

Quality-of-Life Improvement Using Thrombolytic Therapy for Iliofemoral Deep Venous Thrombosis

Anthony J. Comerota, MD, FACS

Jobst Vascular Center, Toledo, OH

Patients with iliofemoral deep venous thrombosis suffer the most severe postthrombotic morbidity. Techniques that effectively remove thrombus from the venous system eliminate venous obstruction and potentially preserve valvular function. This will likely reduce or avoid the postthrombotic syndrome and improve long-term quality of life. To evaluate whether catheter-directed thrombolysis is associated with improved quality of life compared with anticoagulation alone and whether outcome in the thrombolysis group is related to lytic success, 98 patients with iliofemoral deep venous thrombosis who were treated at least 6 months earlier were identified and queried with a validated health-related quality-of-life questionnaire. Sixty-eight patients were identified through the Venous Registry (a national, multicenter venous registry) and were treated with catheter-directed thrombolysis with urokinase, and 30 patients were identified by means of medical record review and were treated with anticoagulation alone. All patients were candidates for thrombolysis; however, the treatment decision was made according to physician preference. The two treatment groups did not differ significantly in average time between the reference hospitalization and first contact. No difference was found in physical functioning and well-being between the groups before the development of deep venous thrombosis. Following treatment, patients receiving catheter-directed thrombolysis reported better overall physical functioning, less stigma, less health distress, and fewer post-thrombotic symptoms compared to those patients treated with anticoagulation alone. Within the thrombolysis group, successful lysis correlated with health-related quality of life. Catheter-directed thrombolysis for the management of patients with iliofemoral deep venous thrombosis significantly improves health-related quality of life compared to similar patients treated with anticoagulation alone. Improved quality of life is related to successful thrombolysis. These data offer a compelling argument for a prospective randomized study. [Rev Cardiovasc Med. 2002;3(suppl 2):S61–S67]

© 2002, 2003 MedReviews, LLC

Key words: Iliofemoral deep venous thrombosis • Postthrombotic syndrome • Quality of life • Catheter-directed thrombolysis • Thrombolysis • Urokinase

The degree to which quality of life (QOL) is improved following thrombolytic management of acute deep venous thrombosis (DVT) is directly related to the reduction of the postthrombotic syndrome compared to standard anticoagulation. The underlying pathophysiology of the postthrombotic

syndrome is ambulatory venous hypertension.¹ Because the important components of ambulatory venous hypertension are luminal obstruction and valvular incompetence,^{2,3} it is intuitively evident that treatment that eliminates luminal obstruction reduces the major com-

ponents who had an underlying venous stenosis corrected after iliofemoral clot lysis had better 1-year patency rates.

The objectively documented outcome of the patients entered into the Venous Registry provided an opportunity to evaluate whether

standard anticoagulation was by the choice of their attending physician; however, all patients were candidates for catheter-directed thrombolysis.

The underlying pathophysiology of the postthrombotic syndrome is ambulatory venous hypertension.

ponent of ambulatory venous hypertension as well as potentially preserving valvular function.

Acute iliofemoral DVT is associated with significant postthrombotic morbidity.⁴⁻⁶ Treatment that removes thrombus from the iliofemoral venous system and restores patency appears to improve the patient's clinical condition and reduces long-term postthrombotic morbidity.⁷⁻¹² Although prior studies have indicated that treatment methods designed to eliminate thrombus from the venous system reduce postthrombotic signs and symptoms,⁷⁻¹⁰ a randomized trial of catheter-directed thrombolysis compared to standard anticoagulation has not been performed.

The Venous Registry was organized as a national multicenter venous registry to assess the impact of catheter-directed thrombolysis in patients with symptomatic DVT.¹³ The outcome was determined by means of phlebography in 287 patients who underwent 312 urokinase (UK) infusions in 303 venous systems with DVT. The patients with iliofemoral DVT had more successful lysis than patients with femoropopliteal DVT. Additional observations indicated that acute DVT responded better than chronic DVT, catheter-directed infusions lysed thrombus more effectively than systemic infusions, and the

catheter-directed thrombolysis for iliofemoral DVT is associated with improved health-related QOL as compared to similar patients with iliofemoral DVT who were treated with standard anticoagulation, and whether the QOL outcome in the thrombolysis group is related to lytic success.

Methods

A newly designed and validated health-related QOL questionnaire¹⁴ was used to query 98 patients who had been hospitalized and treated for iliofemoral DVT 6–44 months earlier (mean 16 months). Sixty-eight patients from the Venous Registry who were treated with catheter-directed thrombolysis were identified, and 30 patients who received heparin anticoagulation

Health-Related Quality-of-Life Questionnaire

An 80-item health-related (HR) QOL questionnaire was used in this study. It contained the Health Utilities Index (HUI) MARK 2/3 version, which includes the nine attributes emotion, cognition, self-care, pain, vision, hearing, speech, ambulation, and dexterity, and additional items and scales specific to DVT.¹⁵ These items included physical functioning, pain, stigma, role functioning, health interference, symptom frequency, bothersomeness, and treatment satisfaction. It also contained the Short Form-12 (SF-12), which was scored to produce two summary measures: the physical component score and the mental component score.¹⁶

Results

Ninety-eight patients were treated for iliofemoral DVT and evaluated with the QOL questionnaire. The patient demographics were essentially similar between the UK treatment group and the anticoagulation-alone treatment group, with the exception that the patients in the UK group

Catheter-directed infusions lysed thrombus more effectively than systemic infusions.

converted to oral anticoagulation for similar iliofemoral DVT were identified by their treating physicians or records from their medical center. Because this was a retrospective evaluation, the treatment was not randomized.

Whether patients were treated with catheter-directed thrombolysis or

were 53 ± 17 versus 60 ± 16 years in the anticoagulation-alone treatment group ($P < .039$).

At the time of initial contact, the patients were asked to recall their pretreatment HR QOL as of the reference hospitalization 6 months to 2 years earlier. The treatment groups did not differ significantly in average

time between the reference hospitalization and the initial contact. No difference was found in functioning and well-being between groups before the development of DVT. After treatment, as reported at the initial follow-up (mean 16 months), patients treated with catheter-directed thrombolysis reported a trend toward a higher mental summary scale ($P = .087$) and improved HUI ($P = .078$). Patients treated with catheter-directed thrombolysis reported better overall physical role functioning ($P = .046$), less stigma, ($P = .033$), less health distress ($P = .022$), and fewer overall symptoms ($P = .006$) compared with patients who were treated with anticoagulation alone (Table 1). The mean scale scores at final follow-up (mean 22 months) show a trend toward less stigma in the lytic group ($P = .10$), and the reduction in health distress and overall symptoms remained significantly less in the patients treated with anticoagulation (Table 1).

A majority of the patients from the thrombolysis group completed the later follow-up questionnaire (48 of 68; 71%), but fewer than half of the anticoagulation-alone patients did (13 of 30; 42%). The analyses presented in Table 1 were repeated on the subset of 61 patients for whom follow-up data were available to assess the possible impact of the loss to follow-up. Interestingly, all of the comparisons favored the thrombolysis group, generally with similar magnitude. Despite the reduced number of patients, the difference remained statistically significant for stigma ($P = .047$), health distress ($P = .005$), and overall symptoms ($P = .027$), but was not significant for overall physical functioning ($P = .19$). A comparison of the patients who dropped out of the study with the patients who were available for follow-up revealed that

Scale Item*	Urokinase (mean \pm SE)	Anticoagulation (mean \pm SE)	P Value
Initial contact (mean 16 months)	n = 68	n = 30	
Health Utilities Index	0.81 \pm 0.02	0.73 \pm 0.03	.078
Physical role functioning	70.78 \pm 3.62	57.06 \pm 5.56	.046
Stigma	83.54 \pm 3.07	71.13 \pm 4.72	.033
Health distress	78.20 \pm 3.20	64.36 \pm 4.87	.022
Overall symptoms	71.40 \pm 2.05	55.80 \pm 4.50	.006
Follow-up (mean 22 months)	n = 48	n = 13	
Health Utilities Index	0.73 \pm 0.03	0.74 \pm 0.07	.94
Physical role functioning	64.12 \pm 4.42	56.59 \pm 8.60	.45
Stigma	82.15 \pm 3.92	67.44 \pm 7.81	.10
Health distress	74.65 \pm 3.84	55.91 \pm 7.65	.036
Overall symptoms	67.74 \pm 3.56	50.68 \pm 7.30	.044

Adjusted for propensity score (education, marital status, age) and number of days since hospitalization.
 * Higher scores represent higher functioning/less interference/fewer symptoms/less distress.
 Modified with permission from Comerota AJ, Throm RC, Mathias SD, et al. Catheter-directed thrombolysis for iliofemoral deep venous thrombosis improves health-related quality of life. *J Vasc Surg.* 2000;32:130-137.

the patients who dropped out had better overall symptoms at initial contact ($P = .020$). A trend was found toward less health distress at initial contact among the patients who dropped out ($P = .084$). Therefore the less symptomatic and less distressed patients were the ones dropping out.

Table 2 evaluates the scores of the thrombolysis group at initial contact (mean 16 months posttreatment; final follow-up mean 22 months posttreatment) by the degree of lysis as determined by posttreatment phlebography. Health distress was less and overall symptoms were significantly fewer in the patients having successful lysis compared with patients in whom treatment failed.

At initial contact, there was a trend toward less stigma in the patients having successful lysis, which became significant by the time of final follow-up (22 months).

Table 3 shows the mean scale scores at initial contact and final follow-up in patients having either partial or complete lysis compared with patients who underwent heparin treatment. Patients demonstrating either partial or complete lytic success had better physical role functioning, less stigma and health distress, and fewer overall symptoms at initial contact. The initial observations of less stigma and health distress and fewer overall symptoms remained significant at 22 months.

Table 2
Mean Scores of Thrombolysis Group by Degree of Lysis

Scale Item*	Failure (mean \pm SE)	Partial (mean \pm SE)	Complete (mean \pm SE)	P Value
Initial contact (mean 16 month)	n = 8	n = 25	n = 18	
Health Utilities Index	0.78 \pm 0.06	0.81 \pm 0.03	0.85 \pm 0.04	.46
Physical role functioning	58.22 \pm 10.50	72.84 \pm 5.88	79.19 \pm 6.91	.26
Treatment satisfaction	77.27 \pm 9.43	91.22 \pm 5.28	81.10 \pm 6.21	.31
Stigma	74.14 \pm 8.24	83.41 \pm 4.62	90.56 \pm 5.42	.25
Health distress	58.68 \pm 7.73	81.63 \pm 4.33	83.88 \pm 5.09	.024
Overall symptoms	52.71 \pm 7.12	78.33 \pm 3.99	79.50 \pm 4.68	.006
Follow-up (mean 22 months)	n = 5	n = 19	n = 13	
Health Utilities Index	0.69 \pm 0.10	0.66 \pm 0.05	0.83 \pm 0.06	.14
Physical role functioning	49.29 \pm 13.82	72.51 \pm 7.72	62.77 \pm 8.56	.33
Stigma	61.70 \pm 10.08	92.88 \pm 5.17	83.47 \pm 6.24	.032
Health distress	50.24 \pm 11.28	84.08 \pm 5.79	73.17 \pm 6.99	.038
Overall symptoms	53.52 \pm 10.25	74.68 \pm 5.40	73.94 \pm 6.35	.18

Adjusted for propensity scores (education, marital status, age) and number of days since hospitalization.

* Higher scores represent higher functioning/less interference/fewer symptoms/less distress. Modified with permission from Comerota AJ, Throm RC, Mathias SD, et al. Catheter-directed thrombolysis for iliofemoral deep venous thrombosis improves health-related quality of life. *J Vasc Surg*. 2000;32:130-137.

The mean scores at initial contact and final follow-up of patients in whom lytic therapy failed were compared with those of the group that underwent anticoagulation treatment alone. Although no benefit to failed lysis was found, no adverse outcome in QOL was found when lytic therapy was unsuccessful.

All patients expressed general satisfaction with their treatment. Interestingly, treatment satisfaction was not related to the treatment the patients received, the success

of thrombolysis, or measures of HR QOL.

Discussion

The results of the treatment of iliofemoral DVT with catheter-directed thrombolysis demonstrate significantly improved HR QOL in many areas of function and well-being in patients treated with catheter-directed UK compared with patients treated with standard anticoagulation. A strong trend toward improvement in the HUI and signif-

icantly better physical role functioning, less stigma, less health distress, and fewer overall symptoms was found with the use of UK. Although the study was observational in nature, the patients were comparable in their reported HR QOL before the onset of their DVT.

It is not surprising that patients who had successful lysis reported better QOL than patients who were lytic failures. The lytic failure group and heparin treatment group were comparable in QOL outcome. No benefit to patients who failed thrombolysis was observed; similarly, the failure of the catheter-directed thrombolysis did not diminish their QOL over the long term compared with standard anticoagulation. The patients' expression of treatment satisfaction was independent of either the success of catheter-directed thrombolysis or long-term QOL. Patients apparently did not link long-term outcome with their treatment of acute DVT, and they were incapable of realizing that the treatment received for the acute DVT could alter subsequent postthrombotic symptoms. Any nonrandomized study has a potential of treatment bias. If treatment bias existed in this study, the patients with more severe symptoms might have been selected for thrombolytic therapy. In this case, the results would be even more dramatic. However, it is also possible that patients who were treated with heparin had more health-related comorbidity at the time of their acute DVT, in which case a worse QOL might be expected in that group. The demographic evaluation and comorbidity evaluation failed to identify any such difference.

Although the patients in the two treatment groups were considered similar, the exact extent of DVT could not be compared between these two groups. The patients treated

Table 3
Mean Scores Comparing Patients Who Had Successful Lysis
Versus Patients Treated with Anticoagulation Alone

Scale Item*	Successful Lysis (mean \pm SE)	Anticoagulation (mean \pm SE)	P Value
Initial Contact (mean 16 months)	n = 43	n = 30	
Health Utilities Index	0.83 \pm 0.03	0.74 \pm 0.03	.032
Physical role functioning	75.68 \pm 4.57	56.59 \pm 5.56	.013
Treatment satisfaction	86.59 \pm 4.25	81.72 \pm 5.18	.49
Stigma	85.98 \pm 4.11	71.32 \pm 5.00	.033
Health distress	82.48 \pm 4.04	64.11 \pm 4.91	.007
Overall symptoms	78.55 \pm 3.44	55.56 \pm 4.19	< .001
Follow-up (mean 22 months)	n = 32	n = 13	
Health Utilities Index	0.71 \pm 0.04	0.73 \pm 0.07	.77
Physical role functioning	68.52 \pm 5.14	56.07 \pm 8.09	.23
Stigma	90.48 \pm 4.11	69.50 \pm 6.71	.014
Health distress	80.25 \pm 4.19	56.32 \pm 6.85	.006
Overall symptoms	74.11 \pm 3.87	50.56 \pm 6.66	.006

Adjusted for propensity scores(education, marital status, age) and number of days since hospitalization.

* Higher scores represent functioning/less interference/fewer symptoms/less distress.

Modified with permission from Comerota AJ, Throm RC, Mathias SD, et al. Catheter-directed thrombolysis for iliofemoral deep venous thrombosis improves health-related quality of life.

J Vasc Surg. 2000;32:130–137.

with catheter-directed thrombolysis always had phlebographic documentation of the proximal extent of their thrombus as a part of the protocol for management. Because that information would not alter the treatment plans for the patients receiving anticoagulation alone, the proximal extent of their venous thrombosis was not defined. Because these patients were identified retrospectively and the criteria for inclusion specified that the index DVT must have occurred 6 months before the completion of the questionnaire, all patients were requested to recall information approximately 6 months or more earlier for their pre-DVT assessment. Although this

is a recognized limitation of this study, the questions addressing the patients' pre-DVT physical functioning focused on objective measures, such as defined physical limitations and days lost from work because of lower-extremity symptoms. Even if there were a recall bias, it would not affect the posttreatment QOL results, because patients' responses were based on their current functioning.

Launois and colleagues¹⁷ developed an HR QOL instrument designed to evaluate chronic venous insufficiency and used it in a large cross-sectional study. They found that psychological functioning, physical functioning, pain, social functioning, and overall QOL were

significantly worse in patients with chronic venous insufficiency than in those without chronic disease. Beyth and colleagues¹⁸ examined patients 6–8 years after acute DVT. Similar to the observations of Launois and colleagues, they found that patients reporting postthrombotic symptoms had worse QOL, which included worse health perception, impairment in physical functioning, and more severe role limitation attributable to physical health, compared with patients without postthrombotic symptoms. Both Launois and colleagues¹⁷ and Beyth and colleagues¹⁸ examined patients with chronic venous disease and did not evaluate any effect of treatment.

Koopman and colleagues¹⁹ assessed QOL in a prospective trial comparing intravenous heparin administered in the hospital with subcutaneous low-molecular-weight heparin administered at home for treatment of acute proximal DVT. Time affected QOL, with improvement of all indicators in both treatment groups. Patients receiving low-molecular-weight heparin, however, had better scores for physical activity and social functioning at the end of the initial treatment (1–2 weeks), which is most likely because most patients were treated as outpatients. No QOL difference was found between treatment groups at 12–24 weeks. Because neither form of heparin dissolves clots, the results indicate that QOL is better when patients are treated as outpatients for acute DVT than when they are treated as inpatients. There was no difference in QOL between treatment groups at 12–24 weeks.

As already discussed, postthrombotic symptoms are related to ambulatory venous hypertension, which correlates with venous obstruction and valvular incompetence.¹⁸ A recent natural history

study of patients with acute DVT demonstrated that patients with the postthrombotic syndrome are more likely than patients without chronic symptoms to have the combination of persistent deep venous obstruction and valvular incompetence as part of their ongoing pathophysiology.¹⁹ Furthermore, patients treated with anticoagulation who had physiologic clot lysis within 3 months of their acute DVT were more likely to retain normal venous valve function than patients with delayed physiologic lysis or persistent thrombosis.²⁰ In light of these observations, it is not surprising that successful catheter-directed thrombolysis resulted in a better QOL than failed thrombolysis or standard anticoagulation. In two earlier prospective, randomized trials of systemic lytic therapy versus anticoagulation for proximal DVT, patients treated with thrombolytic therapy had fewer postthrombotic symptoms than patients treated with anticoagulation alone.^{4,5} In a 5-year follow-up examination of patients with acute DVT who were initially randomized to thrombolytic therapy or anticoag-

ulation, venous function was significantly better in patients who had successful lysis than in patients who did not.⁹

The results after thrombolytic therapy for acute DVT are consistent with those of a large Scandinavian trial comparing venous thrombectomy with anticoagulation for acute iliofemoral DVT. At 6-month, 5-year, and 10-year follow-up, patients treated with venous thrombectomy had better iliac vein patency, improved valvular function, and fewer postthrombotic symptoms than patients treated with standard anticoagulation.^{6,7,21}

These observations suggest that treatment that successfully removes clots from the deep venous system (especially in patients with extensive DVT) is associated with better patient outcome than anticoagulation alone. Until now, outcome assessment of the treatment of acute DVT was based on postthrombotic signs and symptoms, phlebographic findings, and physiologic evaluation of various components of venous function and outflow obstruction. Patients' assessment of their HR QOL may be

the most meaningful long-term outcome. Now a validated instrument exists that can be used as a means of assessing the QOL outcome after acute DVT. The observations from this study cannot be viewed as conclusive but, rather, serve as an attractive hypothesis that catheter-directed thrombolysis with UK for iliofemoral DVT is associated with improved HR QOL compared with standard anticoagulation. These findings offer a compelling argument for a future randomized trial, which should include an HR QOL measure as a part of the outcome analysis. ■

References

1. Nicolaides AN, Schull K, Fernandes E, et al. Ambulatory venous pressures: new information. In: Nicolaides AN, Yao JS, eds. *Investigation of Vascular Disorders*. New York: Churchill Livingstone; 1981:488-494.
2. Shull KC, Nicolaides AN, Fernandes E, Fernandes J. Significance of popliteal reflux in relation to ambulatory venous pressure and ulceration. *Arch Surg*. 1979;114:1304-1306.
3. Johnson BF, Manzo RA, Bergelin RO, Strandness DE. Relationship between changes in the deep venous system and the development of the postthrombotic syndrome after an acute episode of lower limb deep vein thrombosis: a one-to-one six-year followup. *J Vasc Surg*. 1995;21:307-313.
4. O'Donnell TF, Browse NL, Burnand KG, Lea

Main Points

- Acute iliofemoral deep venous thrombosis (DVT) is associated with significant postthrombotic morbidity.
- Patients with postthrombotic syndrome are more likely than patients without chronic symptoms to have the combination of persistent deep venous obstruction and valvular incompetence as part of their ongoing pathophysiology.
- Natural history studies of DVT show that patients with physiologic clot lysis within 3 months of their acute DVT were more likely to retain normal venous valve function than patients with delayed physiologic lysis or persistent thrombosis. Additionally, in a 5-year follow-up examination of patients with acute DVT who were initially randomized to thrombolytic therapy or anticoagulation, venous function was significantly better in patients who had successful lysis than in patients who did not. These observations suggest that treatment that successfully removes clots from the deep venous system is associated with better patient outcome than anticoagulation alone.
- Removing thrombus from the iliofemoral venous system and restoring patency appears to improve clinical condition and reduce long-term postthrombotic morbidity.
- At initial follow-up, patients treated with catheter-directed thrombolysis reported a trend toward a higher mental summary scale and improved HUI, better overall physical role functioning, less stigma, less health distress, and fewer overall symptoms compared with patients who were treated with anticoagulation alone.
- Patients having successful lysis had better physical role functioning, less stigma and health distress, and fewer overall symptoms at initial contact than patients who underwent heparin treatment.

- Thomas M. The socioeconomic effects of an iliofemoral venous thrombosis. *J Surg Res.* 1977;22:483-488.
5. Mavor GE, Galloway JMD. Iliofemoral venous thrombosis. *Br J Surg.* 1969;56:43-59.
6. Hill SL, Martin D, Evans P. Massive vein thrombosis of the extremities. *Am J Surg.* 1989;158:131-135.
7. Plate G, Einarsson E, Ohlin P, et al. Thrombectomy with temporary arteriovenous fistula: the treatment of choice in acute iliofemoral venous thrombosis. *J Vasc Surg.* 1984;1:867-876.
8. Plate G, Eklof B, Norgren L, et al. Venous thrombectomy for iliofemoral venous thrombosis-10 year results of a prospective randomized study. *Eur J Vasc Endovasc Surg.* 1997;14:333-343.
9. Comerota AJ, Aldridge SC. Thrombolytic therapy for acute deep vein thrombosis. *Semin Vasc Surg.* 1992;5:76-84.
10. Jeffrey P, Immelman E, Amoore I. Treatment of deep vein thrombosis with heparin or streptokinase: long-term venous function assessment. In: Proceedings of the Second International Vascular Symposium; September 9-13, 1989; London. Abstract S20.3.
11. Arnesen H, Hoiseth A, Ly B. Streptokinase or heparin in the treatment of deep vein thrombosis: followup results of a prospective study. *Acta Med Scand.* 1982;211:65-70.
12. Elliot MS, Immelman EJ, Jeffrey P. A comparative randomized trial of heparin versus streptokinase in the treatment of acute proximal venous thrombosis: an interim report of a prospective trial. *Br J Surg.* 1979;66:838-843.
13. Mewissen MW, Seabrook GR, Meissner MH, et al. Catheter-directed thrombolysis for lower extremity deep vein thrombosis: report of a national multi-center registry. *Radiology.* 1999;211:39-49.
14. Mathias SD, Prebil LA, Putterman CG, et al. A health-related quality of life measure in patients with deep vein thrombosis: a validation study. *Drug Inf J.* 1999;33:1173-1187.
15. Feeny DH, Torrance GW, Furlong WJ. Health utilities index. In: Spilker B, ed. *Quality of Life and Pharmacoeconomics in Clinical Trials*, 2nd ed. Philadelphia, PA: Lippincott-Raven; 1996:239-252.
16. Ware JE Jr, Kosinski M, Keller SD. SF-12: *How to Score the SF-12 Physical and Mental Health Summary Scales*, 2nd ed. Boston: The Health Institute, New England Medical Center; 1995.
17. Launois R, Reboul-Marty J, Henry B. Construction and validation of a quality of life questionnaire in chronic lower-limb venous insufficiency (CIVIQ). *Qual Life Res.* 1996;5:539-554.
18. Beyth RJ, Cohen AM, Landesfield CS. Long-term outcomes of deep vein thrombosis. *Arch Intern Med.* 1995;155:1031-1037.
19. Koopman MMW, Prandoni P, Pionella F, et al. Treatment of venous thrombosis with intravenous unfractionated heparin administered in the hospital as compared with subcutaneous low molecule weight heparin administered at home. *N Engl J Med.* 1996;334:682-687.
20. Meissner MH, Manzo RA, Bergelin RO, et al. Deep vein insufficiency: the relationship between lysis and subsequent reflux. *J Vasc Surg.* 1993;18:596-602.
21. Plate G, Akesson H, Einarsson E, et al. Long-term results of venous thrombectomy combined with a temporary arterio-venous fistula. *Eur J Vasc Surg.* 1990;4:483-489.