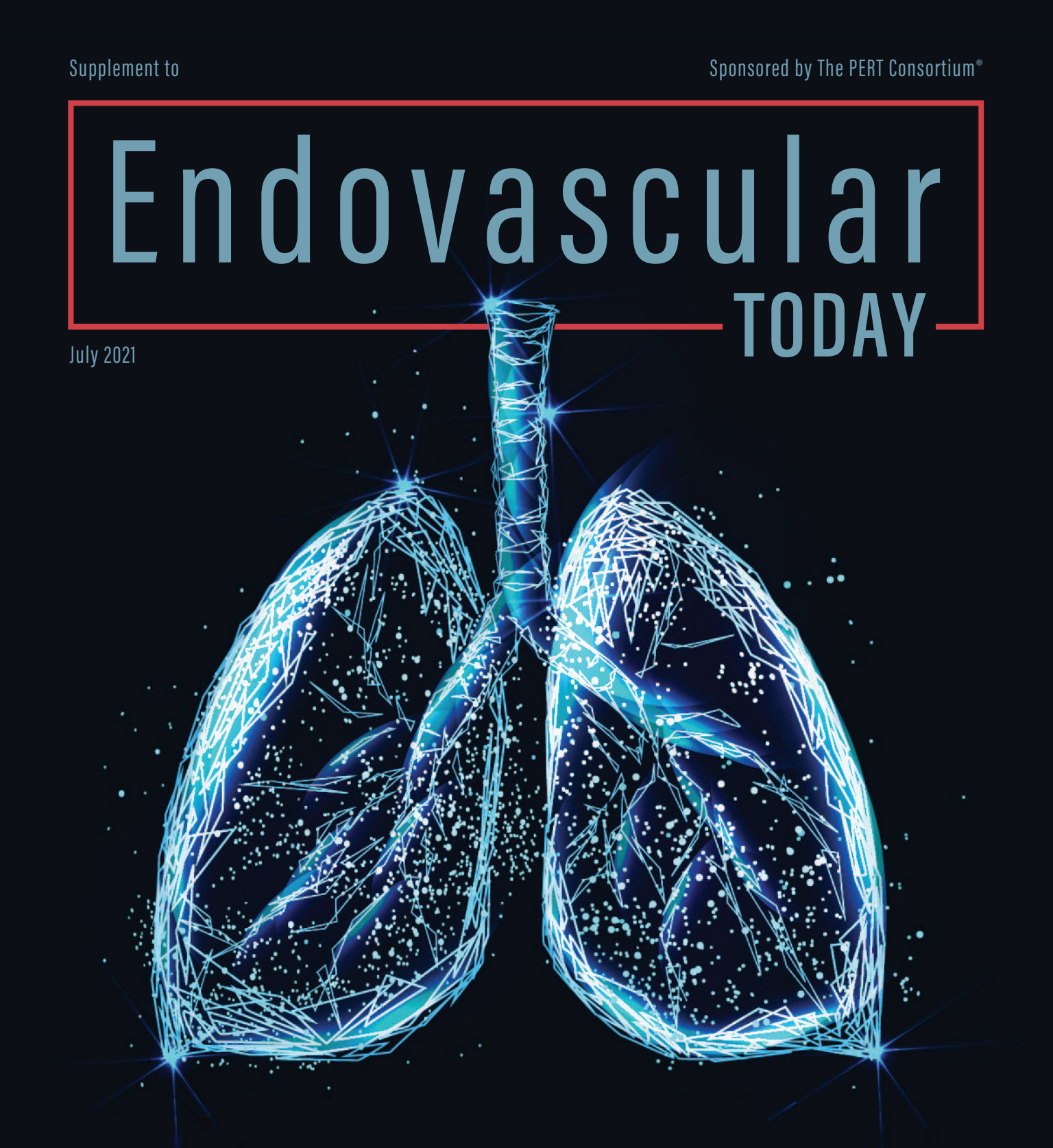
Supplement to

Sponsored by The PERT Consortium®

Endovascular TODAY

July 2021



BRIDGING THE DATA GAP IN PULMONARY EMBOLISM:

Innovative Initiatives From The PERT Consortium®

PERT CONSORTIUM®

BRIDGING THE DATA GAP IN PULMONARY EMBOLISM:

Innovative Initiatives From The PERT Consortium®

TABLE OF CONTENTS

ADVANCING PE CARE, PROMOTING RESEARCH

The National Pulmonary Embolism Response Team (PERT) Consortium® is once again honored to host this supplement of *Endovascular Today*, entitled Bridging the Data Gap in Pulmonary Embolism: Innovative Initiatives From The PERT Consortium®. The National PERT Consortium® is a 501(c)(3) organization founded in 2015 and based in Massachusetts. As implied by the moniker in our name ("Pulmonary Embolism Response Team"), we are dedicated to the team-based treatment of pulmonary embolism (PE). We are a multinational organization and strive to be the vehicle of change to improve the care and survival of patients with PE. The Consortium is comprised of a "coalition of the willing": pulmonologists, emergency physicians, cardiologists, surgeons, radiologists, hospitalists, pharmacists, hematologists, advanced practice providers, and others working collaboratively in the care of patients with PE at our member institutions.

The formal mission of the Consortium is to facilitate the exchange of ideas and information related to the care of patients with PE and advance the science of PE care by performing research, developing advanced treatment protocols, and educating clinicians and community members. The purpose of The PERT Consortium® aligns with our mission—to serve the general public by undertaking activities to advance PE care and promote research. Specifically, the Consortium aims to:

- Promote the adoption of the PERT model in all health care institutions to ensure the prompt diagnosis and treatment of PE
- Expand the current body of scientific evidence regarding the diagnosis and treatment of PE through the promotion and funding of scientific endeavors
- Educate the general public and health care professionals regarding PE diagnosis, treatment, and care

As we reflect on our accomplishments to date, The PERT Consortium® Quality Assurance database is currently the largest PE-centered registry with almost 6,000 patients. Using the backbone of the registry, we have created a robust research infrastructure to begin meaningful clinical projects. Membership in the Consortium has continued to grow, as have educational offerings, clinically oriented initiatives, and publications. Our multiple active committees and projects offer vast opportunities for membership engagement and leadership, both nationally and abroad.

The supplement to *Endovascular Today* highlights a number of our endeavors and program initiatives over this past year, all of which demonstrate our ongoing vision for comprehensive PE care. We have included a thorough review of the challenges encountered during interhospital transfers, a template for management of transitions of PE care (in-hospital, during discharge, and follow-up care), and an update highlighting the promise of our PE registry. Additional contributions describe the participation/cosponsorship of the Consortium in a landmark transatlantic clinical research trial (HI-PEITHO) and our head-on approach to tackling venous thromboembolism during COVID-19.

Finally, our 7th Annual Scientific Symposium, "What Is Known and What We Need to Know: A State-of-the-Art Scientific Update," will be held in Boston on October 15-16, 2021. This year's meeting will be hybrid for those who are unable to attend in person. In 2020, our virtual meeting had more than 1,000 attendees from 38 countries. We are excited to "see" our colleagues at this year's meeting to continue to enhance, expand, and share our knowledge on PE. Please visit www.pertconsortium.org to register and learn more about The PERT Consortium®.

Most importantly, we would like to recognize and thank our industry sponsors for their continued support of The PERT Consortium® and its underlying mission and specifically for their contributions that enable us to produce this informative supplement.

Please enjoy and contact us with further questions as needed. ■

Brent Keeling, MD
President-Elect, PERT Consortium®
Board of Directors

Soophia Naydenov, MD
Past Education Committee Head

The HI-PEITHO Study of Ultrasound-Facilitated, Catheter-Directed Thrombolysis Versus Anticoagulation

The first large randomized controlled trial of an intervention versus anticoagulation for patients with acute intermediate–high-risk pulmonary embolism.

By Stavros V. Konstantinides, MD; Michael R. Jaff, DO, FACP, FACC; and Kenneth Rosenfield, MD, MHCDS

Intermediate–high-risk pulmonary embolism (PE) is a challenging condition to treat for a variety of reasons, including the heterogeneity with which PE presents, the high associated rates of morbidity and mortality, the need for a truly multidisciplinary approach to treatment planning and management, and the lack of level 1 evidence guiding treatment.[1] Further complicating management of acute intermediate–high-risk PE is that there is no clear consensus on which treatment options should be recommended as first-line therapy.[1] Physicians may treat patients presenting with intermediate–high-risk PE medically, without intervention (ie, with anticoagulants alone), or more aggressively, with an interventional approach (eg, surgical embolectomy, systemic thrombolytic therapy, catheter-directed thrombolysis [CDT], or other advanced endovascular intervention).

Part of the reason for lack of consensus can be attributed to the paucity of randomized controlled trials (RCTs) comparing interventional approaches with systemic anticoagulation, the current "standard of care" for patients with intermediate–high-risk PE. There are some notable, well-designed RCTs comparing reperfusion therapies to anticoagulation across all intermediate-risk patients, such as the PEITHO trial testing the thrombolytic agent tenecteplase plus heparin versus heparin alone; however, these trials did not focus on intermediate–high-risk patients because they predated the newer stratification paradigm for this group of patients.[2] Although studies have been published suggesting that anticoagulation alone may not be sufficient for intermediate–high-risk patients, they have largely been observational in nature.[3] Without large head-to-head RCTs comparing interventions with the standard of care for patients with intermediate–high-risk PE, decisions as to whether to pursue advanced treatment options will continue to be based on existing observational data, the patient's clinical presentation, physician experience and preference, and cost.

A thoroughly studied and frequently performed interventional treatment for patients with intermediate-risk PE, with a large volume of published clinical data to date, is ultrasound-facilitated CDT (USCDT), in which CDT is augmented with ultrasound energy to increase the dispersion of the chosen lytic agent into the thrombus. In the only existing RCT comparing an intervention (in this case, USCDT) to anticoagulation alone, USCDT was associated with significantly improved clinical outcomes with no increase in bleeding risk. The study was relatively small and included a broad spectrum of severity within the intermediate-risk patient group (ie, both intermediate–low- and intermediate–high-risk PE).[4] To address this gap in evidence, the Higher-Risk Pulmonary Embolism Thrombolysis (HI-PEITHO) study was recently launched.

WHAT IS THE HI-PEITHO STUDY?

HI-PEITHO (NCT04790370) is a prospective, multicenter RCT comparing USCDT and best medical therapy (BMT; systemic anticoagulation) with BMT alone in patients with acute intermediate–high-risk PE. The primary objective of HI-PEITHO is to assess whether USCDT and anticoagulation are associated with a significant reduction in the composite endpoint of PE-related mortality, cardiorespiratory decompensation or collapse, and/or nonfatal PE recurrence within 7 days of USCDT treatment. The secondary objectives of the trial are to (1) gather additional data, which will add to the existing evidence on the treatment and clinical outcomes of acute intermediate–high-risk PE, and (2) contribute controlled data on catheter-based interventions to the existing evidence base. HI-PEITHO is a joint research study

between The Pulmonary Embolism Response Team (PERT) Consortium®, the University of Mainz and European PEITHO network, and Boston Scientific Corporation.

Study Design

HI-PEITHO is a randomized (1:1), controlled, open-label, multicenter, adaptive-design, parallel-group comparison clinical trial comparing USCDT (EkoSonic endovascular system, Boston Scientific Corporation) plus systemic anticoagulation with systemic anticoagulation alone in patients with acute intermediate–high-risk PE (Figure 1). The null hypothesis (H0) of the study, which has been approved by local site institutional review boards, is that neither treatment is superior to the other in terms of clinical and safety outcomes. The alternative hypothesis (H1) assumes that USCDT will be superior to anticoagulation alone in terms of efficacy without compromising safety (ie, without an increase in major bleeding). The study uses blinded adjudication of the primary composite outcome. The HI-PEITHO trial will include up to 65 sites across the United States and Europe. Target enrollment is 406 to 544 patients, which is based on a statistically robust adaptive trial design including a prespecified planned interim analysis. The trial will follow all rules of clinical research as set forth in the Declaration of Helsinki.

Patients who meet all inclusion and no exclusion criteria will be enrolled in the study upon receipt of written informed consent. Given the urgency for treatment, randomization and initiation of assigned therapy should occur as soon as possible after confirmation of diagnosis. For patients assigned to the USCDT arm, it is recommended to begin the intervention within 2 hours of randomization. Patients will be followed up to 12 months, with follow-up study visits at 7 days, 30 days, 6 months, and 12 months postrandomization. Patients meeting the primary endpoint criteria for cardiorespiratory collapse or decompensation are eligible for rescue reperfusion treatment (such as systemic thrombolysis or CDT). Arbitrary crossover to the intervention (USCDT) arm or use of any other reperfusion treatment after randomization in the absence of primary endpoint criteria or of appropriate justification and documentation of the medical need will be strongly discouraged and considered a protocol deviation.

Patient Inclusion and Exclusion Criteria

Key patient inclusion and exclusion criteria are outlined in Table 1. Given the current context in which HI-PEITHO is being launched, it is important to note that patients who test positive for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection are eligible for the trial if the enrolling investigator believes that the intermediate–high-risk PE is the dominant culprit for the clinical presentation and the qualifying inclusion and exclusion criteria.

Primary Endpoint

The primary endpoint in HI-PEITHO is defined as a composite of PE-related mortality, cardiorespiratory decompensation or collapse, and/or nonfatal PE recurrence within 7 days of initial USCDT treatment. Cardiorespiratory collapse or decompensation is defined as one or more of the following: cardiac arrest or need for cardiopulmonary resuscitation, signs of shock (new-onset arterial hypotension with end-organ perfusion), placement on extracorporeal membrane oxygenation, intubation or noninvasive mechanical ventilation, and/or National Early Warning Score (NEWS) ≥ 9 (Figure 2).[5,6] All outcome components will be adjudicated by an independent clinical events committee, using a blinded adjudication process.

Notably, the primary endpoint of the HI-PEITHO study is a combination of established measures and innovative clinical assessment methods. The NEWS score in particular is a standardized clinical tool for anticipating, detecting, and/or responding to a patient's deterioration and collapse. The peer-reviewed and validated NEWS scoring methodology considers respiratory rate, oxygen saturation, whether supplemental oxygen is required, body temperature, systolic blood pressure, heart rate, and level of consciousness. This comprehensive evaluation has been shown to have greater prognostic accuracy compared to each of its individual

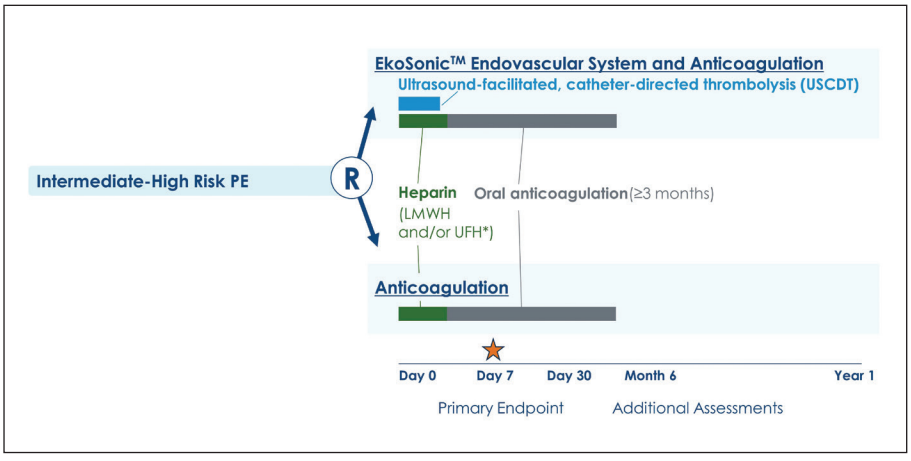
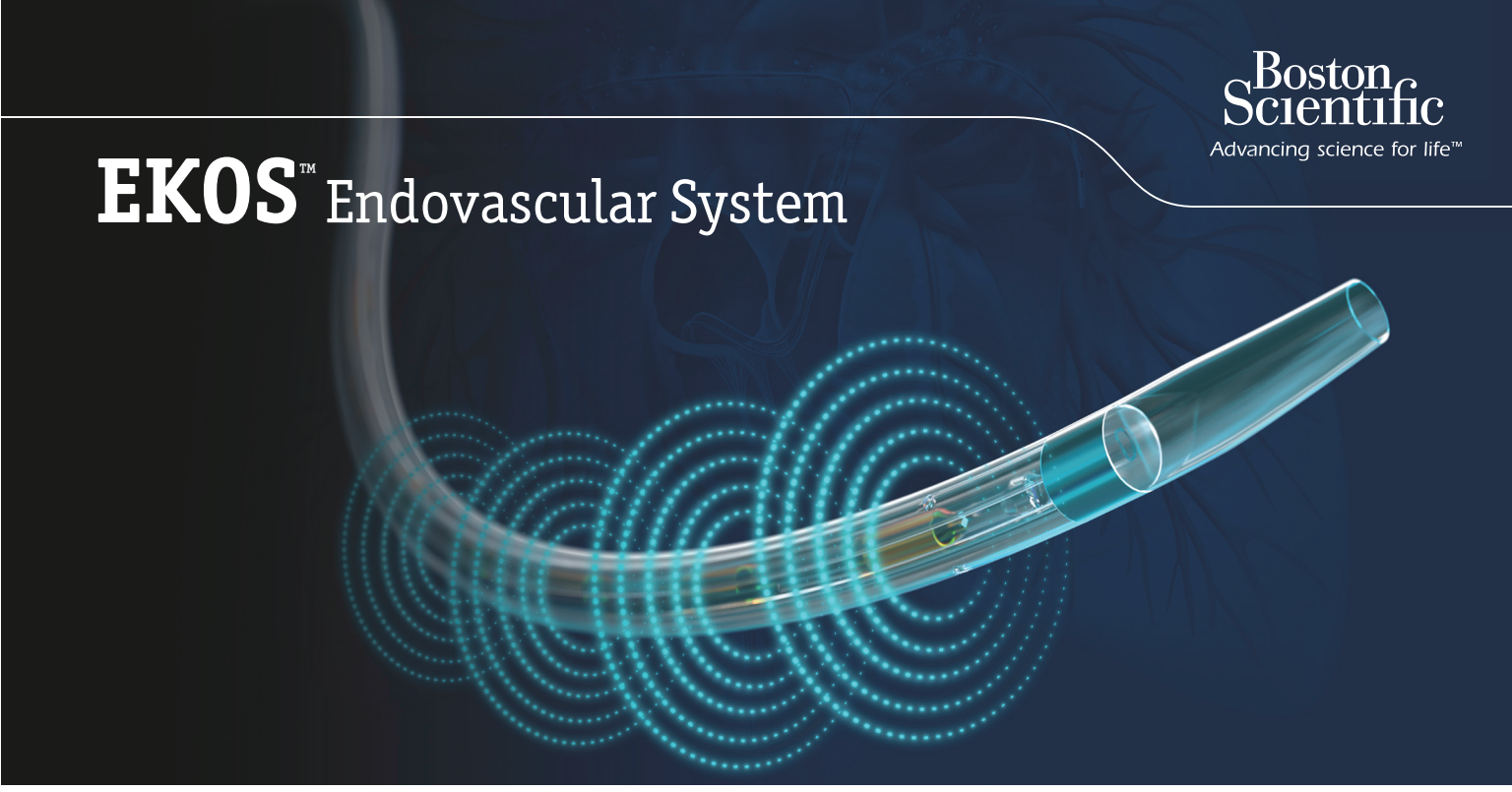


Figure 1. The HI-PEITHO study flow. LMWH, low-molecular-weight heparin; UFH, unfractionated heparin.

Boston Scientific
Advancing science for life™

EKOS™ Endovascular System



A Decade Committed to Clinical Advancement

2014
ULTIMA[1]
Prospective, Multi-Center, Randomized, Controlled Trial

Patients
59 patients with acute submassive PE

2015
SEATTLE II[2]
Prospective, Multi-Center, Single-Armed Trial

Patients
150 patients with acute submassive and massive PE

2018
OPTALYSE[3]
Prospective, Multi-Center, Parallel-Group Trial

Patients
101 patients with acute submassive PE

2021
KNOCOUT[4]
Patient Registry

Patients
1,000 retrospective, 500 prospective

2024
HI-PEITHO[5]
Prospective, Multi-Center, Randomized, Controlled Trial

Patients
406-544 patients with acute intermediate-high risk PE

As the first interventional treatment for patients with acute massive and submassive Pulmonary Embolism (PE), **no other device has been studied as much or for as long as EKOS.**

1. Kucher N et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. Circulation. 2014;129:479-486
2. Piazza G et al. A Prospective, Single-Arm, Multicenter Trial of Ultrasound-Facilitated, Catheter-Directed, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism. The SEATTLE II Study. *J Amer Coll Cardiol: Cardiovasc Interventions* 2015; 8(10):1382-1392.
3. Tapson V et al. A randomized trial of the optimum duration of acoustic pulse thrombolysis procedure in acute intermediate-risk pulmonary embolism. *JACC: Cardiovascular Interventions* 2018; 11(14):1401-1410.
4. An International Pulmonary Embolism Registry Using EKOS (KNOCOUT PE). https://clinicaltrials.gov/ct2/show/NCT03426124?term=KNOCOUT&draw=1&rank=1
5. Ultrasound-facilitated, Catheter-directed, Thrombolysis in Intermediate-high Risk Pulmonary Embolism (HI-PEITHO). https://clinicaltrials.gov/ct2/show/NCT04790370?term=HI-PEITHO&draw=2&rank=1

EkoSonic™ Endovascular System
Indications, Safety and Warnings: CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Directions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions. **INDICATIONS FOR USE:** The EkoSonic Endovascular System is indicated for the: Ultrasound facilitated, controlled and selective infusion of physician-specified fluids, including thrombolytics, into the vasculature for the treatment of pulmonary embolism.•Infusion of solutions into the pulmonary arteries. • Controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature. All therapeutic agents utilized with the EkoSonic Endovascular System should be fully prepared and used according to the instruction for use of the specific therapeutic agent. **CONTRAINDICATIONS:** Not designed for peripheral vasculature dilation purposes. • This system is contraindicated when, in the medical judgment of the physician, such a procedure may compromise the patient's condition. **POTENTIAL COMPLICATIONS:**Vessel perforation or rupture • Distal embolization of blood clots • Vessel spasm • Hemorrhage • Hematoma • Pain and tenderness • Sepsis/Infection • Thrombophlebitis • Tricuspid and pulmonic valve damage • Pulmonary infarct due to tip migration and spontaneous wedging, air embolism, and/or thromboembolism • Right bundle branch block and complete heart block • Intimal disruption • Arterial dissection • Vascular thrombosis • Drug reactions • Allergic reaction to contrast medium • Arteriovenous fistula • Thromboembolic episodes • Amputation • Pneumothorax • Perforation of the pulmonary artery. • Cardiac Arrhythmias – most frequently occurring during placement, removal or following displacement into the right ventricle. PI-726201-AA

TABLE 1. KEY INCLUSION AND EXCLUSION CRITERIA FOR THE HI-PEITHO STUDY

Inclusion Criteria	Exclusion Criteria
▪ Age 18-80 y ▪ A diagnosis of objectively confirmed acute PE ▪ RV/LV ratio ≥ 1.0 ▪ Positive troponin levels (above the upper limit of normal) ▪ Elevated risk of early death/ hemodynamic collapse, defined as exhibiting at least two of the following: – Systolic blood pressure ≤ 110 mm Hg for ≥ 15 min – Respiratory rate > 20/min or SpO_2 < 90% at rest (room air) – Heart rate ≥ 100 bpm, not due to hypovolemia, arrhythmia, or sepsis	▪ Prolonged hemodynamic instability ▪ Need for ICU admission for reasons other than the index PE episode ▪ Body temperature > 39 °C/102.2 °F ▪ Logistical factors limiting the timely availability of interventional procedures to treat acute PE ▪ PE symptom duration > 14 d ▪ Active bleeding ▪ History of intracranial or intraocular bleeding ▪ Stroke or transient ischemic attack within the past 6 mo or previous stroke at any time if associated with permanent disability ▪ Central nervous system neoplasm or metastatic cancer ▪ Major neurologic, ophthalmologic, abdominal, cardiac, thoracic, vascular, or orthopedic surgery or trauma within 3 wk of acute PE index episode ▪ Patients who have received a once-daily therapeutic dose of LMWH or a therapeutic dose of fondaparinux within 24 h prior to randomization ▪ Patients who have received one of the direct oral anticoagulants (apixaban or rivaroxaban) within 12 h prior to randomization

Abbreviations: ICU, intensive care unit; LMWH, low-molecular-weight heparin; PE, pulmonary embolism; RV/LV, right/left ventricular end-diastolic diameter; SpO_2, arterial oxygen saturation.

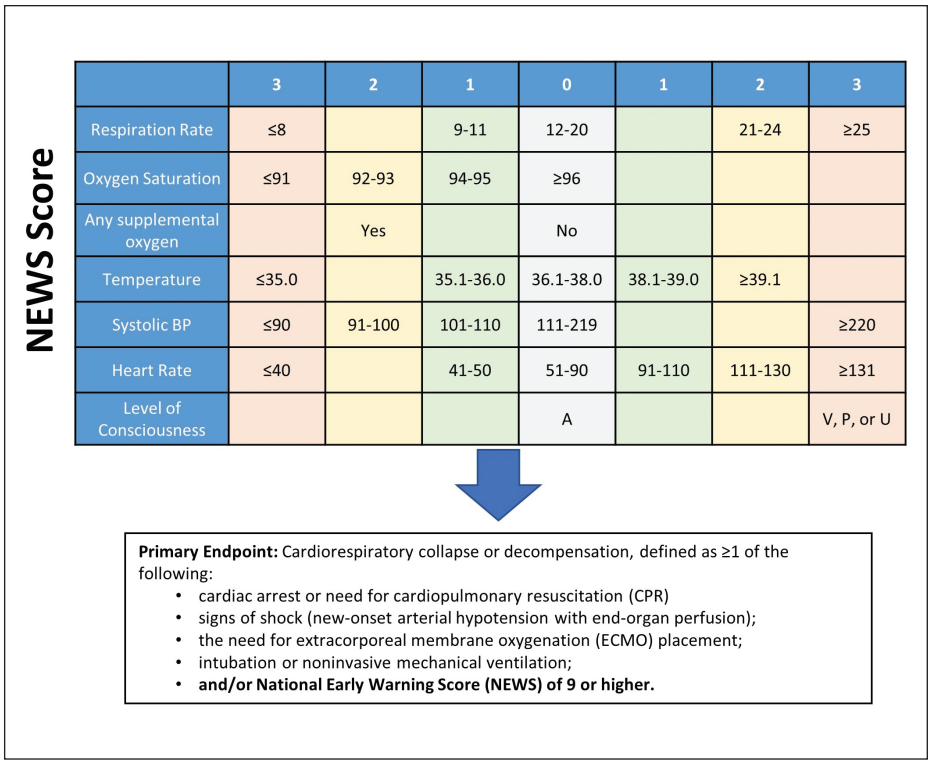


Figure 2. The NEWS score paradigm and composite primary endpoint for HI-PEITHO. NEWS score reproduced from Royal College of Physicians. National Early Warning Score: standardizing the assessment of acute illness severity in the NHS. Report of a working party. London: Royal College of Physicians; 2012.

components.[7] NEWS has been validated in several different clinical settings internationally. When implemented correctly, it has been shown in several single- and multicenter studies to quickly and accurately determine which patients are at highest risk for cardiac arrest, intensive care unit (ICU) admission, and/or death within 24 hours of assessment.[6,8,9]

Key Additional Assessments

In addition to the primary endpoint detailed previously, several other key measures are being collected as part of the HI-PEITHO trial. These include the individual primary outcome components, GUSTO (Global Utilization of Strategies to Open Occluded Coronary Arteries) major (moderate and severe) bleeding within 7 days of treatment, International Society on Thrombosis and Haemostasis

major bleeding, ischemic or hemorrhagic stroke within 7 and 30 days posttreatment, all-cause mortality, symptomatic PE recurrence within 30 days and 6 months, change from baseline right ventricular/left ventricular end-diastolic diameter ratio on echocardiography at 6 months, chronic thromboembolic pulmonary hypertension diagnosis within 12 months, health economic assessments, functional status and quality-of-life measures, and cardiopulmonary exercise testing parameters at select sites.

WHAT IS THE POTENTIAL IMPACT OF HI-PEITHO?

Currently, the existing evidence on intervention beyond BMT for PE suggests that acute intermediate-risk PE remains potentially life-threatening if treated with anticoagulants alone. Although early reperfusion with full-dose intravenous thrombolysis has the ability to improve hemodynamics and, in turn, early clinical outcomes, it is not routinely recommended as first-line therapy because it is associated with a high major (particularly intracranial) bleeding risk. However, newer patient stratification paradigms (classifying patients as either intermediate-low or intermediate-high risk) and USCDT dosing protocols like those tested in the OPTALYSE trial strongly suggest that lower lytic doses with shorter durations of infusion can achieve comparable clinical and better safety outcomes in many patients with acute intermediate–high-risk PE.[10] Consequently, many patients in this risk category may currently be deprived of potentially life-saving therapeutic options.

The goal of HI-PEITHO is to close this evidence gap and provide high-quality clinical data capable of informing future guidelines on the treatment of patients with acute intermediate–high-risk PE. HI-PEITHO is the first large, state-of-the-art international RCT of an interventional PE treatment against the current standard of care using validated, clinically relevant endpoints. It is also the first trial with adequate power to show a significant impact of an interventional approach on the prognosis of patients with intermediate–high-risk PE. The trial is led by expert clinical trialists in PE in the United States and Europe, who have taken care to standardize and precisely define, in the trial protocol, all key aspects of the study design (including time from PE diagnosis and randomization to intervention, USCDT duration and thrombolytic dose, and dose and scheme of anticoagulation regimen). Moreover, the trial protocol includes a clear rule to prevent arbitrary crossover between the treatment arms. Regardless of outcome, there is little doubt that HI-PEITHO will help clinicians manage some of the most challenging cardiovascular patients. ■

Acknowledgments: We thank Alexandra Greenberg-Worisek, PhD, MPH (Boston Scientific Corporation) for providing medical writing assistance.

1. Smith SB, Geske JB, Kathuria P, et al. Analysis of national trends in admissions for pulmonary embolism. Chest. 2016;150:35-45. doi: 10.1016/j.chest.2016.02.638
2. Meyer G, Vicaut E, Danays T, et al. Fibrinolysis for patients with intermediate-risk pulmonary embolism. N Engl J Med. 2014;370:1402-1411. doi: 10.1056/NEJMoa1302097
3. Chatterjee S, Chakraborty A, Weinberg I, et al. Thrombolysis for pulmonary embolism and risk of all-cause mortality, major bleeding, and intracranial hemorrhage: a meta-analysis. JAMA. 2014;311:2414-2421. doi: 10.1001/jama.2014.5990
4. Kucher N, Boekstegers P, Müller OJ, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. Circulation. 2014;129:479-486. doi: 10.1161/CIRCULATIONAHA.113.005544
5. National Early Warning Score (NEWS): Standardising the assessment of acute-illness severity in the NHS. Report of a working party. Royal College of Physicians; 2012.
6. Smith GB, Prytherch DR, Meredith P, et al. The ability of the National Early Warning Score (NEWS) to discriminate patients at risk of early cardiac arrest, unanticipated intensive care unit admission, and death. Resuscitation. 2013;84:465-470. doi: 10.1016/j.resuscitation.2012.12.016
7. Jarvis S, Kovacs C, Briggs J, et al. Aggregate National Early Warning Score (NEWS) values are more important than high scores for a single vital signs parameter for discriminating the risk of adverse outcomes. Resuscitation. 2015;87:75-80. doi: 10.1016/j.resuscitation.2014.11.014
8. Smith ME, Chiovaro JC, O'Neil M, et al. Early warning system scores for clinical deterioration in hospitalized patients: a systematic review. Ann Am Thorac Soc. 2014;11:1454-1465. doi: 10.1513/AnnalsATS.201403-102OC
9. Gerry S, Bonnici T, Birks J, et al. Early warning scores for detecting deterioration in adult hospital patients: systematic review and critical appraisal of methodology. BMJ. 2020;369:m1501. doi: 10.1136/bmj.m1501
10. Tapson VF, Sterling K, Jones N, et al. A randomized trial of the optimum duration of acoustic pulse thrombolysis procedure in acute intermediate-risk pulmonary embolism: the OPTALYSE PE trial. JACC Cardiovasc Interv. 2018;11:1401-1410. doi: 10.1016/j.jcin.2018.04.008

Stavros V. Konstantinides, MD
Center for Thrombosis and Hemostasis
Johannes Gutenberg University Medical Center
Mainz, Germany
Disclosures: Consultancy honoraria and institutional grants from Boston Scientific Corporation.

Michael R. Jaff, DO, FACP, FACC
Peripheral Interventions
Boston Scientific Corporation
Marlborough, Massachusetts
Disclosures: Part-time employee of Boston Scientific Corporation.

Kenneth Rosenfield, MD, MHCDS
Interventional Cardiology and Vascular Medicine
Massachusetts General Hospital
Boston, Massachusetts
krosenfield1@mgh.harvard.edu
Disclosures: Consultant/scientific advisory board, Access Vascular, AngioDynamics, Contego, Philips, Boston Scientific, Surmodics, Janssen, Neptune Med, Magneto, Mayo Clinic, Summa Therapeutics, Thrombolex, Truvic; grants to institution, NIH, Boston Scientific; equity, Access Vascular, Althea Med, Contego, Cruzar Systems, Embolitech, Endospan, JanaCare, Magneto, Orchestra, PQ Bypass, Shockwave, Summa Therapeutics, Thrombolex, Truvic, Valcare; board member, National PERT Consortium®.

Transitions of Care for Patients With Venous Thromboembolism

A review of the barriers and solutions for VTE transitions of care and how The National PERT Consortium® can assist with implementing a VTE transitions of care program.

By Rachel P. Rosovsky, MD, MPH; Geoffrey D. Barnes, MD, MSc; and Geno Merli, MS, MACP, FSVM, FHM

Venous thromboembolism (VTE) is a common disorder affecting 900,000 Americans annually, with a resulting cost of care of $7 to $10 billion per year.[1-4] Acute VTE is estimated to cause 100,000 deaths per year, mainly attributed to the development of a pulmonary embolism (PE).[3] Of patients who survive the acute event, several thousand will develop chronic sequelae, such as postthrombotic syndrome or chronic thromboembolic pulmonary hypertension, which can result in significant morbidity and mortality with a resultant increase in health care costs.[5-7] With the high incidence of VTE and hospitalization, this patient population requires a focused plan to transition their care from the hospital to home.

Transition of care (TOC) is defined as the movement of patients between health care providers or settings. This process, when not effectively completed, can lead to adverse events, higher hospital readmission rates, and increased health costs.[4,7] Anticoagulants are the cornerstone of therapy for VTE and are commonly associated with bleeding and recurrent VTE events secondary to inadequate dosing or failure to comply with treatment plans.[8] These types of medication errors have been implicated as a leading cause of hospital readmissions. The inherent high-risk nature of VTE coupled with associated adverse drug events provide a perfect opportunity to optimize the TOC process for this patient population.[9]

The goals of a VTE TOC program are to provide effective predischarge and ongoing patient education, reduce the risk of recurrent thrombosis by increasing medication adherence, minimize the risk of bleeding, and prevent readmissions.[10,11] The specific objectives of a VTE TOC program include streamlining the evidence-based management of VTE for specific patient populations; providing effective patient education programs, which also includes assessment of patient knowledge; improving patient adherence to prescribed therapy; and outlining core requirements for effective handoffs and communication of the plan of care. To achieve these important objectives, it is essential to identify both the barriers to and the solutions for a successful program, including how to utilize The National Pulmonary Embolism Response Team (PERT) Consortium® to accomplish these goals.

BARRIERS TO VTE TOC

Barriers to VTE TOC are outlined in Table 1. One of the greatest challenges in coordinating a patient's health care across various settings is ensuring effective communication. Because patients with VTE often have multiple specialists involved in their care, determining who is responsible for providing accurate and timely discharge information and instructions, including a follow-up plan, may be difficult. Furthermore, when patients move from the inpatient setting to home or another facility, there may be pending test results that require timely follow-up. A recent study found that over one-third of patients diagnosed with VTE were lost to VTE-specific follow-up, particularly patients who were discharged to a facility rather than home.[12]

The mainstay of therapy for VTE is anticoagulation.[13,14] Determining which anticoagulant to use for each patient requires an in-depth knowledge of a patient's medical comorbidities as well as a comprehensive understanding of the various anticoagulants and their pharmacologic properties. It is also essential for providers to emphasize the importance of and frequently inquire if their patients are taking the anticoagulant correctly. A recent study demonstrated that patients receiving direct oral anticoagulants at nonrecommended doses and/or regimens experienced a higher rate of VTE recurrence than patients who received recommended doses and regimens.[15]

Educating patients about their clinical course, medications, and treatment plans requires time, planning,

PODCASTS WITH THE PERT CONSORTIUM®

In partnership with Janssen Pharmaceuticals, Inc., the following podcasts were developed by The PERT Consortium® to help advance education on the collaborative management of PE.

The PERT Approach

Moderated by:

Richard Channick, MD

Joined by:

Brent Keeling, MD
Christopher Kabrhel, MD
Christina Fanola, MD
Kenneth Rosenfield, MD
Robert Lookstein, MD

Management Pathways for PE

Moderated by:

Emily Gundert, MD

Joined by:

Geno Merli, MD
Jeffrey Kline, MD

VTE Discussion on 2019 ESC Guidelines and Treatment Duration

Moderated by:

Geoffrey Barnes, MD

Joined by:

George Davis, MD
Gregory Piazza, PharmD
Rachel Rosovky, MD

These podcasts were developed by the featured Pulmonary Embolism Response Team (PERT) Consortium® speakers through a sponsorship from Janssen Pharmaceuticals, Inc. Some doctors are also paid consultants for Janssen Pharmaceuticals, Inc.

To learn more visit:

www.pertconsortium.org

or scan the QR code to link to the website

PE=pulmonary embolism, VTE=venous thromboembolism.

PERT CONSORTIUM®

janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

TABLE 1. BARRIERS TO VTE TRANSITIONS OF CARE

Potential Barrier	Population Affected	Necessary Topic or Concern
Communication	Provider to provider	Lack of a point person from the inpatient team Incomplete transfer of information: ▪ Complete and timely discharge summary of hospital course ▪ Pending tests ▪ Anticoagulation plan ▪ Follow-up/postdischarge appointment time and place
	Provider to patient	Education and understanding with regard to: ▪ Etiology of VTE ▪ Treatment plan ▪ Length of anticoagulation ▪ Acute and long-term potential physical, functional, and emotional complications/effects of VTE ▪ Potential complications from treatment ▪ Concerning symptoms for which medical attention is advised ▪ Who and how to call with questions or concerns
System or social supports	Patients	Lack of access to essential resources Lack of support from friends, family, or community
Anticoagulation	Patients	Lack of insurance coverage Unaffordable cost Interaction with other medications Lack of or misunderstanding regarding dose and administration Avoidance of high-bleeding-risk situations Avoidance of NSAIDs or aspirin-containing products unless medically necessary
	Provider	Need for prior authorization Choice of anticoagulant based on patient and drug characteristics (eg, renal failure, liver disease, pregnancy, cancer, obesity)

Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; VTE, venous thromboembolism.

and an understanding of a patient's health literacy. Patients may not fully understand the significance of having a VTE, and once they do, they may grapple with trying to determine the underlying cause. Moreover, patients are often frightened of the consequences and potential long-term sequelae after a VTE, including the possibility of death. Explaining the rationale for the use of anticoagulation as well as the possible side effects can be perplexing and daunting for patients, especially in those who may require long-term use. Patients may also have unusual or exaggerated expectations and anxieties relative to their VTE or anticoagulant and may have questions about the necessity of certain restrictions and their duration.

Possibly one of the biggest obstacles to medication adherence is cost, especially if a patient leaves the hospital without knowing whether the drug is covered by insurance.[16] Given the known side effects and potential lack of understanding regarding the importance of taking anticoagulants regularly, patient compliance may become an issue. However, being compliant with out-of-hospital medication regimens is crucial to recovery from VTE. Another challenge for patients when transitioning from the inpatient setting to home or another facility may be lack of social supports or social systems. Trying to maneuver the health care system alone can be overwhelming, and not having access to essential resources can be detrimental to a patient's health.

Given all of the potential obstacles patients face during this vulnerable time underscores the necessity for smooth transitions from one phase of care to the next.

SOLUTIONS FOR VTE TOC

In order to decrease the morbidity and mortality associated with VTE, determining and operationalizing protocols to ensure access to and adherence and compliance with anticoagulation is critical. Creating a "meds to beds" program whereby a patient would

not leave the hospital without medication in hand addresses the cost and insurance barrier. It is important for patients not only to have easy and affordable access to anticoagulation, but also to understand the rationale behind, side effects of, and how to take this vital medication. Understanding both the disease process and its treatment plays an enormous role in long-term treatment success. This task can be accomplished by providing patients with simple, clear, culturally sensitive, and appropriate information.[10] Visual aids and videos may also help break down complex medical terminology and educate patients about what happened to them and how the medications work. In addition, asking patients to "teach back" what they heard can help gauge their understanding. Offering videos and other educational materials during the acute hospital setting will allow patients the opportunity to ask questions prior to discharge. Patients must also be provided with appropriate contact information if problems or other questions arise after discharge. Furthermore, before leaving the hospital, patients should have a timely (usually within a week) follow-up visit scheduled with a VTE specialist to ensure continuity of care. To take it one step further, many programs have a nurse call the patient within 24 to 48 hours of discharge to inquire about adverse events and medication compliance and address any questions or concerns. Importantly, in order to ensure a smooth transition from the inpatient setting to home (or another facility), the primary inpatient team must provide a comprehensive discharge and follow-up plan, which includes what prompted the admission; a detailed hospital course including any procedures and significant or pending results; a specific anticoagulation plan with rationale for type, dosing, and any concerns for side effects; and the time and place of the follow-up visit.

Finally, the COVID-19 pandemic brought an opportunity to redesign how the medical community delivers health care. By providing telehealth visits to patients with VTE, the costs associated with routine follow-up visits, such as transportation, parking, and having to take time off of work, will be dramatically reduced, which may lead to an increase in follow-up compliance. Further ideas to improve patient follow-up care include a VTE tool kit with solutions that address each of the challenges and barriers faced by patients or an interactive phone application specific to VTE.

MEASURING THE EFFECTS OF A SUCCESSFUL VTE TOC PROGRAM

With any new program, it is important to measure the success and identify opportunities for improvement through clinically meaningful metrics. Metrics specific to a VTE TOC program will mirror the general goals, which are to effectively educate patients about their illness and treatment and develop strategies to minimize the complications associated with those medical conditions. Hospital length of stay and readmission rates are two important outcomes important to both patients and payors alike. Using electronic health records will help identify whether patients have a follow-up visit in place prior to discharge. Medication diaries can be used to assess compliance with home regimens. Patient satisfaction scores and functional assessments are examples of further qualitative measurements.[17]

USING THE PERT CONSORTIUM® TO IMPROVE VTE TOC

The National PERT Consortium®, a 501(c)(3) nonprofit organization founded in 2016 for the purpose of promoting the multidisciplinary care of patients with PE, is ideally posed to help create, implement, and disseminate a VTE TOC program. The PERT Consortium® consists of over 150 institutions and over 1,500 clinicians in the United States and globally, and it is focused on improving outcomes from PE by advancing its recognition, diagnosis, and treatment.[18] PERT teams are on the front lines of managing patients with PE at their institutions.[19] The education and clinical protocols committees of The PERT Consortium® are collaborating with corporate partners to develop a comprehensive VTE TOC program. Furthermore, The PERT Consortium® manages the largest prospective United States registry of PE patients, which serves as a database for future research and clinical innovation. The PERT Consortium® will leverage the infrastructure of this existing registry, which utilizes the user-friendly and rapidly scalable REDCap Cloud platform, to collect TOC metrics to further refine the program.

CONCLUSION

VTE is a major cause of morbidity and mortality, and patients are often hospitalized for the initial treatment. However, care does not stop there, and the transition from inpatient stay to home or another facility is a vulnerable time. Creating a comprehensive VTE TOC program is vital to safely and effectively treat VTE patients. Using The PERT Consortium® to identify barriers and create solutions will help develop a successful VTE TOC program. The PERT Consortium® is also poised to disseminate and measure the effect of the program and further improve on its goals. ■

1. Grosse SD, Nelson RE, Nyarko KA, et al. The economic burden of incident venous thromboembolism in the United States: A review of estimated attributable healthcare costs. Thromb Res. 2016;137:3-10. doi: 10.1016/j.thromres.2015.11.033
2. Heit JA. Venous thromboembolism: disease burden, outcomes and risk factors. J Thromb Haemost. 2005;3:1611-1617. doi: 10.1111/j.1538-7836.2005.01415.x
3. Wendelboe AM, Campbell J, Ding K, et al. Incidence of venous thromboembolism in a racially diverse population of Oklahoma County, Oklahoma. Thromb Haemost. 2021;121:816-825. doi: 10.1055/s-0040-1722189
4. Mahan CE, Borrego ME, Woersching AL, et al. Venous thromboembolism: annualised United States models for

total, hospital-acquired and preventable costs utilising long-term attack rates. Thromb Haemost. 2012;108:291-302. doi: 10.1160/TH12-03-0162
5. Kahn SR, Comerota AJ, Cushman M, et al. The postthrombotic syndrome: evidence-based prevention, diagnosis, and treatment strategies: a scientific statement from the American Heart Association. Circulation. 2014;130:1636-1661. doi: 10.1161/CIR.0000000000000130
6. Pengo V, Lensing AW, Prins MH, et al. Incidence of chronic thromboembolic pulmonary hypertension after pulmonary embolism. N Engl J Med. 2004;350:2257-2264. doi: 10.1056/NEJMoa032274
7. Lin J, Lingohr-Smith M, Kwong WJ. Incremental health care resource utilization and economic burden of venous thromboembolism recurrence from a U.S. payer perspective. J Manag Care Pharm. 2014;20:174-186. doi: 10.18553/jmcp.2014.20.2.174
8. Piazza G, Nguyen TN, Cios D, et al. Anticoagulation-associated adverse drug events. Am J Med. 2011;124:1136-1142. doi: 10.1016/j.amjmed.2011.06.009
9. Jaffray J, Rajpurkar M, Sharathkumar A, et al. Transition of care for patients with venous thromboembolism: Rationale, design and implementation of a quality intervention project conducted at American Thrombosis and Hemostasis Network (ATHN) affiliated sites. Thromb Res. 2018;163:146-152. doi: 10.1016/j.thromres.2018.01.043
10. DeSancho M, Munn JE, Billett HH, et al. Transition of care for pediatric and adult patients with venous thromboembolism: a National Quality Improvement Project from the American Thrombosis and Hemostasis Network (ATHN). Thromb Res. 2021;200:23-29. doi: 10.1016/j.thromres.2021.01.001
11. Trocio J, Rosen VM, Gupta A, et al. Systematic literature review of treatment patterns for venous thromboembolism patients during transitions from inpatient to post-discharge settings. Clinicoecon Outcomes Res. 2019;11:23-49. doi: 10.2147/CEOR.S179080
12. Rokosh RS, Grazi JH, Ruohoniemi D, et al. High incidence of patients lost to follow-up after venous thromboembolism diagnosis—identifying an unmet need for targeted transition of care. Vascular. Published online June 3, 2021. doi: 10.1177/17085381211020969
13. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest. 2016;149:315-352. doi: 10.1016/j.chest.2015.11.026
14. Streiff MB, Agnelli G, Connors JM, et al. Guidance for the treatment of deep vein thrombosis and pulmonary embolism. J Thromb Thrombolysis. 2016;41:32-67. doi: 10.1007/s11239-015-1317-0
15. Trujillo-Santos J, Di Micco P, Dentali F, et al. Real-life treatment of venous thromboembolism with direct oral anticoagulants: the influence of recommended dosing and regimens. Thromb Haemost. 2017;117:382-389. doi: 10.1160/TH16-07-0494
16. Pulleyn T, Kim K, Witt DM, et al. Understanding patients' care barriers in the treatment of venous thromboembolism. J Thromb Thrombolysis. 2019;48:35-41. doi: 10.1007/s11239-019-01880-3
17. Webb D, Kim K, Tak CR, et al. Patient satisfaction with venous thromboembolism treatment. Clin Appl Thromb Hemost. 2019;25:1076029619864663. doi: 10.1177/1076029619864663
18. Rosovsky R, Chang Y, Rosenfield K, et al. Changes in treatment and outcomes after creation of a pulmonary embolism response team (PERT), a 10-year analysis. J Thromb Thrombolysis. 2019;47:31-40. doi: 10.1007/s11239-018-1737-8
19. Rosovsky R, Borges J, Kabrhel C, Rosenfield K. Pulmonary embolism response team: inpatient structure, outpatient follow-up, and is it the current standard of care? Clin Chest Med. 2018;39:621-630. doi: 10.1016/j.ccm.2018.04.019

Rachel P. Rosovsky, MD, MPH
Department of Medicine
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts
rprosovsky@mgh.harvard.edu
Disclosures: Grants to institution from BMS and Janssen; consultant/advisory board for BMS, Dova, Janssen, and Inari Medical.

Geoffrey D. Barnes, MD, MSc
Department of Internal Medicine
Division of Cardiovascular Medicine
University of Michigan Health System
Ann Arbor, Michigan
Disclosures: Consultant to Pfizer, Bristol-Myers Squibb, Janssen, and Acelis Connected Health.

Geno Merli, MS, MACP, FSVM, FHM
Department of Medicine
Thomas Jefferson University Hospitals
Philadelphia, Pennsylvania
Disclosures: None.

EMPHASIZING PREVENTION TO IMPROVE OUTCOMES

AngioVac

The AngioVac System is effective in removing right atrial masses and thrombus-in-transit to assist in the prevention of PE.

angiodynamics

LEARN MORE AT ANGIOVAC.COM

AngioVac Cannula

Indication for Use: The AngioVac Cannula is indicated for use as a venous drainage cannula and for removal of fresh, soft thrombi or emboli during extracorporeal bypass for up to 6 hours.
Contraindications: The following contraindications are applicable:

- Do not use if the patient has severe arterial or venous vascular disease.
- The device is contraindicated in the removal of chronic firmly adherent intravascular material (e.g., atherosclerotic plaque, chronic pulmonary embolism).
- The device is contraindicated for use in the right heart or pulmonary arteries during active cardiopulmonary resuscitation.

Refer to Directions for Use and/or User Manual provided with the product for complete Instructions, Warnings, Precautions, Possible Adverse Effects and Contraindications prior to use of the product. CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician.

AngioVac Circuit

Indication for Use: This circuit is indicated for use in procedures requiring extracorporeal circulatory support for periods of up to six hours.
Contraindications: Refer to the AngioVac Cannula Directions for Use (DFU) for procedure-specific contraindications.
Refer to Directions for Use and/or User Manual provided with the product for complete Instructions, Warnings, Precautions, Possible Adverse Effects and Contraindications prior to use of the product. CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician.

The Interhospital Transfer Project of The PERT Consortium®: A Call to Action for Pulmonary Embolism

Addressing the gap in knowledge in interhospital transfer of patients with pulmonary embolism.

By Charles B. Ross, MD, DFSVS; Parth Rali, MD; and Belinda N. Rivera-Lebron, MD, MS, FCCP

Interhospital transfer (IHT) for critically ill patients is an established area of clinical research that spans the discipline of medicine.[1-8] Areas like trauma, stroke, and ST-segment elevation myocardial infarction (STEMI) have well-established protocols for IHT. Each critical illness has been studied to understand differences in patient characteristics and outcomes between patients transferred to institutions more capable of providing advanced comprehensive care. Processes of care have been studied with laudable goals of improvements in early recognition of the need for transfer, avoidance of delays, safe conduct of patients in transfer, and regionalization of care. Resource utilization and complications comparing patients directly admitted to comprehensive centers versus those transferred, such as intensive care unit (ICU) length of stay, costs, and rates of readmission, have been studied. A recent Pubmed search (April 25, 2021) documents the degree of scientific investigation of IHT: 458 citations for "interhospital transfer" and "mortality"; 314 citations for "interhospital transfer" and "trauma"; 140 citations for "interhospital transfer" and "stroke"; 99 citations for "interhospital transfer" and "STEMI"; 40 citations for "interhospital transfer" and "sepsis"; and 33 citations for "interhospital transfer" and "pregnancy." However, the search strategy for "interhospital transfer" and "pulmonary embolism" yielded only one citation, which was a case report.[9]

The National Pulmonary Embolism Response Team (PERT) Consortium®, founded in 2015, is dedicated to promoting multidisciplinary care of patients with pulmonary embolism (PE).[10,11] Presently, there are more than 125 member institutions in the United States and seven internationally, with professional membership representing at least 10 different specialties.[12] PE is the third most common cardiovascular cause of death and is estimated to be responsible for 60,000 to 100,000 deaths in the United States annually.[13,14] Over the past decade, there has been rapid evolution in advanced care, including critical care support and interventional therapies for PE patients.[15] However, many patients with PE first present to hospitals that are incapable of providing such care, making the process of IHT a potential barrier to their outcome. The key here is process, which represents the continuum from first diagnostic consideration of PE to safe arrival at the receiving center. Within this continuum, especially in the case of high- and intermediate–high-risk PE, there are points of critical decision-making and rapid execution that must be managed correctly and decisively to improve chances of survival. Unlike trauma and STEMI for which advanced trauma life support and advanced cardiac life support exist to guide practitioners, no such guidance has been developed and disseminated for PE.

IHT AND PE: A CRITICAL GAP IN KNOWLEDGE AND EFFORT

As noted, there has been little IHT research in PE. In 2015, a group at Vanderbilt presented an early report of the structure and function of their PE network.[16] They reported 31 patients, comparing 14 transferred from network hospitals and 17 directly admitted to Vanderbilt University Hospital. No mortality differences were reported. Recently, a group from Beth Israel Deaconess Medical Center reported 1,994 patients with acute PE, 682 (34.2%) of whom were transferred.[17] PE-related and overall mortality were higher in transferred patients, and advanced therapies were more commonly used in transferred patients. However, there was no statistical difference in mortality in the subgroup of submassive and massive PE patients who received care in the ICU. These data still form an early and incomplete picture about the importance of well-executed transfer for critically ill PE patients. The number of deaths that occur between PE diagnosis and arrival at the destination center is unknown. PE-related mortality due to transfer delays, for reasons ranging from initial failure to recognize the need for transfer, bed unavailability at receiving hospitals,

lack of extracorporeal membrane oxygenation (ECMO) circuit availability, and even suboptimal weather, has not been defined.

With the multidisciplinary collaboration within The PERT Consortium®, the gap in evidence, research, and education of frontline practitioners targeted toward IHT of PE as compared to other critical illnesses has been recently recognized. In 2019, support for initial research was awarded in the form of an unrestricted, investigator-initiated grant from Boston Scientific Corporation to begin the process of investigation and quality improvement in IHT for PE. The IHT project (IHTP) became the work of the clinical protocols committee (CPC) of The PERT Consortium®. Its primary goal was to develop a step-by-step guide to the stabilization and transfer of critically ill PE patients. Additional goals included identification of existing barriers in the IHT process and increasing awareness and education on definitive PE care.

THE IHTP

The IHTP is organized into work groups (WGs) and subcommittees to address the following four needs:

- WG 1: Identify and review critical processes and issues associated with IHT for PE
- WG 2: Identify problems and barriers to transfer of PE patients by surveying both transferring and receiving providers through a structured interview process
- WG 3: Analyze data from The PERT Consortium® database to compare characteristics and outcomes of transferred versus directly admitted PE patients
- WG 4: Disseminate findings to frontline practitioners as well as receiving physicians

WGs 1, 2, and 3 mainly include members of the CPC. WG 4 collaborates with the education committee of The PERT Consortium® and will include webinars, podcasts, and development of teaching materials. WG 1's project was felt to be especially critical to the overall IHTP and has been completed in partnership with members of the CHEST Pulmonary Vascular Disease Network.[18] Progress made to date includes manuscript preparation, submission, review, and revision for WG 1. WG 2 and WG 3 have manuscripts currently in development. The IHTP is recognized by all participants as a call to action to begin investigative and quality improvement research in IHT for PE. The IHTP is the beginning—not the end.

GENERAL CONSIDERATIONS FOR IHT FOR PE

After a PE patient is diagnosed and risk stratified, initiation of anticoagulation is the first step in PE management. Then, the frontline clinician must decide if the patient needs to be admitted to that presenting institution, transferred to another institution, or discharged home. That clinician may consider transfer if the patient has been diagnosed with an intermediate- or high-risk PE, the patient has complex medical problems, the facility lacks advanced PE treatment options, the facility lacks beds or expertise to treat for such a patient, or a patient has a high bleeding risk. Transfer of a critically ill patient begins with a call from the transferring facility to the receiving institution's call/transfer center.

Each receiving institution has a protocol in place to stimulate the call center, such as the activation of the institution's PERT or other accepting provider. Physician-to-physician communication will be promptly initiated. In most receiving centers, a single physician is the point person and triages the call with subsequent involvement of the PE interventionalist, ECMO service provider, and/or cardiac surgeon depending on the situation. Important basic patient information must be obtained in the call, such as vital signs including trends in heart rate, blood pressure, and respiration; oxygenation status and support; mentation and patient comfort or distress; historical features such as syncope and presence or absence of visible trauma; comorbidities; bleeding risks and review for contraindications to thrombolysis; and available family support. It is of utmost importance to establish if systemic anticoagulation has been administered. If it has not, the receiving physicians will help advise the transferring team to do so promptly.

Requests for transfer may differ depending on the status of the patient. The type of transport (air vs ground) will also depend on the severity of illness and availability of transport crew. Patients presenting to and being transferred from an emergency department differ from those transferred from an ICU. Additionally, hemodynamic optimization prior to transfer is key in achieving a safe and successful transfer.

An example of a difficult transfer call would be as follows:

> A woman in her early 40s with obesity collapses after rising from her hospital bed on postoperative day 2 after a total abdominal hysterectomy. After a brief period of cardiopulmonary resuscitation, return of spontaneous circulation is achieved. PE is strongly suspected. She is moved to the ICU where a transthoracic echocardiogram shows a markedly dilated right ventricle with a positive McConnell's sign. She is awake and alert but seems to be in distress. She has a small laceration and hematoma on the back of her scalp from the fall. Blood pressure is 90/50 mm Hg and heart rate is 130 bpm. Two vasopressors have been initiated for hemodynamic support. Her $Sa0_2$ on high-flow oxygen is 90%. The resuscitating physician and team have done an excellent job and call for transfer with strong suspicion of PE.

Management of this patient is affected by many factors. Some considerations that transferring and receiving practitioners may encounter include: Is the transferring physician willing to start systemic anticoagulation? If the patient experiences cardiac arrest again and given no other available recourse, will systemic thrombolysis be administered?

If the patient cannot be adequately oxygenated, is the transferring physician able to manage her airway and perform a hemodynamically neutral intubation? Is the transferring physician willing to try a intravenous fluid bolus while awaiting transfer? Can the patient be safely transferred? Should it be by air or by ground? What's the weather? What's the condition of metro traffic? Can you dispatch your mobile ECMO team to the patient to initiate ECMO prior to transfer?

In this sample case, there is a contraindication to administration of systemic tissue plasminogen activator (tPA). However, what if the scenario was different and there were no contraindications? Every PERT receiving team has encountered frontline physicians who are hesitant to administer tPA. The same frontline physicians who readily administer tPA for stroke (which has become standard practice) are often unsure about its use for high-risk PE. This may serve to unnecessarily raise the risk of deterioration in transfer and highlights the rudimentary state of our education and support of frontline providers of PE care as compared to stroke.

Although the most dramatic transfer dilemmas often arise in cases of high-risk PE, patients with intermediate–high-risk PE also require careful consideration. Conundrums arise when transfer is delayed, and patient care must ensue at the facility requesting transfer.

Finally, what about issues of futile care? Frequently, PERTs at advanced centers are asked to accept transfer of patients critically ill with PE, only to later learn that the patient in question is terminally ill from other causes such as a widely metastatic tumor. Bed shortages exist, and especially during the pandemic, such transfers could consume critical resources for patients in greater need. Issues of end-of-life care arise frequently with PE, and these need to be dealt with in a more forthright and appropriate manner.

CONCLUSION

Management of PE through multidisciplinary PERTs has often been called the "coalition of the willing." The importance of the multidisciplinary nature of a PERT on the call with a frontline provider during a PE crisis cannot be overemphasized. The PERT receiving specialists may be especially helpful in guiding frontline physicians away from high-risk intubation or toward appropriate administration of systemic thrombolysis. Experience and collaboration are key, but research, data, and education are ultimately needed to clarify and improve the systems process. Above all, education is fundamental to advance the IHT of PE patients into the future, and The PERT Consortium®'s IHTP represents only the beginning. ■

1. Heincelman M, Gebregziabher M, Kirkland E, et al. Impact of patient-level characteristics on in-hospital mortality after interhospital transfer to medicine services: an observational study. J Gen Intern Med. 2020;35:1127-1134. doi: 10.1007/s11606-020-05659-8
2. Shannon EM, Zheng J, Orav EJ, et al. Racial/ethnic disparities in interhospital transfer for conditions with a mortality benefit to transfer among patients with Medicare. JAMA Netw Open. 2021;4:e213474. doi: 10.1001/jamanetworkopen.2021.3474
3. Arthur KR, Kelz RR, Mills AM, et al. Interhospital transfer: an independent risk factor for mortality in the surgical intensive care unit. Am Surg. 2013;79:909-913. doi: 10.1177/000313481307900929
4. Mueller SK, Fiskio J, Schnipper J. Interhospital transfer: transfer processes and patient outcomes. J Hosp Med. 2019;14:486-491. doi: 10.12788/jhm.3192
5. Van Diepen S, Widimsky P, Lopes R, et al. Transfer times and outcomes in patients with ST-segment-elevation myocardial infarction undergoing interhospital transfer for primary percutaneous intervention: APEX-AMI insights. Circ Cardiovasc Qual Outcomes. 2012;5:437-444. doi: 10.1161/CIRCOUTCOMES.112.965160
6. Vora AN, Holmes DN, Rokos I, et al. Fibrinolysis use among patients requiring interhospital transfer for ST-segment elevation myocardial infarction care: a report from the US National Cardiovascular Data Registry. JAMA Intern Med. 2015;175:207-215. doi: 10.1001/jamainternmed.2014.6573
7. Grotta JC. Interhospital transfer of stroke patients for endovascular treatment. Circulation. 2019;139:1578-1580. doi: 10.1161/CIRCULATIONAHA.118.039425
8. Holena DN, Kaufman EJ, Hatchimonji J, et al. The impact of interhospital transfer on mortality benchmarking at level III and IV trauma centers: a step toward shared mortality attribution in a statewide system. J Trauma Acute Care Surg. 2020;88:42-50. doi: 10.1097/TA.0000000000002491
9. McDonald C, Laurie J, Janssens S, et al. Successful provision of inter-hospital extracorporeal cardiopulmonary resuscitation for acute post-partum pulmonary embolism. Int J Obstet Anesth. 2017;30:65-68. doi: 10.1016/j.ijoa.2017.01.003
10. Rosovsky R, Borges J, Kabrhel C, Rosenfield K. Pulmonary embolism response team: inpatient structure, outpatient follow-up, and is it the current standard of care? Clin Chest Med. 2018;39:621-630. doi: 10.1016/j.ccm.2018.04.019
11. Rosovsky R, Zhao K, Sista A, et al. Pulmonary embolism response teams: purpose, evidence for efficacy, and future research directions. Res Pract Thromb Haemost. 2019;3:315-330. doi: 10.1002/rth2.12216
12. The PERT Consortium. Accessed July 13, 2021. http://www.pertconsortium.org
13. Centers for Disease Control and Prevention. Blood clots: a serious but preventable medical condition. Accessed May 2, 2021. http://www.cdc.gov/ncbddd/dvt/documents/blood-clots-fact-sheet.pdf
14. Rivera-Lebron B, McDaniel M, Ahrar K, et al. Diagnosis, treatment, and follow-up of acute pulmonary embolism: consensus practice from the PERT Consortium. Clin and Appl Thromb Hemost. 2019;25:1076029619853037. doi: 10.1177/1076029619853037
15. Giri J, Sista AK, Weinberg I, et al. Interventional therapies for acute pulmonary embolism: current status and principles for the development of novel evidence: a scientific statement from the American Heart Association. Circulation. 2019;140:e774-e801. doi: 10.1161/CIR.0000000000000707
16. Bloomer TL, Thomassee EJ, Fong PP. Acute pulmonary embolism network and multidisciplinary response team approach to treatment. Crit Pathw Cardiol. 2015;14:90-96. doi: 10.1097/HPC.0000000000000049
17. Beyer S, Secemsky E, Carroll B. Outcomes of patients with acute pulmonary embolism who undergo interhospital transfer. J Am Coll Cardiol. 2021;77(18 suppl 1):1821.
18. Rali P, Sacher D, Rivera-Lebron B, et al. Interhospital transfer of patients with acute pulmonary embolism (PE): challenges and opportunities. Chest. Published online July 13, 2021. doi: 10.1016/j.chest.2021.07.013

Charles B. Ross, MD, DFSVS
Chief of Vascular and Endovascular Services
Piedmont Heart and Vascular Institute
Atlanta, Georgia
Disclosures: None.

Parth Rali, MD
Associate Professor, Thoracic Medicine and Surgery
Lewis Katz School of Medicine
Temple University
Philadelphia, Pennsylvania
Disclosures: Consultant to Janssen.

Belinda N. Rivera-Lebron, MD, MS, FCCP
Associate Professor of Medicine
Division of Pulmonary, Allergy and Critical Care Medicine
Department of Medicine
University of Pittsburgh School of Medicine
Pittsburgh, Pennsylvania
riveralebronbn@upmc.edu
Disclosures: Board of Directors, PERT Consortium®; consultant, Janssen, Bayer, Bristol-Myers Squibb.

Indigo® System | Mechanical Thrombectomy

LIGHTNING™ 12

Intelligent Aspiration *Powered by Penumbra ENGINE®*

"The median **Indigo** device introduction to removal time was **37.0 min**, which is the **FASTEST** published time in prospective mechanical thrombectomy studies for **acute PE**"[a,b]

– As published in JACC-CI regarding the EXTRACT-PE study

a. Sista AK, Horowitz JM, Tapson VF, et al. Indigo aspiration system for treatment of pulmonary embolism: results of the EXTRACT-PE trial. *J Am Coll Cardiol Cardiovasc Interv.* Jan 13, 2021. Epublished doi:10.1016/j.jcin.2020.09.053.

b. Trial device used was Indigo Aspiration System and catheter was limited to the Indigo System CAT™8 used in conjunction with the SEP8 on a per case basis. Lightning 12 was not available at time of trial.

The clinical results presented herein are for informational purposes only, and may not be predictive for all patients. Individual results may vary depending on patient-specific attributes and other factors.

Caution: Federal (USA) law restricts these devices to sale by or on the order of a physician. Prior to use, please refer to the Instructions for Use (IFU) for complete product indications, contraindications, warnings, precautions, potential adverse events, and detailed instructions for use. Please contact your local Penumbra representative for more information.

To view the complete IFU Summary Statements, scan the QR code below

Follow us on Twitter

@PenVascular

Penumbra

COVID-19 and Venous Thromboembolic Disease: Where Are We Today?

What is currently known about the pathophysiology of the SARS-CoV-2 virus, prevalence of venous thromboembolism in COVID-19 patients, and the current approach to anticoagulation.

By Andrew J. P. Klein, MD, and Victor Tapson, MD

The devastating impact of COVID-19 on global health care delivery, especially intensive care medicine, has been unparalleled. A substantial contributor to this impact is the predilection of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus for the respiratory tract, which in turn leads to an elevated transmission rate along with a propensity for lung infection and severe hypoxemia frequently requiring intensive care unit (ICU) level of care. Early in the pandemic, numerous reports emphasized an increased incidence of venous thromboembolism (VTE) in the setting of SARS-CoV-2 infection, prompting many to suggest a change in VTE prophylaxis for these patients.[1] In addition, autopsy reports suggested multiple thrombi present in the lungs of COVID-19 patients, raising the specter of a viral-induced coagulopathy and/or vasculitis.[2] By coupling this concept with the well-described "cytokine storm"[3] induced by this coronavirus, the lungs have the potential to be damaged on all levels, further escalating the challenge in caring for these patients.

PATHOPHYSIOLOGY OF SARS-CoV-2

At the basic level, SARS-CoV-2 relies on the angiotensin-converting enzyme 2 (ACE 2) and transmembrane serine protease 2 (TMPRSS2) receptors for cell entry.[4] These critical host entry receptors are both heavily concentrated within the pulmonary vascular endothelium and in alveolar epithelial cells, which explains in part the tremendous pulmonary pathophysiology seen with COVID-19. The vascular endothelium is a dynamic system, and its activation triggers a cascade of inflammation via numerous cellular mechanisms. The cytokine storm phenomenon ensues, with elevated levels of biomarkers including fibrinogen, interleukin-6, von Willebrand factor, tumor necrosis factor-α, C-reactive protein, D-dimer, and others. Additionally, the endotheliopathy induced by SARS-CoV-2 infection can induce a hypercoagulable state, leading to an increase in the incidence of thromboembolism (including arterial thrombosis), also termed as "CAC" or COVID-19–associated coagulopathy.[5] In a landmark early autopsy study of COVID victims, the lungs showed diffuse alveolar damage, severe endothelial injury, and a unique preponderance of widespread thrombosis with microangiopathy in the vascular beds.[2] This hypercoagulable state along with a high prevalence of traditional risk factors for VTE among COVID-19 patents, such as immobility, central venous catheters, and critical illness, has further spurred interest into how to prevent these vascular events.

PREVALENCE OF VTE IN COVID-19 PATIENTS

The true prevalence of VTE in patients with COVID-19 is unclear and varies widely among studies. This is due to the tremendous difficulty in performing CTA on many patients due to fear of spread, as well as the critically ill, severely hypoxemic nature of these patients precluding their safe transport outside of the ICU. Evidence for this most recently came from a single-center study at a New York academic hospital examining the number of pulmonary embolism response team (PERT) activations during the pandemic. In this study, Finn and colleagues reported a much lower use of CTA for the definitive diagnosis of pulmonary embolism (PE) in COVID-19 patients compared to historical controls (58.1% vs 92.3%; $P = .001$), likely leading to an underdiagnosis of PE in these patients.[6] The literature is also fraught with the confounders of various strategies of anticoagulation used in these patients, which makes the true incidence unknown to date. Kollias et al recently demonstrated a pooled prevalence of PE and deep vein thrombosis of 32% (95% CI, 25%-40%) and 27% (95% CI, 21%-34%), respectively, across 47 studies performed through the end of September 2020.[7] Although the true prevalence is unknown and the numbers vary by study, all reported studies show a higher incidence of VTE in COVID-19 patients compared to those without COVID-19 based on historical data. Even in view of potential selection bias in clinical studies, the numbers are high.

TABLE 1. SUMMARY OF THE NATIONAL PERT CONSORTIUM® POSITION STATEMENTS ON THE DIAGNOSIS AND TREATMENT OF PE IN COVID-19 PATIENTS

PERT Consortium® Position Statements on COVID-19 and PE
▪ A multidisciplinary approach to diagnose and treat patients with PE is encouraged.
▪ Carefully assess the contribution of COVID-19 lower respiratory tract involvement to the presenting hemodynamic and gas exchange abnormalities and whether these abnormalities are out of proportion and require exploration for an alternative explanation such as PE.
▪ Because patients with COVID-19 may exhibit a hypercoagulable state, the index of suspicion for concurrent PE should be high. In patients with clinical and imaging findings not entirely explained by COVID-19, evaluation for PE should be strongly considered.
▪ Elevated D-dimer, in and of itself, should not be used to diagnose suspected PE.
▪ PERT consultation should take into account COVID-19 testing and results as a means of risk stratification and to protect allied health care providers from risk of viral transmission.
▪ For patients with mild COVID-19 symptoms and low-risk PE, outpatient treatment or early discharge may be considered, with close follow-up.
▪ Indications and contraindications for thrombolysis remain unchanged.
▪ Consider systemic thrombolysis as a viable alternative in certain COVID-19 patients who are appropriate for advanced therapy but in whom an invasive approach may not be available because of limited resources or concerns about viral transmission.
▪ The risk-benefit ratio of medical and interventional therapy may require adjustment in patients with concurrent COVID-19 and PE.
▪ PERT consultation provides a mechanism for evaluation of complex interventional options by a multidisciplinary group of PE experts.
▪ Transfer of care for a patient with PE and COVID-19 should be requested when needed services are not available at the originating institution and are necessary for best care of the patient.
▪ The potential benefit versus risk should be carefully considered on a case-by-case basis via direct communication between physicians from transferring and receiving institutions. PERTs can aid in this decision.
▪ Follow-up assessment of patients with COVID-19 and PE is critical to address issues surrounding anticoagulation, follow-up testing, recovery and persistent symptoms, and psychologic well-being.
▪ When possible, follow-up visits should be virtual. If persistent symptoms or concern for right ventricular failure exist, long-term follow-up visits may be best evaluated in person.
▪ Monitoring and collection of data obtained during follow-up visits will help the medical community understand the unique impact of concurrent COVID-19 and PE. Facilities caring for patients with COVID-19 and PE are encouraged to join the complimentary PERT Consortium® COVID-19/PE registry, which provides important data on presentation, assessment, and management of patients with COVID-19 and PE and helps shape real-time decision-making and patient-level care as this pandemic unfolds.
▪ In all care of patients infected with COVID-19, exposure should be limited, without compromising the medical information necessary to make critical evidence-based management decisions.
▪ Digital platforms for information exchange enable reduced exposure and facilitate real-time decision-making by a multidisciplinary team such as a PERT.
▪ Careful and thoughtful advanced planning for interventional or operative procedures, particularly regarding required personnel and equipment, will expedite procedures and minimize staff exposure.

Abbreviations: PE, pulmonary embolism; PERT, pulmonary embolism response team.
Reprinted from Chest, 158, Rosovsky RP, Grodzin C, Channick R, et al. Diagnosis and treatment of pulmonary embolism during the coronavirus disease 2019 pandemic: a position paper from the National PERT Consortium, 2590-2601, 2020, with permission from Elsevier.

ANTICOAGULATION IN COVID-19 PATIENTS

The higher prevalence of VTE in COVID-19 patients has prompted numerous studies evaluating various levels of aggressiveness of prophylactic anticoagulation in an attempt to effectively prevent this potentially fatal complication. Most recently, the INSPIRATION randomized trial, conducted at 10 centers in Iran, showed no difference between intermediate-dose (enoxaparin, 1 mg/kg daily) and standard prophylactic dose (enoxaparin, 40 mg daily) anticoagulation in 562 COVID-19 patients admitted to the ICU on the composite endpoint of adjudicated venous or arterial thrombosis, treatment with extracorporeal membrane oxygenation, or mortality within 30 days.[8] However, in this trial, mortality in each group was > 40% (ie, much higher than at most United States academic hospitals treating a large number of COVID-19 patients), and thus it is unclear if these results can be extrapolated to United States centers. Several multicenter randomized trials (ACTIV-4a,[9] ATTACC,[10] PROTHROMCOVID,[11] REMAP-COVID[12]) evaluating various anticoagulant dosing

strategies for VTE prophylaxis in hospitalized COVID-19 patients have been conducted. The preliminary report for those patients with severe COVID-19 enrolled in the REMAP-CAP, ACTIV-4a, ATTACC open-label, adaptive, multiplatform, randomized, anticoagulation trials (> 400 sites worldwide in total) has been released,[13] but the final report should offer useful insight.

These and other trials involving various permutations of antithrombotics, antiplatelets, and other strategies to combat VTE in these patients have been recently summarized.[14] At present, there is no single risk score that has been proven to effectively predict which patients with COVID-19 are at the highest risk for VTE nor the optimal prophylaxis or treatment for these patients. Currently, clinicians must use the available data combined with clinical judgment regarding patient-specific risk factors for both VTE and bleeding. When all of the clinical trial data are ultimately available for analysis, we must rigorously and critically analyze them, taking into account the various forms of bias that are present in most and use them to the best of our abilities.

PERT Consortium® Consensus Recommendations

The pandemic has also provided a unique forum for the creation and expansion of PERTs across the globe. Born from a multidisciplinary approach to VTE, The National PERT Consortium® is the largest organization in the world specifically dedicated to improving outcomes in acute PE. The PERT Consortium® has provided consensus recommendations for the diagnosis, treatment, and follow-up of patients with acute PE[15] and recently provided an update for COVID-19 patients.[16] The position statements are summarized in Table 1. The PERT Consortium® emphasizes the need for a multidisciplinary approach in those patients who may have two simultaneous critical cardiopulmonary conditions (COVID-19 and PE) while being limited in diagnostic testing abilities, all in a setting designed to optimize patient outcomes while protecting health care personnel from viral transmission.

CONCLUSION

The complexity of care required to optimize outcomes in critically ill patients with COVID-19 is staggering. Standardized treatment protocols based on the most recent literature must constantly evolve, and this requires a true multidisciplinary team. No one specialty can offer the medical literature vigilance nor the expertise required in such a constantly changing clinical environment; thus, clinicians should consider the creation of COVID-19 teams with expertise in pulmonary, critical care, cardiology, hematology/oncology, vascular medicine,[17] vascular surgery, cardiothoracic surgery, radiology, and pharmacy to ensure the development of order sets that are as standardized as the available evidence base will permit to successfully prevent and treat VTE in critically ill COVID-19 patients. Sound clinical judgment by these expert teams will still be required in this complex and continuously changing area of medicine. ■

1. Tan BK, Mainbourg S, Friggeri A, et al. Arterial and venous thromboembolism in COVID-19: a study-level meta-analysis. Thorax. Published online February 23, 2021. doi: 10.1136/thoraxjnl-2020-215383
2. Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. N Engl J Med. 2020;383:120-128. doi: 10.1056/NEJMoa2015432
3. Fajgenbaum DC, June CH. Cytokine storm. N Engl J Med. 2020;383:2255-2273. doi: 10.1056/NEJMra2026131
4. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 2020;181:271-280.e8. doi: 10.1016/j.cell.2020.02.052
5. Iba T, Connors JM, Levy JH. The coagulopathy, endotheliopathy, and vasculitis of COVID-19. Inflamm Res. 2020;69:1181-1189. doi: 10.1007/s00011-020-01401-6
6. Finn MT, Gogia S, Ingrassia JJ, et al. Pulmonary embolism response team utilization during the COVID-19 pandemic. Vasc Med. Published online April 4, 2021. doi: 10.1177/1358863X21995896
7. Kollias A, Kyriakoulis KG, Lagou S, et al. Venous thromboembolism in COVID-19: a systematic review and meta-analysis. Vasc Med. Published online April 4, 2021. doi: 10.1177/1358863X21995566
8. INSPIRATION investigators; Sadeghipour P, Talasaz AH, Rashidi F, et al. Effect of intermediate-dose vs standard-dose prophylactic anticoagulation on thrombotic events, extracorporeal membrane oxygenation treatment, or mortality among patients with COVID-19 admitted to the intensive care unit: the INSPIRATION randomized clinical trial. JAMA. 2021;325:1620-1630. doi: 10.1001/jama.2021.4152
9. Anti-thrombotics for adults hospitalized with COVID-19 (ACTIV-4). Clinicaltrials.gov website. Accessed June 7, 2021. https://clinicaltrials.gov/ct2/show/NCT04505774
10. Houston BL, Lawler PR, Goligher EC, et al. Anti-thrombotic therapy to ameliorate complications of COVID-19 (ATTACC): study design and methodology for an international, adaptive Bayesian randomized controlled trial. Clin Trials. 2020;17:491-500. doi: 10.1177/1740774520943846
11. Standard vs high prophylactic doses or anticoagulation in patients with high risk of thrombosis admitted with COVID-19 pneumonia (PROTHROMCOVID). Clinicaltrials.gov website. Accessed June 7, 2021. https://clinicaltrials.gov/ct2/show/NCT04730856
12. Randomized, embedded, multifactorial adaptive platform trial for community-acquired pneumonia (REMAP-CAP). Clinicaltrials.gov website. Accessed June 7, 2021. https://clinicaltrials.gov/ct2/show/NCT02735707
13. The REMAP-CAP, ACTIV-4, ATTACC investigators; Zarychanski R. Therapeutic anticoagulation in critically ill patients with Covid-19—preliminary report. medRxiv. 2021. doi: 10.1101/2021.03.10.21252749
14. Talasaz AH, Sadeghipour P, Kakavand H, et al. Recent randomized trials of antithrombotic therapy for patients with COVID-19: JACC state-of-the-art review. J Am Coll Cardiol. 2021;77:1903-1921. doi: 10.1016/j.jacc.2021.02.035
15. Rivera-Lebron B, McDaniel M, Ahrar K, et al. Diagnosis, treatment and follow up of acute pulmonary embolism: consensus practice from the PERT Consortium. Clin Appl Thromb Hemost. 2019;25:1076029619853037. doi: 10.1177/1076029619853037
16. Rosovsky RP, Grodzin C, Channick R, et al. Diagnosis and treatment of pulmonary embolism during the coronavirus disease 2019 pandemic: a position paper from the National PERT Consortium. Chest. 2020;158:2590-2601. doi: 10.1016/j.chest.2020.08.2064
17. Han H, Barnes GD. PERTinent new insights into venous thromboembolism risk and management in hospitalized patients with COVID-19. Vasc Med. Published online May 20, 2021. doi: 10.1177/1358863X211012776

Andrew J. P. Klein, MD
Piedmont Heart Institute
Piedmont Healthcare
Atlanta, Georgia
andrew.klein@piedmont.org
Disclosures: Board of Trustee member of The PERT Consortium® (unpaid position).

Victor Tapson, MD
Cedars-Sinai Medical Center
Los Angeles, California
victor.tapson@cshs.org
Disclosures: Board of Trustee member of The PERT Consortium® (unpaid position).

FlowTriever®
Thrombectomy System

INDUSTRY LEADING CLINICAL RESEARCH

The FlowTriever® system has been studied more than any other mechanical thrombectomy device for the treatment of pulmonary embolism.

464

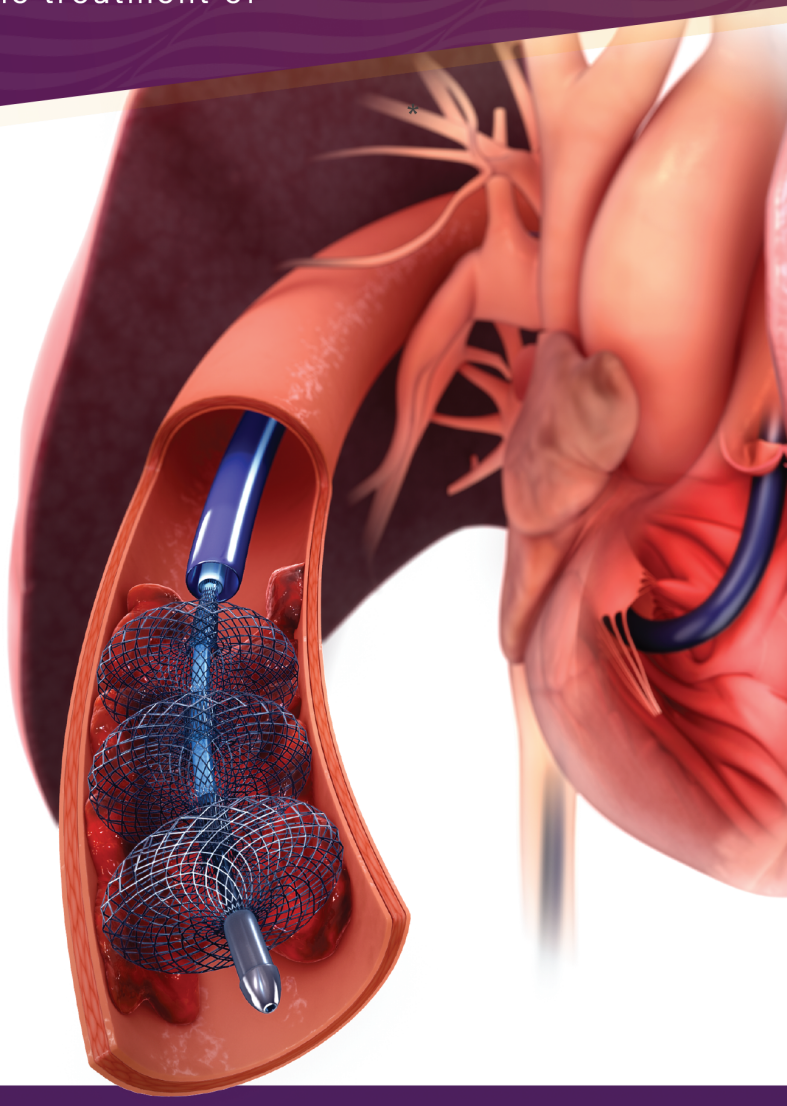
Acute PE Patients

0

Device-Related Deaths

0.6%

Acute Mortality



Patients studied in peer reviewed papers and conference presentations

1. Tu T., Toma C., Tapson V.F., et al. A prospective, single-arm, multi-center trial of catheter-directed mechanical thrombectomy for intermediate-risk acute pulmonary embolism: the FLARE study. JACC Cardiovasc Interv. 2019; 12: 859-869 2. Wible B.C., Buckley J.R., Cho K.H., Bunte M.C., Saucier N.A., Borsa J.J., Safety and efficacy of acute pulmonary embolism treated via large-bore aspiration mechanical thrombectomy using the Inari FlowTriever device. J Vasc Interv Radiol. 2019; 30: 1370-1375 3. Toma C,Toma C, Khandhar S, Zalewski AM, D'Auria SJ, Tu TM, Jaber WA. Percutaneous thrombectomy in patients with massive and very high-risk submassive acute pulmonary embolism. Catheter Cardiovasc Interv. 2020;1–6. 4. Graif, A., Patel, K.D., Wimmer, N.J., Upparapalli, D., Kaneria, A., Leung, D. et al. Large-Bore Aspiration Thrombectomy versus Catheter-Directed Thrombolysis for Acute Pulmonary Embolism: A Propensity Score–Matched Comparison JVIR volume 31, issue 12, p2052-2059, Dec 1 2020 5. Nezami, N., Chockalingam, A., Cornman-Homonoff , J. et al. Mechanical thrombectomy for pulmonary embolism in patients with patent foramen Ovale. CVIR Endovasc 3, 89 (2020). 6. Markovitz M, Lambert N, Dawson L, Hoots G. Safety of the Inari FlowTriever device for mechanical thrombectomy in patients with acute submassive and massive pulmonary embolism and contraindication to thrombolysis. Am J Interv Radiol 2020;4:18 7. Toma, C. FLASH registry Transcatheter Cardiovascular Therapeutics scientific symposium of the Cardiovascular Research Foundation on held online October 14-18, 2020.

Indications:

The FlowTriever System is indicated for (1)The non-surgical removal of emboli and thrombi from blood vessels (2) Injection, infusion and/or aspiration of contrast media and other fluids into or from a blood vessel The FlowTriever System is intended for use in the peripheral vasculature and for the treatment of pulmonary embolism. The Triever Catheters are intended for use in peripheral vasculature and for the treatment of pulmonary embolismTriever Catheters are also intended for use in treating clot in transit in the right atrium.

INARI MEDICAL®

9 Parker #100, Irvine, CA 92618

MM-01020_A; MCO-00065

The Promise of The PERT Consortium® PE Registry

A registry to inform physicians about the modern state of pulmonary embolism care, including risk stratification, diagnosis, and treatment.

By Eric A. Secemsky, MD, MSc, RPVI, FACC, FSCAI, FSVM; Jay Giri, MD, MPH; and Robert Lookstein, MD, MHCDL, FSIR, FAHA, FSVM

Pulmonary embolism (PE) is the third leading cause of worldwide cardiovascular death.[1] However, significantly fewer resources have been put into research related to innovation in care delivery for this disease than the top two leading causes of cardiovascular death: myocardial infarction and stroke. Although evidence-based pathways for care delivery fueled by evolving therapeutics paired with registry-based assessments for quality improvement are the norm for these conditions, such a coordinated system has been largely absent from the acute PE space.

PERT CONSORTIUM® PE REGISTRY

The last large-scale multicenter registry dedicated exclusively to the study of acute PE patients enrolled patients in the mid-1990s. The International Cooperative Registry for Pulmonary Embolism (ICOPER) enrolled 2,454 patients with acute PE at 52 institutions in 1995-1996.[2] A series of seminal publications arose from these efforts that were instrumental in defining prognosis, treatment patterns, and outcomes for a wide range of real-world, hospitalized PE patients. This work has largely persisted as the gold standard for observational research in acute PE, even as the field itself has continued to evolve. For instance,

- University of Kentucky
- Beaumont Health
- Columbia University Medical Center
- University of Michigan
- Henry Ford Health System
- University of Cincinnati
- Ohio Health
- Mount Sinai Health System
- Gates Vascular
- Cedars-Sinai
- Penn Presbyterian
- Doylestown Hospital
- Marshfield Clinic
- Ellis Hospital
- CCF
- CHS Mercy Buffalo
- Lancaster General
- MGH
- UCLA
- Loyola
- Lahey
- Piedmont
- Englewood Health
- Spectrum Health
- Carle Foundation
- University of Virginia
- Delray Medical Center
- Allegheny Health
- Gundersen Health
- Emory
- Thomas Jefferson
- Northeast Georgia Medical Center
- St. Francis
- Jamaica Hospital

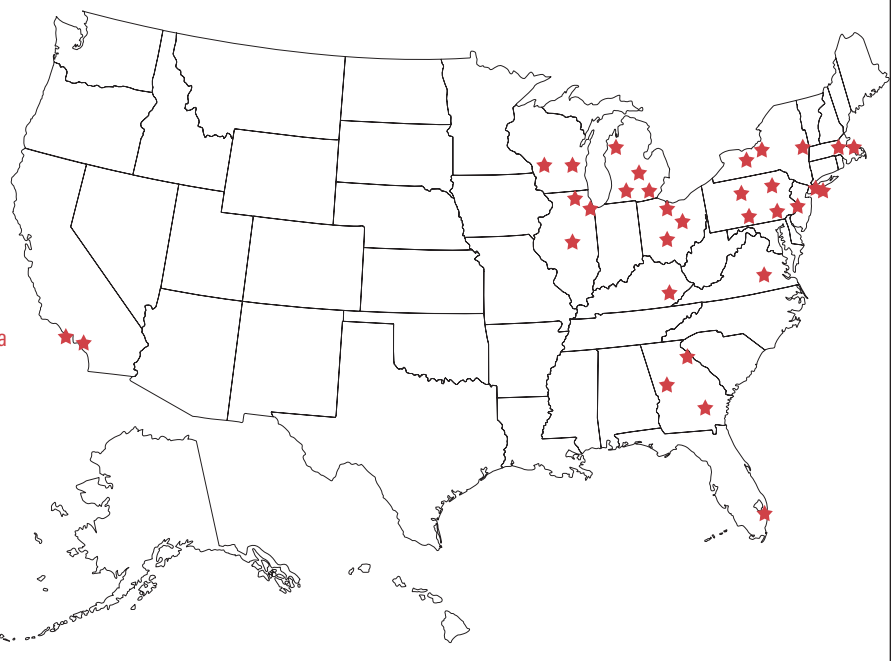


Figure 1. Participating centers in The PERT Consortium® PE Registry.

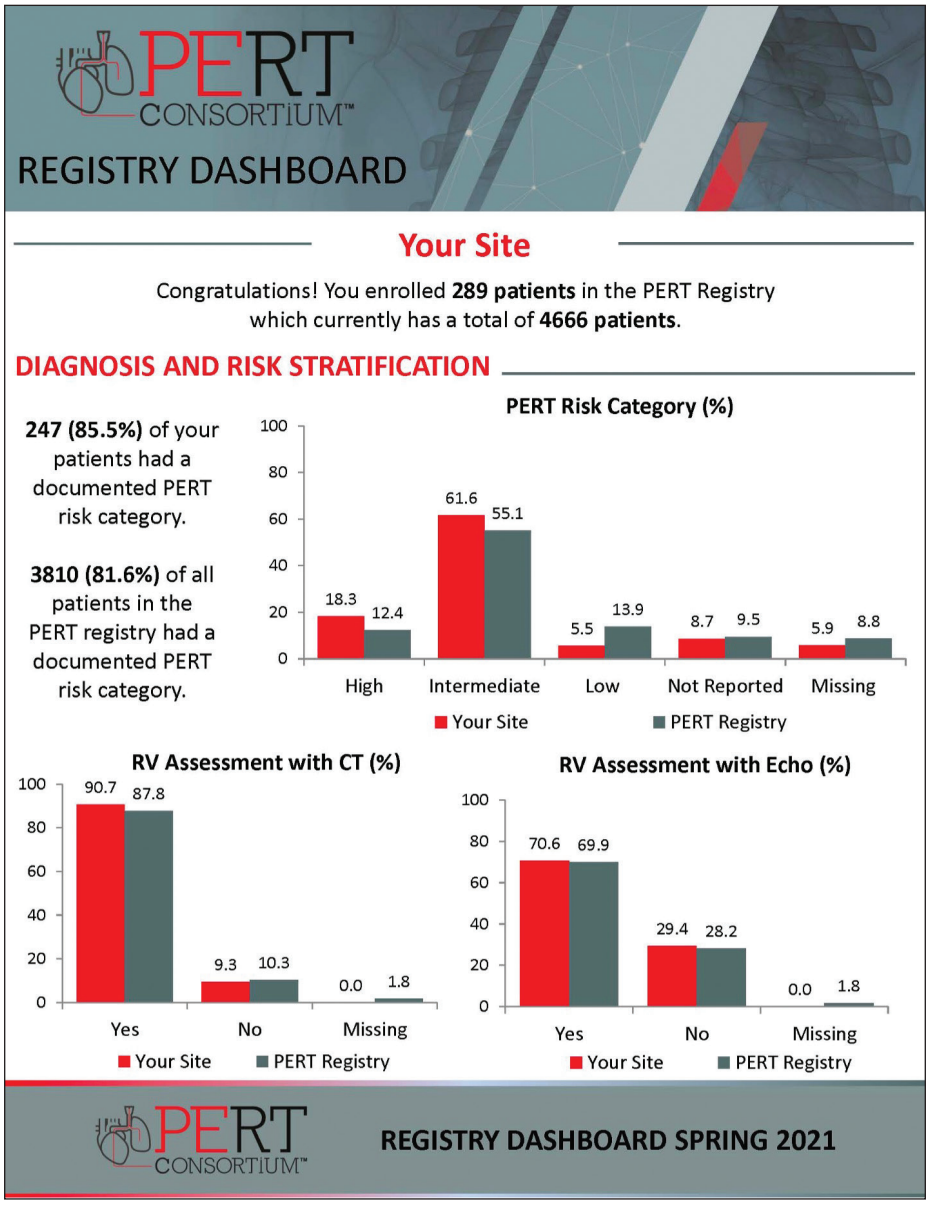


Figure 2. Representative image of the PERT Consortium® PE Registry dashboard.

in 1996, direct oral anticoagulants had barely been theorized, much less developed. Imaging technologies for assessing the pulmonary circulation and the right heart were primitive compared to today's standards. Additionally, the rapidly evolving wide range of interventional technologies we now have for acute pulmonary artery revascularization was nonexistent. These are just a few of the myriad issues that clearly need reassessment in modern, large, real-world PE populations.

It is on this background that The National Pulmonary Embolism Response Team (PERT) Consortium® embarked on a mission to create a modern PE registry. Utilizing the backbone of member sites in the organization, The PERT Consortium® has assembled a broad group of > 30 hospitals that submit data on an ongoing basis regarding hospitalized patients with PE. Member institutions submitting data vary in size, region, technologic capacity, and academic status (Figure 1). More than 4,600 patients have been entered in the registry to date, representing diversity in age, gender, race, and comorbidity profiles. For instance, the average age of a registry patient is 61 years, with a wide range of ages represented (SD, 18 years). Of all patients, currently 53% are female and 39% are of minority race. PERT activations were performed 56% of the time in the emergency department, whereas the remaining patients were consulted on in various hospital locations. Furthermore, 25% of patients were transferred from another institution prior to PERT activation to receive advanced PE care.

Additional data collected by the registry include signs and symptoms at presentation, risk factors for PE, laboratory and imaging studies, noninvasive and invasive therapies, in-hospital events, and longitudinal follow-up. These data are critical in estimating and categorizing PE-related risks and understanding expected prognoses. Importantly, in addition to participating sites having access to their own PE data, centers are provided quarterly dashboards with information on how their site-specific quality metrics (eg, length of stay, in-hospital events, follow-up visits, readmissions) vary compared with other participating centers (Figure 2).

Furthermore, a newly formed PERT Consortium® Research and Publications Committee launched this year. This 12-member committee, made up of national leaders in PE care and representing various medical specialties and disciplines, was developed to facilitate the

use of the registry to answer pressing scientific questions regarding the management of patients hospitalized with PE. The committee has developed a research proposal application process to allow members of the PERT community to apply and lead scientific investigations for national presentation and peer-reviewed publication. The anticipation is that the registry can assist in eliminating the many data gaps that exist in current PE management.

This modern PE registry has a slightly different focus than ICOPER given the knowledge gained in the past and the specific areas of uncertainty that exist now. Specifically, registry patients are captured through the activation of PERTs, thus enriching the registry by focusing on the management of intermediate- and high-risk patients. Not incidentally, this is where most of the current controversy in prognosis and care lies, as management of low-risk PE patients is decidedly more algorithmic in the modern era. The PERT Consortium® PE Registry has the promise to better determine how contemporary hospitalized PE patients are being managed, obtain benchmark rates for adverse events, and provide much-needed longitudinal follow-up data on survivors of PE.

CONCLUSION

At its core, The PERT Consortium® PE Registry is a quality assessment and improvement tool for participating institutions. In an arena where level 1 data to guide the management of hospitalized PE patients are sparse, the ability for an institution to benchmark its processes and outcomes against like-minded peer institutions is invaluable. Similar to ICOPER before it, The PERT Consortium® PE Registry also holds considerable promise for informing PE practitioners and the medical community at large about the modern state of PE care. This includes important assessments regarding the evolution of risk stratification, diagnosis, and treatment of PE as well as observational analysis of the care delivery model of the PERT itself. ■

1. Goldhaber SZ, Bounameaux H. Pulmonary embolism and deep vein thrombosis. Lancet. 2012;379:1835-1846. doi: 10.1016/S0140-6736(11)61904-1
2. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). Lancet. 1999;353:1386-1389. doi: 10.1016/s0140-6736(98)07534-5

Eric A. Secemsky, MD, MSc, RPVI, FACC, FSCAI, FSVM
Director, Vascular Intervention
Section Head, Interventional Cardiology and Vascular Research
Richard A. and Susan F. Smith Center for Outcomes Research in Cardiology
Beth Israel Deaconess Medical Center
Assistant Professor of Medicine
Harvard Medical School
Boston, Massachusetts
esecemsk@bidmc.harvard.edu
Disclosures: Research grants to BIDMC from NIH/NHLBI K23HL150290, Harvard Medical School's Shore Faculty Development Award, AstraZeneca, BD, Boston Scientific, Cook, CSI, Laminate Medical, Medtronic and Philips; consulting/speaking, Abbott, Bayer, BD, Boston Scientific, Cook, CSI, Inari, Janssen, Medtronic, Philips, and VentureMed.

Jay Giri, MD, MPH
Director, Peripheral Intervention
Assistant Professor of Medicine
Hospital of the University of Pennsylvania
Philadelphia, Pennsylvania
jay.giri@pennmedicine.upenn.edu
Disclosures: Research funds from and advisory board, Inari Medical, AstraZeneca, and Boston Scientific Corporation.

Robert Lookstein, MD, MHCDL, FSIR, FAHA, FSVM
Professor of Radiology and Surgery
Icahn School of Medicine at Mount Sinai
New York, New York
robert.lookstein@mountsinai.org
Disclosures: Advisory board and consultant for Medtronic and Boston Scientific Corporation; consultant for Penumbra.

THE PERT CONSORTIUM®

We would like to recognize and thank the continued support of our industry partners.

angiodynamics

Boston Scientific

INARI MEDICAL®

janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Penumbra

PERT CONSORTIUM®

REGISTER NOW

Pulmonary Embolism: What is Known, and What We Need to Know: A State of the Art and Scientific Update

In-person and hybrid options available!

7TH ANNUAL

Pulmonary Embolism Symposium

Sponsored by the PERT Consortium®

Register now at https://pertconsortium.org/register

Renaissance Boston Waterfront Hotel • 606 Congress Street • Boston, MA 02210

The business meeting will take place on Thursday followed by the annual Scientific Symposium on Friday and Saturday.

OCTOBER	THURSDAY	FRIDAY	SATURDAY
2021	14	15	16

This This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Boston University School of Medicine and PERT Consortium. Boston University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Boston University School of Medicine designates this live activity for a maximum of 15 AMA PRA Category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

@pertconsortium

contact@pertconsortium.org