Thrombolytic Therapy for Peripheral CTOs

The role of this therapy has expanded, allowing for successful treatment of more patient groups.

BY AMIR MOTARJEME, MD

The role of thrombolytic therapy in the treatment of arterial chronic total occlusions (CTOs) has changed in the past several years, partly due to the introduction of hydrophilic catheters and wires, and partly due to the popularity of subintimal recanalization, in addition to frequent application of stents, in particular the self-expandable nitinol stents. Thrombolytic therapy is still the treatment of choice in acute and subacute arterial occlusions and graft thrombosis, despite the commonly used mechanical thrombectomy catheters. From hundreds of thrombolytic therapy articles published in European and North American literature, there are only a few reports regarding thrombolytic therapy in chronic arterial occlusions.[1-6]

In 1985, after an accidental clot lysis of a 1-year-old thrombosed femoropopliteal graft, we undertook a prospective study to evaluate the results of thrombolysis using urokinase in all arterial occlusions longer than 3 cm, regardless of the length and chronicity of the occlusions. In this series, 276 arterial occlusions were treated in 268 patients (147 men, 121 women; age range, 31 to 90 years). The length of occlusion ranged from 3 cm to 66 cm, with a median of 17 cm.

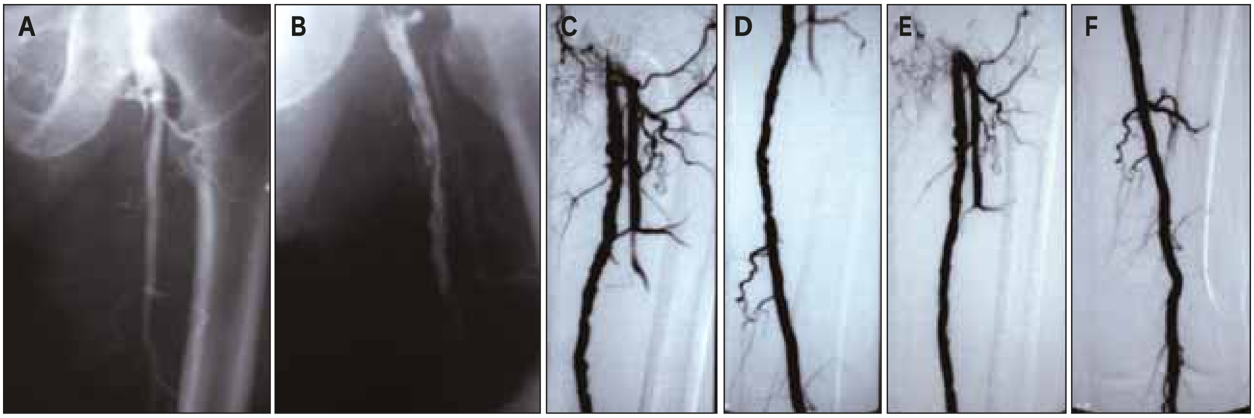

Figure 1. Total occlusion of the superficial femoral artery (SFA) from its origin (A) and a 6-hour postthrombolysis arteriogram (B). Twenty-four–hour postthrombolysis arteriogram showing multiple stenoses of the SFA (C, D). Postangioplasty arteriogram (E,F).

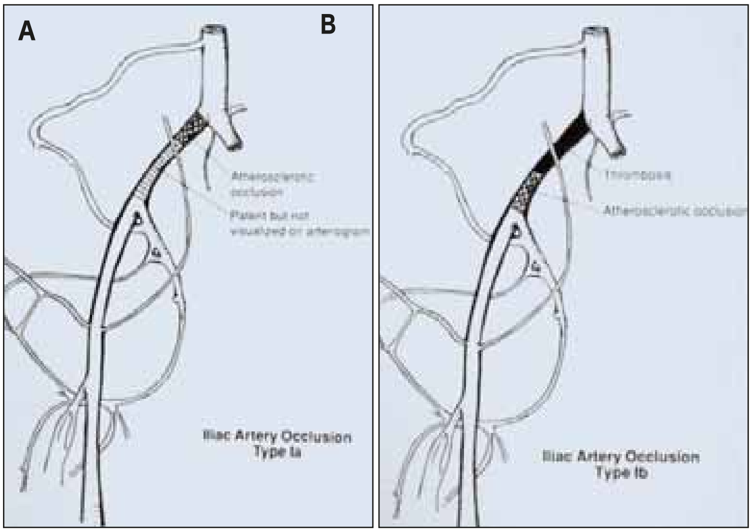

Figure 2. Schematic drawing of type Ia (A) and Ib (B) iliac artery occlusions.

The duration of occlusion was documented by an arteriogram in 25% of the cases, or by a history of a sudden onset of pain, coldness, and numbness of the lower limbs in 13% of patients. The duration of the occlusion was undetermined in the remaining 62%. Seventeen patients had arterial occlusions older than 2 years proven by previous arteriograms. Among patients with occlusions of the SFAs, 39 had occlusion of one or both SFAs, extending from the origin at the common femoral artery (CFA). Fifty percent of the patients had intermittent claudication from 8 months to 10 years. Only 12% of the patients complained of intermittent claudication of less than 8 months' duration. Fifty-eight patients had severe peripheral vascular occlusive disease and were treated for limb salvage. Surprisingly, 80% of chronic arterial occlusions responded favorably to thrombolysis. These lesions included long-segment occlusion of the iliac arteries, occlusion of the SFA from the origin, and very long-segment occlusions extending below the trifurcation of the popliteal artery. As seen in Table 1, all treated arteries responded very well; the larger iliac arteries had the highest success rate.

Most arterial occlusions (more than a few centimeters in length) are associated with some degree of arterial thrombosis, and thus may be more difficult to recanalize mechanically. This finding, combined with the experience that arterial stenosis and short-segment occlusions are more amenable to PTA than longer lesions, makes it reasonable to use thrombolysis as the initial step in treatment. The advantage of thrombolysis administered both systemically and locally prior to PTA and acute arterial occlusions is well established.[7,8]

Intra-arterial infusion of urokinase began a new era in thrombolytic therapy, demonstrating lower rates of hemorrhagic complications and more effective thrombolysis.[9] Concurrent advances in the availability of smaller catheters (3 F and 4 F), development of an open-end injectable guidewire, and utilization of coaxial systems have increased the rate of success due to both a better delivery system and fewer complications. In the absence of bleeding complications, lytic therapy can be continued until complete clot lysis is achieved. The author has treated patients with local intra-arterial infusion of urokinase as long as 5 days without bleeding. A prolonged, low-dose urokinase infusion is essential in long-segment chronic thrombotic occlusions. Rapid resolution of a fresh clot in the arterial system by intra-arterial infusion of urokinase has been demonstrated by McNamara et al,[9] who used an initial high dose of 240,000 U/h for 4 hours. Although this might be justifiably effective in acute arterial occlusions, more treatment time is essential in the treatment of chronic arterial thrombotic disease,

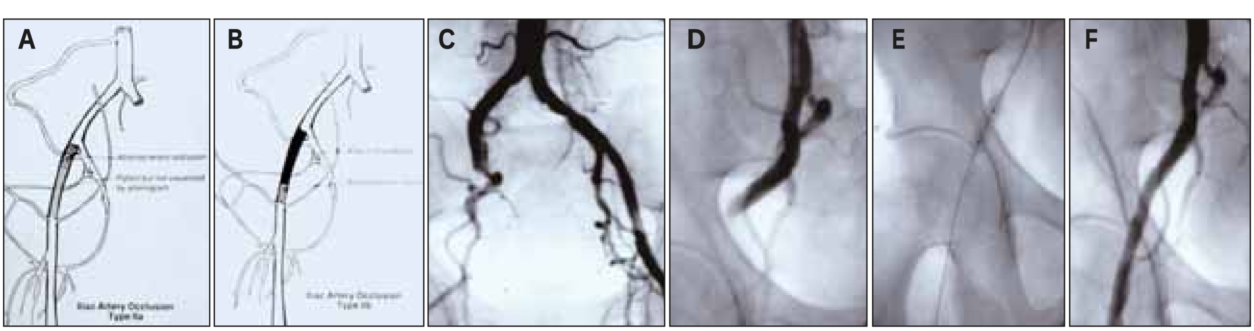

Figure 3. Schematic drawing of type IIa (A) and IIb (B) occlusion of the iliac arteries. Occlusion of the right external iliac artery (C). Postthrombolysis arteriogram showing almost total clot lysis (D). There is still a short-segment occlusion of the distal external iliac artery that was later recanalized and dilated (E). Postthrombolysis and angioplasty arteriogram shows patent external iliac artery (F).

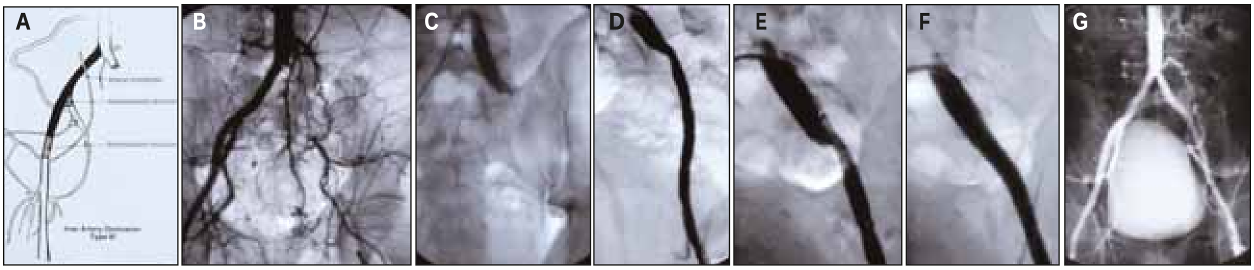

Figure 4. Schematic drawing of type III iliac artery occlusion (A). An arteriogram showing total occlusion of the left common and external iliac arteries. There is reconstitution of the internal iliac artery (B). Four-hour (C) and 24-hour (D) postthrombolysis arteriograms showing a single stenosis of the distal common iliac artery, not responding to balloon angioplasty. Delivery and deployment of a short 308 Palmaz stent (Cordis Corporation, a Johnson & Johnson company, Miami, FL) via a contralateral approach (E, F). A bilateral iliac arteriogram showing total patency of the left common and external iliac arteries. The internal iliac artery remains occluded at its origin (G).

both with and without atherosclerotic disease.

We have achieved complete thrombolysis in a short-segment, chronic arterial occlusion, but complete clot lysis of long-segment occlusions might not be achieved by thrombolysis alone. Furthermore, an underlying atherosclerotic occlusion prevents the flow of thrombolytic agent to the distal thrombus. Increasing the area of interface between the clot and the fibrinolytic agent is not essential for a fresh clot, but it appears to be of significant value in the treatment of CTOs. Thus, clot maceration, a process undertaken during thrombolysoangioplasty, a process alternating thrombolytic therapy and angioplasty, is not only effective, but also necessary to achieve adequate dissolution of thrombus. The author made this observation in clinical experience in which more than 50% of the long-segment, chronic arterial occlusion required further thrombolytic therapy to remove residual thrombus after a successful recanalization and dilatation. An additional short course of postdilatation lytic therapy resulted in complete clot lysis and patency of the segment. This experience has been shared by other investigators in principle, if not in exact clinical application.[10-13]

SFA OCCLUSIONS

Occlusion of the SFA occurs in many patterns, although three variations are common: (1) varying length segmental occlusions in the adductor canal, (2) occlusion of the SFA from the origin down to the popliteal runoff in the adductor canal, and (3) varying length occlusions involving both the superficial femoral and the popliteal arteries.

An occluded SFA frequently contains several areas of severe stenosis or short-segment occlusions, with one or more areas of thrombosis (Figure 1). Thus, it is difficult to predict the occlusive elements in an occlusion seen on angiogram. Thrombolysis, in the author's experience, is the key to a successful angioplasty because it enables identification of the variable patterns present in an occlusion.

TABLE 1. THROMBOLYSIS OF CHRONIC ARTERIAL OCCLUSIONS

Artery	Total	Success	Rate (%)
Iliac	54	44	81
Common femoral	17	13	76
Superficial femoral	150	119	79
Popliteal	39	31	79
Others	16	14	87
Total	276	221	80

TABLE 2. PRIMARY STENTING OF CHRONIC ILIAC ARTERY OCCLUSIONS							
Investigator	No. of Patients	Primary Success	Complications	Surgical Intervention	Short-Term Reocclusion	1-Year Patency	5-Year Patency
Rees, et al. Radiol. 1989	15	12/15 (80%)	3/15 (20%)	2/15 (13%)	1/15 (6.6%)	N/A	N/A
Yedlicka, et al. JVIR. 1994	11	8/11 (73%)	0	0	0	67%	N/A
Vorwerk, et al. Radiol. 1995.	127	103/127 (81%)	12/127 (11.6%)	6/127 (5.8%)	4/127 (3%)	81/127 (64%, 87%)	54%
Dyet, et al. JVIR. 1997.	72	67/72 (93%)	5/72 (7%)	4/72 (5.5%)	2/72 (2.7%)	85%	N/A
Henry, et al. J Endovasc Surg. 1998	105 stent 69	92/105 (88%)	5/105 (4.8%)	9/105 (8.5%)	7/105 (6.7%)	74.7%	56%
Motarjeme Pre-Stent Lysis	65	63/65 (97%)	1/65 (1.5%)	1/65 (1.5%)	0/65 (0%)	88%	Primary: 79%, secondary: 91%

ILIAC ARTERY OCCLUSIONS

Iliac artery occlusions have been thought to be resistant to treatment by angioplasty, except for short-segment lesions. Other investigators have experienced an unacceptable high complication rate.[14,15] The author has reported a success rate of 81% in recanalization of iliac artery occlusions using thrombolysis[16] before stents were available. After the introduction of balloon-expandable and self-expandable stents, recanalization of chronically occluded iliac arteries became more feasible, and successful primary stenting of iliac artery occlusions was reported by many investigators. We, on the other hand, still practice presenting thrombolysis, and our data show a higher success rate, better long-term patency rates, and fewer complications (Table 2).

To enhance the understanding of this approach to treating iliac artery occlusions, the lesions are classified into three types.

Type I

Type I lesions are an occlusion of the common iliac artery with patent internal and external iliac arteries and are subdivided into types Ia and Ib.

Type Ia is an occlusion of the proximal end of the common iliac artery, by atherosclerotic plaque. Type Ia occlusions are associated with no, or very little, arterial thrombosis. Because the common iliac artery has no side branches, the entire iliac artery is nonvisualized on arteriograms and is thought to be entirely occluded, even though the occlusion is only limited to the proximal end. Thrombolysis is occasionally effective in softening this type of occlusion.

Type Ib is an atherosclerotic occlusion of the distal end of the common iliac artery and thrombosis of the proximal iliac segment. Thrombolysis is very effective in this type of occlusion and facilitates the successful recanalization of the atherosclerotic segment (Figure 2).

Type II

Type II lesions consist of patent common and internal iliac arteries with occlusion of the external iliac artery to the level of the CFA run-off, which is revascularized by deep iliac circumflex and inferior epigastric arteries just proximal to the inguinal ligament. Type II lesions are divided into IIa and IIb. The entire external iliac artery appears occluded in type IIa lesions, while the occlusion is limited to the proximal segment. In this type of lesion, there is limited or no thrombosis, although thrombolysis appears to help soften the atherosclerotic lesion.

"Bleeding complications of thrombolysis are mainly due to concomitant heparin therapy."

In type IIb lesions, the atherosclerotic occlusion is located at the distal aspect of the external iliac artery, with thrombus filling the proximal segment to the bifurcation of the common iliac artery (Figure 3). Thrombolysis is extremely effective in recanalization of this type of lesion.

Type III

Type III lesions involve occlusion of the entire iliac artery from the aorta to the CFA. The occlusion of the internal iliac artery begins prior to occlusion of the common and/or external iliac arteries. The extent of arterial thrombosis is related to the site of the primary atherosclerotic occlusion. Thrombolysis is very effective in almost all of these cases, except when the occlusion takes place at the very proximal end of the common iliac artery (Figure 4).

CONCLUSION

Using thrombolysis, the author has improved the success rate in recanalizing occluded iliac arteries to almost 100%. The long-term patency is improved because stenting is limited to a short-segment atherosclerotic disease rather than a long-segment arterial thrombosis.

It is the author's opinion that thrombolytic therapy enhances the ability to perform angioplasty and stenting of lesions that are usually considered to be difficult or not amenable to this method of therapy. The rate of success is related to location, age, and length of occlusions. Thrombolysis is quite successful in larger vessels, such as the aorta and iliac arteries. Chronic occlusions of the superficial femoral and popliteal arteries can also be frequently treated with lytic agents. Thrombolysis of chronic occlusions of the tibial arteries is not as successful as therapy in the larger arteries. This finding may be due to softer, less-organized areas of occlusions that are frequently present at the core of lesions in larger vessels.

Bleeding complications of thrombolysis are mainly due to concomitant heparin therapy. Since initiating the use of lower doses of heparin to maintain the PTT between 45 and 60, the author has not observed any serious bleeding problems. Occurrence of local hematoma could be prevented by early recognition and timely exchange of the arterial sheath for a larger size. Development of a small local hematoma does not call for cessation of therapy, but rather for exchange of the sheath for a larger size to stop the bleeding at the puncture site.

Overall, lytic therapy offers a new dimension in percutaneous catheter treatment of arterial occlusive disease. This conclusion is particularly true in patients with limb salvage who have no effective alternative therapy.[17] This method of treatment has also helped define the significant role of thrombosis in arterial occlusive disease. ■

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