared with existing literature. For instance, Badesha et al[7] reported a primary and secondary patency rate of 74% and 90% at 12 months, respectively, in patients who were predominantly treated with Vici Venous stents, Sinus-Venous stents, and Zilver Vena stents; although, a small minority of patients in this review received arterial stents. Similarly, Majeed et al[8] investigated outcomes in patients with PTS and NIVL mainly treated with repurposed arterial stents such as Wallstent, SMART, and E-Luminexx. In the former group, 76% primary patency rate and 92% secondary patency rate was observed at 12 months, whereas 96% primary patency rate and 100% secondary patency rate was noted in the latter

group. There are multiple potential reasons for this observed improvement. Previous systematic reviews contained studies published during the early phases of dedicated venous stenting, where reintervention occurred in patients with asymptomatic in-stent stenosis of >50%.[36] In addition, the inclusion of deep venous stenting in clinical guidelines[4,52] has promulgated the uptake of this procedure hence vascular centers will accrue more experience in stenting over time and practice will evolve to incorporate novel technology. For instance, the VIDIO trial[53] and subsequent research[54] highlighted that IVUS imaging is a superior imaging modality for deep venous stenting when compared with venography; at our vascular centers, IVUS imaging is used as standard in all procedures to size and measure stents.

This review summarized the different procedural practices used by vascular centers internationally. At our vascular center, magnetic resonance venography is the imaging modality of choice to assess the extent of deep venous disease before stenting. Its advantages over duplex ultrasound imaging include the ability to detect subtle morphological changes such as smaller-caliber diseased veins or post-thrombotic webs, whereas the absence of ionizing radiation supports its application in younger patients.[55] Most studies are performed before and after dilation of stents; adequate predilation is vital so that the fibrotic vein is adequately expanded before stenting, whereas postdilation ensures that the stent wall achieves apposition against the native vein to minimize the risk of stent migration. Overall, eight cases of stent migration were observed in this review. Choosing the ideal dedicated venous stent requires various considerations. Rigid closed-cell stents provide high radial force hence are ideal for stenting in NIVL pathology, whereas flexible open-cell stents are more suited for deployment in the iliofemoral region where hip flexion occurs. Novel designs may be able to incorporate the benefits of both open- and closed-cell stents.

There was a paucity of data comparing stent patency between patients treated with hybrid interventions versus endovascular intervention. Only van Vuuren et al[23,27] reported patency outcomes stratified by hybrid versus endovascular intervention hence the pooling of these data would have led to imprecise estimates, thus precluding any meaningful statistical analysis. Given that the published literature[56] has demonstrated that good inflow from the profunda femoral vein and femoral vein is associated with significantly higher patency rates, future research should evaluate how adjunctive procedures such as endophlebectomy and AVF formation impact patency.

This review highlighted a diversity of postoperative anticoagulation regimes. Antithrombotic agents that were used included low-molecular-weight heparin, VKA, DOACs, and antiplatelet agents. The length of treatment varied between different centers. Nonetheless, it was observed that anticoagulation use was usually longer in patients with PTS to reflect the prothrombotic nature of the collagen-rich veins found in these patients. Current consensus among deep venous interventionalists is that treatment should occur for a minimum of 6 to 12 months;[57] this was supported by the findings in this study. The advent of direct oral anticoagulants provides a convenient option for anticoagulation as regular monitoring is no longer necessary (in most patients), and a less lifestyle restricting regimen is necessary. However, evidence on the optimal postoperative antithrombotic regime is still lacking. Consequently, results from multicenter research trials such as the ARIVA trial[58] will be welcomed.

This review demonstrates that deep venous stenting can engender good ulcer healing rates. Historically, superficial venous incompetence was thought to be the main precipitant of venous ulceration.[59] However, improvements in diagnostic imaging have revealed that deep venous obstruction plays a significant role in the development of ulceration through venous hypertension[59] and evidence now highlights that correcting superficial incompetence in isolation can be ineffective in managing severe ulcers.[60] In addition, to sustain ulcer healing after stenting a patent deep venous system must be maintained into the medium and long term;[61] this notion is supported by this review, which demonstrated inferior healing rates in patients with PTS where in-stent thrombosis was more common. Vascular centers should now consider deep venous stenting as an adjunct to superficial venous interventions for the management of ulceration. It is anticipated that data from the DEVELOP trial[62] will provide further information on this.

The conclusions drawn from this review must be considered in the context of the significant level of heterogeneity demonstrated in the evidence. The included research consisted mainly of low-quality single-arm observational studies with inherent selection and observer bias. The studies were diverse in nature and used different inclusion criteria. For example, some studies exclusively recruited patients with complete deep venous occlusion, thus representing the most severe disease, whereas other studies included individuals with underlying malignancy or thrombophilia who were more likely to suffer from a loss of patency hence the outcomes do not represent a uniform set of patients. There were also variations in procedural techniques, with some centers lacking access to IVUS, whereas others chose to perform poststenting venoplasty in a selection of their patients. The absence of a standardized follow-up assessment protocol precluded the pooling and analysis of clinical changes after intervention and therefore a direct comparison of results between studies. There were also variations in the type of clinical symptom assessment scales (VCSS or Villalta) or methods used to analyze pain, edema, and claudication. There is a need for

reporting guidelines to promote standardization of future deep venous stenting research so that comparable and poolable data can be collected.

Complications related to in-stent stenosis can arise due to poor collateral-vein inflow and noncompliance with a postintervention anticoagulation protocol (anticoagulation and compression hosiery).[42,63] The impact of these factors on symptom improvement could not be explored due to heterogeneous reporting. In addition, stent patency was assessed using surveillance duplex ultrasound scanning. Despite this imaging modality being safe, inexpensive, and noninvasive, there are limitations associated with imaging of iliocaval stents in obese patients, when there is overlying bowel gas, or when there is an overlap of devices.[64] Given that this procedure is highly operator dependent, it may have been that certain complications were missed.

The length of follow-up in deep venous stenting research is shorter than peripheral arterial disease where outcomes from large multicenter trials have reported patency outcomes up to 5 years after intervention.[65] In light of the predilection for deep venous disease to affect younger patients, there was limited evidence on the 5- to 10-year safety profile and patency outcomes of dedicated venous stents. This is necessary for a robust assessment of the clinical effectiveness of these devices so that they can be incorporated into the toolkit of all vascular centers.

Health-related quality of life was only reported up to 12 months after intervention, and there was a lack of exploration into the impact of complications on quality of life. This is a pertinent limitation when considering that the target population mainly consists of young individuals who are unlikely to have many comorbidities at baseline. Therefore, any complications that arise from the procedure or postintervention anticoagulation could have a significant impact on quality of life. Moreover, further evidence is needed on whether improvements in quality of life are sustained postoperatively.

CONCLUSIONS

Deep venous stenting using dedicated venous stents is a safe and effective intervention for treating chronic deep venous disease. Good patency rates and symptomatic improvement can be achieved in the midterm however there is a paucity of data to make reliable conclusions about long-term safety and patency outcomes. In addition, further evidence is required to determine the optimal poststenting anticoagulation regime; the results from ongoing research will be welcomed. Finally, guidelines are needed to establish a standardized reporting protocol similar to that found in arterial disease research.

AUTHOR CONTRIBUTIONS

Conception and design: AB, SB, NT, AD, TK
Analysis and interpretation: AB, GK, TK
Data collection: AB, AH
Writing the article: AB, GK
Critical revision of the article: AB, SB, AH, NT, AD, TK
Final approval of the article: AB, SB, GK, AH, NT, AD, TK
Statistical analysis: AB, GK, AH
Obtained funding: Not applicable
Overall responsibility: AB

DISCLOSURES

T.K. and S.A.B. have received honorarium for presentations at Medtronic, Boston Scientific, Bentley, and Philips.

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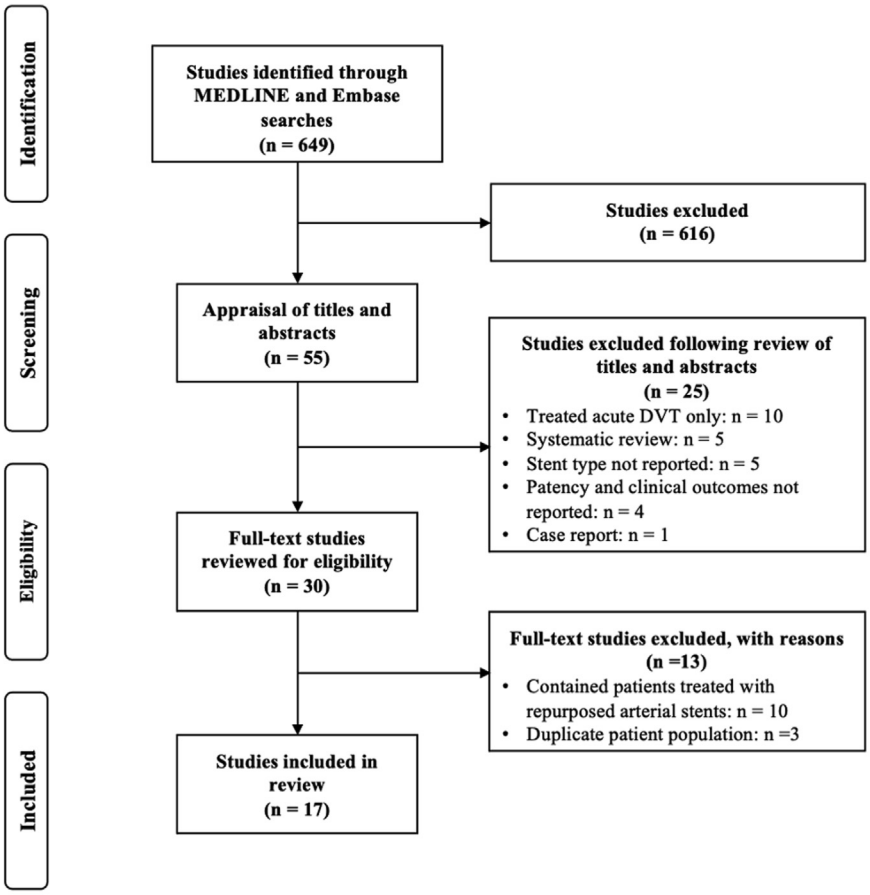
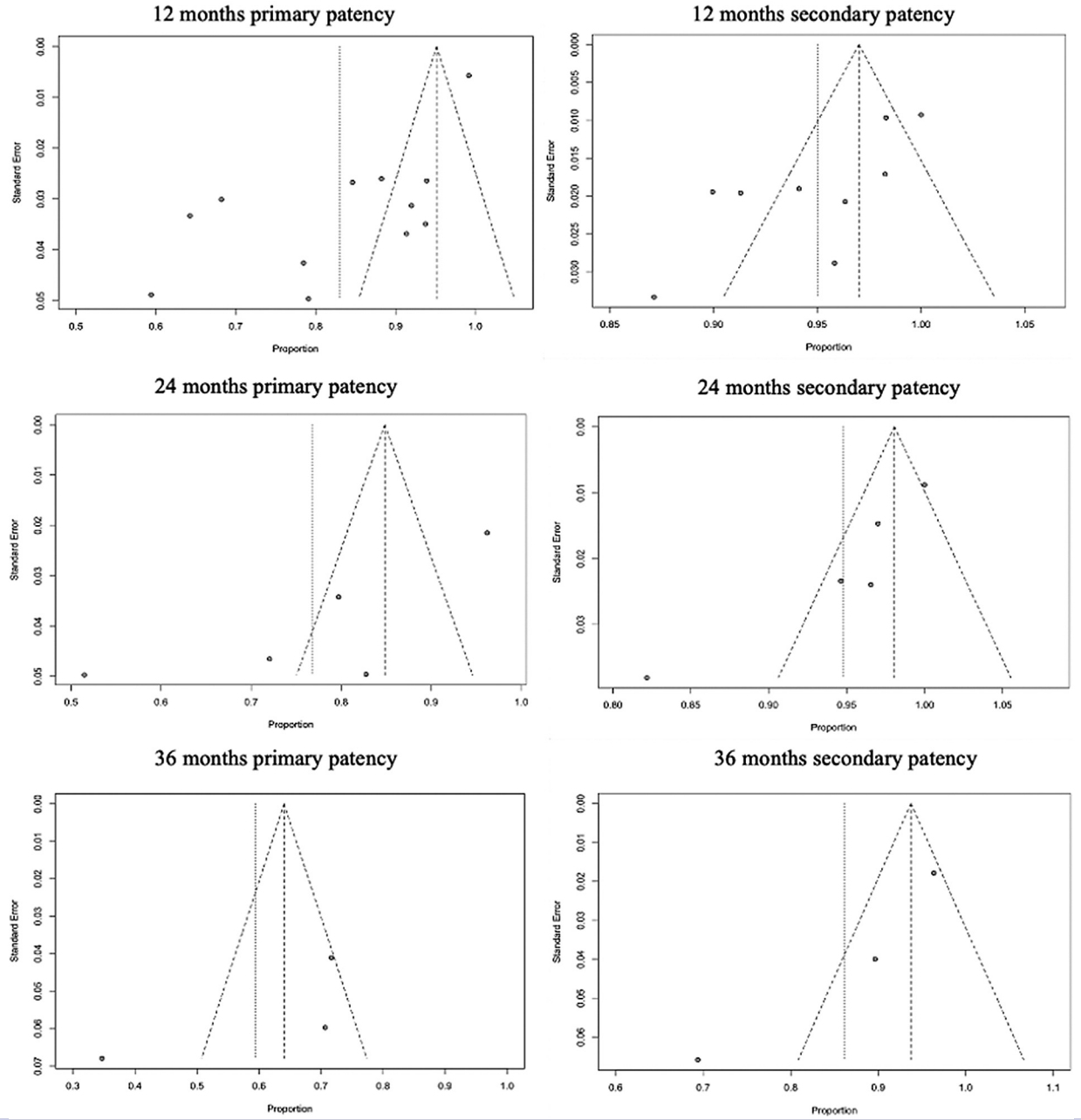
Submitted Aug 17, 2023; accepted Nov 5, 2023.



Supplementary Fig 1 (online only). Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. *DVT*, Deep vein thrombosis. Adapted from Moher et al.[66]



Supplementary Fig 2 (online only). Funnel plots of the primary patency and secondary patency analysis.

Supplementary Table I (online only). Search strategy

1.	POSTTHROMBOTIC SYNDROME/ or POSTTHROMBOSIS SYNDROME/
2.	Post thrombotic syndrome.ti,ab.
3.	Postthrombotic syndrome.ti,ab.
4.	Non-thrombotic iliac vein lesion*.ti,ab.
5.	Nonthrombotic iliac vein lesion*.ti,ab.
6.	CHRONIC VENOOCCLUSIVE DISEASE/ or CHRONIC VENOUS INSUFFICIENCY/ or CHRONIC VEIN INSUFFICIENCY/
7.	Chronic venous disease.ti,ab.
8.	"VEIN INSUFFICIENCY"/ or "CHRONIC VEIN INSUFFICIENCY"/
9.	Venous insufficiency.ti,ab.
10.	May Thurner Syndrome.ti,ab.
11.	Venous occlusive disease.ti,ab.
12.	Chronic occlusive venous disease.ti,ab.
13.	Non thrombotic occlusion.ti,ab.
14.	Nonthrombotic occlusion.ti,ab.
15.	Post thrombotic occlusion.ti,ab.
16.	Postthrombotic occlusion.ti,ab.
17.	Stent*.ti,ab.
18.	Angioplasty.ti,ab.
19.	Vascular patency.ti,ab.
20.	Endoprosthesis.ti,ab.
21.	"VENOUS STENT"/
22.	Zilver vena.ti,ab.
23.	Sinus venous.ti,ab.
24.	Sinus obliquus.ti,ab.
25.	Vici venous stent*.ti,ab.
26.	Venovo.ti,ab.
27.	Abre.ti,ab.
28.	Blueflow.ti,ab.
29.	BeYond.ti,ab.
30.	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
31.	17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
32.	30 and 31
33.	limit 32 to yr="2010 -Current"

Supplementary Table II (online only). Procedural characteristics and medical management

Study	Patients receiving a dedicated venous stent	Puncture site	Perioperative venoplasty	Postoperative anticoagulation	Follow-up protocol
Hong et al[20]	Venastent: 123 Zilver Vena: 122	CFV	Predilation in all patients Postdilation: 185 patients	Rivaroxaban 20 mg once daily for 3 months	Clinical assessment at 3 and 12 months CT venography or venography at 12 months
Lichtenberg et al[21]	BLUEFLOW: 67	DNM	DNM	Postoperative anticoagulation provided (DNM regime)	Clinical assessment at 30 days, 6 months, 12 months, and 24 months Venography or DUS at 12 months
Morris et al[29]	Vici Venous: 107 Venovo: 26 Zilver Vena: 9 Abre: 65	FV	Predilation and postdilation in all patients	LMWH for 2 weeks followed by VKA for ≥6 months	Clinical assessment at 6 weeks, 6 months, and 1 year DUS at 1 day, 2 weeks, 6 weeks, 6 months, and 12 months
Murphy et al[30]	Abre: 167	FV	Predilation and postdilation in all patients	VKA or DOAC for ≥6 months in patients with NIVL and ≥12 months in patients with PTS	Clinical assessment and DUS at 30 days, 6 months, and 12 months Multiplanar pelvic x-ray at 12 months
Piao et al[31]	Sinus-XL: 11 Veniti: 10 Sinus-Venous:[a] Venovo:[a]	FV	Predilation in all patients DNM postdilation	Oral anticoagulation (DNM drug) for ≥12 months	Clinical assessment and DUS at 2 weeks, 3 months, 6 months, and 12 months
Powell et al[32]	Venovo: 125	FV or PV	Predilation and postdilation in all patients	Lifelong aspirin 81 mg for all patients DOAC for patients with risk factors for in-stent restenosis	Clinical assessment and DUS at 3 weeks, 3 months, 6 months, 12 months, and annually thereafter
Razavi et al[33]	Vici Venous: 200	FV: 175 PV: 16 JV: 5 JV and FV: 4	Predilation: 134 patients Postdilation: 184 patients	PTS patients: anticoagulation (DNM drug) for 6 months followed by aspirin for ≥6 months PTS patients with a history of recurrent DVT or occlusion: anticoagulation (DNM drug) for ≥12 months NIVL patients: aspirin for ≥12 months	Clinical assessment at 1 month, 6 months, 12 months, and annually thereafter DUS at 12 months, 24 months, and 36 months
Salem et al[34]	Zilver Vena: 58	PV: 37 FV: 11 GSV: 6 SSV 3 Contralateral FV: 1 Additional access via the R IJV: 7	Predilation in all patients DNM postdilation	DOAC for 3 months and clopidogrel for 6 months Extended anticoagulation for patients with thrombophilia or recurrent DVTs	Clinical assessment and DUS at 1 month, 3 months, 6 months, 12 months, and annually thereafter

Supplementary Table II (online only). Continued.

Study	Patients receiving a dedicated venous stent	Puncture site	Perioperative venoplasty	Postoperative anticoagulation	Follow-up protocol
Lichtenberg et al[35]	Venovo: 79	FV	Predilation and postdilation in all patients	VKA or DOAC for 6 months in patients with NIVL and 12 months in patients with PTS	Clinical assessment and DUS at 30 days, 6 months, 12 months, and 24 months
Black et al[36]	Vici Venous: 88sinus-XL: 6Zilver Vena: 1	FV, however JV was accessed if FV was unsuccessful	Predilation and postdilation in all patients	LMWH for 2 weeks followed by long-term oral anticoagulation (DNM drug)	Clinical assessment and DUS at 1 month, 6 months, 12 months, and 24 months
Lichtenberg et al[22]	Sinus-Obliquus: 48Sinus-Venous: 15Venovo: 6	FV, however CFV was accessed in some patients with NIVL	Predilation and postdilation in all patients	LMWH postoperatively followed by DOAC for 6 months in patients with NIVL and 6-12 months in patients with PTS	Clinical assessment and DUS at 1 month, 6 months, and 12 months
van Vuuren et al[23]	Sinus-Venous and Sinus-XL:[a]	DNM	Predilation and postdilation in all patients	LMWH postoperatively followed VKA for 6 months	Clinical assessment and DUS at 2 weeks, 6 weeks, 3 months, 6 months, and 12 months
Stuck et al[24]	Sinus-Obliquus, Vici Venous, Zilver Vena, Sinus-XL Flex, and Sinus-Venous:[a]	FV or PV	Predilation in all patients DNM postdilation	LMWH, DOAC, or VKA for 3 months in patients with NIVL and 6 months in patients with PTS	Clinical assessment and DUS at 3 months, 6 months, 12 months, and annually thereafter
Lichtenberg et al[25]	Vici Venous: 75	FV, however CFV accessed in some patients with NIVL	Predilation in all patients DNM postdilation	LMWH postoperatively followed by VKA for 6 months	Clinical assessment and DUS at 1 month, 6 months, and 12 months
de Wolf et al[26]	Sinus-Venous: 75	FV	Predilation and postdilation in all patients	LMWH postoperatively followed by VKA for 6 months	Clinical assessment and DUS at 2 weeks, 6 weeks, 3 months, 6 months, and 12 months
van Vuuren et al[27]	Sinus-XL, Sinus-XL Flex, Sinus-Venous, Sinus-Obliquus, Vici Venous, Zilver Vena, Venovo:[a]	Mid-FV below the inflow of the main PFV branches	Predilation and postdilation in all patients	LMWH postoperatively followed by VKA for 6 months or >6 months if stent stenosis, stent configuration problems, hyper coagulability, or history of recurrent DVT	DNM
Stuck et al[28]	Sinus-XL Flex: 10	DNM	DNM	VKA or DOAC (DNM regime)	Clinical assessment and DUS at 3 months, 6 months, and 12 months

CFV, Common femoral vein; *CIV*, common iliac vein; *CT*, computed tomography; *DNM*, does not mention; *DOAC*, direct oral anticoagulant; *DUS*, duplex ultrasound scan; *DVT*, deep vein thrombosis; *EIV*, external iliac vein; *FV*, femoral vein; *IVC*, inferior vena cava; *GSV*, great saphenous vein; *JV*, jugular vein; *LMWH*, low-molecular-weight heparin; *NIVL*, nonthrombotic iliac vein lesion; *PFV*, profunda femoral vein; *PTS*, post-thrombotic syndrome; *PV*, popliteal vein; *R IJV*, right internal jugular vein; *SFJ*, saphenofemoral junction; *SSV*, short saphenous vein; *VKA*, vitamin K antagonist.
[a]Does not mention number of patients treated with this stent.

Supplementary Table III (online only). Clinical outcomes measured using the Venous Clinical Severity Score (VCSS), revised Venous Clinical Severity Score (rVCSS), and Villalta scale.

Study	Baseline score	Post-stenting score	P value
VCSS			
Powell et al[32]	Median: 7 (IQR = 5, 9)	3 months: 4 (IQR = 3, 6) 6 months: 4 (IQR = 2, 6) 12 months: 3 (IQR = 3, 5)	<.001 <.001 <.001
Razavi et al[33]	Mean: 9.7 ± 4.9	12 months: 5.5 ± 4.2	DNM
van Vuuren et al[23]	Median: 7 (range: 5-9)	12 months: 4 (range: 2.5-7.0)	<.001
de Wolf et al[26]			
PTS subgroup	Median: 8 (range: 3-21)	12 months: 5 (range: 0-16)	≤.001
NIVL subgroup	Median: 6 (range: 2-19)	12 months: 4 (range: 1-16)	.019
van Vuuren et al[27]			
PTS subgroup	Median: 7 (range: 0-21)	12 months: 5 (range: 0-18) 24 months: 4 (range: 0-14)	Significant improvement[a]
NIVL subgroup	Median: 5 (range: 0-19)	12 months: 4 (range: 0-16) 24 months: 3 (range: 0-7)	Significant improvement[a]
Hybrid subgroup	Median: 8 (range: 3-18)	12 months: 5 (range: 0-13) 24 months: 4 (range: 0-15)	Significant improvement[a]
rVCSS			
Hong et al[20]	Mean: 7.6 ± 3.9	3 months: 4.6 ± 2.7 6 months: 3.2 ± 2.3	DNM DNM
Lichtenberg et al[21]	Median: 8 (IQR = 2)	6 months: 4 (IQR = 4) 12 months: 4 (IQR = 3.5)	<.001 <.001
Murphy et al[30]			
PTS subgroup	Mean: 8.8 ± 5.0	6 months: 5.5 12 months: 5.0	DNM DNM
NIVL subgroup	Mean: 9.0 ± 4.5	6 months: 4.7 12 months: 4.3	DNM DNM
Lichtenberg et al[35]	Mean: 9.1 ± 4.2	1 month: 5.1 ± 4.0 6 months: 4.1 ± 2.2 12 months: 4.1 ± 3.1 24 months: 4.2 ± 2.8	<.001 <.001 <.001 <.001
Lichtenberg et al[22]	Mean: 9.0 ± 4.3	1 month: 5.2 ± 4.0 6 months: 4.9 ± 2.8 12 months: 4.8 ± 2.9	DNM DNM <.001
Stuck et al[24]			
PTS subgroup	Mean: 7.8 ± 6.0	Latest follow-up: 4.1 ± 5.0	<.001
NIVL subgroup	Mean: 6.5 ± 4.0	Latest follow-up: 2.8 ± 2.0	DNM
Lichtenberg et al[25]	Median: 8 (range: 4-27)	1 month: 5 (range: 1-15) 6 months: 4 (range: 0-15) 12 months: 4 (range: 1-19)	<.001 <.001 .001
Stuck et al[28]	Mean: 5.0 ± 3.9	Latest follow-up: 2.0 ± 2.9	.05
Villalta			
Morris et al[29]			
Open cell subgroup	Median: 13 (IQR = 9, 15)	Post-stenting: 8 (IQR = 5, 12)	<.001
Closed cell subgroup	Median: 14 (range: 3-27)	Post stenting: 8.5 (IQR = 5, 12)	<.001
Murphy et al[30]			
PTS subgroup	Mean: 11.1 ± 6.1	6 months: 5.7 12 months: 5.0	DNM DNM
NIVL subgroup	Mean: 11.5 ± 5.4	6 months: 4.5 12 months: 4.3	DNM DNM
Salem et al[34]	Mean: 16.8 (range: 10-31)	DNM	N/A

Supplementary Table III (online only). Continued.

Study	Baseline score	Post-stenting score	P value
Black et al[36]	Median: 14 (range: 5-33)	6 months: 8 (0-33) 12 months: 8 (1-33) 24 months: 8 (1-33)	DNM DNM DNM
van Vuuren et al[23]	Mean: 10.5 ± 4.2	12 months: 5.3 ± 3.8	<.001
Stuck et al[24]			
PTS subgroup	Mean: 6.5 ± 4.0	Latest follow-up: 4.1 ± 5.0	<.001
NIVL subgroup	DNM	Latest follow-up: 2.8 ± 2.0	DNM
van Vuuren et al[27]			
PTS subgroup	Median: 10 (range: 2-27)	12 months: 5 (range: 0-20) 24 months: 4 (range: 0-16)	Significant improvement[a]
NIVL subgroup	DNM	DNM	DNM
Hybrid subgroup	Median: 11 (range: 3-21)	12 months: 5 (range: 0-14) 24 months: 5 (range: 0-18)	DNM
Stuck et al[28]	Mean: 10 ± 3	Latest follow-up: 4 ± 2	.02

DNM, Does not mention; *IQR*, interquartile range; *NIVL*, nonthrombotic iliac vein lesion; *PTS*, post-thrombotic syndrome.
[a]Significant symptomatic improvement was observed although the *P* value was not stated.

Supplementary Table IV (online only). Baseline and post-stenting pain, venous claudication, and edema

	Baseline pain			Post-stenting pain		
Study	Overall	PTS	NIVL	Overall	PTS	NIVL
Hong et al[20]	172/245[a]	N/A	b	12 months: 126/245[a]	N/A	b
Lichtenberg et al[21]	Mean rVCSS: 2.2 ± 0.4	DNM	DNM	12 months: 0.6 ± 0.7	DNM	DNM
Powell et al[32]	Median VAS score: 7 (range: 5-9)	DNM	DNM	3 months: 2 (range: 0-5) 6 months: 2 (range 0-6) 12 months: 4 (range 0-5)	DNM	DNM

	Baseline venous claudication			Post-stenting venous claudication		
van Vuuren et al[23]	132/200[a]	88/151	44/49	12 months: 17/200[a]	12 months: 15/152[a]	12 months: 2/48[a]
de Wolf et al[26]	40/75[a]	25/40	16/35	12 months: 9/41[a]	12 months: 7/25[a]	12 months: 2/16[a]

	Baseline edema			Post-stenting edema		
Lichtenberg et al[25]	76/82[c]	DNM	DNM	12 months: 14/75[c]	DNM	DNM

DNM, Does not mention; *NIVL*, nonthrombotic iliac vein lesion; *PTS*, post-thrombotic syndrome; *VAS*, visual analog scale.
[a]Pertains to number of patients.
[b]All patients had NIVL disease.
[c]Pertains to number of limbs.

Supplementary Table V (online only). Health-related quality of life

Study	Scoring instrument		Baseline score ± standard deviation	Follow-up score	*P* value
Murphy et al[30]	VEINES-QoL	PTS subgroup	Mean: 49.1 ± 1.8	6 months: 68.2 ± 2.8 12 months: 69.0 ± 2.6	DNM DNM DNM DNM
		NIVL subgroup	Mean: 46.8 ± 3.0	6 months: 71.5 ± 3.0 12 months: 71.8 ± 3.1	
Powell et al[32]	CIVIQ-20		Median: 58	Latest follow-up: 28	<.00001
Razavi et al[33]	CIVIQ-20		Mean: 55.4 ± 19.5	12 months: 41.4 ± 20.2	DNM

CIVIQ-20, ChronIc Venous dIsease quality of life Questionnaire; *DNM*, does not mention; *NIVL*, nonthrombotic iliac vein lesion; *PTS*, post-thrombotic syndrome; *VEINES-QoL*, VEnous INsufficiency Epidemiological and Economic Study—Quality of Life.

Supplementary Table VI (online only). Mid- to long-term primary- and secondary-patency rates

Study	Primary patency			Secondary patency		
	Overall	PTS	NIVL	Overall	PTS	NIVL
Hong et al[20,a]	12 months: 99.2%	N/A	b	DNM	N/A	DNM
Lichtenberg et al[21]	6 months: 92% 12 months: 80%	6 months: 87% 12 months: 73%	6 months: 100% 12 months: 92%	DNM	DNM	DNM
Morris et al[29]	12 months: open-cell group = 63%, closed-cell group = 65%	DNM	DNM	12 months: open-cell group = 93%, closed-cell group = 90%	DNM	DNM
Murphy et al[30]	12 months: 88%	12 months: 80%	12 months: 99%	12 months: 94%	12 months: 89%	12 months: 100%
Piao et al[31,c]	36 months: 35%	b	N/A	36 months: 71%	b	N/A
Powell et al[32]	18 months: 81%	DNM	DNM	18 months: 98%	DNM	DNM
Razavi et al[33]	12 months: 85% 24 months: 80% 36 months: 72%	12 months: 80% 24 months: 74% 36 months: 64%	12 months: 97% 24 months: 97% 36 months: 96%	12 months: 98% 24 months: 97% 36 months: 96%	DNM	DNM
Salem et al[34,c]	6 months: 93% 12 months: 91% 24 months: 82% 36 months: 71% 48 months: 64% 60 months: 60%	b	N/A	6 months: 100% 12 months: 98% 24 months: 97% 36 months: 90% 48 months: 83% 60 months: 81%	b	N/A
Lichtenberg et al[35]	24 months: 95.5%	24 months: 96%	24 months: 95.5%	24 months: 100%	24 months: 100%	24 months: 100%
Black et al[36,c]	12 months: 59% 24 months: 51%	b	N/A	12 months: 87% 24 months: 82%	b	N/A
Lichtenberg et al[22]	6 months: 94%12 months: 94%	DNM	DNM	6 months: 96% 12 months: 96%	DNM	DNM
van Vuuren et al[23]	12 months: 68%	12 months: 71%	12 months: 92%	12 months: 90%	12 months: 90%	12 months: 100%
Stuck et al[24]	12 months: 79% 24 months: 72%	12 months: 75%	12 months: 89%	24 months: 95%	24 months: 94%	24 months: 100%
Lichtenberg et al[25]	12 months: 94%	DNM	DNM	12 months: 96%	DNM	DNM
de Wolf et al[26]	3 months: 99%6 months: 96% 12 months: 92%	DNM	DNM	3 months: 100% 6 months: 100% 12 months: 100%	DNM	DNM
van Vuuren et al[27]	DNM	60 months: 64%	60 months: 90%	DNM	60 months: 89%	60 months: 100%

DNM, Does not mention; *NIVL*, nonthrombotic iliac vein lesion; *N/A*, not applicable; *PTS*, post-thrombotic syndrome.
[a]All patients had NIVL disease.
[b]Equal to the patency rate for the overall study population.
[c]All patients had PTS.

Supplementary Table VII (online only). Patency analysis for the overall study population

Time interval	Primary patency (95% CI)	Primary-assisted patency (95% CI)	Secondary patency (95% CI)
12 months[20-26,29,30,33,34,36]	83% (76%-90%)	90% (85%-96%)	95% (92%-98%)
24 months[24,33-36]	77% (62%-91%)	87% (74%-100%)	95% (89%-100%)
36 months[31,33,34]	59% (36%-83%)	80% (60%-100%)	86% (71%-100%)

CI, Confidence interval.