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Endovascular Stenting and Factor Xa Inhibitors for Filter-Associated Chronic IVC Occlusion: A Case Series

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Case series
Patients: Male, 48-year-old • Male, 75-year-old • Male, 46-year-old
Final Diagnosis: Chronical inferior vena cava occlusion • postthrombotic syndrome
Symptoms: Bilateral lower extremity swelling • hyperpigmentation and refractory venous ulcerations
Clinical Procedure: —
Specialty: Radiology

Objective: Rare disease
Background: Chronic inferior vena cava (IVC) occlusion is a serious long-term complication of inferior vena cava filters (IVCFs) placement, which can lead to severe post-thrombotic syndrome (PTS). Endovascular management associated with anticoagulation may be one of limited options. Here, we present 3 patients with chronic filter-associated IVC occlusion managed with endovascular stenting and Factor Xa inhibitor infusion.
Case Reports: Case 1: A 48-year-old man who presented bilateral lower-extremity swelling, hyperpigmentation, and refractory venous ulcerations with a permanent IVCFs placements 16 years before admission was diagnosed as having filter-associated chronic IVC occlusions. Recanalization was performed through endovascular therapy, and factor Xa inhibitor was selected for antithrombotic therapy. Although in-stent occlusion was discovered on the left limb during 1-year follow-up, relief of symptoms was achieved at 36-month follow-up.
Case 2: A 75-year-old man with a 6-year history of bilateral lower-extremity swelling, hyperpigmentation, and refractory venous ulcerations was found to have chronic IVC occlusions due to permanent IVCFs. Endovascular therapy and factor Xa inhibitor were chosen for revascularization, and symptomatic relief and stents patency were maintained until the last follow-up (30 months).
Case 3: A 46-year-old man diagnosed with filter-associated chronic IVC occlusions underwent endovascular stenting and factor Xa inhibitor infusion. Improvement was shown during the first-year follow-up, but recurrence of symptoms and in-stent occlusions were discovered at 18-month follow-up for anticoagulation withdrawal.
Conclusions: Despite risks of in-stent occlusions, factor Xa inhibition associated with endovascular may be a safe and feasible management of filter-associated chronic IVC occlusion.

Keywords: Vena Cava, Inferior • Endovascular Procedures

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Introduction

Inferior vena cava filters (IVCFs) have been widely used for over 40 years to prevent pulmonary embolism (PE) in acute proximal deep venous thrombosis (DVT) patients who have contraindications to anticoagulation [1-5]. Some IVCFs placed in the last 2 decades were retrievable, but most of them were permanent [6-11]. An increasing number of studies focused on the long-term complications of IVCFs have been published [6,8-10,12,13].

Chronic filter-associated inferior vena cava (IVC) occlusion is a serious long-term complication of IVCFs placement [6], with incidence ranging from 2% to 30% [6,8,14]. Some patients with symptomatic filter-associated IVC develop severe post-thrombotic syndrome (PTS), yet treatment options are still limited [15]. Because of the unsatisfactory patency rate of open venous femorocaval bypass reconstruction [16,17], endovascular treatment has become the first-line intervention [18-21]. There is also no consensus on use of antithrombotic medications after iliocaval stent placement [22,23]. Factor Xa inhibitors, whose mechanism is based on direct, reversible, and selective inhibition of free and clot-bound Factor Xa [24], has shown promising results in venous thromboembolism prevention [25] and antithrombotic medications after stenting [26,27].

This case series presents 3 patients with chronic filter-associated IVC occlusion managed with endovascular stenting and Factor Xa inhibitor infusion.

Interventional Therapy

With patents supine, bilateral percutaneous accesses were performed through popliteal veins under guidance of ultrasound. An anterograde venogram was used to assess the venous obstruction from the introduced sheath (MAK mini access kit; Merit Medical systems, Inc.). A guide wire (V-18 Control Wire; Boston Scientific Corporation) was directed through femoro-ilio-caval vein obstructions under guidance of an angiographic catheter (VER 135°, Cordis Corporation) or support catheter (CXI Support Catheter; Cook, Inc.). Then, a Flexor Check-Flo Introduce Sheath (8-F, 90-cm Raabe Modification, Cook, Inc.) replaced the former sheath and was placed in the iliofemoral vein, which expedited advancement through the lesions. Balloon catheters (Armada; Abbott Vascular), with diameter of 4-14 mm and length of 60-150 mm, were used for percutaneous transluminal angioplasty (PTA). Balloon dilations were performed with a "kissing balloon" technique in the IVC, and the filters were displaced sideways. Two self-expandable stents (Wallstent; Boston Scientific Corporation; E-Luminexx; Bard, Inc.) (14-16mm diameter; 90-120mm length) were implanted across the IVCFs and released in the IVC simultaneously. The bilateral stent re-dilations were performed simultaneously after stents were deployed. Depending on the length of the occluded vein, 2-6 stents were placed to ensure sufficient outflow.

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Figure 1. (**A**) A 48-year-old man with a history of a permanent filter (Simmons Bard Inc.) placement for postoperative PE 16 years ago presented with hyperpigmentation and recurrent non-healing venous ulcers on both legs. (**B**) CTV revealed bilateral external iliac vein (EIV) and IVC occlusion. (**C**) Five stents were deployed for revascularization. (**D**) Significant improvements of hyperpigmentation and venous ulcers at 1-year follow-up.

Case Reports

Case 1

A 48-year-old male patient was admitted for a 16-year history of bilateral lower-extremity swelling, as well as 1 week of exacerbation. This patient, who had a right femoral fracture reduction, received a permanent IVCF (Simmons Bard, Inc.) for postoperative PE (dyspnea, hemoptysis, and confirmed by pulmonary artery CTA) 16 years ago, and he was safely discharged after treatment with advice that oral anticoagulation (warfarin, dosage unknown) should last for 1 year. Bilateral lower-extremity swelling presented after hospital discharge. However, 5 years ago, edema, redness, hyperpigmentation, and lipodermatosclerosis appeared and progressed, and refractory venous ulcerations were treated by dressing (**Figure 1A**). Meanwhile, red cord-like abdominal wall masses emerged and visibly engorged. He was diagnosed with severe post-thrombotic

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syndrome (PTS) due to filter-associated chronic IVC occlusions, and was assessed as C6 based on the CEAP classification. Computed tomographic venography (CTV) (**Figure 1B**) and anterograde venogram revealed bilateral external iliac vein (EIV) and IVC occlusion. Based on guidelines for PTS [23], endovascular therapy, compression stockings (ECS), and anticoagulation were used.

After laboratory results confirming no contraindication, the endovascular therapy was performed without complications, details of which were described above. Four self-expandable stents including 2 Wallstent (16-90 mm and 14-90 mm, Boston Scientific Corporation) and 3 E-Luminexx (14-120 mm, Bard, Inc.) were implanted for revascularization of IVC and bilateral EIV (**Figure 1C**). Anticoagulation therapy (rivaroxaban 20 mg per day) and ECS were initiated postoperatively and the patient was advised to continue this lifelong. Improvements in clinical symptoms with relief of swelling, pain, and heaviness were reported postoperatively, and venous ulcer healing subsequently reached complete epithelization, which was assessed as C5 after surgery.

Follow-ups were routinely performed at 1, 3,6, 12 months and then annually, which included clinical examination, duplex ultrasound, or anterograde venogram. Positive outcomes were enhanced after discharge; however, re-occlusion was discovered in the left limb during 1-year follow-up. The left limb later successfully received PTA, but stent patency still could not be maintained for long. He was treated with ECS and pharmacotherapy, and clinical impairments were not observed at the final follow-up (39 months), which was assessed as C4 (**Figure 1D**).

Case 2

A 75-year-old man with a history of permanent IVCFs (Simmons Bard, Inc.) placement for right lower-extremity DVT in a local hospital 14 years ago presented to the hospital due to bilateral lower-extremity swelling, hyperpigmentation, and refractory venous ulcerations for 6 years, as well as 2 months of exacerbation (**Figure 2A**). He was taking 75-mg warfarin per day, without monitoring the international normalized ratio (INR). Severe PTS (C6) caused by filter-associated chronic IVC occlusions was diagnosed, and a subsequent anterograde venogram confirmed bilateral EIV and IVC occlusion (**Figure 2B**). Based on guideline for PTS [23] and patient preference, endovascular therapy was chosen, and 6 self-expandable stents (Wallstent, Boston Scientific Corporation) were deployed for revascularization (**Figure 2C**). Anticoagulation therapy (rivaroxaban 20 mg per day) and ECS were initiated postoperatively and he was advised to continue taking these lifelong. Improvements in clinical symptoms with relief of swelling, pain, and heaviness were reported postoperatively, and venous ulcer healing

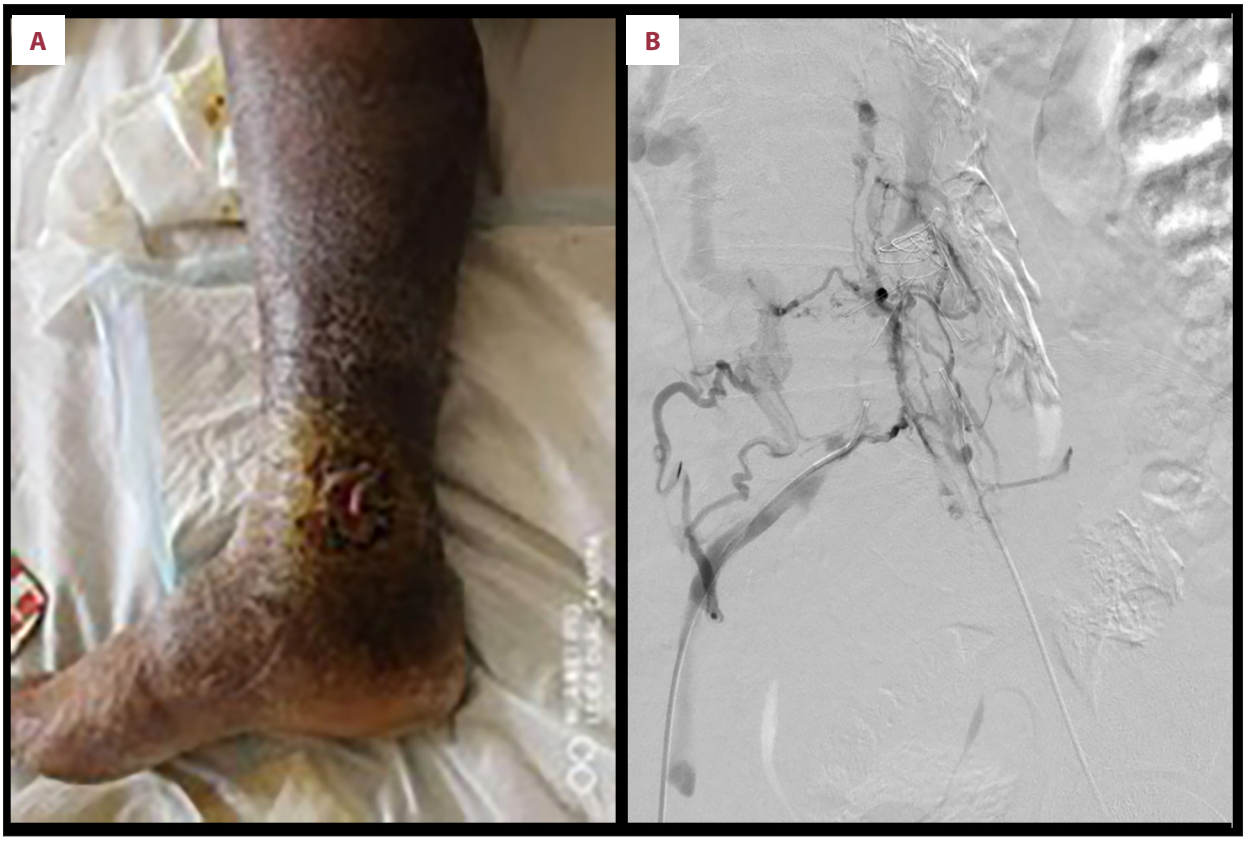

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Figure 2. (**A**) A 74-year-old man who had permanent filter (Simmons Bard Inc.) placement for right lower-extremity DVT 14 years ago presented with hyperpigmentation and recurrent non-healing venous ulcers on both legs. (**B**) An anterograde venogram showed chronic post-thrombotic obstruction of the lower IVC and bilateral iliofemoral vein, with numerous collateral veins. (**C**) After stents deployment, a venogram showed venous outflow without remaining obstruction. (**D**) Significant improvements of hyperpigmentation and venous ulcers in follow-ups.

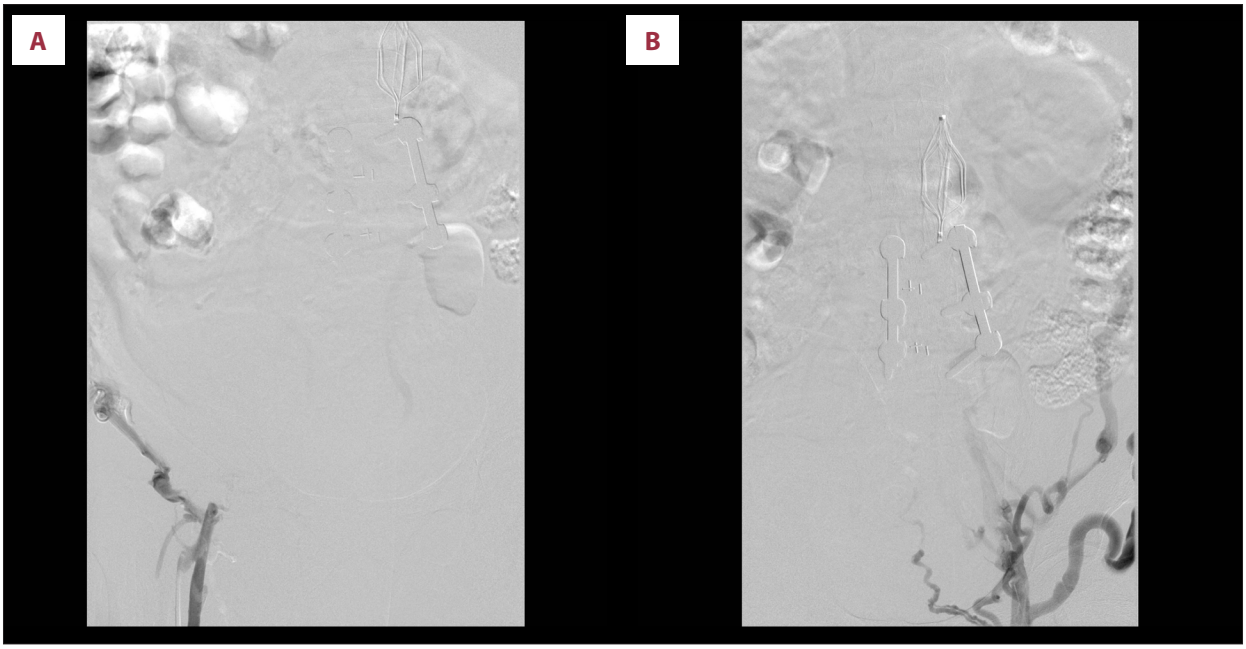

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Figure 3. (**A, B**) Anterograde venogram showed chronic post-thrombotic obstruction of lower IVC and bilateral iliofemoral vein with numerous collateral veins. (**C**) Balloon dilations were performed with a "kissing balloon" technique in the IVC. (**D**) After stents deployment, a venogram showed venous outflow without remaining obstructions.

subsequently reached complete epithelization, with CEAP classification C5 at discharge.

He had regular follow-ups after discharge, and relief of symptoms (CEAP classification was C4) and stent patency both maintained a satisfactory outcome (**Figure 2D**) through the last follow-up (30 months).

Case 3

A 46-year-old man came to the hospital because of bilateral lower-extremity swelling, hyperpigmentation, and refractory venous ulcerations for 2 years. He had a history of multiple fractures caused by major trauma 4 years ago. Bilateral lower-extremity DVT was discovered before surgery, then a filter (Aegisy,

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LifeTech Scientific Corporation) was placed due to contraindication of anticoagulation, which was not removed. Bilateral EIV and IVC occlusion were discovered by anterograde venogram (**Figure 3A, 3B**), the CEAP classification at the time of presentation was C6, and similar treatments including endovascular therapy (4 self-expandable stents including 3 Wallstent and 1 E-Luminexx) (**Figure 3C, 3D**), anticoagulation (rivaroxaban 20 mg per day) and ECS were successfully performed. Satisfactory postoperative recovery was obtained, and the venous ulcers were subsequently healed, with a CEAP classification at discharge of C5.

At 1-month, 3-month, 6-month, and 12-month follow-ups, improvement in symptoms was shown, but in-stent occlusions were identified by recurrence of symptoms and imaging confirmation on CTV, discovered at 18-month follow-up for anticoagulation withdrawal, and he refused to undergo a re-intervention.

Discussion

This case report presents 3 patients with severe PTS caused by filter-associated chronic IVC occlusion, and promising outcomes of factor Xa inhibitors associated with endovascular therapy were confirmed.

Presentations of filter-associated chronical IVC occlusion vary from asymptomatic disease to severe PTS, which include severe limb pain, severe lower-extremity swelling, venous claudication, and even refractory venous ulceration [6,8-10,14,15]. Only a small proportion of them result in severe PTS, whose manifestations generally involve bilateral limbs and have a significant negative impact on quality of life [19,21,28]. As in previous studies [19,21,28,29], the 3 cases in this report presented with severe PTS that negatively impacted quality of life (CEAP classification all reached C6). In addition to clinical presentations, diagnosis of filter-associated chronical IVC occlusion is mostly based on duplex ultrasound, CTV, and anterograde venograms [19,21,28,29], which may also provide a reference for selecting the optimal treatment strategy.

Treatments of severe PTS with bilateral iliac vein and vena cava occlusion usually include compression-based therapies, pharmacotherapy, and endovascular procedures, according to guidelines [23,30], and they must be completely administered. The first principle of endovascular procedures should be detection and elimination of iliac vein and vena cava obstructions [19,21]. Various stent placement techniques were used in former studies, including fenestrated stents, double-barrel stent technique, bifurcation reconstruction with 2 Gianturco Z-stents, and cephalad stents terminated below IVCFs [18,19,21,28,29]. Multiple stent placement techniques were used simultaneously in most reports; the technical success rate ranged from 85% to 100%, and the primary stent patency rates in short-term follow-up ranged from 32% to 70% [18,19,21,28,29]. The double-barrel technique was most commonly used in previous reports, but none focused on a single technique. In our 3 cases (6 limbs) of chronic filter-associated IVC occlusion, the technical success rate was 100%, and the primary stent patency rate was 83.33%, which is consistent with former studies [18,19,21,28,29]. Compared with other techniques, the "double-barrel" stent technique appears to have a higher stent patency rates and lower risk of complications, but further case reports and observational studies are needed.

Choosing the appropriate post-intervention management for venous stenting is challenging [22]. With insufficient evidence of effectiveness, exercise and ESC are still widely recommended to treat PTS, with the goals of reducing symptoms in guidelines [23,29,30]. In the present cases we adopted those strategy, and follow-ups showed improved daily functions. In addition, antithrombotic medications to prevent stent malfunction significantly affect long-term outcomes, but consensus is lacking [22,31]. Some extrapolations from antithrombotic therapy in peripheral artery stenting were obtained, whereas anticoagulation seems to have a more important role than antiplatelet therapy in the venous system [32]. A combination of anticoagulation and antiplatelet therapy after stenting was reported to be associated with better patency without causing bleeding complications [33,34], but this is not widely accepted due to lack of large, multi-center analyses. In former studies, long-term warfarin used to be recommended for patients with PTS or after stenting [22], while factor Xa inhibitors, especially rivaroxaban, were demonstrated to a more effective management [26, 27]. Long-term anticoagulation with rivaroxaban was chosen to maintain stent patency in the present study, which resulted in only 1 limb re-occlusion.

Conclusions

Despite risks of in-stent occlusions, Factor Xa inhibition associated with endovascular may be a safe and feasible management of filter-associated chronical IVC occlusion. Efforts to prevent IVCF-related complications are needed.

Department and Institution Where Work Was Done

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Patient Consent

All patient consents have been obtained.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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