Journal of the Society for Cardiovascular Angiography & Interventions 3 (2024) 102049

JSCAI

The official journal of the Society for Cardiovascular Angiography & Interventions

Original Research

A Safety and Feasibility Single-Arm Study of a Novel Catheter Thrombectomy Device for the Treatment of Pulmonary Embolism (ENGULF)

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ABSTRACT

Background: Despite advances in therapy options, pulmonary embolism (PE) continues to carry a high risk of mortality and morbidity. Currently, therapeutic options are limited with only 2 US Food and Drug Administration-cleared catheter-based embolectomy devices approved for the treatment of intermediate-risk PE. The novel Hēlo PE thrombectomy catheter (Endovascular Engineering, Inc) has a flexible and collapsible funnel with an internal agitator for a dual mechanism of treatment for acute PE. We sought to investigate the safety and feasibility of the novel Hēlo PE thrombectomy catheter in intermediate-risk PE.

Methods: A prospective, single-arm feasibility study evaluating the Hēlo PE catheter was performed in patients presenting with intermediate-risk PE. Patients underwent preprocedural and postprocedural computed tomography angiography. Primary efficacy was the difference in preprocedural to postprocedural right ventricle/left ventricle (RV/LV) ratio. Primary and secondary safety outcomes were all-cause mortality, major life-threatening bleeding, device-related serious adverse events, pulmonary or cardiac injury, and clinical decompensation at 48 hours postprocedure and at 30 days.

Results: A total of 25 patients from 8 centers were consented and included in the analysis. Preprocedural computed tomography angiography revealed an RV/LV ratio of 1.53 ± 0.27. All patients underwent a successful thrombectomy procedure. Postprocedure, the RV/LV ratio was reduced to 1.15 ± 0.18, translating into a 23.2 ± 12.81% decrease from baseline. No patients underwent adjunctive thrombolysis. Two patients had adjunctive catheter-directed embolectomy with an alternative device. Two patients had postprocedural anemia requiring transfusion but did not meet criteria for major life-threatening bleeding by VARC-2 criteria. There were no major adverse events including no deaths, major bleeding, pulmonary injury, or vascular complications at 48 hours or 30 days post procedure.

Conclusions: In this multicenter first-in-human study, use of the Hēlo PE thrombectomy catheter was feasible and safe for the treatment of acute PE.

Abbreviations: CTA, computed tomography angiography; LV, left ventricular; PA, pulmonary artery; PE, pulmonary embolism; RV, right ventricular; SAE, serious adverse event.

Keywords: catheter-directed embolectomy; intermediate-risk; pulmonary embolism.

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https://doi.org/10.1016/j.jscai.2024.102049
Received 6 March 2024; Received in revised form 27 March 2024; Accepted 4 April 2024
Available online 3 May 2024

Introduction

Despite advances in the treatment of pulmonary embolism (PE), there continues to be substantial mortality associated with this disease.[1] In particular, patients with right ventricular (RV) strain on cardiac imaging and myocardial injury based on elevated biomarkers remain at high risk for mortality at 30 days.[2]

In the past decade, there have been notable innovations in the management of intermediate-risk PE with the introduction of minimally invasive catheter-based devices, including directed thrombolytic therapy and mechanical thrombectomy.[3–7] Currently, there are only 2 Food and Drug Administration-cleared catheter-based thrombectomy systems in the United States: the FlowTriever (Inari Medical), a 16F-24F suction-based thrombectomy system, and the Lightning Indigo (Penumbra Inc), an 8F-16F continuous suction-based system. With the large-bore FlowTriever device, there have been case reports of hemodynamic instability due to disruption in the mechanics of the RV and right-sided cardiac valves.[3] Conversely, smaller bore catheter systems that rely only on suction may lack the ability to debulk substantial thrombus and risk significant blood loss.[8]

The Hēlo PE thrombectomy system (Endovascular Engineering, Inc) was designed to address the limitations of currently available suction embolectomy systems. The Hēlo PE catheter is uniquely designed as a 16F delivery catheter incorporated with a collapsible 24F funnel tip, which allows for clot engagement similar to a large-bore system but with a smaller device profile. The device has dual articulations to facilitate navigation in the pulmonary arterial system. Furthermore, an internal agitator within the funnel aids in mechanical disruption and ingestion of thrombus, particularly those that are more fibrotic and organized, to augment and not rely on continuous suction properties alone. The aim of this first-in-human study was to investigate the safety and feasibility of the Hēlo PE thrombectomy catheter for the treatment of patients with intermediate-risk PE.

Table 1. Demographics and baseline characteristics.

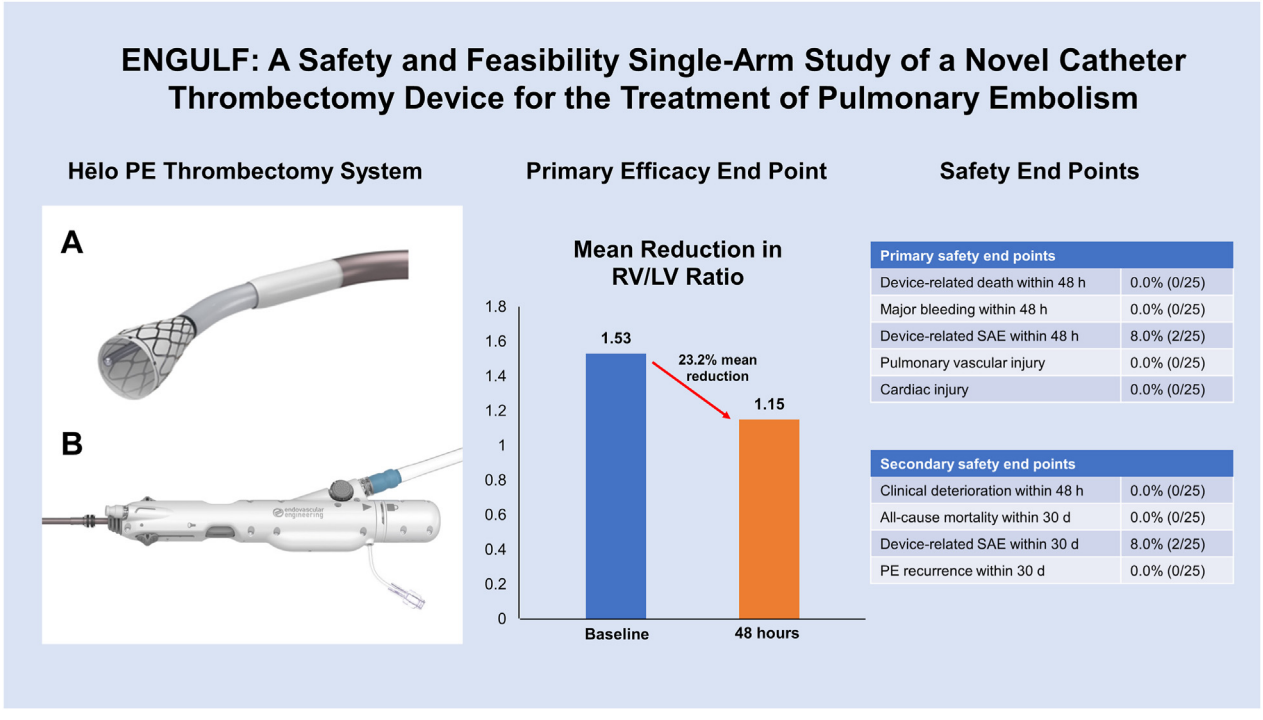
Variable	N = 25
Age, y	66.1 ± 11.97
Male sex	64% (16/25)
Race	
Black or African American	28.0% (7/25)
Other/multiple	12.0% (3/25)
White	60.0% (15/25)
Body mass index, kg/m^2	31.0 ± 4.22
Systolic blood pressure, mm Hg	130.4 ± 20.68
<90 mm Hg	0 (0/25)
Heart rate, bpm	91.1 ± 20.38
SpO_2 >90%	100% (25/25)
Prior deep vein thrombosis	16.0% (4/25)
Prior pulmonary embolism	12.0% (3/25)
Prior hyperlipidemia	48.0% (12/25)
Prior chronic obstructive pulmonary disease	12.0% (3/25)
Creatinine, mg/dL	1.1 ± 0.26
Elevated troponin	88% (21/24)
Elevated B-type natriuretic peptide	80% (20/25)

Values are mean ± SD or % (n/N).

Methods

Study design

The ENGULF study (A Safety and Feasibility Single-Arm Study of a Novel Catheter Thrombectomy Device for the Treatment of Pulmonary Embolism) is a prospective, single-arm study to assess the safety and feasibility of the Hēlo PE thrombectomy system. The study included consecutive patients aged 22 to 90 years presenting with symptoms of an acute, intermediate-risk PE with symptom duration ≤14 days and evidence of proximal PE by computed tomography angiography (CTA) with right ventricular/left ventricular (RV/LV) ratio >0.9. Intermediate-risk PE was defined to include intermediate-low or intermediate-high



Central Illustration.
Primary efficacy and safety end points. (**A**) Illustration of the Hēlo PE thrombectomy system in its "open funnel" configuration. (**B**) Illustration of the integrated handle of the Hēlo PE thrombectomy system Primary efficacy end point showing a 23.2% reduction in RV/LV ratio at 48 hours. Primary and secondary safety end points showing 0% all-cause mortality at 30 days. LV, left ventricle; RV, right ventricle; SAE, serious adverse events.

Table 2. Procedural characteristics.

Characteristic	N = 25
Pulmonary artery pressure, mm Hg	
Baseline	50.5 ± 14.33
Postprocedure	43.1 ± 11.30
Procedure time, min	57.4 ± 21.87
Blood loss, mL	345.6 ± 168.20
Length of hospital stay, d	4.2 ± 2.00
Postprocedural escalation to intensive care	4% (1/25)

Values are mean ± SD or % (n/N).

risk based upon the European Society of Cardiology criteria.[9] Full inclusion and exclusion criteria are included in Supplemental Table S1. Patients meeting all eligibility criteria and providing informed consent were enrolled in the study.

This study was conducted under Food and Drug Administration Investigational Device Exemption approval and oversight. The study protocol was approved at each participating center through a central or local institutional review board and the study was registered on ClinicalTrials.gov (NCT05597891). The trial was conducted in compliance with good clinical practices for medical devices and in accordance with ethical principles based on the Declaration of Helsinki.

Study definitions and end points

The primary efficacy end point was the difference in RV/LV ratio from baseline to 48-hour postprocedure or discharge (whichever was sooner) assessed by CTA. The primary safety end point was the rate of device-related major adverse events at 48 hours, defined by a composite of all-cause mortality, life-threatening, disabling, or major bleeding Valve Academic Research Consortium-2 (VARC-2),[10] and device-related serious adverse events (SAEs). The VARC-2 definitions for bleeding events were used as a prespecified protocol agreed upon by the United States Food and Drug Administration. Device-related SAEs were a composite of clinical deterioration, pulmonary vascular injury, or cardiac injury. Clinical deterioration was defined as unplanned treatment-related events such as endotracheal intubation, unexpected requirement for mechanical ventilation, arterial hypotension (>1 hour or requiring the use of vasopressors) or shock, cardiopulmonary resuscitation, persistent worsening in oxygenation and emergency surgical embolectomy. Additional secondary safety end points were 30-day rates of all-cause mortality, device-related SAEs, and symptomatic recurrence of PE (Supplemental Table S2).

Device and procedures

The Hēlo PE thrombectomy system is a catheter-based mechanical thrombectomy device intended for removal of thrombi from the pulmonary arteries. The single-use system is introduced through a 16F sheath and connects to any commercially available vacuum pump. A funnel at the distal end of the catheter is controlled by the handle and expands to 24F. The compound curves of the catheter and funnel allow for effective navigation and sweeping motion in the pulmonary arteries for clot engagement. The integrated handle is operated manually by the clinician during the procedure and features a side port that allows for flushing, pressure monitoring, and injection of contrast. A motorized agitator wire inserted in the inner lumen of the catheter connects to the handle where a control button activates suction alone or with agitation (Central Illustration). The agitator's shaped tip does not extend distal to the catheter funnel at any point during use and is designed to mechanically disrupt emboli within the distal region of the catheter lumen to assist with clot aspiration. The agitator may be disconnected, removed, and reintroduced through the catheter lumen during use.

Invasive hemodynamics by right heart catheterization were obtained at baseline and postprocedure. Baseline and postprocedural pulmonary angiograms were encouraged but not required by the study protocol. Procedural times were defined as first skin puncture to final access site closure. The Hēlo PE catheter procedural time was defined as time of first introduction of Hēlo PE catheter to time of catheter removal. Procedural success was defined as the ability of the Hēlo thrombectomy system to access the site of the embolus, the ability to position the system and expand the funnel at the site of the embolism, successful aspiration and removal of thrombus and the ability to retrieve and remove the catheter system intact. The use of adjunctive treatments including thrombolytic therapy or other devices within the intraprocedure or postprocedure period was recorded as protocol deviations unless utilized for treatment of a clinical deterioration.

Table 3. Efficacy outcomes.

Outcome	N = 25
Baseline RV/LV ratio	1.53 ± 0.27
48-h RV/LV ratio	1.15 ± 0.18
Reduction in RV/LV ratio from baseline to 48 h	0.38 ± 0.29
Reduction in RV/LV ratio from baseline to 48 h, %	23.2 ± 12.81
Reduction in thrombus burden based upon prethrombectomy and postthrombectomy pulmonary angiograms (n = 12)	83.8 ± 22.4

Values are mean ± SD.
LV, left ventricular; RV, right ventricular.

Clinical data collection

Patient presentation and demographics were collected at baseline, procedure characteristics during the procedure, and outcomes were collected at 48 ± 24 hours or at discharge (whichever was sooner) and at 30 days postprocedure. Echocardiographic information was collected when performed as standard of care and site interpretation of RV dilation, RV hypokinesis, septal flattening, RV systolic pressure, tricuspid annular plane systolic excursion score, clot visualized in the heart, and LV ejection fraction was recorded.

A protocol required CTA was performed at baseline and at 48 hours (± 24 hours) or at the time of discharge (whichever came first). All CTA were independently reviewed by the Vascular Ultrasound Core Laboratory (VasCore, Massachusetts General Hospital, Boston, MA) to assess the RV/LV ratio. Thrombus burden was assessed quantitatively using and reported based on the modified Miller score as described in previous literature.[11,12]

All available baseline and postprocedure thrombectomy pulmonary angiograms were acquired using a standard protocol. An independent angiographic core laboratory (Yale Cardiovascular Research Group, New Haven, CT) reviewed and analyzed matched angiograms (Supplemental Table S3). Thrombus burden was assessed at baseline and after thrombectomy using manual planimetry of the visualized radiographic thrombus area (Medis, QXAngio version 7.3). Angiographic thrombus was defined as a discrete intraluminal filling defect with defined borders with or without associated contrast staining. Only arteries that were targeted and instrumented by the device were analyzed by angiographic thrombus burden reduction. The reduction in thrombus area was defined as the difference in baseline to postprocedure thrombus area. Angiograms were analyzed for evidence of intraprocedural and postprocedural complications including distal embolization, dissection, vessel spasm, and/or perforation.

Statistical analysis

Descriptive statistics were calculated for baseline and procedural characteristics, and all primary and secondary end points. Categorical variables are summarized as counts and percentages. Continuous variables are summarized as means and standard deviation. Descriptive analysis was performed using Microsoft Excel (Microsoft Corporation).

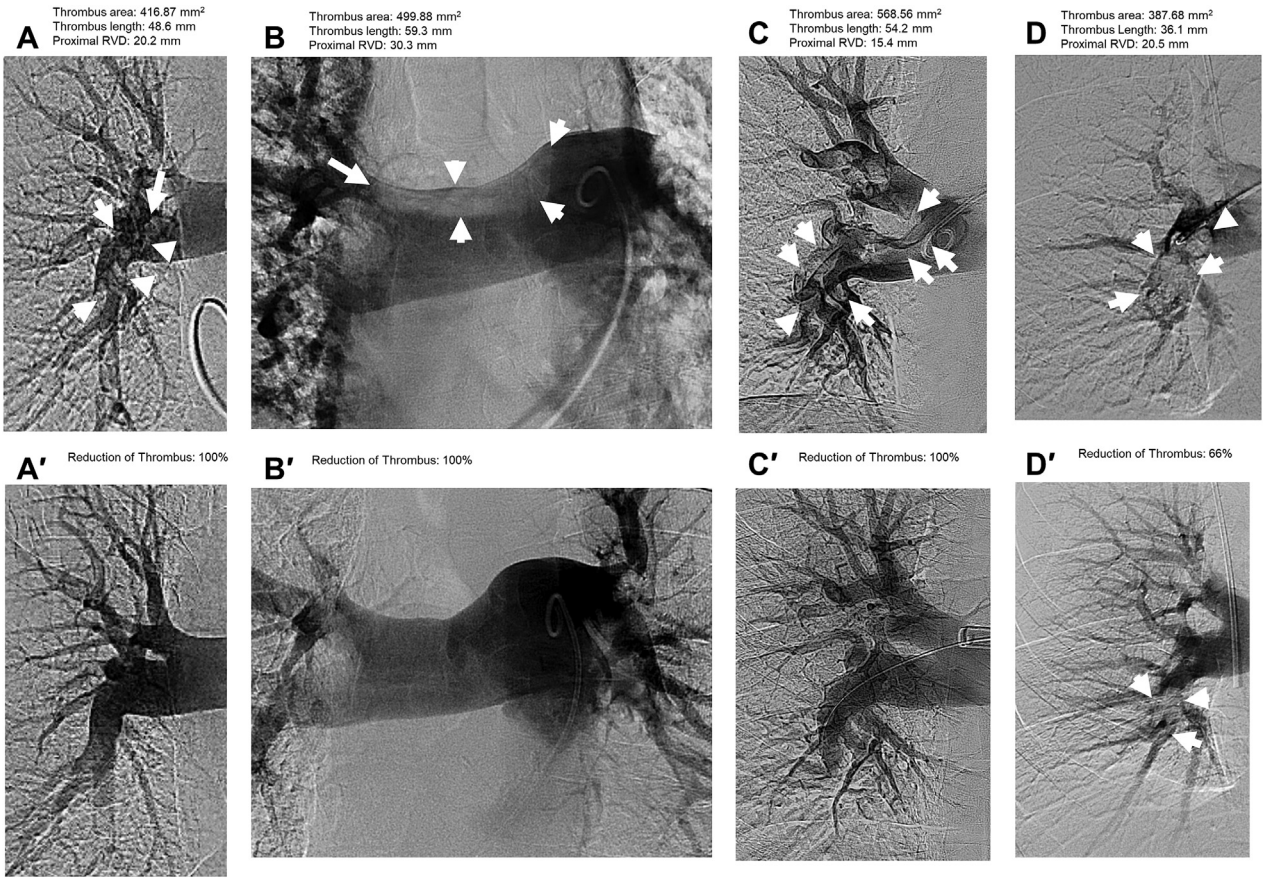


Figure 1.
Representative examples of angiograms before and after the use of the Hēlo PE thrombectomy system. (**A**) Preprocedure: thrombus located in the right interlobar pulmonary artery with an area of 416.87 mm^2 and length of 48.6 mm; proximal RVD 20.2 mm. (**A′**) Postprocedure. Thrombus reduction of 100%. (**B**) Preprocedure: thrombus located in the saddle with an area of 499.88 mm^2 and length of 59.3 mm; proximal RVD 30.3 mm. (**B′**) Postprocedure. Thrombus reduction of 100%. (**C**) Preprocedure: thrombus located in the right interlobar pulmonary artery with an area of 568.56 mm^2 and length of 54.2 mm; proximal RVD 15.4 mm. (**C′**) Postprocedure. Thrombus reduction of 100%. (**D**) Preprocedure: thrombus located in the right interlobar pulmonary artery with an area of 387.68 mm^2 and length of 36.1 mm; proximal RVD 20.5 mm. (**D′**) Postprocedure. Thrombus reduction of 66%. Residual thrombus area 130.24 mm^2 and length of 19.5 mm. RVD, reference vessel diameter.

Results

A total of 25 patients were enrolled at 8 sites across the United States. The mean age of the population was 66 ± 12 years, 64% were male, and 60% were white. The mean systolic blood pressure at enrollment was 130 ± 21 mm Hg, and none of these patients had systolic blood pressure ≤90 mm Hg. Patient demographics and baseline characteristics are reported in Table 1. Of the patients, 76% had bilateral and 24% had unilateral thrombus. The majority of patients received conscious sedation and all had femoral access. The mean procedure time from device insertion to removal was 57 ± 21.87 minutes. All patients completed the procedure successfully. Two patients underwent adjunctive thrombectomy with the FlowTriever system for residual thrombus and no patient received adjunctive thrombolytic therapy. The mean length of stay was 4.2 ± 2.0 days, and only 1 patient required an escalation of care postprocedure to the intensive care unit (Table 2).

Efficacy outcomes

The mean pretreatment RV/LV ratio was 1.53 ± 0.27, and the mean RV/LV ratio at 48 hours was 1.15 ± 0.18, resulting in a mean reduction of 0.38 ± 0.29 or a 23.2 ± 12.81% reduction (Table 3). The right heart catheterization mean pulmonary artery (PA) systolic pressure was 50.5 ± 14.3 mm Hg preprocedure and 43.1 ± 11.3 mm Hg postprocedure. The modified Miller score was 15.65 ± 0.27 at baseline and 13.09 ± 2.66 at 48 hours, resulting in a reduction of 2.57 ± 2.41 or 16.5 ± 15.26%. Paired pre and post angiograms were available in 12 patients (48%) and in pulmonary arteries targeted and instrumented by the Hēlo thrombectomy system, there was a thrombus burden reduction of 83.8 ± 22.4% (Figure 1).

Safety outcomes

At 48 hours, there were no deaths, VARC2 major bleeds, cardiac or pulmonary injuries, or clinical deteriorations. Eight percent of patients had device-related SAEs reported (Central Illustration) as procedure-related blood loss or anemia requiring transfusion but neither met criteria for VARC-2 major life-threatening bleeding.

Discussion

This prospective first-in-human study demonstrates the safety and feasibility of the Hēlo PE thrombectomy catheter in the treatment of patients with acute intermediate-risk PE. The Hēlo PE thrombectomy catheter was safe, and successfully reduced the RV/LV ratio (–0.38, 23.4%) and reduced the angiographic thrombus area burden.

The Hēlo PE thrombectomy catheter system is unique in its ability to deliver an expandable 24F funnel to the PA in its compressed

configuration through a 16F sheath, allowing full expansion once it reaches its target location. The smaller access size offers significant benefits including, lower bleeding and vascular complications, improved navigation from the femoral vein to the PA, and a lower likelihood of hemodynamic instability during the procedure.[3] Beyond its smaller access size, the unique design of the Hēlo PE thrombectomy catheter is its flexible expandable distal funnel combined with the rotating agitator that augments the continuous suction used for thrombectomy to allow for better mechanical disruption and removal of larger thrombus volumes.

This first-in-human feasibility study demonstrates proof of concept of the Hēlo PE catheter and these initial results suggest at least similar thrombus removal compared to other thrombectomy devices. The reduction in RV/LV ratio of –23.2 ± 12.8% at 48 hours is similar to currently approved devices (25.1% with FlowTriever and 27.3% with Indigo).[7,8] Furthermore, the ENGULF study included 1 of the first core-lab adjudicated pulmonary angiographic analyses to objectively and prospectively measure thrombus burden reduction in arteries targeted for treatment with the device. This showed greater than 80% reduction in arteries specifically targeted by the device. From an overall thrombus reduction perspective, the use of the device was associated with a 16.5% decrease in the modified Miller score which is in line with other thrombectomy devices.[7]

Use of the Hēlo PE thrombectomy device was safe, with no deaths, clinical deteriorations, PE recurrence, pulmonary injuries, or cardiac injuries reported within 30 days of the procedure. Two patients had device-related blood loss requiring transfusion; however, this did not meet the a priori VARC-2 major bleeding definition. To further mitigate intraprocedural bleeding, additional device iterations are underway to improve the catheter performance based on investigator feedback, including an audible flow indicator and clot catcher that emits an auditory signal to alert the operator of unobstructed blood flow during suction use, indicating that the clot has either been removed and/or the device should be repositioned. There were 2 patients who underwent adjunctive thrombectomy with the FlowTriever system. The decisions to utilize adjunctive devices were made to further treat residual thrombus but not due to hemodynamic or intraprocedural instability.

Limitations

This early feasibility study is a first-in-human experience and is not designed to assess efficacy or to compare outcomes to other devices.

The protocol mandating pre and postdevice pulmonary angiography was changed after study initiation due to investigator concerns about overall contrast utilization related to both the procedure and 2 mandatory CT scans, thus limiting the available data for core-lab adjudicated thrombus reduction analysis and may affect the interpretability of these results.

The study was designed to evaluate device performance and procedural 30-day outcomes and did not assess long-term clinical outcomes. Furthermore, the device was evaluated in intermediate-risk PE patients, and the role of this device in high-risk PE has not been determined.

Conclusions

ENGULF is the first prospective, feasibility study of the Hēlo PE thrombectomy device system for the treatment of patients with intermediate-risk PE. This study demonstrated that the device reduced the RV/LV ratio by 23.2% and that there were no major procedural or 30-day complications. A prospective approval study is underway for the treatment of acute PE (NCT05597891).

Peer review statement

Editor-in-Chief Alexandra J. Lansky had no involvement in the peer review of this article and had no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Deputy Editor Suzanne J. Baron.

Declaration of competing interest

Taisei Kobayashi reports institutional research funding from Inari Medical, Boston Scientific, and Endovascular Engineering. Eric A. Secemsky: consultant for Abbott Vascular, Boston Scientific, Cordis, Endovascular Engineering, Medtronic, and Philips; equity in Endovascular Engineering. Julie C. Bulman: consultant – Argon Medical Devices and Endovascular Engineering. Mohannad Bisharat: consultant – Abbott, Inari, Cordis, Bard BD, Philips, Argon, and Medtronic. D. Christopher Metzger: National PI or Co-PI – C-GUARDIANS (InspireMD) and PERFORMANCE III (Contego Medical); speaking and proctor honoraria – Abbott Vascular; advisory board – Boston Scientific; speaking honoraria – Penumbra. Ido Weinberg: VasCore received institutional research support from Endovascular Engineering as the vascular ultrasound core laboratory for the ENGULF study. Venu Vadlamudi: consultant – Portola Medical, Baylis Medical Technologies, Inventure, Endovascular Engineering, Inari Medical, Penumbra, MIVI Neuroscience, Stryker Neurovascular, Medtronic Neurovascular; equity in Endovascular Engineering. William H. Matthai Jr: Research support – Inari Medical. Alexandra J. Lansky: institutional research support – Endovascular Engineering. Jay Giri: Institutional research support from Inari Medical, Boston Scientific, and Endovascular Engineering. Jay Giri reports consulting fees from Inari Medical and Boston Scientific and equity in Endovascular Engineering. Andrew J. Klein, Salomao Faintuch, Jeffrey L. Weinstein, Yonatan Bitton-Faiwiszewski, Russell D. Rosenberg, Amr Saleh, and Ecaterina Cristea report no financial interests.

Funding sources

The ENGULF study was sponsored by Endovascular Engineering, Inc.

Ethics statement and patient consent

This study was conducted under US Food and Drug Administration Investigational Device Exemption approval and oversight. The study protocol was approved at each participating center through a central or local institutional review board and the study was registered on ClinicalTrials.gov (NCT05597891). The trial was conducted in compliance with good clinical practices for medical devices and in accordance with ethical principles based on the Declaration of Helsinki. All patients provided informed consent.

Supplementary material

To access the supplementary material accompanying this article, visit the online version of the *Journal of the Society for Cardiovascular Angiography & Interventions* at 10.1016/j.jscai.2024.102049.

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