The Heart Surgery Forum #2015-1307
18 (6), 2015 [Epub December 2015]
doi: 10.1532/hsf.1307

Online address: http://journal.hsforum.com

Early Outcomes of Pharmacomechanical Thrombectomy in Acute Deep Vein Thrombosis Patients

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ABSTRACT

Background: Acute lower extremity deep vein thrombosis (DVT) occurs due to obstruction of large veins by thrombus and its clinical findings are pain and swelling. If not treated, it can cause morbidity and mortality. Oral warfarin or low molecular weight heparin are applied in traditional treatment. However, recently, endovascular procedures have gained increasing popularity in deep vein thrombosis. In this study we aimed to compare our early results of pharmacomechanical thrombectomy (PMT) versus oral anticoagulation for acute deep vein thrombosis.

Methods: We comprised 50 patients presented with acute DVT between January 2013 and June 2014, who received either adjusted subcutaneous low molecular weight heparin (LMWH) or PMT followed by intravenous unfractionated heparin (UFH) for 5 days. Warfarin was administered to PMT patients for 3 months and at least 6 months for the control group.

Results: Median follow-up was 14 months (6-18 months). Recanalization within 6 months was found in 84.0%, femoral venous insufficiency was found in 36.0%, and postthrombotic syndrome (PTS) was found in 28.0% of the patients who received PMT treatment. The mean duration of symptoms was 11.0 days (range, 3-20 days). The mean duration of the procedure was 78.1 minutes (range, 55-100 min).

Conclusion: In contrast to medical therapy in the treatment of deep vein thrombosis, usage of catheter-directed thrombolysis experienced early recanalization with higher thrombus resolution. PMT with adjunctive thrombolytic therapy is an effective treatment modality in patients with significant DVT. Also, early thrombus removal in patients with acute DVT prevents development of postthrombotic morbidity. We believe that the efficacy and usage will increase with the experience of surgeons in the future.

INTRODUCTION

Deep vein thrombosis (DVT) is the abnormal coagulation of blood in deep veins, which can result in obstruction of the vena cava and venous disorders. If not promptly treated, DVT may be complicated by pulmonary embolism (PE) in the acute stage and in later stages may cause post-thrombotic syndrome (PTS), which can affect the patient's capacity for life and work.

Awareness of and efforts to prevent DVT in the United States have increased in recent years, but the incidence of DVT remains high, and approximately 275,000 patients are affected by DVT each year [Heit 2008].

The present treatments for DVT include surgery, anticoagulant therapy, and combined anticoagulant and thrombolytic therapy. In 1980, the U.S. National Institutes of Health sug¬gested that thrombolytic therapy can be used as the standard treatment for acute DVT and PE. At that time, it was used mainly for disease of the peripheral venous system. As interventional techniques have developed rapidly in recent years, PMT has become widely used, and the results of new clinical trials have been published frequently. Venography results after PMT indicate that it can achieve better short-term efficacy than anti¬coagulant therapy alone; it can also reduce the complications of DVT. The results from long-term follow-up indicate that pharmacomechanical thrombectomy (PMT) can significantly reduce the probability that PTS will occur after DVT [Manninen 2012].

MATERIAL AND METHODS

This retrospective study involved a total of 50 patients who had experienced symptoms of acute DVT for <14 days between January 2013 and July 2014, who were treated with either PMT or warfarin. Both groups contained 25 patients.

We aimed to compare warfarin with PMT on treatment safety and efficacy of acute DVT in lower limbs. The study endpoints included the evolution of DVT and treatment efficacy and safety, which were assessed with frequent duplex ultrasounds.

Warfarin sodium was routinely started before hospital discharge; this treatment was continued for at least three months for PMT patients and at least 6 months for the control group. The dose was adjusted to maintain an international normalized ratio of 2.0 to 2.5. Adjuvant elastic compression therapy was recommended for one year.

The primary symptoms were limb swelling, discoloration, pain, and venous claudication in the majority of patients. Duplex ultrasonography was used to diagnose DVT.

Inclusion Criteria

Age 20-75 years; onset of symptoms <14 days; first time verified deep vein and thrombosis limited to the upper thigh.

Received June 9, 2015; received in revised form July 21, 2015; accepted August 10, 2015.

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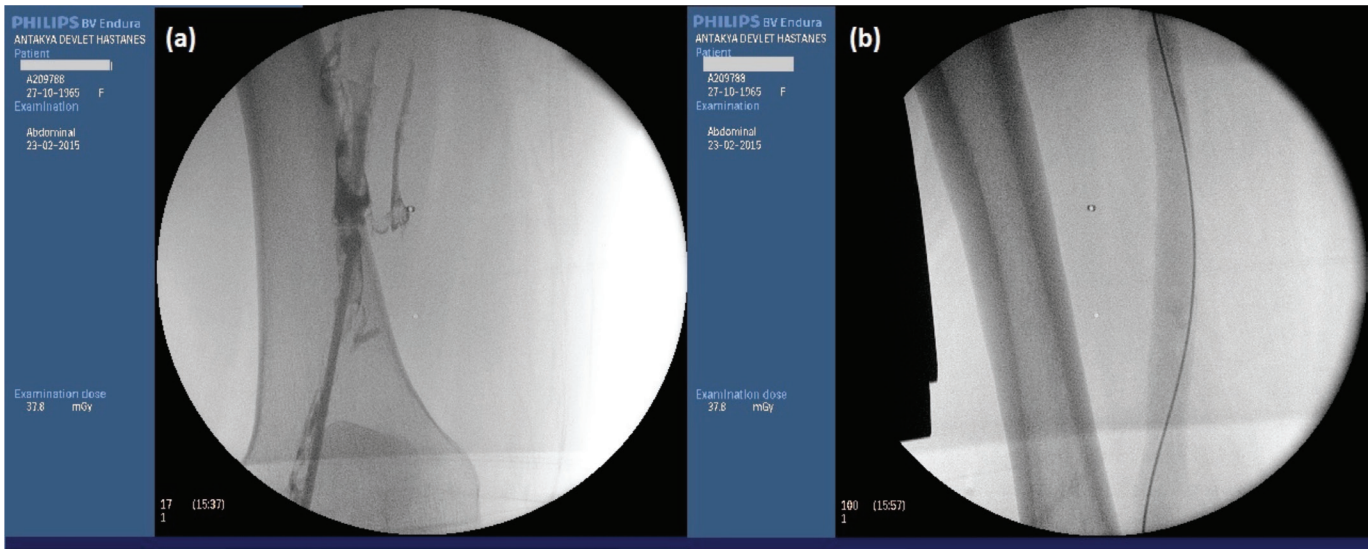

Preoperative (a) and postoperative (b) venography of a pharmacomechanical thrombectomy patient.

Exclusion Criteria

Anticoagulant therapy before trial entry; contraindication to thrombolytic treatment, including: bleeding diathesis, hemorrhagic stroke, major surgery <1 month, severe hypertension, severe renal failure.

Surgical Technique

Retrievable vena cava filter (Angel Catheter) was inserted selectively at the beginning of the procedure with local anesthesia through the femoral vein on the intact side, at the infrarenal level. Next, the patient was placed in a prone position, and access was obtained under ultrasound guidance. Local anesthesia was performed on the popliteal area. Then a 0.35 inch guide wire was inserted to the popliteal vein by using Doppler ultrasound. A 6F sheath was inserted in the popliteal vein through the guide wire. With the infusion of radiocontrast agent, it was found that deep veins were filled with thrombus (Figure, A). Afterwards, the guide wire was pulled out and a Cleaner 6F rotational thrombectomy catheter was inserted through the sheath. A thrombectomy catheter was started by using recombinant tissue plasminogen activator (t-PA; Alteplase). Popliteal, superficial femoral and deep veins were opened gradually. The procedure was ended following the observation that the veins were be entirely open in controlled venography (Figure, B).

Heparin infusion was started with a dose of 1000U/h for 24 hours. A vena cava filter (Angel Catheter) was pulled out on postoperative day 1. All attempts at both implantation and retrieval of the filter were safely accomplished. No complication related to filter placement occurred.

All interventions were performed by the same surgical team.

Statistical Analysis

The data gathered from the study was analyzed using SPSS (Statistical Package for Social Sciences) 22.0 for Windows. For the data evaluation number, percentage, mean and standard deviation were used as the descriptive statistical methods. Chi-square test was used for the comparison of groups of variables. T test was used to determine the differentiation state of the two groups. A P value <.05 was considered statistically significant. All statistical analyses were performed using SPSS software.

RESULTS

From January 2013 to June 2014, we recruited 50 patients with acute DVT, who received either adjusted subcutaneous low molecular weight heparin (LMWH) or PMT followed by intravenous unfractionated heparin (UFH) for 5 days.

Risk factors for DVT are listed in Table 1. All patients presented with severe swelling or pain, or both; median follow-up was 14 months (6-18 months). 6 PMT patients (39.0%) had a femoropopliteal thrombosis and 18 PMT patients (61.0%) had an iliofemoral venous thrombosis. The mean duration of symptoms was 11.0 days (range, 3-20 d). The mean duration of the procedure for the patients participating in the study was 78.1 ± 10.7 min. (range, 55-100 min).

Recanalization within 6 months was found to be significantly higher in the PMT group (n = 21, 84%) than in the control group (n = 14, 56%) ($\times^2 = 4.667$; $P = .031$ <.05). Femoral venous insufficiency was not significantly different in the two groups; n = 9 (36%) in the PMT group and n = 15 (60%) in the control group ($\times^2 = 2.885$; $P = .089$ >.05). Postthrombotic syndrome was found to be significantly less in the PMT group (n = 7, 28%) than in the control group (n = 14, 56%) ($\times^2 = 4.023$; $P = .045$ <.05) (Table 2).

There was no major complications and mortality.

Study Limitations

There were limitations to our study. This report is a retrospective observational analysis of patients who underwent treatment with a new technique for venous thrombus

Table 1. Risk Factors for DVT Patients

Predisposing factors	PMT	Control
Malignancy, n (%)	4 (16)	5 (20)
Smoking, n (%)	10 (40)	12 (48)
Immobilization, n (%)	3 (12)	5 (20)
Hypercoagulable state, n (%)	5 (20)	7 (28)
Orthopedic surgery, n (%)	5 (20)	4 (16)
Idiopathic, n (%)	4 (16)	6 (24)

DVT indicates deep vein thrombosis; PMT, pharmacomechanical thrombectomy.

Table 2. Postoperative Evaluation of Two Groups

	PMT	Control	x^2	*P*
Recanalization within 6 months , n (%)	21 (84)	14 (56)	4.667	.031
Femoral venous insufficiency, n (%)	9 (36)	15 (60)	2.885	.089
Postthrombotic syndrome, n (%)	7 (28)	14 (56)	4.023	.045

PMT indicates pharmacomechanical thrombectomy.

extraction. Although we are encouraged by the excellent outcomes presented, we cannot be absolutely certain that the lytic agent conferred additional benefit to PMT.

DISCUSSION

Venous thromboembolism (VTE) is estimated to occur in 350,000 to 600,000 persons per year in the United States alone, of which over 250,000 cases represent first episodes of deep vein thrombosis (DVT) [U.S. Department of Health and Human Services 2008]. The management of DVT has traditionally been anchored in a longstanding view of the disease as an acute condition involving an initial period of high risk of pulmonary embolism (PE), followed by a progressively reduced risk of patient harm over time. As a result, DVT therapies have been judged primarily on their ability to prevent symptomatic PE, early thrombus progression, and recurrent venous thromboembolism [Kearon 2008].

Patients with iliofemoral DVT, defined as DVT involving the iliac vein and/or common femoral vein, are at significantly increased risk of both PTS and recurrent VTE [Kahn 2008; Delis 2004]. Although the completed studies had significant methodological limitations, the preponderance of the evidence suggests that clinical outcomes are likely to be superior with use of endovascular therapy in such patients. Therefore, patients with acute iliofemoral DVT who are at low projected risk of bleeding should be provided with a balanced discussion of the risks and possible benefits of nonurgent endovascular thrombolytic therapy for the purpose of PTS prevention. Given the lack of conclusive evidence of benefit, a very low threshold should be applied to exclude patients if there are risk factors for bleeding. Patients with asymptomatic DVT and isolated calf DVT should not undergo thrombolysis since the risks of major PTS are low [Ginsberg 2001]. Patients with chronic femoropopliteal DVT should not undergo catheter-directed thrombolysis since it is ineffective in that scenario [Mewissen 1999].

Vedantham et al evaluated several mechanical thrombectomy devices used as an adjunct to catheter-directed thrombolysis. They concluded that mechanical thrombectomy alone was inadequate and that pharmacologic thrombolysis significantly improved outcomes [Vedantham 2002]. Bush et al drew the same conclusions when they demonstrated more effective thrombus extraction after adding a lytic agent to rheolytic thrombectomy [Bush 2004].

After initial treatment, patients' symptoms of acute DVT, such as leg swelling, tightness, and pain, typically disappeared rapidly. In our ultrasonographic observations, the following factors were primarily responsible for the immediate resolution of these symptoms: (a) recovery of venous obstruction (i.e., recanalization) and (b) the development of bypassing collateral veins. As observed by Thomas et al [Thomas 1971], the resolution of these symptoms is primarily the result of bypassing collateral veins, which are typically detected around the occluded vein segment immediately following warfarin treatment. In the present study, patients undergoing PMT experienced rapid resolution of their symptoms, which primarily resulted from effective thrombolysis and early vein recanalization.

A review of the relevant literature suggests that catheter-directed thrombolysis (CDT) and LMWH substantially influence thrombus regression and prevent recurrent DVT [Enden 2009].

In our study, recanalization occurred in 84% of the PMT group after 6 months of treatment. However, only 56% of the control group experienced recanalization at 6 months.

Decousus et al demonstrated the initial efficacy of filters for the prevention of pulmonary embolism in deep vein thrombosis patients [Decousus 1998].

Currently, the vast majority of filters implanted worldwide are of the permanent type, but their use is associated with a number of long-term complications such as IVC thrombosis, filter migration, perforation, etc. Non-permanent filters represent an important alternative, and in particular retrievable filters are an attractive option because they may be either left in place permanently or safely retrieved after quite a long period when they become unnecessary [Imberti 2012].

All attempts at both implantation and retrieval of the filter were safely accomplished. No complication related to filter placement occurred. Our results demonstrate that both placement and removal of the retrievable vena cava filter can be accomplished safely and that this type of filter is useful to prevent pulmonary embolism during treatment of deep venous thrombosis of the lower extremity.

Early reports suggest that PMT is safe and may be cost-effective with an acceptable safety profile and encouraging mid-term results [Karthikesalingam 2011].

Conclusion

Use of the cleaner thrombectomy device is a promising alternative to current treatment modalities for the management of DVT in a single session of pharmacomechanical thrombolysis. Addition of lytic agent to PMT facilitates thrombus extraction, decreases overall interventional treatment time, and improves patient outcomes. PMT with adjunctive thrombolytic therapy is an effective treatment modality in patients with significant DVT.

In conclusion, our short-term results suggest that PMT treatment is as safe as anticoagulation and provides greater thrombus resolution and earlier recanalization, which may preserve venous function and further prevent PTS.

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