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Aspiration mechanical thrombectomy for treatment of acute iliofemoral and central deep venous thrombosis

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ABSTRACT

We describe our experience with the Indigo CAT™ aspiration mechanical thrombectomy (AMT) system in 20 patients. A modification of the AMT technique was done in 7 patients (35%) whereby a snare was used instead of a separator. Technical success by intravascular ultrasound (IVUS) was noted in 8 patients (40%) while symptom improvement was noted in all patients prior to discharge. In 4 patients (20%), occlusion was noted on first post-operative day ultrasound; remainder demonstrated venous patency. Snare use was associated with higher technical success (85.7% versus 15.4%, $p = 0.004$) and less procedural blood loss (235 ± 40 cc versus 300 ± 55 cc, $p = 0.04$) compared to the separator.

1. Introduction

Percutaneous thrombectomy for symptomatic acute iliofemoral/central deep venous thrombosis (DVT) can be accomplished via catheter-directed thrombolysis (CDT), mechanical thrombectomy (MT) with AngioJet rheolytic thrombectomy system (Boston Scientific, Marlborough, Mass), and aspiration mechanical thrombectomy (AMT) using devices such as Indigo AMT system (Penumbra, Inc, Alameda, Calif) or AngioVac (AngioDynamics, Latham, NY).

The Indigo CAT AMT system can be utilized to aspirate thrombus in select vascular systems. The catheter has a curved tip and connects to a vacuum pump (the Penumbra Engine®) which generates suction through negative pressure (-29 inHg or 98.2 kPa). The catheter is available in a variety of sizes depending on the caliber of the target vessel. CAT 12 (12 Fr) can aspirate approximately 300 mL/s compared to 160 mL/s with CAT 8 (8 Fr). The separator is the third component of the system that can be used to clear thrombus from the catheter.[1] The variety of catheter sizes, easy navigation and trackability make the Indigo CAT AMT an attractive thrombectomy system. Also, thrombolytic agents such as alteplase are not needed. The main disadvantages include blood loss and theoretical risk of vessel trauma. The blood loss can now be mitigated by the use of Lightning™ Intelligent Aspiration Tubing that monitors blood flow in real time and provides feedback to the operator audiovisually.

The aim of this report is to summarize our experience with the indigo CAT™ AMT system and to describe a modification of the AMT technique with use of a snare instead of a separator.

2. Methods

2.1. Type of research study

From January to December, 2020, records of all patients with acute iliofemoral/central DVT who had AMT performed using the Indigo CAT™ system were retrospectively analyzed. Informed consent was obtained from patients. Institutional review board (IRB) permission was granted for publication of the study.

2.2. Inclusion and exclusion criteria

Symptomatic patients with acute iliofemoral/central DVT, including iliofemoral caval venous stent thrombosis, who underwent single session AMT with Indigo CAT™ system were included. CDT was not performed after use of Indigo system as these procedures were performed during the COVID-19 pandemic and bed utilization was extremely restrictive. CDT would have required intensive care unit stay which was not feasible at that time. Indications for thrombectomy included extensive iliofemoral DVT with or without caval involvement, persistence of severe symptoms despite medical management and anticoagulation and presentation within 2 weeks from the onset of symptoms. Patients in our subset were not felt to be appropriate candidates for other thrombectomy modalities (such as CDT and AngioJet) due to one or more of the following conditions:

(1) Advanced age (≥65 years),
(2) Baseline renal insufficiency (serum creatinine ≥ 1.5 mg/dL),

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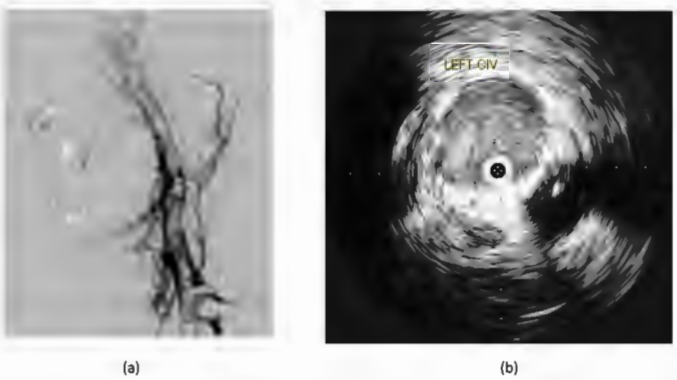

Fig. 1. (a) Acute iliofemoral deep venous thrombosis (DVT) noted by venography. Early collateralization and multiple venous filling defects are noted, (b) Common iliac vein seen with intravascular ultrasound showing dilated appearance and significant thrombus burden.

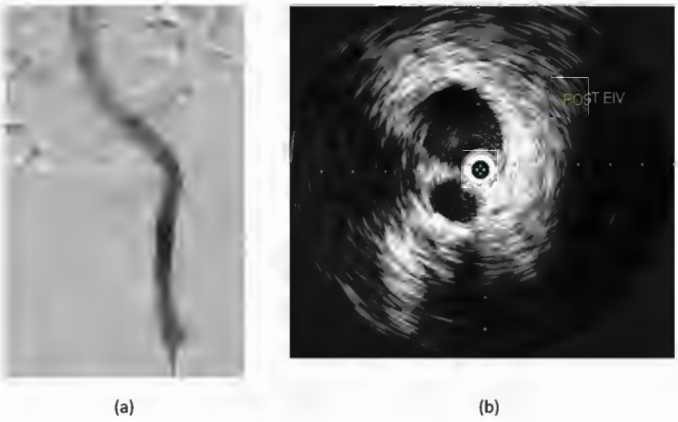

Fig. 2. (a) Establishment of venous patency and inline flow after aspiration mechanical thrombectomy on venography, (b) Intravascular ultrasound demonstrating clearance of thrombus from the external iliac vein after aspiration mechanical thrombectomy with Indigo system.

(3) History of recent major surgery (within 4 weeks of presentation),
(4) History of metastatic cancer,
(5) History of major spontaneous bleeding,
(6) History of recent major trauma (within 4 weeks of presentation)

2.3. Technical success

Intravascular ultrasound (IVUS) was performed before and after AMT (Figs. 1 and 2). Technical success of the thrombectomy procedure was arbitrarily chosen as the resolution of ≥ 50% of the thrombus on IVUS after AMT intraoperatively.

2.4. Procedural details

All procedures were performed under general anesthesia. Systemic anticoagulation was not withheld for the procedure. Patients were positioned prone for the procedure. The popliteal vein was accessed using micro-puncture kit percutaneously under ultrasound guidance. An 11 Fr sheath was utilized for all patients through which both 8Fr and 12Fr Indigo CAT catheters could be inserted easily. All patients had venography and IVUS performed before and after the AMT. In addition to AMT, balloon maceration of thrombus was done with angioplasty balloon in select patients. At the conclusion of the procedure, manual pressure was held at the access site for hemostasis.

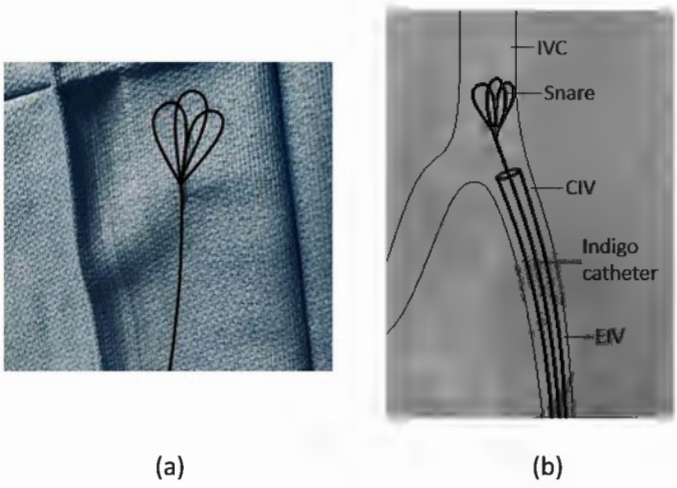

Fig. 3. (a) Loop snare, with three interlaced nitinol loops, provides mechanical disruption of the thrombus through rotational manipulation, (b) Representative image superimposed on fluoroscopic image: the loop snare is rotated just above the Indigo catheter while the system is actively on aspiration mode. IVC – inferior vena cava, CIV – common iliac vein, EIV – external iliac vein.

2.5. AMT device

Components and catheters of the Indigo CAT^{TM} system have been described previously.[1] In this study, CAT 8 (8Fr) was used from January to August, 2020. From August onwards, we used the CAT 12 (12Fr) system once it became available.

2.6. Modification of AMT technique

The Indigo CAT^{TM} system has a separator that can disrupt the thrombus into smaller fragments that are then aspirated. As described previously, this separator can also be used to clear thrombus from the catheter.[1] During our initial experience, we utilized the separator. However, the AMT technique was then modified to include the use of a 7F snare with loop diameter size of 25 or 30 mm (EN Snare, Merit Medical, South Jordan, Utah) instead of the separator (Fig. 3) for the purposes of mechanical disruption, removal of thrombus and thrombus clearance from the catheter itself. Some observations that led to this modification included: persistence of considerable thrombus burden despite separator use, high cost of separator and relative lack of perceptual and haptic feedback with separator.

2.7. Statistical analysis

Statistical analysis was performed using a commercially available statistics program (Prism software, Irvine, Calif). Mean and standard deviations were reported. Where appropriate, Fisher's exact test or *t*-test was used. $P < 0.05$ was considered as significant.

3. Results

3.1. Demographics

20 patients underwent AMT with the Indigo CAT^{TM} as the primary thrombectomy modality. Seven (35%) patients were male (Table 1). Mean age was 62 ± 14 years (range 30–84 years). Seven (35%) patients were ≥ 65 years. Major comorbidities included hypertension (11, 55%), renal insufficiency (8, 40%), diabetes (5, 25%) and active malignancy (5, 25%). Five (25%) patients also had a history of major surgery in the 4 weeks prior to presentation while 3 (15%) patients had a history of major spontaneous bleeding. 15 (75%) patients had a prior history of DVT and/or PE.

Table 1
Demographic details of patients ($n = 20$) who underwent aspiration mechanical thrombectomy with Indigo CAT™ system.

Variable	*N* (%)
Age in years (mean, range)	62 ± 14 (30–84)
Gender	
Male	7 (35)
Female	13 (65)
Comorbidities*	
Hypertension	11 (55)
Renal insufficiency	8 (40)
Diabetes	5 (25)
Active malignancy	5 (25)
History of recent major surgery	5 (25)
History of major spontaneous bleeding	3 (15)
Iliofemoral DVT	8 (40)
Iliofemoral DVT with IVC extension	12 (60)
Prior history of DVT with or without PE	15 (75)
Thrombosis in pre-existing stent	7 (35)
PE at presentation along with DVT	3 (15)
BMI (kg/m^2)	
< 25	3 (15)
25–30	12 (60)
> 30	5 (25)
Thrombophilia conditions ($n = 15$)*	
Hyperhomocysteinemia	4 (20)
Protein C or S deficiency	1 (5)
Antithrombin deficiency	1 (5)
Prothrombin gene mutation	2 (10)
Factor V Leiden mutation	2 (10)
Factor VIII elevation	5 (25)

* Some patients had more than one comorbidity or thrombophilia conditionDVT – deep venous thrombosis, PE – pulmonary embolism, BMI – body mass index

3.2. Thrombophilia data

Thrombophilia testing was performed in 15 patients at the discretion of the treating physician (Table 1). The most common thrombophilia conditions in this patient cohort were factor VIII elevation (25%) and hyperhomocysteinemia (20%).

3.3. Clinical and procedural parameters

CAT-8 system was used in 7 patients while CAT-12 system was used in 13 patients. Technical success was noted in 8 patients (40%); remaining patients having >50% residual thrombus on IVUS after AMT. Snare use was associated with higher technical success (85.7% versus 15.4%, $p = 0.004$). There was no significant association between technical success and use of CAT-8 or 12 systems ($p = 0.26$). No peri-procedural complications were noted. In 4 patients (20%), venous occlusion was noted on ultrasound done on the first post-operative day; the remainder demonstrated venous patency with residual thrombus. Among patients with occlusion, two had prior history of DVT while one had prior history of major spontaneous bleeding.

Snare was used instead of the separator in 7 (35%) patients. For the purposes of analysis, two groups were formed on the basis of the use of the snare (Table 2). Stenting was done selectively; it was performed in a total of 4 patients (20%). Out of these 4 patients who underwent stenting, one had snare utilization.

3.4. Follow up and clinical success

Symptom improvement was seen in all patients prior to discharge. Mean follow-up was 4.3 ± 3.9 months (range 6 weeks – 1 year). At follow up, symptomatic improvement continued to be noted in all patients in terms of grade of edema and pain score. The improvement in Venous Clinical Severity Score (VCSS), edema grade and pain score was noted in both groups (Table 2). Trends towards greater improvement in pain score and edema grade were noted with snare use but the association was not statistically significant. On follow-up ultrasound (done at 6 weeks, and 3–6 month follow-ups thereafter), 14 (70%) of the treated limbs were still found to be patent. Of these 14 limbs, 5 had snare usage at the time of thrombectomy.

3.5. Anticoagulation status

During the hospital stay, all patients received therapeutic dose of enoxaparin for anticoagulation. Post-discharge, all patients were continued on therapeutic anticoagulation for at least 3 months. Details of anticoagulation regimen are mentioned in Table 3. Direct acting oral anticoagulants (DOACs) such as apixaban (45%) and rivaroxaban (30%) were the most commonly prescribed anticoagulants. Choice of anticoagulation agent was dependent on a number of factors including surgeon preference, patient preference, affordability and tolerance to side effects of the medication. In some patients, extended anticoagulation was considered as part of secondary DVT prophylaxis strategy. This included the use of apixaban (2.5 mg twice daily) or rivaroxaban (10 mg once daily) long term. The decision to employ such a strategy was complex and involved consideration of a multitude of factors including nature

Table 2
Clinical and procedural parameters in patients who underwent aspiration mechanical thrombectomy with Indigo CAT™ system.

Parameter	Group 1 (snare used), $n = 7$	Group 2 (snare not used), $n = 13$	*p*-value
Technical success	6 (85.7%)	2 (15.4%)	**0.004***
Occlusion on POD 1 ultrasound	1 (14.2%)	3 (23.1%)	0.56
Use of thrombolytic agent	2 (28.6%)	3 (23.1%)	0.59
Mean ± SD change in VCSS before and after intervention	- 3.25 ± 0.5**	- 1.75 ± 1.3**	0.06
Mean ± SD change in pain score before and after intervention	- 5.75 ± 0.96**	- 4.5 ± 3.1**	0.8
Mean ± SD change in edema grade before and after intervention	- 2.5 ± 0.58**	- 1.25 ± 0.96**	0.08
Mean estimated blood loss during procedure (in mL)	235 ± 40	300 ± 55	**0.04***
Mean procedural time (in minutes)	69 ± 26.6	62 ± 17.3	0.33
Mean time from onset of symptoms to intervention (days)	11	13.23	0.8
Use of CAT 8 system	3 (42.8%)	4 (30.7%)	0.47
Use of CAT 12 system	4 (57.1%)	9 (69.3%)	0.47
Adjunctive balloon maceration of thrombus	4 (57.1%)	6 (46.2%)	0.5
Iliofemoral venous angioplasty and stenting	1 (14.3%)	3 (23.1%)	0.4
History of prior DVT (post-thrombotic)	5 (71.4%)	10 (77%)	0.3
Time from symptom onset to intervention	11.3 ± 2.5 days	9.6 ± 3.8 days	0.3

* Bold face *p*-value indicates statistical significance
** Negative value indicates decreasePOD – post-operative day; SD – standard deviation; VCSS – Venous Clinical Severity Score

Table 3
Details of anticoagulation at discharge in patients who underwent aspiration mechanical thrombectomy with Indigo CAT™ system.

Anticoagulant	*N* (%)
Apixaban	9 (45)
Enoxaparin	1 (5)
Rivaroxaban	6 (30)
Warfarin	4 (20)

of DVT (provoked versus unprovoked), history of recurrent DVT or PE, absence of absolute contraindications to anticoagulation, patient's age and functional status, patient preference, patient compliance and results of thrombophilia panel.[2]

4. Discussions

This study showed that Indigo CAT™ is a reasonable thrombectomy option for patients, including octogenarians, patients with baseline renal insufficiency, cancer or recent major surgical intervention. These are patient subsets who would otherwise have been excluded from intervention due to high risk for complications from other thrombectomy modalities. Majority of patients did not require ICU stay (90%) and were not administered thrombolytic agents (75%). Technical success in this study was gauged by IVUS in this study rather than venography because IVUS is more sensitive than venography.[3] A previous study reported technical success by venography alone as 60% after use of Indigo CAT AMT system.[1]

Other thrombectomy modalities include CDT, AngioJet, Clottriever (Inari Medical Inc, CA, USA) and AngioVac. CDT involves placement of a catheter in the proximity of the thrombus under fluoroscopic guidance. Thrombolytic agent is then slowly infused through the catheter for 24–48 h. Patients undergoing CDT generally require close monitoring in the intensive care unit. CDT can rarely cause major bleeding, including intracranial hemorrhage. Use of thrombolytic agents is considered prohibitive in conditions including, but not limited to, active hemorrhage, recent stroke, recent major surgery or trauma, uncontrolled hypertension, thrombocytopenia, intracranial tumor, prior history of major spontaneous bleeding and suspicion of infected thrombus.[4] Pharmacomechanical thrombectomy can be performed via AngioJet. It actively aspirates and delivers thrombolytic agent via power pulse spray mode. The 8Fr ZelanteDVT™ catheter is used in the treatment of DVT with AngioJet. However, use of AngioJet has been associated with post-procedural acute kidney injury (AKI) and pancreatitis.[5,6] ClotTriever is a mechanical thrombectomy device that does not involve the use of thrombolytic agents. It has a nitinol coring element and a collection basket for the thrombus. There is minimal blood loss with the use of ClotTriever device.[7] The main disadvantage of the system includes potential entanglement of the coring element or basket with pre-existing IVC filters or stents. The AngioVac system involves a veno-venous bypass circuit whereby thrombus is removed via a suction cannula (22 Fr) and then returned to the patient through a reinfusion venous cannula. The main risks with the device are related to its relative inflexibility while navigating tortuous vessels and access site complications.[8] In the current study, no patients experienced post-operative renal failure, bleeding or access site complications with the use of Indigo CAT AMT device.

Snare provides mechanical fragmentation of the thrombus which can then be aspirated by the catheter. Because of this nature, the principle of snare use is based on mechanical thrombectomy devices such as ClotTriever and FlowTriever (Inari Medical Inc, CA, USA). There is a theoretical embolic risk with fragmentation of thrombus with snare use. However, increased risk of intraoperative or post-operative PE due to snare use was not observed clinically in this study or previous ones.[1] Any thrombus fragments are quickly aspirated by the Indigo CAT AMT system; hence occurrence of PE is highly unlikely. The snare can also capture larger thrombus fragments which can then be removed in their entirety. Snare may thus offer an effective alternative to the separator. The use of snare has been described previously in cardiac literature for atrial thrombus retrieval[9] and pulmonary embolectomy,[10] neurology literature for cerebral artery thromboembolectomy[11,12] and venous literature for cavoiliac thrombectomy without the use of AMT device.[13] The maneuverability and complete expansion of the snare maybe limited by factors such as chronicity of clot and caliber of the vessel. Snare use was associated with less blood loss compared to the separator. This maybe related to the more efficient clearance of thrombus compared to separator which may limit the time the device is actively suctioning in the patient's body.

Significant residual thrombus was seen by IVUS in the majority of patients (60%) despite AMT. However, patency was noted on both post-operative day 1 ultrasound as well as follow up ultrasound in at least 70% patients. Despite significant residual thrombus noted on IVUS, symptomatic improvement was seen in all patients at discharge. This suggests that the creation of a flow channel with establishment of inline flow, despite residual thrombus, can provide symptomatic improvement for patients.[14]

5. Study limitations

The main limitations of the study include its retrospective nature, small sample size, need for more granular data and relatively short follow-up. Analysis of post-intervention outcomes is limited by the heterogeneity of patient characteristics.

6. Conclusions

AMT with Indigo CAT™ system is a reasonable thrombectomy modality, especially in patients considered high risk for complications from other thrombectomy modalities. Use of snare with AMT may improve technical success while reducing procedural blood loss.

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Ethical approval

All procedures in patients were performed with informed consent. Institutional review board (IRB) permission was obtained for data collection and analysis.

Guarantor/overall responsibility

Taimur Saleem

Declaration of Competing Interest

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Royalty, Veniti Inc. (Dr. Seshadri Raju), US Patent, IVUS diagnostics and Iliac vein stent design (Dr. Sedhadri Raju).

CRediT authorship contribution statement

Taimur Saleem: Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing. **Robert Fuller:** Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Seshadri Raju:** Writing – original draft, Writing – review & editing.

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