Review Article

Interventional Cardiology

Emergent pulmonary embolectomy associated with clot in transit using FlowTriever aspiration device

Abstract

Clot in transit (CIT) possesses a high mortality rate if left untreated hence timely management is required. Various treatment options, including endovascular procedures, are available. Currently, no consensus exists on superior treatment modality. Nevertheless, a multidisciplinary approach with a case-based evaluation seems the most appropriate. In the event of thrombolysis contraindication and hemodynamic instability, percutaneous mechanical thrombectomy should be considered. The success of the procedure is dependent on proper patient selection, as well as appropriate procedure guidance. The FlowTriever (Inari Medical Inc., Irvine, CA, USA) has proven efficacious for CIT treatment in several case reports. Based on the literature review, five out of six patients with CIT treated with the FlowTriever were discharged alive. Furthermore, the FLARE study reported an acceptable effectiveness profile in patients with Pulmonary Embolism (PE). This article presents currently available percutaneous mechanical thrombectomy alternatives focusing on the potential of the FlowTriever aspiration device.

Keywords: Clot-in-transit • Right atrial thrombus • Pulmonary embolism • Catheter directed thrombolysis • Percutaneous mechanical thrombectomy

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Introduction

Clot-in-Transit (CIT), described as a free-floating acute thrombus usually in the right atrium or right ventricle [1], has a high likelihood of fatal pulmonary embolism. Unlike other thrombi, CIT are typically serpiginous, highly mobile, and pose a high risk of mortality [2]. CIT may result from deep venous thrombosis or form in situ, primarily when atrial fibrillation occurs [3]. This particular subset of cardiopulmonary thromboembolic disease has a variable prevalence ranging from 4% to 18%. Prevalence depends upon the severity of Pulmonary Embolism (PE), "Results from the Italian Pulmonary Embolism Registry" reported a prevalence of 16% in high-risk patients, 3.8% in intermediate-risk, and 0.3% in low-risk patients [1]. Right Heart Thrombus (RiHT) is associated with a high mortality rate, almost 91% if left untreated [4]. The overall short-term mortality rate was 27.1%; however, the mortality rates associated with no therapy, anticoagulation, surgical embolectomy, and thrombolysis were 100%, 28.6%, 23.8%, and 11.3%, respectively. Garvey et al. (2020) found that all-cause mortality by seven days was higher in CIT patients when compared to PE alone (12.5% vs. 5.1%, P=0.02) [5].

Aim

The purpose of this article is to provide an overall comprehensive update on the Inari FlowTriever system, and the potential impact in treating both CIT and intermediate-high risk pulmonary embolic disease.

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Risk Assessment of PE and CIT

Clot in transit should be suspected in all patients with PE and right ventricular dysfunction. The most validated risk-assessment tool for acute PE patients and CIT is Transthoracic Echocardiography (TTE). This test can reveal the free-floating thrombus, septal mobility or flattening, and right ventricular systolic function [3].

Transesophageal Echocardiography (TEE) helps obtain a more precise amount of ventricle-valve information, site of attachment of the thrombus, and involvement of right and left pulmonary arteries. Still, TEE has a limited sensibility and specificity for acute PE diagnosis [6].

During thrombectomy, intraoperative TEE provides real-time surveillance during atrial entry and helps to visualize the residing thrombus [7,8]. It can potentially reduce the likelihood of serious sequela, including chordae tendineae damage and consecutive arrhythmia provocation. Additionally, TEE monitoring decreases the need for fluoroscopy, thereby reducing the risks associated with ionizing radiation and contrast administration. A case described by Nezami et al. presented a safe and effective use of TEE guidance during CIT removal [7].

Computed Tomography (CT) is the optimal imaging modality, especially in hemodynamic instability [9]. CT Pulmonary Angiography (CTPA) is the current standard of care in PE and provides accurate diagnosis with rapid turnaround time [10]. CTPA allows direct visualization of pulmonary arteries, cardiac thrombus, pericardial abnormalities, and musculoskeletal injuries associated with the etiology of chest pain and shortness of breath [10].

Intravascular Ultrasound (IVUS) is an invasive imaging modality that can accurately characterize CIT before and during an embolectomy [11]. Intracardiac ultrasound (ICE) is another type of invasive procedure guidance. Both may prove more practical. Interventional cardiologists widely use ICE, as it allows a single operator [12]. It eliminates the need for TEE, concurrently avoiding tracheal trauma. Furthermore, ICE decreases procedure and fluoroscopy time [12]. Chen et al., in their case report, described a successful ICE-guided right atrial thrombus aspiration using FlowTriever [13]. Similarly, IVUS has been employed in cardiac interventions, including embolectomy procedures [14]. The increased cost and less availability may be limiting factors in the more widespread utilization of IVUS and ICE compared to the more readily available TTE or TEE.

As part of the clinical criteria, hemodynamically unstable patients defined as systolic blood pressure sBP<90 mm Hg at the time of CIT diagnosis, make up the High-Risk Pulmonary Embolism (HRPE) group. Intermediate-Risk Pulmonary Embolism (IRPE) includes patients with sBP ≥ 90 mmHg who present with Right Ventricle Dysfunction (RVD) or biochemical signs of myocardial injury. Low-Risk Pulmonary Embolism (LRPE) comprises subjects who did not fulfill the criteria for HRPE or IRPE [15].

Therapies and Thrombectomy Systems for PE and CIT

There is no consensus on the optimal therapy for CIT and PE, and treatment selection is still widely debated. Anticoagulation (AC) is indicated for low-risk PE or CIT in situ [16,17]. Athappan et al., compared treatment options for CIT and PE and found that the mortality associated with AC alone was significantly higher than surgical embolectomy or thrombolysis (37.1% vs. 18.3% vs. 13.7%, respectively) [4]. In patients with intermediate, and high-risk PE plus CIT, thrombolysis significantly reduced 30-day mortality compared to heparin alone (20% vs. 80%) [18]. Some controversy has arisen with systemic thrombolysis in treating giant right atrial thrombosis and clot fragmentation, with subsequent fatal results related to cardiogenic shock development [19]. Surgical embolectomy has shown to have significant complication risks such as intraprocedural and postsurgical bleeding, cardiac tamponade, and severe secondary infections [20].

Recently, mechanical endovascular thrombectomy has seen increased utilization for patients exhibiting contraindications to lytic therapy. Aside from limited individual case reports and descriptive commentaries, there are currently no large prospective or retrospective studies regarding the best minimally invasive procedures to treat CIT with or without concomitant PE.

The AngioVac (AngioDynamics, Latham, NY, USA) is the first aspiration thrombectomy device capable of removing intravascular material such as thrombus (including those located in the atrium), tumors, and foreign bodies [21]. It is a vein-to-vein bypass device requiring dual vein employment. Ultrasound guidance during venous access is preferable to avoid arterial puncture, especially when utilizing wide catheters. The immediate availability of Extracorporeal Membrane Oxygenation (ECMO) is always valuable and can be vital in the event of unexpected clot dislodgement and clinical deterioration. It is a robust system that requires operator experience and a cardiovascular setting, including a perfusionist.

AngioJet (Boston Scientific), a system that combines active aspiration and power pulse lytic delivery, has been fallen out of favor due to complications such as bradycardia, hemoptysis, and hemodynamic collapse when used in the central venous system or PE [22]. Indigo Device (Penumbra Inc.) is a mechanical aspiration system that has shown to be less effective due to the small French

size (8-12 French system); however, it can be safely used in pulmonary embolism with segmental or subsegmental branch involvement. Its use in CIT has not been thoroughly investigated [23].

The FlowTriever (Inari Medical Inc., Irvine, CA, USA) is a relatively flexible thrombectomy device that allows moderately comfortable navigation through the right ventricular outflow tract down to segmental pulmonary branches. It is available in various sizes, the biggest being a 24 Fr catheter, making it favorable in patients with extensive thromboembolic burden. In addition, the 20 Fr cannula permits the coaxial navigation of a second 16 Fr sheath that can improve the access into a more subsegmental level. The FLARE study, conducted from 2016 to 2017, demonstrated the safety and effectiveness of the FlowTriever System for acute intermediate-risk PE [24]. Although its use for treating CIT has not been fully assessed, early case reports show promising results. When compared with AngioVac, it appears less rigid and easier to maneuver through the heart.

Summary Case Reports of CIT Treated with FlowTriever

In the literature review, we found 6 case reports of CIT with or without PE [7,13,20,25] the mean age was 72 years (range 44 to 88), and 3 of 6 patients were males. In two patients, Deep Vein Thrombosis (DVT) was confirmed as the origin of the thrombi, the other three patients presented with atrial fibrillation but DVT was not confirmed, and the remaining patient did not have atrial fibrillation nor was DVT confirmed. Contraindication for thrombolysis or surgical thrombectomy included recent surgery (brain and hips), gynecological-obstetric bleeding, recent ischemic stroke, and age. Symptoms varied from lightheadedness, dyspnea, syncope and cardiac arrest. In three patients ECG showed right ventricular strain, and troponin was elevated in four of them (range 0.4-0.91 ng-mL-1). Two patients had measurements of mean pulmonary artery pressure and oxygen saturation pre and post-procedure. Atrial thrombectomy was successful in all patients; however, in a patient with intra-operatory pulseless electrical activity, repeated TTE revealed a new embolus in RA. After PE thrombectomy, two patients had minimal residual PE, and the other four had residual bilateral subsegmental PE. Five patients were discharged alive; the patient who presented with pulseless electrical activity had their code status changed to do not resuscitate and died a few hours later.

Discussion

The prevalence of CIT has been reported around 4% among all patients with acute PE [25]. The overall mortality rate has ranged from 27.1% in 2002 to 12.5% in 2020 [5,26]. The 30-day all-cause mortality predictors included low systolic blood pressure (<90 mm Hg), right ventricular dysfunction, and the simplified Pulmonary Embolism Severity Index [15]. Clinically, CIT should be suspected in patients with heart failure, pre-existing central venous catheters, hypotension with PE, or signs of more severe PE, including right ventricular dysfunction and hemodynamic instability [5]. While there is no consensus about the treatment, the authors' recommendations suggest a multidisciplinary approach with a case-based evaluation to define the more appropriate therapy, including bridging to ECMO. If untreated, the consequences can be catastrophic, with mortality reported as almost a 91% [27]. Patients with intermediate-risk PE (with evidence RV strain on imaging and biochemical markers, without overt hemodynamic instability) systemic thrombolysis prevented hemodynamic decompensation but increased risk of major hemorrhage and stroke when compared with placebo plus heparin [28]. In this group of patients (intermediate-risk PE), catheter-directed thrombolysis was superior to anticoagulation with heparin alone in reversing RV dilation at 24 hours and presented a similar rate in bleeding complications (3 cases in CDT vs. 1 in heparin, P=0.61) [29]. Similar results should be considered when treating patients with CIT and PE. In intermediate-risk PE, with absolute contraindications of thrombolysis, mechanical thrombectomy surges as a therapeutic alternative. The FLARE (FlowTriever Pulmonary Embolectomy Clinical Study), a prospective single-arm (without comparative group) study, reported an acceptable effectiveness profile in patients with PE compared to that observed with catheter-directed thrombolysis with an average right ventricle/left ventricle (RV/LV) ratio reduction of 25.1%, a composite major adverse events rate of 3.8%, and additionally short ICU and hospital stays [24].

When choosing a treatment for CIT and PE, the factors to consider are whether there is a contraindication for thrombolysis, whether the patient's hemodynamics are compromised, the patient's RV/LV ratio, previous failures to respond to conservative therapies, risks of deterioration, and operator experience. Optimizing CIT and PE treatment in patients with contraindication to lysis in some specific situations can be problematic; as an example, a patient with Patent Foramen Oval (PFO) and entrapped clot may benefit from a surgical approach that can remove the clot and treat the PFO.

Proceeding with mechanical thrombectomy requires expertise and versatility to adapt to different available devices in the market. Angiovac (AngioDynamics Inc., Latham, NY, USA), an FDA-

approved aspiration device, has been reported with conflicting results. Major technical concerns include stiffness of the device as well as maneuverability and risk of RV perforation. It requires an extracorporeal circulation setting, including a perfusionist not always available, thus precluding intervention in non-cardiovascular centers. Five cases were reported by Al-Hakim et al., in which technical success, defined as successful removal of some thrombus combined with the reduction of the Miller score index (the extent of thrombus in each part of the pulmonary arteries), was achieved in two of the four patients with massive PE. Four patients died at a mean time of 7.3 days, all having presented with massive PE and one death related to catheter perforation [30]. A small series by Donaldson et al. reported two of three patients with failure to perform embolectomy [31].

The use of the FlowTriever device (Inari Medical, Irvine, CA, USA) for CIT, has been recently described in multiple case reports as a mechanical and suction alternative with all patients having a clinical contraindication for lysis and surgical thrombectomy. The device demonstrates significant versatility to navigate the central and segmental branches, and its large bore (16 Fr, 20 Fr, or 24 Fr) permits clot removal without needing extracorporeal bypass. It is relatively safe if the technical recommendations are followed. There is a valve mechanism designed to avoid a potential air embolism. One of the advantages is that it does not require cardiopulmonary bypass or extracorporeal filtration. As concluded in the FLARE study, percutaneous mechanical thrombectomy with the FlowTriever system appears safe and effective for treatment of acute intermediate PE presenting significant improvement in RV/LV ratio and minimal major bleeding [24].

This review has some limitations. First, there are limited case reports to validate the results of the use of FlowTriever in the treatment of clot in transit with or without PE. Second, the scientific significance is smaller because case reports present level 4 of evidence. Lastly, publication bias may play a role if only successful results are published.

Conclusion

Clot-in-transit should be suspected in all patients with pulmonary embolism and right ventricular dysfunction as it may be an early sign of fatal PE. Therefore, to determine the best treatment, it is essential to assess the risk of PE and CIT using the imaging modalities available, preferably TTE, TEE or CTPA. Currently, anticoagulation therapy is the best treatment option for in situ RiHT and CIT associated with low-risk PE. As hemodynamic instability increases, other therapies such as systemic thrombolysis, surgical embolectomy, ECMO, mechanical thrombectomy, or a combination of these become necessary. Optimal management would depend on the severity of PE, comorbidities and clinical state of the patients, technical resources, and experience of the interventionalist. Under circumstances where there is a contraindication to surgical embolectomy or lytic therapy, percutaneous mechanical thrombectomy can be a promising life-saving alternative. Still, more evidence is needed to determine the most efficacious approach and to reach a consensus on patient selection criteria. The FlowTriever system is a valuable tool for treating CIT and PE, especially in patients with absolute contraindications to thrombolysis. This device stands out against others in the current market because it allows for easy navigation, large clot volume removal, and minimal blood loss. Nonetheless, the operator's experience and skill remain an essential factor to consider when deciding to use FlowTriever to treat CIT or PE.

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