

Transcatheter Thrombolysis with High-Dose Bolus Tissue Plasminogen Activator in Iatrogenic Arterial Occlusion After Femoral Arterial Catheterization

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Abstract

Purpose: To assess the efficacy of percutaneous local thrombolysis with high-dose bolus recombinant tissue plasminogen activator (rt-PA) in patients with acute limb ischemia due to arterial thrombosis after cardiac catheterization.

Methods: We treated eight patients (7 men; mean age 56 years) with thrombotic occlusion of both the common femoral artery (CFA) and external iliac artery (EIA) in six patients and of the CFA only in two patients. Two 5 mg boluses of rt-PA were injected into the proximal clot through a 5 Fr end-hole catheter and subsequently two additional boluses of 5 mg rt-PA were given through a catheter with multiple side-holes. In case of a significant amount of residual thrombus, a continuous infusion of 2.5 mg/hr of rt-PA was started.

Results: Successful lysis was achieved in all patients. The mean duration of lysis was 2 hr 41 min. The mean total amount of rt-PA delivered was 23.16 mg. In four patients unmasked flow-limited dissections confined to the CFA were managed by prolonged balloon dilatation, while in the remaining four patients with extension of the dissection to the external iliac artery one or two Easy Wallstents were implanted. There was prompt relief of lower limb ischemic symptoms and signs in all patients. Two groin hematomas were conservatively treated. Clinical and color Doppler flow imaging follow-up with a mean duration of 15 months, showed no reappearance of ischemic symptoms or development of restenosis in any of the patients. One patient died 6 months after thrombolysis.

Conclusions: Transcatheter thrombolysis with high-dose bolus rt-PA is a safe and effective treatment in patients with iatrogenic arterial occlusion after femoral catheterization. Underlying dissections should be treated by prolonged balloon dilatation but stent implantation is often required.

Key words: Thrombolysis—Iatrogenic complications—Arterial thrombosis—Cardiac catheterization

Peripheral vascular complications after cardiac catheterization represent a significant problem with increasing incidence among traumatic vascular injuries, especially when complex cardiovascular procedures are performed [1, 2]. Acute ischemia from intimal dissection or thrombosis following femoral artery injury, although not always limb-threatening, can seriously compromise walking exercise, which is an important component of cardiac rehabilitation in these patients [3]. Surgical repair is performed in such cases, including major vascular reconstruction in 9% of patients [4], but up to 50% of those presenting with critical ischemia may suffer permanent disability after operation [5]. On the other hand, iatrogenic acute thrombotic occlusions respond well to local delivery of thrombolytic agents [6, 7], but this type of treatment has not been stressed sufficiently in the literature.

The purpose of the present study was to assess the efficacy of percutaneous local thrombolysis with high-dose bolus recombinant tissue plasminogen activator (rt-PA) in patients with acute limb ischemia due to iliofemoral arterial thrombosis after cardiac catheterization.

Table 1. Patient data

Patient no., sex and age	Lesion location	Lesion length	Duration of limb ischemia
1 M, 43 years	CFA + EIA	12.8 cm	4 days
2 M, 64 years	CFA + EIA	13.9 cm	24 hr
3 M, 71 years	CFA + EIA	11.5 cm	2 hr
4 M, 38 years	CFA	4.8 cm	36 hr
5 F, 72 years	CFA + EIA	13.8 cm	3 hr
6 M, 42 years	CFA	5.2 cm	2 days
7 M, 61 years	CFA + EIA	13.9 cm	7 days
8 M, 55 years	CFA + EIA	14.6 cm	5 days

CFA, common femoral artery; EIA, external iliac artery; M, male; F, female.

Materials and Methods

Between September 1997 and November 1999, out of 1658 consecutive cardiac catheterization procedures, eight patients (1 woman, 7 men; mean age 56 years, range 38–72 years) who developed acute limb ischemia following cardiac catheterization for diagnostic or therapeutic indications, were treated by catheter-based techniques. The ordinary Seldinger technique was applied in all femoral arterial punctures. In all cases the cardiac intervention was completed and after sheath removal manual compression was applied at the puncture site for an average period of 15 min. Clinical signs of limb ischemia included absent femoral arterial pulses, pallor and diminished skin temperature of the cannulated leg. No patient experienced rest pain. In six patients disabling claudication was manifested immediately after their mobilization. The mean duration of limb ischemia was 2 days 14 hr (range 2 hr to 7 days). All patients were in clinical category I (Viable) according to the SVS/ISCVS standards for acute limb ischemia [8]. Color Doppler flow imaging (CDFI) revealed in all cases absence of flow in the proximal common femoral artery (CFA), due to occupation of the lumen by thrombotic material, in combination with a damped waveform at the distal CFA peripheral to the occlusion. Diagnostic angiography through a contralateral femoral approach showed thrombotic occlusion of both proximal CFA and external iliac artery (EIA) in six patients and of the CFA only in two patients. The mean length of occlusion was 11.3 cm (range 4.8–14.6 cm). Both superficial femoral artery and profunda femoris were patent in all patients (Table 1).

All patients were classified as ASA 3 according to the American Society of Anesthesiologists' Physical Status Classification [9] and were considered as being of high risk for surgical repair of their iliofemoral thrombosis.

Our protocol of transcatheter thrombolysis for acute peripheral arterial thrombosis was applied. After intra-arterial administration of 5000 IU of heparin, a 5 Fr end-hole catheter was advanced through the contralateral femoral access used in the angiography and its tip embedded in the proximal portion of the occlusion, following some gentle disruption of the thrombotic material at this location with a 0.035-inch hydrophilic guidewire (Terumo, Tokyo, Japan). Initially, two 5 mg boluses of rt-PA (Actilyse, Boehringer, Germany) were injected into the clot at an interval of 10 min in order to initiate lysis and facilitate subsequent manipulations. Following this, the occlusion was negotiated carefully with the 0.035-inch hydrophilic guidewire and, after successful passage, the end-hole catheter was exchanged for a 5 Fr Mewissen (Boston Scientific, Watertown, MA, USA) catheter with 20 side-holes (10

cm infusion length) in such a way that the infusion part of the catheter was positioned within the thrombus while its tip was occluded by the guidewire. Two additional 5 mg boluses of rt-PA were given at an interval of 10 min. In the two cases with thrombus confined to the CFA, only one additional bolus was given through the initial end-hole catheter after this had been advanced further into the clot. Ten minutes after the last bolus an angiogram was performed, in order to check for the extent of thrombus dissolution, and in case of a significant amount of residual thrombus a continuous infusion of 2.5 mg/hr of rt-PA was started using a calibrated infusion pump. During infusion of the lytic agent, concurrent intravenous heparin at a dose of 500 IU/hr was given to prevent rethrombosis. Laboratory monitoring consisted of baseline and 2-hourly determinations of plasma fibrinogen and activated partial thromboplastin time (APTT).

Successful lysis was defined as the restoration of antegrade flow with complete or near-complete clearance of thrombus. After the completion of lysis, unmasked occlusive dissections were managed promptly by prolonged (10 min) inflation of a standard angioplasty balloon of a diameter equal to that of the relatively normal artery adjacent to the lesion being treated; the measurement was made directly from a film-screen angiogram, resulting in slight overdilation of the vessel. The degree of apposition of the dissected intima and underlying media was checked angiographically at the end of balloon angioplasty with anteroposterior and oblique imaging, using as a criterion of success rapid flow with a fast contrast medium wash-out through the dissected area. In case of persistent flaps falling across the lumen, one or two self-expandable stents (Easy Wallstent, Schneider, Bülach, Switzerland) were deployed in order to establish a widely patent smooth lumen.

Four hours after sheath removal all patients were started on heparin for 24 hr and continued afterwards on long-term antiplatelet therapy. The follow-up protocol included clinical investigations by ankle blood pressure measurements and CDFI at 1 day, 3, 6 and 12 months following the procedure and then yearly thereafter.

Results

Successful lysis was achieved in all eight patients. The mean duration of lysis was 2 hr 41 min (range 45 min to 4.5 hr). The mean total amount of rt-PA delivered was 23.16 mg (range 15–29 mg). A completion angiogram at the end of thrombolysis revealed flow-limiting dissection located at the proximal CFA in four patients, while in the remaining four patients the dissection extended well above the inguinal ligament at the ipsilateral EIA. In two patients residual thrombi adherent to the vessel wall were noted, but they did not compromise flow. No peripheral emboli were detected angiographically in any of the patients. Percutaneous transluminal angioplasty with prolonged balloon inflation was performed in all cases and the result was considered satisfactory by angiographic criteria in the four cases with dissection limited to the CFA. In the other four cases with EIA involvement, balloon angioplasty alone failed to reattach the dissected intima and therefore self-expandable Easy Wallstents were deployed through a contralateral femoral access.

In three of four cases, placement of a single stent in the EIA was thought to be adequate (Fig. 1), but in the fourth case gross irregularity of the CFA lumen with persistent

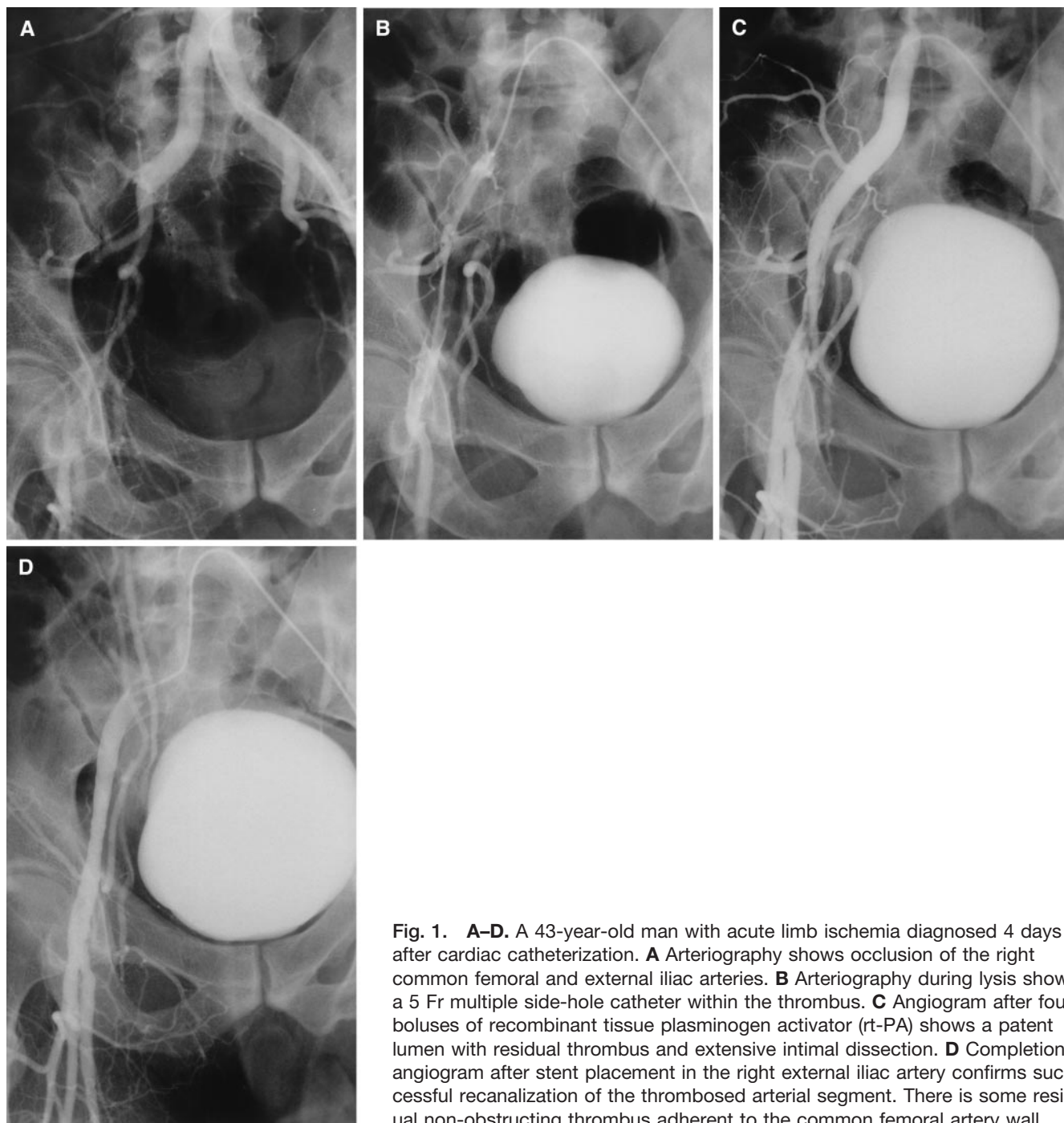


Fig. 1. A–D. A 43-year-old man with acute limb ischemia diagnosed 4 days after cardiac catheterization. **A** Arteriography shows occlusion of the right common femoral and external iliac arteries. **B** Arteriography during lysis shows a 5 Fr multiple side-hole catheter within the thrombus. **C** Angiogram after four boluses of recombinant tissue plasminogen activator (rt-PA) shows a patent lumen with residual thrombus and extensive intimal dissection. **D** Completion angiogram after stent placement in the right external iliac artery confirms successful recanalization of the thrombosed arterial segment. There is some residual non-obstructing thrombus adherent to the common femoral artery wall.

obstruction of flow led us to place a second stent in such a way that the proximal CFA, above the femoral bifurcation, was also covered; the final angiogram showed complete restoration of a patent smooth lumen with no residual stenoses.

Complications included groin hematomas in two cases: one at the occluded site when the cardiac catheter had been placed and the other at the interventional contralateral puncture site. They developed during the infusion phase of thrombolysis, at 4 hr and 3 hr respectively, and were both treated

with prolonged local pressure. Fortunately, in both cases at that time recanalization of the occluded segment had already been achieved and the infusion was stopped with no development of rethrombosis. In the first of those cases, there were some residual wall-adherent, non-obstructing thrombus at the EIA, as well as an intimal flap at the CFA that was effectively treated by prolonged balloon dilatation; in the second case a stent was eventually positioned.

There was prompt relief of lower limb ischemic symptoms and signs in all patients. Clinical and CFDI follow-up

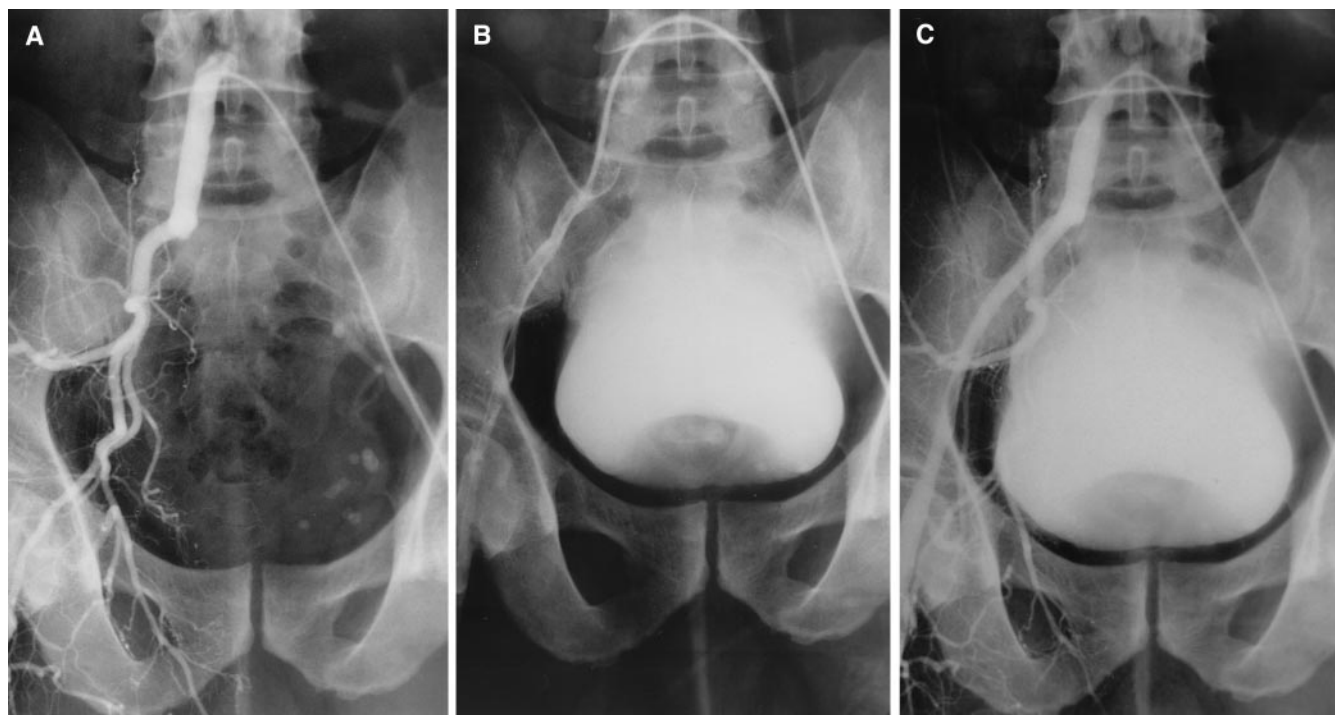


Fig. 2. A–C. A 71-year-old man with acute limb ischemia diagnosed 2 hr after cardiac catheterization. **A** Arteriography shows occlusion of the right proximal common femoral and external iliac arteries. **B** An angiogram after two boluses of rt-PA shows a significant amount of thrombus. Intimal dissection of the right proximal common femoral artery is also noted. **C** Final result after successful stenting of the right external iliac artery and common femoral artery above the femoral bifurcation.

with a mean duration of 15 months (range 6–24 months) showed no reappearance of ischemic symptoms or development of restenosis at the site of intervention in any of the patients. One 71-year-old man died from acute myocardial infarction 6 months after thrombolysis, having shown no signs of restenosis at 3-month follow-up (Fig. 2).

Discussion

Subintimal passage of the guidewire or catheter during percutaneous arterial manipulations usually results in postponement of the procedure with no sequelae to the vessel patency [10], but in a minority of cases this is the cause of arterial thrombosis [11]. In such cases vascular surgery represents the traditional treatment. Because iliofemoral vessels in patients with coronary disease are also affected in most cases by atherosclerosis, their surgical repair usually requires a reconstructive procedure in addition to thrombectomy [12]. These open surgical procedures, although very often performed under general anesthesia, are potentially hazardous, since they increase the stress load in these patients, many of whom are in an unstable condition; in addition the existing hematoma and local tissue injury frequently found in such iatrogenically traumatized areas predispose to postoperative infection, especially if interposition of a synthetic graft is needed [3].

Transcatheter thrombolysis seems to be an acceptable alternative to primary surgical revascularization in iatrogenic

acute thrombotic occlusions, although there are no large series in the literature supporting its widespread use in everyday clinical practice [13–16]. The most commonly used lytic agents for intra-arterial thrombolysis in such cases are streptokinase and urokinase, often with the adjunct of catheter suction [10, 15, 16]. As a lytic agent, recombinant tissue plasminogen activator (rt-PA) is superior to streptokinase [17], and although there is no difference in efficacy or safety between rt-PA and urokinase, the rate of thrombolysis with rt-PA tends to be more rapid during the first hours of the procedure [18, 19]. In addition, rt-PA is associated with fewer side-effects of nausea and vomiting compared with urokinase [19]. Regarding rt-PA delivery, it seems that an initial high-dose transthorbus bolus, followed by continuous infusion, significantly accelerates lysis without compromising outcome [20]. This was also our experience in the present study, where the duration of successful lysis was satisfactorily short.

We consider our technique of transcatheter thrombolysis to be simple and convenient. Our experience from this study, as well as from similar cases of acute iliac thrombosis caused by underlying atheroma, shows that the tip of a 5 Fr end-hole catheter can easily be introduced into the proximal portion of the non-organized thrombus and the first two boluses can be effectively delivered at this position; the resultant softening of thrombotic material makes subsequent manipulations of a 0.035-inch steerable hydrophilic guidewire through the oc-

clusion much easier and safer, by reducing intraluminal resistance during its advancement. Both types of infusion catheters, the 5 Fr end-hole and the Mewissen multiple side-hole, show in our experience excellent trackability over the 0.035-inch Terumo guidewire and can be positioned fairly easily in the thrombus. Another advantage of our technique is that after the bolus the patient can be transferred to a nearby close-surveillance area before the infusion phase is started, making the angiography suite available for another procedure.

Regarding the underlying cause of thrombosis, i.e., occlusive dissection, atherectomy devices such as the Simpson atherocath have been involved in the removal of intimal flaps falling across the lumen [21], but in clinical practice these devices have significant disadvantages, since they are rigid, creating difficulty in tortuous arteries and making the contralateral approach almost impracticable. Successful percutaneous balloon angioplasty of iatrogenic arterial dissections has also been reported in iliac, renal and mesenteric vessels as well as the distal aorta [22, 23]. In recent years intravascular stents such as the Palmaz and the Strecker have been placed successfully for reducing angioplasty-induced intimal flaps in iliac vessels [24, 25]. In our patients we tried initially to achieve apposition of the intima and underlying media by prolonged inflation of a standard angioplasty balloon of appropriate diameter. Careful angiographic monitoring showed this to be successful only in flaps localized to the CFA, while in more extensive dissections involving the EIA deployment of a stent was thought to be essential for salvage of the procedure. We decided to use the Easy Wallstent because in our experience it has excellent trackability over the aortic bifurcation, is repositionable after partial deployment, can be introduced through a relatively small (7 Fr) sheath, expresses an effective radial force and, finally, undergoes less shortening compared with the conventional type of Wallstent. In three cases stents were placed so that their distal end did not extend below the level of the inguinal ligament, following the widely accepted clinical practice of avoiding stenting of the CFA [26]. In the fourth case, after deployment of the EIA stent the CFA intimal flaps were still obstructing flow on a check angiogram, despite previous prolonged balloon dilation, so a second stent extending to the proximal CFA was deemed necessary; this practice has also been followed occasionally by other investigators [27].

It is interesting that in all our cases arterial thrombosis became apparent only after completion of the coronary catheterization procedure. The explanation we offer is that either the guidewire was redirected by the operator to the true lumen after initial dissection, or it followed a subintimal route with spontaneous re-entry to the true lumen; the second mechanism would explain more convincingly the more extensive dissections also involving the EIA. This extensive vessel injury, in combination with perhaps excessively firm external compression applied after sheath removal, may have created a severe obstruction to flow in the iliofemoral region which resulted in acute thrombosis. We also do not fully

understand why, of those cases with a dissection localized in the CFA, in two of them the thrombus was confined to that region while in the other two the thrombosis extended proximally to the ipsilateral EIA. One possible explanation may be that in the former two patients the level of systemic anticoagulation was sufficiently high to prevent extension of the thrombosis more centrally, as is often the case in patients with coronary disease.

Regarding complications, most bleeding during catheter lysis occurs at sites of arterial puncture—not only from the access site but also from recent arterial punctures for catheterization—and is usually treated conservatively [28]. This was also our experience: the two groin hematomas were treated with prolonged local pressure. We attribute these nonsignificant complications mainly to the short mean duration of lysis, as Sullivan et al. [29] have also shown, in addition to the small-caliber intravascular devices we used.

In conclusion, transcatheter thrombolysis with high-dose bolus rt-PA seems to be a safe and effective treatment in patients with iatrogenic arterial occlusion after femoral catheterization, provided it is promptly diagnosed with proper clinical examination and CDFI. Percutaneous transluminal angioplasty with prolonged balloon inflation is almost always needed as a complementary procedure, and in approximately half of the cases an additional self-expandable endoprosthesis should be placed in order to treat more extensive dissections proximal to the CFA. Further studies with a larger number of patients and a longer follow-up are needed to justify this method as common practice in treating such increasingly encountered iatrogenic vascular injuries, aiming finally to replace the more complex and distressing surgical procedures.

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