

Ultrasound-Facilitated Thrombolysis in Treating DVT

Rapid and complete clot clearance using the EKOS Lysis System offers promising treatment for DVT.

BY RODNEY A. RAABE, MD

Deep venous thrombosis (DVT), which occurs in more than 250,000 Americans each year, is a common condition associated with serious clinical sequelae.^{1,2} Pulmonary embolism, the most significant acute complication of DVT, has an inpatient mortality rate of 12%.³ Postthrombotic syndrome (PTS), the most prevalent complication of DVT, is chronic venous insufficiency that develops in approximately two thirds of patients with iliofemoral DVT.^{4,5}

PTS presents clinically months or years after DVT as the result of valvular incompetence and venous obstruction. Residual thrombus may permanently damage venous valves, thereby causing reflux, and preventing adequate venous return from the limb.¹ The resulting venous hypertension causes symptoms ranging from edema, heaviness, pain, claudication, and hyperpigmentation to varicose veins, lipodermatosclerosis, and skin ulceration, in severe cases.^{1,2,6}

Although both valvular incompetence and venous obstruction may contribute to the development of PTS, the combination of these factors tends to be associated with the more severe symptoms.^{7,8} Rapid resolution of thrombus in DVT is thought to

aid in preserving valvular function.^{9,10} By maintaining valvular integrity and rapidly eliminating residual venous obstruction, complete clot lysis may result in improved clinical outcomes by preventing symptoms of PTS.⁸

LIMITATIONS OF CURRENT DVT TREATMENTS

Clinical management of DVT includes anticoagulation therapy, surgical thrombectomy, and endovascular techniques. Anticoagulation therapy with unfractionated or low-molecular-weight heparin followed by oral anticoag-

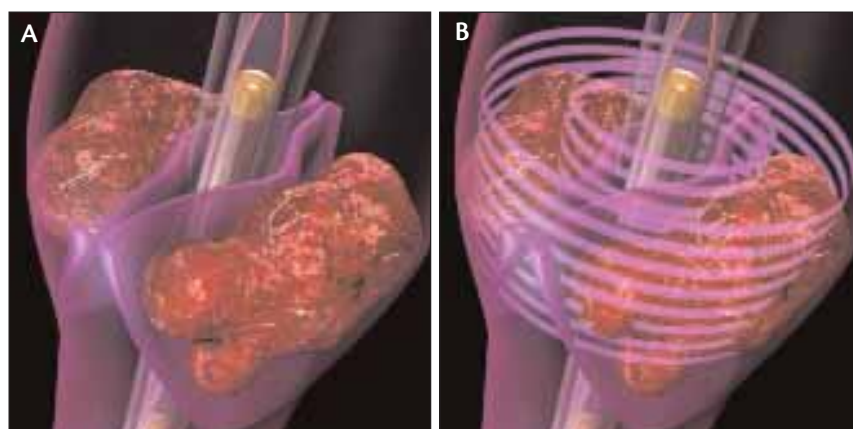


Figure 1. Graphic illustration of radially delivered ultrasound energy penetrating the venous valves to impact thrombus that is difficult to reach. The EKOS device (EKOS Corporation, Bothell, WA) in place (turned off) between the venous valves (A). The EKOS device turned on with the energy penetrating the valves to enhance clot resolution.

ulants is the standard of care for acute DVT, providing there is no contraindication to such.^{5,6,11} Anticoagulation therapy is effective in preventing thrombus propagation, however, it does not dissolve existing clot, leaving the venous obstruction often unresolved.² Due to associated operative mortality, surgical thrombectomy is reserved for patients contraindicated for thrombolysis and refractory to other treatments.^{2,11} Systemic thrombolysis, although demonstrated to reduce PTS symptoms more effectively than anticoagulation therapy, is associated with a significant increase in major bleeding complications.¹¹

Endovascular techniques include catheter-directed thrombolysis and percutaneous mechanical thrombectomy (PMT). Catheter-directed thrombolysis has demonstrated efficacy in achieving complete and partial lysis in many DVT patients, resulting in fewer PTS symptoms 1 year after treatment; however, long lysis times and higher risk of major bleeding complications compared to standard anticoagulation therapy have prevented widespread use of the technique.^{6,11} A number of PMT devices are available that macerate and aspirate clot using either rotational or hydrodynamic mechanisms. In most cases, PMT does not completely eliminate the thrombus, requiring adjunctive thrombolytic therapy to completely resolve residual clot.^{3,12} Procedures with PMT devices often require additional time in busy interventional labs, and often there is still the need to complete treatment with percutaneous catheter infusions.

IMPACT OF ULTRASOUND

The EKOS Lysus System combines high-frequency, low-power ultrasound with simultaneous catheter-directed thrombolytics to accelerate clot dissolution in the peripheral vasculature. The exposure of nonfragmenting ultrasound to thrombus has no lytic effect on its own. However, the combination of directed ultrasound with local lytic infusion accelerates the thrombolytic process.¹³ Ultrasound-enhanced lytic therapy works by first loosening or disassociating the fibrin mesh to make more surface area of the fibers available to the lytic agent. At the same time, acoustic microstreaming caused by the ultrasound waves drives the lytic agent away from the catheter deep into the loosened clot. This endovascular treatment results in reduced procedural time and allows for lower doses of therapeutic agents, thereby reducing the potential for hemorrhagic complications.

One unique feature of the ultrasound is that 99.6% of the energy emanating from the transducers will penetrate venous valves and impact the hard-to-reach clot located behind them (Figure 1). Other endovascular techniques, including catheter-directed thrombolysis alone and percutaneous mechanical thrombectomy have



Figure 2. The Lysus multilumen drug delivery catheter and removable ultrasound core wire. Application of radial ultrasound energy along the axis of the infusion catheter enhances permeability and penetration of lytic agent into clot.

limited access to clot trapped behind valves. Exposure of the entire clot to ultrasound enhances complete clearing of the occlusion, with significantly less infusion time (often less than 24 hours).

THE EKOS LYSUS SYSTEM

The EKOS system consists of a 5.2-F, multilumen drug delivery catheter with one central lumen and three separate infusion ports (Figure 2). Each drug lumen incorporates a series of laser-cut, microinfusion pores that focus the delivery of drug for optimum interface with the ultrasound waves. Infusion patterns are available in sizes from 6 cm to 50 cm. The central lumen is used to house the EKOS Ultrasound Core wire.

Each catheter has a matched Ultrasound Core wire that incorporates a series of miniature ultrasound transducers spaced approximately 1 cm apart to deliver the ultrasound energy evenly along the entire infusion pattern. The system is driven by a control unit that automatically adjusts the power to the optimum level for each of the ultrasound transducers based on ambient conditions in the vessel.

THE ULTRASOUND-ACCELERATED THROMBOLYSIS PROCEDURE

The catheter is positioned in the clot using a standard .035-inch guidewire. The guidewire is replaced with the ultrasound core wire. An infusion of the lytic agent is started per standard hospital protocol, along with a nominal flow of saline to serve as a coolant in the central

TABLE 1. SUMMARY OF TREATED OCCLUSIONS

Occlusion Site	Number of Cases (%)
Lower extremity (n=25)	
Inferior vena cava	2 (8)
Isolated iliac	1 (4)
Iliofemoral	14 (56)
Femoropopliteal	4 (20)
Popliteal	3 (12)
Upper extremity (n=17)	
Brachiocephalic/jugular	3 (18)
Axillosubclavian	13 (76)
Brachial	1 (6)
Other (n=3)	
Hepatic	2 (67)
AV fistula	1 (33)

lumen. Ultrasound is then started and delivered simultaneously with the infusion of lytic agent.

The control unit will automatically optimize the power delivery of each ultrasound transducer. A series of thermal couples are placed at various points along the infusion pattern to transmit ambient vessel conditions. As clot is dissolved and blood flow is re-established, changes monitored by the thermal couples are relayed to the control unit, which automatically increases power to the transducers in that area. This power change is displayed graphically in the form of a power log on the control unit. Changes in the power log may indicate recanalization and serve as an early indicator of an opportunity to perform early angiographic assessment.

CLINICAL RESULTS

Forty patients (55% male) with 45 DVT occlusions of the upper and lower extremities were treated using the EKOS Lysis System from September 2004 to February 2006, in an open enrollment reg-

istry across seven centers in the US. Treatment lengths of the EKOS drug delivery catheter ranged from 6 cm to 50 cm based on the length of the occlusion, with an average occlusion length of 28.5 cm. Fifty-six percent of occlusions occurred in the lower extremities, 38% were located in the upper extremities, and the three remaining occlusions involved one fistula and two hepatic vein occlusions (Table 1). Catheter-directed lytic infusions were performed using reteplase (47%), urokinase (24%), alteplase (16%), and tenecteplase (13%).

Technical success, defined as catheter positioning within the clot and simultaneous ultrasound delivery with lytic infusion, was 100%. Average time to complete lysis was 24.7 hours, less than half the average lysis time observed in the National Venous Thrombolysis Registry (53.4 hours), a prospective multicenter study that demonstrated the feasibility of catheter-directed thrombolysis for the treatment of iliofemoral DVT.¹⁴ There were two major bleeding complications (4.4%), which also compares favorably to the National Venous Thrombolysis Registry with a major bleeding complication rate of 11%. There were no incidents of intracranial hemorrhage.

Complete lysis (>90% lysis based on angiographic assessment) was achieved in 71% of DVT cases, and an additional 20% of cases achieved partial lysis. Table 2 compares the results of the EKOS study to those of the National Venous Thrombolysis Registry. Of the clots treated with ultrasound-accelerated thrombolysis, 42% were acute (<10 days old), 33% were chronic, 11% were acute on chronic occlusions, and the age of the remaining six clots (13%) was not reported.

CONCLUSIONS

Ultrasound-accelerated thrombolysis with the EKOS Lysis System offers a promising treatment for DVT, with shorter infusion duration and lower lytic drug dosage compared to traditional catheter-directed thrombolysis, potentially reducing associated hemorrhagic complications. The ability to achieve complete clot lysis, including

TABLE 2. COMPARISON OF CLINICAL RESULTS IN THE EKOS STUDY VERSUS THE NATIONAL VENOUS THROMBOLYSIS REGISTRY

	EKOS Study (n = 45)	National Venous Thrombolysis Registry (n = 287)
Average Infusion Time	24.7 hours	53.4 hours
Lysis at final angiography		
Complete lysis (>90%)	71%	31%
Partial lysis	20%	52%
No lysis	9%	17%

clearing clot behind valves, without altering the technique offers potential benefit in prevention of PTS symptoms by rapidly eliminating venous obstruction and preserving valvular function.

The use of the EKOS Lysis System offers a rapid way to initiate thrombolytic therapy for DVT in a busy interventional practice. The ability to quickly place an infusion catheter under fluoroscopic and ultrasound guidance with nontraumatic thrombolyses (performed in usually less than 24 hours) offers a substantial improvement in previous DVT thrombolysis. The lower total dose of thrombolytic drug reduces bleeding and other infusion complications. The absence of mechanical fracturing of the thrombus prevents rare but inadvertent development of pulmonary embolus during the procedure. The new therapy has allowed efficient, safe, and practical thrombolytic therapy for the treatment of DVT in a very time-efficient manner. Additional studies need to be performed to confirm the reduction in postthrombotic syndrome and to convince primary care physicians, emergency department physicians, and others of the importance of referring patients for this therapeutic option. ■

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insufficiency. The recurrent and unrelenting debilitating nature of this condition is clearly an entity to be prevented if at all possible. The long-term costs and frequent need for medical treatment signify the negative impact of chronic venous insufficiency.

Thrombolysis in the iliofemoral venous segment has sufficiently good success and low complication rates that it can be considered a good therapy. The different available modalities of thrombolysis with pharmacologic, mechanical, and pharmacomechanical methods provide a range of treatment options from which to choose, such that different patient issues can be accommodated. Striking clinical results from successful thrombolysis are quite compelling, and failed thrombolysis generally results in no clinical detriment to the patient in terms of the severity of the thrombotic process or its chronic sequelae. Based on the literature currently available, thrombolysis or pharmacomechanical thrombectomy with treatment of underlying lesions for acute iliofemoral venous thrombosis should be considered for symptomatic patients with a reasonable life expectancy. Patients with chronic iliofemoral venous occlusion and related symptoms can also benefit from endovascular interventions in an effort to alleviate their symptoms and reduce the clinical sequelae of postthrombotic syndrome. ■

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