Early and Long-Term Outcomes of Venous Stent Implantation for Iliac Venous Stenosis After Catheter-Directed Thrombolysis for Acute Deep Vein Thrombosis

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Background: Although stent implantation is used worldwide for peripheral arterial disease, there is little data on the safety and long-term patency of stents implanted for venous disease.

Methods and Results: We studied 13 patients with 14 lesions (6 males, 7 females, mean age: 63.2±10.2 years) diagnosed with venous stenosis and who underwent venous stenting. We examined the location of the stenosis, safety of venous stenting, implantation success rate, and long-term stent patency rate. All patients were suffering from venous stenosis in the left common iliac vein because of iliac vein compression syndrome. No major complications occurred during stent implantation. Acute stent occlusion occurred in 1 patient, who was given additional thrombolytic therapy. Of the 13 patients, 10 underwent venography or contrast-enhanced computed tomography (CT) during mid-term follow-up (mean: 12.9±16.1 months), and only 1 stent was occluded, resulting in a patency rate of 90.0%. The latter patient decided to stop taking warfarin soon after stent implantation. Furthermore, 5 patients underwent contrast-enhanced CT to assess the long-term patency of their stents (mean: 79.6±31.2 months), and none was occluded.

Conclusions: Venous stents display a high long-term patency rate, and hence are a useful tool for treating iliac venous stenosis. (Circ J 2014; 78: 1234–1239)

Key Words: Deep vein thrombosis; Iliac vein compression syndrome; Venous stenosis; Venous stents
Venous Stenting for Iliac Venous Stenosis

All 13 patients underwent venous stent implantation between May 2000 and June 2008. The following information was obtained for each case: intravascular ultrasound (IVUS) scan findings; the number, size, and type of stents used; the stent implantation site; and whether thrombolysis or concurrent rheolytic thrombectomy for acute DVT. During the procedure, all patients underwent full anticoagulation with unfractionated heparin through the side port of the introducer sheath. The heparin dose was adjusted to produce an activated partial thromboplastin time of twice the control value. After the procedure, all the patients were started on additional warfarin. The unfractionated heparin was discontinued after a therapeutic prothrombin time-international normalized ratio (PT-INR) had been obtained. The warfarin dose was adjusted to produce a PT-INR of 1.5–2.5.

Follow-up
Acute stent patency (within 2 weeks of stent implantation) and mid-term stent patency (approximately 1 year after stent implantation) were assessed with venography or contrast-enhanced CT; 3 patients were lost to mid-term follow-up, and we evaluated long-term stent patency (>3 years later) with contrast-enhanced CT in 5 patients. We diagnosed post-thrombotic syndrome based on the CEAP classification.

Results
The characteristics of the 13 patients (6 males, 7 females; mean age 63.2±10.2 years) enrolled in this study are shown in Table 1. During the same period, there were 74 cases of DVT for which catheter-directed thrombolysis was performed in our hospital, and the stent implantation rate was 17.6%. All patients were suffering from acute DVT or venous stenosis in the left common iliac vein because of iliac vein compression syndrome and continued to exhibit symptoms such as leg swelling and pain or venous stasis related to venous stenosis after thrombolytic therapy. One patient had stenotic lesions in both the left common iliac and external iliac vein. Thrombophilia, including protein S deficiency and antithrombin deficiency, was detected in 2 patients.

Stents
The stent implantation sites were the left common iliac vein in 13 lesions and the left external iliac vein in 1 lesion. Easy Wallstents (Boston Scientific) were implanted into 7 patients, SMART stents (Cordis, Bridgewater, NJ, USA) were implant-
Complications Related to Stent Implantation
No major complications occurred during stent implantation; 1 patient exhibited in-stent thrombosis immediately after stent implantation. There were no complications such as pulmonary thromboembolism, vascular injury, major bleeding, stent fracturing, or stent migration.

Retrieval of the IVC Filters
All the IVC filters that had been implanted in the patients with acute DVT were successfully retrieved after thrombolysis and stent implantation. No complications related to IVC filter implantation or retrieval occurred.

Mid-Term Follow-up
We administered warfarin-based anticoagulation therapy to all patients; 3 patients were lost to the mid-term follow-up; 1 patient suffered leg swelling because of a stent occlusion during the mid-term follow-up period (mean follow-up period: 12.9 ± 16.1 months). Imaging studies (venography: 6 patients, contrast-enhanced CT: 4 patients) were performed for the remaining 10 patients to verify whether the stents were occluded, but stent occlusion was only detected in 1 patient. Thus, the stent patency rate for the mid-term phase was 90.0%.

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Table 2. Details of Stent and Implantation
| Case no. | Stent Diameter (mm) | Length (mm) | Predilatation | Post-dilatation | Additional thrombolytic therapy after stenting |
|----------|---------------------|-------------|---------------|-----------------|-----------------------------------------------|
| 1        | Easy Wallstent      | 10          | 50            | –               | –                                             |
| 2        | Easy Wallstent      | 12          | 50            | +               | –                                             |
| 3        | Easy Wallstent      | 10          | 65            | –               | –                                             |
| 4        | SMART               | 12          | 60            | +               | –                                             |
| 5        | SMART               | 12          | 40            | +               | +                                             |
| 6        | SMART               | 10          | 60            | +               | +                                             |
| 7        | Easy Wallstent      | 12          | 50            | +               | +                                             |
| 8        | Easy Wallstent      | 10          | 65            | +               | +                                             |
| 9        | Luminexx            | 10          | 100           | +               | –                                             |
| 10       | Easy Wallstent      | 12          | 50            | +               | +                                             |
| 11       | Easy Wallstent      | 12          | 30            | +               | –                                             |
| 12       | SMART               | 10          | 40            | +               | +                                             |
| 13       | SMART               | 10          | 40            | +               | –                                             |

Table 3. Follow-up Data
| Case no. | Occlusion in acute phase | Occlusion in mid-term phase | Diagnostic method | Warfarin therapy (duration) | Recurrence of VTE | Prognosis |
|----------|--------------------------|-----------------------------|-------------------|-----------------------------|------------------|-----------|
| 1        | –                        | –                           | Venography        | Discontinued (84 months)    | Died of tongue cancer |
| 2        | +                        | –                           | Venography        | Continuing                  | –                |
| 3        | –                        | Not examined                | –                  | Discontinued (48 months)    | –                |
| 4        | –                        | –                           | Venography        | Discontinued (51 months)    | –                |
| 5        | –                        | –                           | Venography        | Discontinued (45 months)    | –                |
| 6        | –                        | –                           | Venography        | Continuing                  | –                |
| 7        | –                        | –                           | Enhanced CT       | Continuing                  | –                |
| 8        | –                        | –                           | Venography        | Continuing                  | Died of postoperative ileus |
| 9        | –                        | +                           | Enhanced CT       | Discontinued (28 months)    | –                |
| 10       | –                        | not examined                | –                  | Discontinued (32 months)    | –                |
| 11       | –                        | not examined                | –                  | Discontinued (6 months)     | –                |
| 12       | –                        | –                           | Enhanced CT       | Continuing                  | –                |
| 13       | –                        | –                           | Enhanced CT       | Continuing                  | –                |

VTE, venous thromboembolism.
Venous Stenting for Iliac Venous Stenosis

A 69-year-old woman (case no. 9) was admitted because of acute proximal DVT, and catheter-directed thrombolysis was initiated. After the clot had been dissolved, we implanted a stent (Luminexx, 10×100 mm) in a severe stenotic lesion in her left common iliac vein, which had been caused by iliac compression syndrome. After stent implantation, adequate stent expansion was confirmed by venography and IVUS. After discharge, the patient stopped taking warfarin of her own accord (10 days after stenting); however, her left leg subsequently began to swell. Complete obstruction from in-stent thrombosis was detected by CT at 1 month after stent implantation (Figure 2). Catheter-directed thrombolysis was not performed, but anticoagulation therapy was resumed, but despite long-term anticoagulation therapy, recanalization was not achieved. Finally, we ceased the anticoagulation therapy at 28 months according to the patient’s wishes. After cessation of anticoagulation therapy, exacerbation of lower limb swelling has not been observed.

Long-Term Follow-up

The mean follow-up after stent implantation was 79.9±29.8 months (range 28–117 months). During follow-up, 2 patients died of tongue cancer and postoperative ileus, respectively. No deaths because of venous thromboembolism occurred. We list the long-term outcomes of anticoagulation therapy in Table 3. At the time of the last follow-up examination, 7 patients had

Table 4. Review of Venous Stenting Studies

| Year   | Author          | n  | Acute phase patency rate (%) | Chronic phase patency rate (%) | Follow-up (months) | Diagnostic method          |
|--------|-----------------|----|-------------------------------|-------------------------------|--------------------|-----------------------------|
| 1998   | Binkert et al13 | 8  | 100                           | 100                           | 35                 | Venous US                   |
|        |                 |    |                               |                               |                    | Venography                  |
| 2000   | Patel et al14   | 10 | 100                           | 80                            | 36                 | Venous US                   |
| 2000   | O’Sullivan et al15 | 35    | 93.6                          | 93.6                          | 12                 | Venous US                   |
| 2001   | Heijmen et al16 | 6  | 100                           | 83                            | 12                 | Venous US                   |
| 2001   | Hurst et al17   | 17 | –                             | 79                            | 14–17              | Venography                  |
|        |                 |    |                               |                               |                    | Venous US                   |
| 2002   | Lamont et al18  | 15 | 93                            | 87                            | 16                 | Venous US                   |
| 2005   | Kwak et al19    | 22 | 96                            | 95                            | 24                 | Venous US                   |
| 2006   | Kim et al20     | 18 | 100                           | 88                            | 6                  | Venography                  |
| 2008   | Hartung et al21 | 29 | 89.7                          | 78.9                          | 63                 | Venous US                   |
| 2012   | Funatsu and Nakamura22 | 20    | 95                            | 93.8                          | 50                 | Venography                  |
|        |                 |    |                               |                               |                    | Venous US                   |
|        |                 |    |                               |                               |                    | Enhanced CT                 |
|        | Present study   | 13 | 92.3                          | 90.0                          | 79.9               | Venography                  |
|        |                 |    |                               |                               |                    | Enhanced CT                 |

Representative Case of Stent Occlusion

Figure 1. Stent occlusion during the acute phase (case 2). (A) Stent (Easy Wallstent, 12×50 mm) implanted after thrombolytic therapy. (B) After stent implantation. (C) At 2 days after stent implantation, catheter-directed thrombolytic therapy (Fountain infusion system, 5Fr×10 cm) was initiated because of stent occlusion (yellow arrows). (D) Final imaging examination.
Bolysis is being increasingly used to treat DVT and venous disease. Stent implantation for venous stenosis is a catheter intervention for venous disease and is considered to be an effective treatment for venous stagnation. In our hospital, venous stents are implanted in patients with venous stasis because of severe stenosis after complete thrombolysis. On the other hand, we exclude young subjects or with a rich collateral through the pelvic venous plexus.

All patients in the present series were suffering from left common iliac vein stenosis. The left common iliac vein is often compressed (iliac compression syndrome) because it runs behind the right iliac artery, and in some patients there is a pelvic venous spur in this region. As a result, the left leg is prone to venous stagnation and DVT.

To treat the patients with DVT, we placed a sheath in the popliteal vein ipsilateral to the lesion and performed stent implantation. After stent implantation, stent expansion was confirmed by IVUS. The 6 patients who exhibited inadequate stent expansion were treated with additional low-pressure balloon dilatation. Vascular injury, bleeding, infection, and pulmonary embolism were absent as complications, but 1 patient suffered in-stent thrombosis just after stent implantation. In that patient, venous stenosis and a thrombus developed in the distal part of the lesion, probably because of in-stent thrombus formation.

Catheter-directed thrombolysis was highly effective, but venous stenosis remained in the distal portion of the lesion.

stopped taking anticoagulants, and 6 patients were continuing to receive anticoagulation therapy. The mean duration of anticoagulant therapy in the patients who ceased treatment was 42.0±24.1 months. None of the surviving patients who had ceased anticoagulation therapy developed recurrent venous thromboembolism. Contrast-enhanced CT was performed to examine the long-term stent patency in 5 patients (including 2 patients who had discontinued anticoagulation therapy; mean duration of stent implantation: 79.6±31.2 months). Good stent patency was observed in all 5 patients, and none of the stents had fractured.

Only 1 patient had leg swelling according to the CEAP classification (C3), but post-thrombotic syndrome was not observed in any other patient (CEAP classification: C0).

**Discussion**

Venous stenosis can lead to blood flow stagnation and cause DVT. Also, the administration of anticoagulation therapy alone in patients with poor collateral vessels can lead to leg swelling, pain, and skin ulcers because of venous stenosis. Therefore, it is important to treat stenotic lesions in such patients.

In recent years, the use of catheter interventions for vascular disease has spread rapidly in conjunction with the development of catheter devices. In addition, catheter-directed thrombolysis is being increasingly used to treat DVT and venous disease. Stent implantation for venous stenosis is a catheter intervention for venous disease and is considered to be an effective treatment for venous stagnation. In our hospital, venous stents are implanted in patients with venous stasis because of severe stenosis after complete thrombolysis. On the other hand, we exclude young subjects or with a rich collateral through the pelvic venous plexus.

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**Figure 2.** Stent occlusion during the mid-term phase (case 9). (A) Stent (Luminexx, 10×100 mm) implanted after thrombolytic therapy. (B) After stent implantation (yellow arrowheads indicate the stent). (C) Contrast-enhanced CT (4 days after stent implantation; green arrows show stent patency). (D) Contrast-enhanced CT (1 month after stent implantation; blue arrows show stent occlusion).
Blood flow stagnation was also observed at this site, and so an additional stent was implanted. After treatment, no recurrence developed during the chronic phase of the patient’s condition. Only 1 patient developed stent obstruction in the acute phase and that patient did not undergo balloon dilatation after stent implantation. Angiography performed just after stent implantation suggested that the stent might not have been large enough. Therefore, it was considered that blood flow stagnation led to the formation of a thrombus. The patient’s blood flow was restored by catheter-directed thrombolysis, and no recurrence was observed.

IVC filters are often required in cases of acute DVT treated with a catheter intervention. In this study, we implanted retrievable IVC filters in all patients. After completion of the catheter intervention, the IVC filters can be retrieved. However, implantation of a permanent IVC filter increases the risk of recurrent DVT, so IVC filters should only be implanted during the catheter intervention. In this study, all of the IVC filters were successfully retrieved.

Of the 10 patients in whom we were able to assess stent patency during the mid-term follow-up phase, occlusion was only observed in 1 patient. After discharge, the latter patient exhibited good patency, and there were no fractured stents.

Thus, stent implantation is considered to be an appropriate treatment for venous stent obstruction in patients with proximal deep vein thrombosis. Circ J 2012; 76: 2697–2704.

Conclusions

In conclusion, venous stent implantation for iliac venous stenosis is associated with a high long-term patency rate and is an effective and safe therapy.

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