REVIEW ARTICLE

Envisioning acute iliofemoral deep venous thrombolysis jockeying on the horse of interventional radiology: A systematic review

Gaurav Vedprakash Mishra[1, 2], Pankaj Banode[3], Anurag Luharia[4]*

[1]Pro-Vice Chancellor, [2]Department of Radio-diagnosis, Acharya Vinoba Bhave Rural Hospital, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research (Deemed to be University), Wardha-442001 (Maharashtra) India, [3]Department of Interventional Radiology, Acharya Vinoba Bhave Rural Hospital, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research (Deemed to be University), Wardha-442001 (Maharashtra) India, [4]Radiation Physicist and Radiation Safety Officer, Acharya Vinoba Bhave Rural Hospita, Datta Meghe Institute of Higher Education and Research (Deemed to be University), Wardha-442001 (Maharashtra) India

Abstract

Deep Venous Thrombosis (DVT) is a venous disease which develops in lifestyles involving sedentary postures or where the individual works in a sitting or standing posture for prolonged periods of time. The incidence of this disease has been increasing recently owing to preference of sedentary lifestyles in the modern world. Coming onto the frontiers of its diagnosis and treatment, either conservatively or surgically, minimally invasive treatment involving interventional radiological perspectives has been catching much attention lately as it has been observed to deliver acceptable results in terms of the quality of life of the patients as well as thrombus clearance within the affected venous vasculature. This draft houses a systematic review of articles dwelling over the aspect of various treatment techniques and studies on deep venous thrombolysis incorporating interventional radiological aspects.

Keywords: Thrombosis, Venous Thrombosis, Thrombolysis, Deep Venous Thrombolysis, Interventional Radiology, Vascular Interventional Radiology

Introduction

The term "iliofemoral DVT" refers to an obstruction or occlusion of the deep venous vasculature involving the iliac and/or common femoral vein which may or may not present with additional occluded veins leading to a functional occlusion to the normal venous outflow with reference to the laterality of affected lower limb [1-2]. This invariably has a sequelae of a group of findings termed together as "Post Thrombotic Syndrome" (PTS) which may occur either early or late in the timeline depending upon the severity of the occlusion or thrombosis of the affected lower limb and the level of occlusion in terms of its proximal or distal location [3-7].

Scoring systems for PTS

One of the much utilized scoring systems for PTS for the purposes of not only diagnosing the syndrome but also for categorizing and/or grading the same with reference to the severity of presentation of PTS is the Villalta scoring system [8-9]. It was devised and presented from a cross

sectional study including 100 cases of DVT which have had their follow-up from 6 months until 36 months. The scoring system is based on five symptoms viz pain in the affected limb, cramps in the affected limb, heaviness of affected limb, paresthesia involving the affected limb and pruritus affecting the limb involved. This scoring system also bases itself upon six clinical signs viz pretibial edema, induration of the overlying skin, hyper-pigmentation of the overlying skin, redness, any evidence of venous dilatation or venous ectasia with pain on compression of calf. The scoring system rating of 5 or greater along with a presenting venous ulcer diagnoses a case with PTS. A Villalta score of 5 to 9 addresses mild form of PTS whereas a score of 10 to 14 addresses moderate PTS. A score of 15 or greater addresses a severe form of PTS [8-9].

The Villalta scoring system has been used and utilized for the purposes of not only grading the diagnosis of PTS but also for the classification of severity of the presenting syndrome, evaluation of long term follow up of patients of PTS and their treatment prospectively through an array of vital researches in literature [10-21].

The Ginsberg scoring system for PTS was an outcome reported through a cross sectional study where the phenomenon of PTS was seen as a presentation in cases of hip and/or knee arthro-plasty where there was reporting of both swelling a swell as pain in the affected lower limb for at least 1 month duration with prolonged standing as a contributing factor and having undergone relief in both pain and swelling of the affected lower limb upon elevation of the same, all of which should have been taking place at least if not beyond 6 months of initial reporting of DVT [22].

The Ginsberg score was utilized in a research study which examined the effects of usage of compression stockings in the prevention and treatment of PTS [23].

The Villalta and Ginsberg scoring systems were compared by Kahn et al in another research study which concluded that Ginsberg scoring system diagnosed only those patients who had a severe disease presentation as compared to that of Villalta scoring system – Ginsberg scoring system showing higher mean Villalta scores at the same time [24]. The Ginsberg scoring system is still being utilized in additional studies related to prevention and treatment of PTS using graduated compression stockings [25].

The Brandjes scoring system [9, 26] was reported as an outcome from another trial study which examined the role of compression stockings utilization in cases with proximal DVT presenting with symptoms. The scoring system is similar to Villalta's as in points being allocated against various criteria – subjective and objective criteria which were a choicest combination of other systems developed for scoring of PTS [26-27]. Cases were diagnosed with PTS if they had a score same across 2 or more consecutive visits spanning a time period of 3 months. A score of 3 was equal to mild to moderate PTS, 4 or more pointing to a severe form of PTS. The score was based upon allocation of points as against certain subjective and objective criteria and the presence of a venous ulcer graded the case as a severe form of PTS. Kolbach *et al*. [28] utilized the Brandjes scoring system and compared the presenting cases against the Ambulatory Venous Pressure (AVP) values showing a strong association/correlation between the two.

Table 1: Villalta's PTS scoring system [8]

Symptoms/signs	None	Mild	Moderate	Severe
Symptoms				
Pain	0	1	2	3
Cramps	0	1	2	3
Heaviness	0	1	2	3
Paresthesia	0	1	2	3
Pruritus	0	1	2	3
Signs				
Pretibial edema	0	1	2	3
Skin induration	0	1	2	3
Hyperpigmentation	0	1	2	3
Redness	0	1	2	3
Venous ectasia	0	1	2	3
Pain in calf compression	0	1	2	3
Venous ulcer	absent			present

Table 2: Brandjes's PTS scoring system [9]

Subjective criteria		Objective criteria	
Symptoms	**Score**	**Signs**	**Score**
Spontaneous pain in calf	1	Calf circumference increased by 1 cm	1
Spontaneous pain in thigh	1	Ankle circumference increased by 1 cm	1
Pain in calf of standing / walking	1	Pigmentation	1
Pain in thigh on standing / walking	1	Venectasia	1
Edema of foot/calf	1	Newly formed varicosis	1
'Heaviness' of leg	1	Phlebitis	1
Spontaneous pain and pain of standing / walking	1	Venous ulcer	4
Impairment of daily activities	1		

The Widmer scoring system [9, 29] was prepared to calibrate and grade chronic venous insufficiency of the lower limb. It was utilized in studies related to PTS by Widmer *et al*. [29]. This scoring system was also a part of a Cochrane Systematic Review based upon evaluation of wearing compression stockings towards mitigating the severity of signs and symptoms of PTS [30]. Kolbach *et al*. [28] showed a moderate association/correlation in between the Widmer scoring system and Brandjes scoring system with k value equal to 0.52 in their study.

Another scoring system prepared for grading the severity of chronic venous insufficiency on the basis of clinical signs is the CEAP scoring system wherein C stands for clinical signs, E stands for etiology of the presenting disease, A stands for the anatomic distribution of the presenting disease and finally P stands for the pathophysiologic status and condition of the disease presented [31]. Here, in this system of scoring, the scoring is done into 7 classes based on the above 4 criteria. Depending upon the class the grading is done as per Table 4 – from C_0 to C_6, with $C_{0\text{-}6,A}$ as asymptomatic and $C_{0\text{-}6,s}$ as symptomatic disease. Depending upon the etiology of the underlying disease, it is classified as congenital, primary or secondary and denoted as E_C, E_P and E_s respectively.

Table 3: Widmer's PTS scoring system [29]

Stage	Symptoms
1	Ankle flare, subclinical edema
2	Edema, pigmentation, lipodermatosclerosis, white (skin) atrophy
3	Leg ulcer, leg ulcer as a part of past history

Table 4: CEAP scoring system [31]

Class	Signs
0	No visible or palpable signs of venous disease
1	Telangiectases, reticular veins, malleolar flare
2	Varicose veins
3	Edema without skin changes
4	Skin changes related to venous disease such as pigmentation, venous eczema, lipodermatosclerosis
5	Above skin changes associated with healed ulceration
6	Above changes associated with active ulceration

The anatomic distribution/site is denoted as A_s for superficial sites, A_d for deep sites and A_P for perforating sites. The pathophysiology is denoted as P_R in case of pathologic reflux, P_o in case of pathologic obstruction and $P_{R,O}$ in case of presence of both reflux and obstruction at the same time. This scoring system has been used to diagnose PTS in multiple research studies [16, 18, 32-37].

Venous Clinical Severity (VCS) Score was devised basing itself on the CEAP scoring system (9, 38) with additional three points allocated toward differences or multiplicity in any conservative therapy or management followed previously such as utilization of graded compression stockings in cases of PTS with or without conservative treatment and finally the compliance of the patient eventually summing up to a maximum score of 30. Wahlgren *et al*. [39] used VCS in their research study to diagnose and/or grade PTS severity. Kolbach *et al*. [28] compared VCS with other scoring systems and inferred a k value of 0.22 which represented a poor association/correlation. Meissner *et al*. [40] on the other hand inferred on comparing VCS as against CEAP scoring systems that there was a good association/correlation in between both the scoring systems whilst statistically significant interobserver variability for the descriptors of pain, inflammation and pigmentation out of a total of 10 descriptors of pain, varicose veins with more than 4 mm diameter, venous edema, skin pigmentation, inflammation, induration, number of active ulcers, duration of active ulceration in months, diameter of the largest ulcer in centimeter and compliance to compressive therapy in terms of wearing graded compressive stockings on the affected lower limb.

Literature search strategy on research studies on acute iliofemoral DVT

A systematic search for literature was conducted on the 5th of September, 2023 at 1:50 pm on PubMed and Medline search databases using the keywords – DVT OR deep venous thrombolysis OR aspiration OR removal OR villalta score OR post thrombotic syndrome OR pts OR complications AND iliofemoral vessels Filters: randomised controlled trials, systematic reviews, systematic review and meta-analyses, free full text, in the last 5 years.

This displayed a list of 31 articles out of which there were no duplications. So, all 31 articles were screened by title and abstract for their eligibility. One additional article was included in the form of a systematic review. Upon this stage, 6 articles were excluded on grounds of mismatching inclusion and exclusion criteria, inadequate sample size, differences in primary or secondary outcomes etc. Now, 14 more articles were excluded on similar grounds on further exploration. A total of 8 articles were included for generation of systematic review of literature and defining the research gap for this present study (Table 5). The same is represented in the form of a flow chart (Figure 1).

Table 5: Literature search strategy results

Author	Research Focus	Conclusion	Observations
Comerota *et al*. (2019) [41]	Symptom severity and severity of PTS	Both anticoagulant therapy alone as well as augmentation of the same with PCDT do not affect the occurrence of PTS	Severity of PTS was less in pharmacomechanical catheter directed thrombolysis with anticoagulant therapy group of patients. Here, only one group was subjected to PCDT
Catherine *et al*. (2019) [44]	Effect on patency rates after PCDT – single or multi-stage intervention	There is no statistically significant effect of single or multiple stage CDT intervention on vessel patency	Unless thrombolysis is complete, occurrence of rethrombosis is high resulting in decreased patency rates
Lichtenberg e*t al*. (2021) [45]	Effect of pharmacomechanical CDT versus CDT alone with reference to vessel patency rates	Patency rate at 6 months in systemic or catheter directed thrombolysis versus pharmacomechanical catheter directed thrombolysis was 68% versus 94%	Pharmacomechanical element when added to catheter directed thrombolysis improves the extent of thrombus removal, results in better recanalization and improves patency rates
Notten *et al*. (2021) [46]	Long term effects of Ultrasound accelerated CDT	PTS develops in all cases but severity is less in those cases with CAVA	CDT reduces absolute risk for PTS development but does not completely cure it. Only severity is reduced which is not statistically significant with similar impact on quality of life
Pouncey *et al*. (2020) [47]	Effects of PCDT as against CDT on post thrombotic syndrome and vessel patency.	PCDT and CDT show similar long term outcomes with nearly equal to each other where vessel patency for PCDT is slightly greater than CDT but not statistically significant	PCDT and CDT both are good treatment options for iliofemoral DVT cases. PCDT provides slightly better vessel patency rates with less lytic dosage and less severity of PTS on long term follow up
Razavi *et al*. (2021) [48]	Immediate results of venography and clinical outcomes of PCDT.	Good removal of thrombus by PCDT. Residual thrombus burden does not correlate with occurrence of PTS but reduces its severity with improvement in quality of life but this is not statistically significant either.	More complete the lysis of thrombus at PCDT, less are the chances of the patient developing severe PTS later on. But PTS only gets delayed, not cured or competely ruled out

Continued...

Author	Research Focus	Conclusion	Observations
Dopheide *et al*. (2018) [49]	Use of AngioJet Zelante DVT device and its early clinical outcomes.	AngioJet Zelante DVT device is able to provide single session treatment. Vessel patency rates are effectively restored	Novel technique used here employs advancing catheter across thrombus slowly and also uses 27- degree rotation of catheter
Zheng *et al*. (2022) [50]	Use of pigtail catheter with Angiojet device.	Pigtail catheter crushing helps in vessel patency restoration augmented with use of pharmacomechanical aspiration devices like AngioJet	Use of pigtail catheter for crushing is a novel technique with a good thrombus removal rate

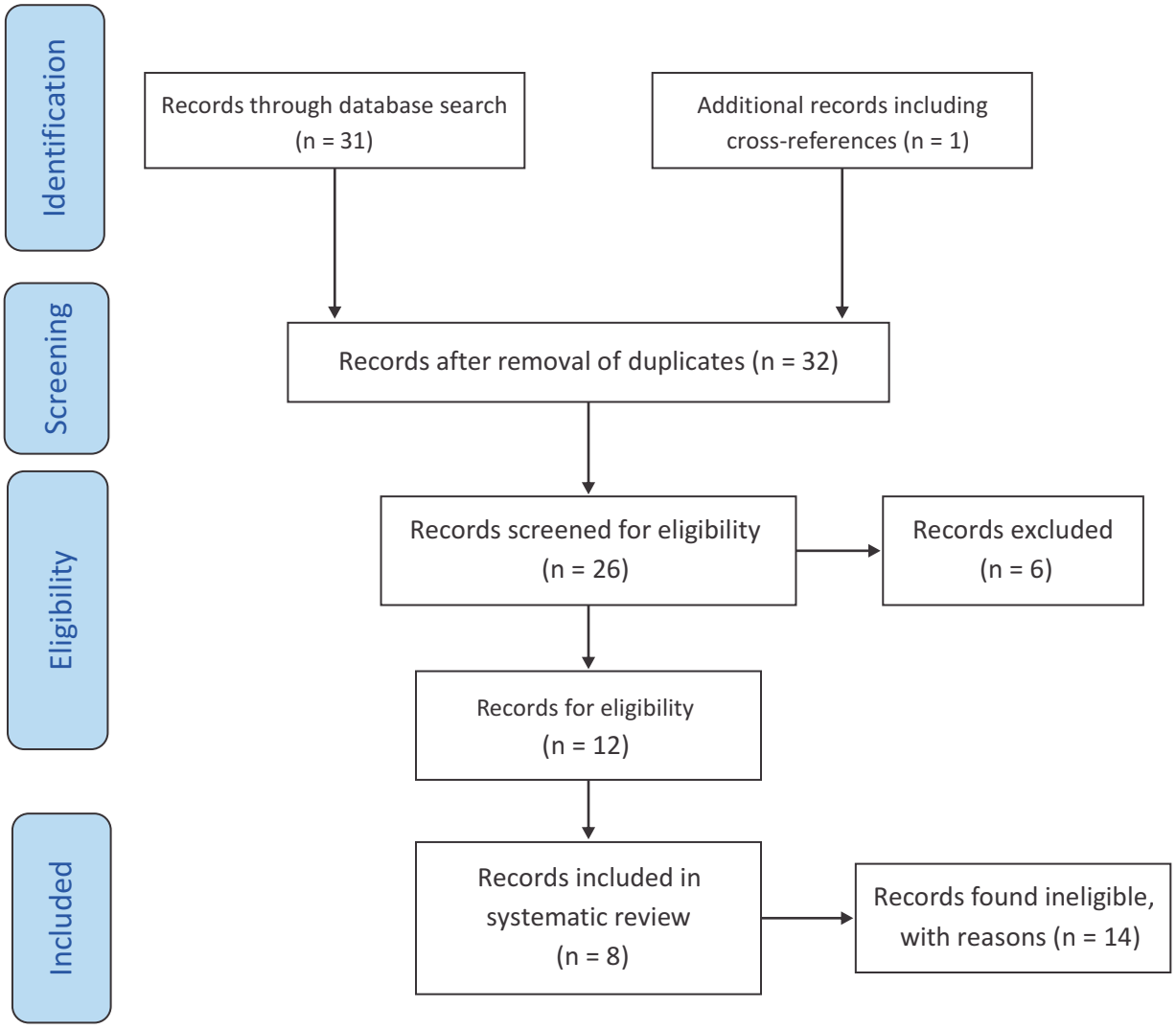

Figure 1: PRISMA Chart – flowchart showing the literature search strategy for the present review

The Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis Trial (ATTRACT) carried out earlier inferred that PTS as a sequel was not prevented but delayed in the timeline with less severity of presenting symptoms [41-43]. Here, ATTRACT stands for, supposedly the most extensive of randomized controlled trials based upon examining the results and outcomes of catheter directed interventions for DVT [42-43]. The main outcome of the trial was that there was no reduction in the frequency of PTS and/or the Quality of Life (QoL) of patients affected by PTS over a follow up period of 2 years post Pharmacomechanical Catheter-Directed Thrombolysis (PCDT) with augmented anticoagulation drug therapy as against another study group of patients having been administered anticoagulation drug therapy alone without PCDT [42-43]. There have been multiple research studies carried out to assess the outcomes of iliofemoral DVT recently which aptly bring out valuable results and a new direction towards future management [44-50].

The study carried out by Zheng et al. [50] made the use of a novel technique where there was utilization of a pigtail catheter in order to create a 'niche' within the lodged thrombus and then use of thrombolytic techniques to aspirate the thrombus and remove it safely, thereby reducing the thrombus load. Use of pigtail catheter along with pharmacomechanical catheter directed thrombolytic techniques involved the rotation of the pigtail catheter by an angle of 270 degree from the starting point as reported in literature leading to better outcome in the form of thrombus load reduction subject to removal and/or aspiration of the lodged thrombus from the site of venous flow obstruction.

A novel technique quite similar to the above technique titled "**Banode-Mishra Technique (BMT) for acute deep venous iliofemoral thrombolysis**" also utilizes pigtail catheter and use of pharmacomechanical catheter directed thrombolytic techniques with rotation of the pigtail catheter by an angle of 90 degree. The technique has been registered under the Copyright Office, Department of Promotion of Industry and Internal Trade, Government of India with diary number **21369/2022-CO/L** and ROC number **L-123704/2023**. The certificate of registration is also sent to the editorial team for kind reference and perusal as a part of evidence.

Conclusion

The purpose of this review has been to gather information regarding the prevalent modes of investigation and reasons thereto for the same as to why and how they are carried out. The setting of acute iliofemoral DVT invariably leads to PTS and perhaps the only good contribution vascular interventional procedures pertaining to thrombus removal/aspiration/suction can contribute to further delaying the complications of PTS down the timeline and adding to the productive timespan for the overall benefit of the concerned patients. In addition to all the techniques listed in literature enriching itself second after second, the angular approach whilst creating anintrathrombotic 'niche' followed by injection of thrombolytic agent utilising pharmacomechanical catheter directed thrombolytic techniques surely appears to be an open ground where experts in the field of vascular interventional radiology may further hustle with iliofemoral DVT to excel at enhancing not just the number of years but also to the quality of those years in the lives of all concerned.

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***Author for Correspondence:**

Dr. Gaurav Vedprakash Mishra, 35A, 'Abhiruchi', Opp. Prahaar School, Bank of India Colony, Nalwadi, Wardha (Maharashtra) India

Email:drgvmishra@gmail.com Cell:9171391739

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