

Frugal Pharmacomechanical Catheter Directed Thrombolysis for Ilio-Femoral Deep Vein Thrombosis (IFDVT) in Resource Poor Setting – Is It Any Good?

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DOI: <http://dx.doi.org/10.21276/ijcmsr.2020.5.3.6>

How to cite this article: Sitaram Barath, Hari Ram, Ayush Tambi. Frugal pharmacomechanical catheter directed thrombolysis for ilio-femoral deep vein thrombosis (IFDVT) in resource poor setting – is it any good?. International Journal of Contemporary Medicine Surgery and Radiology. 2020;5(3):C17-C21.

A B S T R A C T

Introduction: Pharmacomechanical Catheter-directed thrombolysis (CDT) for the treatment of acute iliofemoral deep venous thrombosis (IFDVT) has the advantages of thrombus removal, restoration of the vein patency, and preservation of valvular function. It also allows venoplasty of the underlying vein lesions. However the cost of dedicated devices is usually limiting factor in resource poor settings. The aim of the study was to assess the efficacy, safety, short-term patency rates, and incidence of post-thrombotic syndrome (PTS) following CDT treatment of IFDVT using frugal technique using low cost materials and drugs.

Material and methods: This is a retrospective study of all adult patients who underwent Pharmacomechanical CDT for the treatment of acute, nonrecurrent, radiologically proven IFDVT at the Department of vascular interventional radiology in Geetanjali medical college and hospital (a tertiary referral hospital), between December 2016 and November 2019. Total 42 patients were included in study.

Results: 42 patients underwent Pharmacomechanical CDT for treatment of acute IFDVT. Balloon angioplasty was performed in 32 (76%) patients. two bleeding events One major and one pulmonary embolism causing deaths occurred. 12% patients had symptoms of mild PTS. None of the patient had moderate or severe PTS or occurrence of venous ulceration.

Conclusion: Pharmacomechanical CDT is a safe and effective treatment option for patients with acute IFDVT, with good technical end result. Prompt thrombus lysis along with adjunctive treatment of vein lesions can help reduce rate of rethrombosis and the subsequent development of PTS.

Keywords: Pharmacomechanical Catheter-Directed Thrombolysis, Deep Venous Thrombosis, Post-Thrombotic Syndrome, Venoplasty

INTRODUCTION

The treatment of patients with iliofemoral lower-extremity deep venous thrombosis (IFDVT) involving the iliac, femoral, and popliteal veins remains challenging. Short and long-term complications contribute to patient morbidity and health care costs, due to increased incidences of venous thromboembolism and recurrent DVT.¹ In the acute setting, treatment is aimed at restoring venous patency, preventing thrombus extension, and reducing the incidence of pulmonary embolism. Long term treatment goals include reducing the incidence of recurrent thrombosis and risk of chronic venous insufficiency and postthrombotic syndrome (PTS). The current standard of care is systemic anticoagulation, which can prevent thrombus propagation, with this however, endogenous fibrinolysis is required for clot dissolution. Consequently, larger-volume clots, particularly ilio-femoral DVTs, are a therapeutic challenge, as anticoagulation

often fails to restore venous patency and thus predisposes to recurrent thrombosis and chronic complications due to associated venous valvular disruption.

Adjunctive treatments with external compressive devices such as graded-compression stockings also have been shown to be ineffective for preventing PTS.² These results highlight the need to perform more effective early intervention before irreversible venous damage occurs. These limitations have prompted the development of endovascular thrombus removal and dissolution strategies, including catheter-directed thrombolysis (CDT), pharmacomechanical CDT, and percutaneous mechanical thrombectomy. However problem with CDT is long duration of treatment and PCDT is high cost of dedicated equipment. In this study we have used a frugal way of doing PCDT in resource poor settings. Current research aimed to study the short and long term safety and efficacy of frugal Pharmacomechanical CDT using a wide bore guide catheter for mechanical debulking

of clot followed by 24 hour catheter directed lysis with urokinase with or without venoplasty if required.

MATERIAL AND METHODS

This is a retrospective study of all adult patients who underwent Pharmacomechanic CDT for the treatment of acute, nonrecurrent, radiologically proven IFDVT at the Department of vascular interventional radiology in Geetanjali medical college and hospital (a tertiary referral hospital), between December 2016 and November 2019. Total 42 patients were included in study.

The sampling method was non probability convenience sampling. The data was collected retrospectively from medical record department and follow up were taken telephonically and also in outpatient department.

Inclusion criteria

Patients with Doppler evidence of ilio-femoral DVT up to 14 days from onset of symptoms included in study that were more than or equal to 18 years of age.

Exclusion criteria

Patients less than 18 years of age.

Chronic DVT, recurrent DVT or sub-acute DVT of more than 14 days duration were excluded. Bedridden patients, systemic malignancy, pregnancy and DVT limited only to femoral and popliteal vein were also excluded from study.

Frugal equipment

Cook shuttle sheath 7f was used for aspiration and debulking of clot. 50 cc leurolock syringe was used for suction. Cragg Mcnamara 5f perfusion catheter with 50 cm perfusion zone was used for CDT. Urokinase was used as a fibrinolytic agent in all the cases. Large diameter Atlas balloon from Bard was used for venoplasty.

Procedure steps

1. Preoperatively patient was kept Nil by mouth for 8 hours. The leg was shaved.
2. The patient was kept prone on the table. Intravenous sedation in the form of nalbuphine and midazolam was used in pain sensitive or apprehensive patients.
3. Puncture for popliteal vein access was made just below the knee joint.
4. 10 French sheath was placed in the vein. Extent of the deep venous system thrombosis was confirmed by

venogram. (Figure 1a)

5. The occluded segment was crossed with hydrophilic angled tip guidewire and cook shuttle sheath combination keeping in mind not to cross the junction of IVC and CIV. This was done to avoid chances of pushing thrombus upstream. The junction of IVC and CIV is usually stenotic and cause of DVT and works as a barrier for pulmonary thromboembolism. However if the patient had pulmonary thromboembolism to begin with or had IVC thrombus then an IVC filter was placed from jugular vein access before starting Pharmacomechanic CDT.
6. Suction was done with small to and fro motion of shuttle sheath using 50 cc leurolock syringe. The cycle was repeated several times for the entire length of vein up to the puncture site.
7. When debulking was no more possible a check venogram was performed to look for extent of debulking and evidence of stenosis or residual clot burden.
8. At this stage finally the wire was crossed in IVC and 5f Cragg Mcnamara perfusion catheter was placed. Advantage of this catheter is valve at the distal end hence eliminating need of an occluder wire. 50 cm perfusion zone enables to cover near about entire length of thrombus from popliteal vein till lower ivc.
9. This was Sutured and secured in place for 24 hours.
10. Urokinase 1lac units bolus and 1 lac units continuous infusion per hour was started through catheter. Heparin 500 units continuous infusion was given through sheath. As a standard protocol every patient received fibrinolysis for 24 hours.
11. Check venogram was done at 24 hours to look for extent of recanalization and proximal stenotic lesion. Stenotic lesion was dilated with balloon and residual clots removed via suction if any. We did not use stents. (Figure 1 B To1 e)
12. Puncture site hemostasis was obtained by manual compression.
13. Systemic anticoagulation was started which was given a minimum of 6 months, initially injectable and then oral preferably a NOAC. NOAC helps further reduction of hospital stay as patients don't have to wait for therapeutic INR achievement in contrast to vitamin k antagonists. Patient was usually discharged next day.

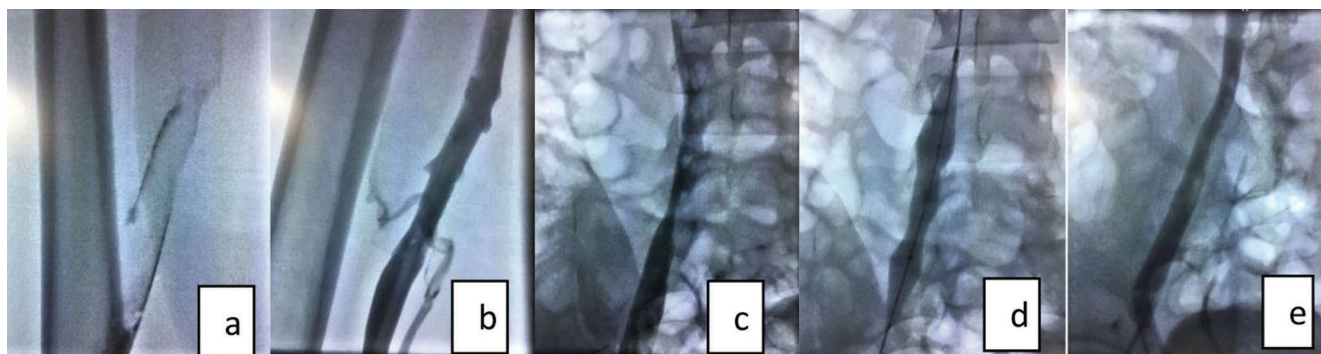


Figure-1(a to e): shows a representative case showing acute thrombus in the deep venous system seen as central filling defect on venogram (1a). Following pharmacomechanic CDT the thrombus has cleared (1b) exposing stenosis of distal CIV (1c), also evident on balloon plasty image (1d). Check venogram obtained post venoplasty showing good patency (1e).

Assessment of outcome

A total thrombus score was calculated before and after completion of CDT by adding the scores for the following seven vein segments: inferior vena cava, common iliac vein, external iliac vein, common femoral vein, proximal and distal segments of femoral vein, and popliteal vein. Scores were 0 when the vein was patent, 1 in case of a partially occluded vein, and 2 in case of a completely occluded vein. Each segment was given a score, resulting in possible total thrombus scores of 0–14.³

The early efficacy of CDT was defined based on post lysis thrombus score and clot lysis grade at the end of the procedure. Lysis grade was calculated by dividing the difference of the total pre- and post lysis thrombus scores by the pre lysis score, resulting in a grade III indicating 100% lysis with no residual clots, a grade II indicating 50%–99% lysis, and a grade I indicating less than 50% lysis. Lysis grades II and III (ie, >50%) were considered successful outcomes.

Bleeding complications were considered major if it led to fall in haemoglobin by at least 2g/dL, required transfusion of at least 2U of packed red blood cells, were retroperitoneal, intracranial, or in a critical organ, or contributed to death. PTS was diagnosed after 6 months to 24 months based on the Villalta scale (table 1) with assessment of five patient-rated venous symptoms and six clinician-rated physical signs.⁴

STATISTICAL ANALYSIS

The data was processed in Microsoft excel, tabulation done, and statistical averages and relevant proportion were calculated. Charts and tables prepared for simplification of data.

RESULTS

Out of 42 patients in our study 16(38%) were male and 26 (62%) were female.(figure 2a) The age ranged from 18 years to 70 years. The number of cases as per age distribution are given in (figure 2b).

Left side was predominantly involved and constituted 76% cases. Right side was involved in 17% cases and 7% patient had IVC extension. One patient had bilateral DVT. (Figure 3)

Out of 42 patients 32 (76%) had underlying stenosis or external compression and underwent venoplasty. We did not use stent in any of the cases.(Figure 4)

Successful outcome was obtained in 95% of cases. The extent of recanalization achieved is described in (table 2).

Complications

4 patients developed rethrombosis out of which one underwent retreatment. One patient had dissection leading to rethrombosis. 2 patients developed major bleed. One had hemarthrosis and another one had rectus abdominus muscle hematoma. One patient died due to massive PE.

On long term follow up 2 patients developed cerebral venous sinus thrombosis highlighting the fact that these patients are prone for thrombosis elsewhere.(Table 3)

On follow up ranging from 6 months to 3 years 56% of patients were asymptomatic. 32% of patients had some symptoms of PTS but not significant as per Villalta score. 12% had mid PTS. None of the patients had moderate or

Patient rated venous symptoms	
Pain	
Cramps	
Heaviness	
Paraesthesia	
Pruritus	
Clinician rated signs	
Pretibial edema	
Skin induration	
Hyperpigmentation	
Pain during calf compression	
Venous ectasia	
Redness	

Each sign/symptom is rated as 0 (none), 1 (mild), 2 (moderate), or 3 (severe), and the scores are summed to produce a total score where by a score 0-4 excludes PTS, a score of 5-9 indicates mild PTS, 10-14 indicates moderate PTS, and a score of > 15 or venous ulcer indicates severe PTS.

Table-1: Villalta Scale for Assessment of PTS

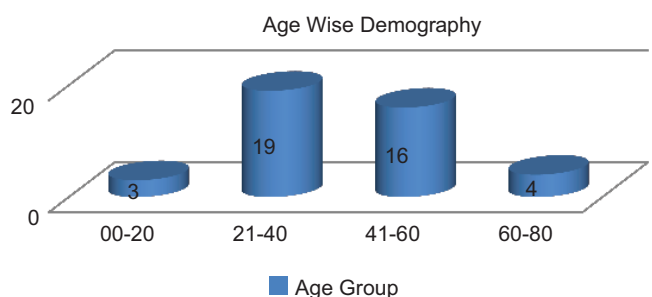
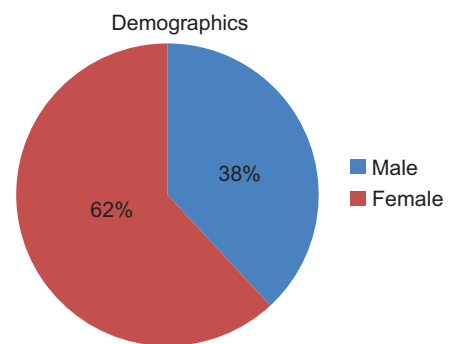


Figure-2a and 2b: Shows demographic data in terms of gender and different age groups.

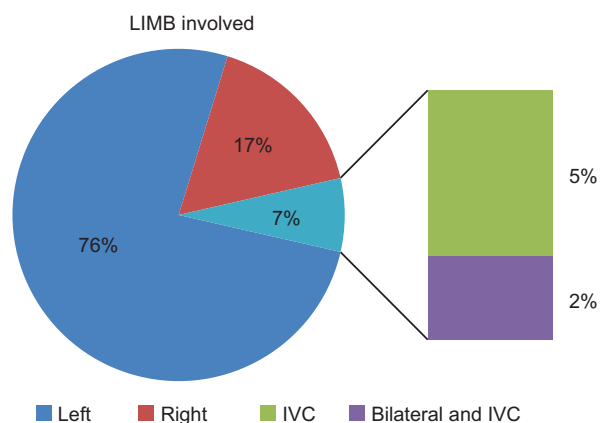


Figure-3: Shows laterality of DVT, as well as whether extension to IVC was present.

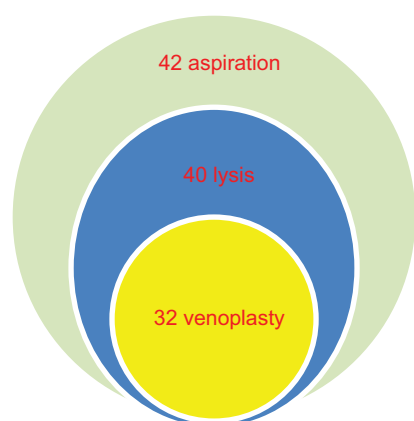


Figure-4: Shows number of patients and types of procedure received for restoring vein patency.

Grade of thrombolysis	% Recanalization	No of pts	Percentage
I	0-50	2	5
II	51-99	31	74
III	100	9	21
	Total	42	100

Table-2: Showing grading of thrombolysis and extent of recanalization.

Complications	Number of Pts
Rethrombosis	2+2
Bleed	2
Dissection	1
Death/PE	1
CVT	2
Total	8

Table-3: Showing short term or long term complications. One patient of dissection and another of bleed also developed rethrombosis.

PTS Score	No of pts	Percentage
0	19	56
1-4	11	32
5-9	4	12
10-14	0	0
>15 Or ulcer	0	0
No follow up	8	

Table-4: Showing incidence of PTS as per Villalta score.

severe PTS or ulceration.(Table 4). 8 patients were lost to follow up.

DISCUSSION

The different treatment modalities for IFDVT are anticoagulation alone, systemic thrombolysis, CDT and percutaneous mechanical thrombectomy coupled with CDT. Anticoagulation therapy alone However has high rates of subsequent PTS and venous ulcers, especially with IFDVT, demanding other treatment options targeting thrombus removal and restoration of vein patency.^{5,6} Systemic thrombolysis has been associated with serious bleeding

events.⁷ Locally delivered thrombolytic therapy in CDT helps to lyse the thrombus, protects valve function, and maintains venous patency. The reported decreased incidence of recurrent thrombosis and PTS after CDT made it the preferred modality for treatment of IFDVT.⁸

A major disadvantage of CDT is the long infusion time, during which intensive care monitoring is required. To overcome this limitation pharmacomechanical CDT, in which mechanical thrombus removal is combined with CDT was developed. Many reports indicate that pharmacomechanical thrombolysis with active mechanical fragmentation of the thrombus with or without aspiration is associated with shorter treatment time, lowers total doses of thrombolytic agent, shorter intensive care unit and hospital stays, and therefore reduced costs.⁹

However the devices used in pharamcomechanic CDT are still quite costly and beyond reach of many patients in resource poor settings. Hence we used this frugal technique to further reduce the cost. However in the quest of reducing cost we should not end up reducing safety and efficacy. Also since there is wide variation in the treatment strategies we tried to standardize our technique.

In our study we achieved adequate recanalization that in 95% of patients with a complete lysis obtained in 21% of cases. This is comparable to studies done by Ly B et al and Sillessen et al.^{10,11}

We did venopalsty in 76% of cases however we did not stent any vein in our study. We had 4 rethrombosis constituting 10%. So despite not stenting our long term and short term patency rate is comparable to many studies. 82% in Baekgaard N et al and 78% in Bjarnason H et al.^{12,13} This needs to be further studied whether stenting is really required.

On follow up ranging from 6 months to three years four (12%) of our patients developed mild PTS. None had moderate or severe symptoms or venous ulceration. the incidence of PTS in ATTRACT trial was 42%, Although the ATTRACT study did not report a lowered risk for all-severity PTS in CDT-treated patients compared with those treated with oral anticoagulation only, their incidence of moderate-to-severe PTS was significantly lower in the CDT group (18 vs. 24%; P=0.04).¹⁴

Bleeding is known to be the main complication related to CDT.⁸ Bleeding rate in our study was 4.76%, with only one major bleeding event 2.38%. Similar rates of minor and major bleeding were reported in ATTRACT study.¹⁴ One of the patient developed PE (2.3%) leading to death.

CONCLUSION

Pharmacomechanic CDT is a safe and effective treatment option for patients with acute IFDVT, with good technical end result. Prompt thrombus lysis along with adjunctive treatment of vein lesions can help reduce rate of rethrombosis and the subsequent development of PTS.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 03-06-2020; **Accepted:** 25-06-2020; **Published online:** 21-07-2020