The PERT Consortium® COVID-19 PE Registry: Introduction and Implementation

A discussion of the goals of the registry and what types of data are being collected and reported.

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The novel coronavirus disease 2019 (COVID-19) was first identified in Wuhan, China, in December 2019 and is currently spreading around the world, with over 9.2 million cases and more than 476,000 deaths as of June 24, 2020.[1,2] Although patients often present with respiratory insufficiency, those with the most severe form of the disease develop multiorgan failure. In those patients, one of the most significant poor prognostic features is the development of coagulopathy.[3] Early studies out of China have demonstrated that individuals who have elevated circulating D-dimer levels are at significantly increased risk of mortality compared with individuals who do not.[3,4] This finding has been confirmed in several other studies around the world.[5-8] Research has also shown that, similar to the SARS-CoV virus, pathologic fibrin thrombi are found within the pulmonary vasculature of affected patients. The coagulopathic state associated with COVID-19 and the resultant increased thrombin generation can increase the risk of venous thromboembolism (VTE), including pulmonary embolism (PE). Prior to the COVID pandemic, the incidence of PE was estimated at 1 to 2 per 1,000 individuals in the United States per year, accounting for at least 100,000 deaths per year.[9] Although the exact incidence of VTE associated with COVID-19 is currently unknown, reports range from as low as 1% in general wards to as high as 31% in intensive care units.[5,10-19] Given the prothrombotic state conferred by COVID-19 infection and the resultant higher incidence of PE and its associated morbidity and mortality in affected patients, there is an urgent need to study this unique population. Understanding the characteristics, prevention and treatment modalities, and outcomes of patients with COVID-19 who develop PE and how they compare to PE patients without COVID-19 is crucial as this pandemic continues. By characterizing the findings in COVID-19 patients with PE through the Pulmonary Embolism Response Team (PERT) Consortium® COVID-19 PE registry, future diagnostic and treatment algorithms can be optimized to improve outcomes and reduce related morbidity and mortality.

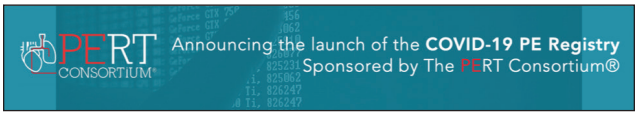

Figure 1. Announcement of the COVID-19 PE registry on the PERT Consortium® website (pertconsortium.org).

THE PERT CONSORTIUM®

The PERT Consortium® is a 501(c)(3) nonprofit organization founded in 2016 for the purpose of promoting the multidisciplinary care of patients with PE. The PERT Consortium® is ideally positioned to implement this essential project (Figure 1). Its membership represents > 150 institutions and > 1,500 clinicians in the United States and globally, and it is focused on improving outcomes for patients with PE by advancing its recognition, diagnosis, and treatment. PERT teams are on the front lines of managing patients with PE at their institutions and therefore are in the essential position to treat COVID-positive patients with PE. Moreover, the PERT Consortium®, in conjunction with the Boston Clinical Research Institute, manages an already established and mature database that is the largest prospective United States registry of PE patients to date. The PERT Consortium® is leveraging the infrastructure of this existing registry, which utilizes the user-friendly and rapidly scalable REDCap Cloud platform, to collect the necessary information for the COVID-19 PE registry and quickly scale it up to obtain data and address the impact of this rapidly growing disease.

THE COVID-19 PE REGISTRY

Goals and Participation

The goal of the COVID-19 PE registry is to utilize the existing infrastructure of a robust multicenter PE database to (1) identify the clinical characteristics, diagnostic strategies, treatment approach, and short- and long-term outcomes of all patients diagnosed with both COVID-19 and PE; and (2) compare the mechanisms of triage and systems of care and delivery between patients with

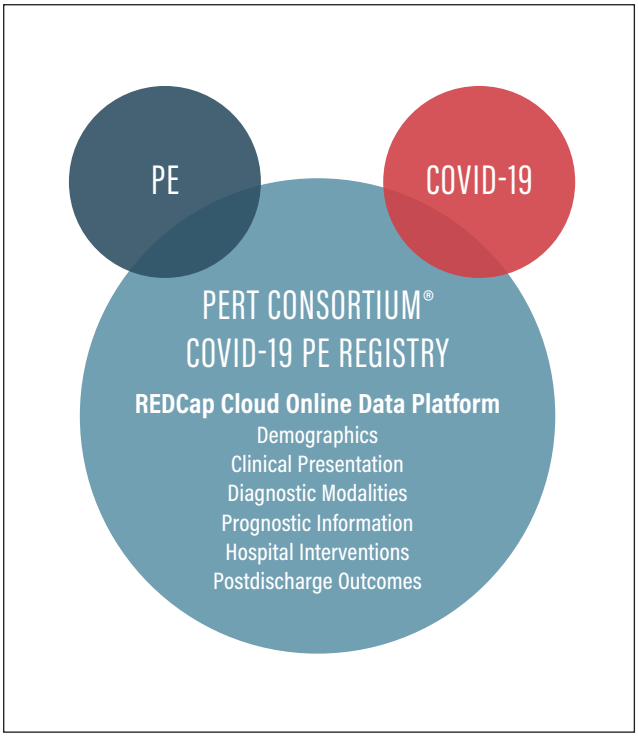

Figure 2. Embedding the COVID-19 PE registry into the existing PERT Consortium® database.

both COVID-19 and PE to historical PE controls from the existing PERT registry. This is being accomplished by collecting data from established participating sites by nesting a distinct COVID-19 PE registry within the existing data collection tool and inviting any other institution (regardless of membership status in the PERT Consortium® or participation to date in the registry) to join the COVID-19 PE registry and submit data for every PE occurring in COVID-19 patients at their institution (Figure 2). Participation is being offered without any cost centrally. Central institutional review board approval (IRB) is being orchestrated and achieved by the PERT Consortium® or local IRB approval at individual sites if preferred.

PERT Consortium® has created a deidentified observational registry within an existing large multi-institutional database dedicated to the study of patients with PE to capture the clinical characteristics and outcomes of patients with confirmed COVID-19 and PE. A major benefit of this registry is the ability to utilize historical data from the existing PE registry as a control group.

The PERT Consortium® contributing member institutions exist throughout the United States as well as in Europe, China, Asia, and Africa. Several of the participating United States institutions are located within current

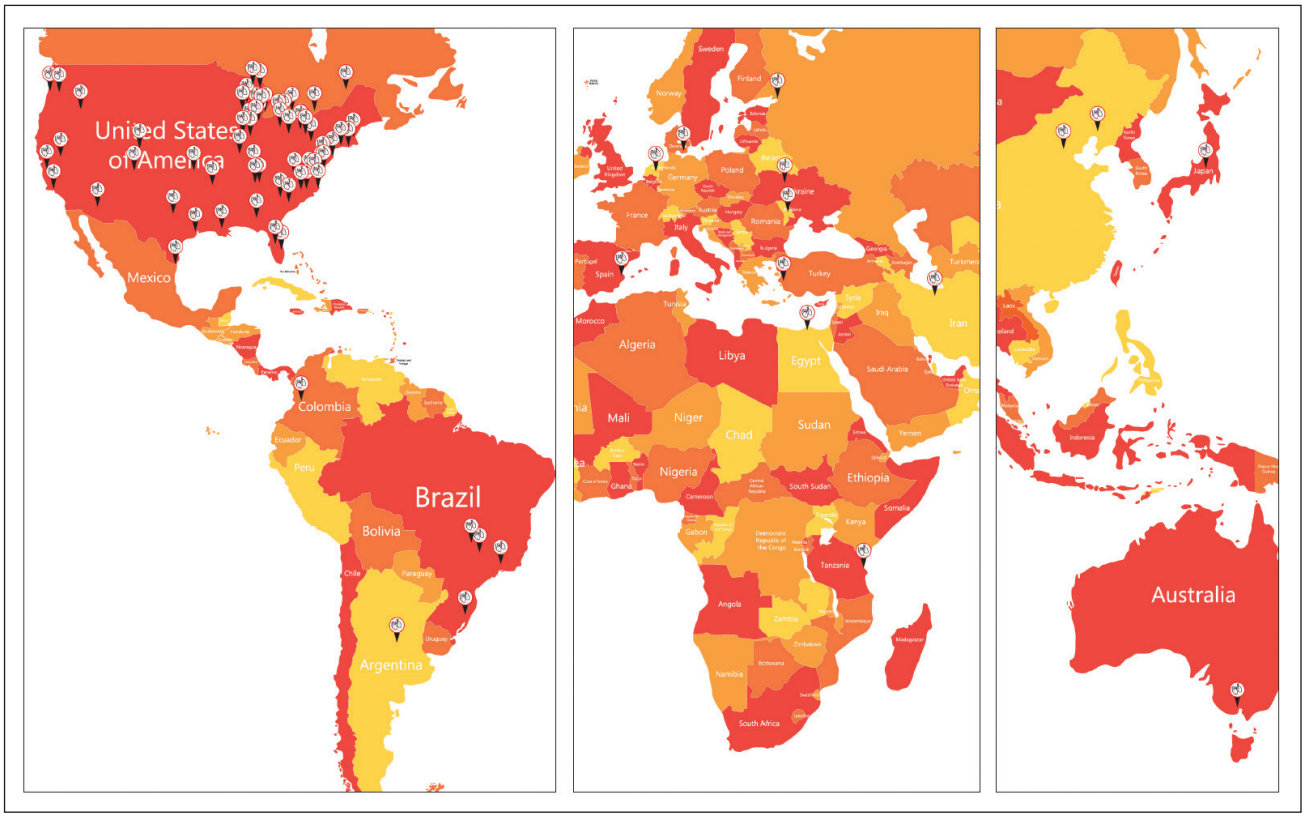

Figure 3. Map of PERT Consortium® sites around the world.

CURRENT PARTICIPATING SITES IN THE PERT CONSORTIUM® COVID-19 PE REGISTRY

- Abbott Northwestern
- Advent Health Orlando
- Allegheny Health
- AtlantiCare
- Augusta University
- Aurora Health
- Baptist Health System
- Baptist Health South Florida
- Beaumont Health
- Beth Israel Deaconess
- Cancer Treatment Centers of America
- Carle Foundation
- Catholic Health/Mercy Hospital of Buffalo
- Cedars-Sinai
- Christiana Care
- Cleveland Clinic
- Columbia University
- Community Foundation of Eastern CT
- Detroit Medical Center
- Duke University
- East Carolina University
- Edward-Elmhurst Heart Hospital
- Ellis Hospital
- Emory University
- Englewood Hospital
- Essentia Health St. Mary's Medical Center
- Gates Vascular/Kaleida Health
- Geisinger
- Grady Memorial
- Grandview Medical Center
- Gundersen Lutheran
- Henry Ford Hospital
- Infirmary Health
- Inova
- Jacobi Medical Center
- Jamaica Hospital
- Jefferson
- Jefferson Township
- Kobe University
- Lahey Medical Center
- Lancaster General
- Lenox Hill Hospital
- Loyola
- MacNeal Hospital
- Marshfield Clinic
- Massachusetts General Hospital
- Mayo Clinic
- Medical University of South Carolina
- MedStar
- Memorial Hermann
- Methodist Hospital
- Mission Hospital
- Mount Sinai Health System
- Newton-Wellesley Hospital
- Northeast Georgia Medical Center
- Northwestern Memorial/Bluhm
- NYU Langone
- Ohio Heart & Vascular
- Ohio State University
- Oklahoma State University
- Palos Community Hospital
- Penn Medicine Piedmont
- Providence Hospital
- Rhode Island Hospital
- Riverside Medical Center
- SSM Health
- Saint Vincent Hospital
- Southern Illinois Healthcare
- Spectrum Health
- St. Joseph Mercy
- Temple University Hospital
- Thomas Jefferson University Hospital
- Trinity Health
- UC Davis
- UC Health
- UW Health
- University of California
- University of Chicago
- University of Kentucky
- University of Michigan
- University of Minnesota
- University of Pittsburgh
- University of Rochester
- University of Tennessee
- University of Virginia
- University of Wisconsin
- Vanderbilt
- Weill Cornell
- Yale University

COVID-19 hot spots, which ensures that a cohort enriched with affected patients will be entered into the COVID-19 PE registry. Current participating sites are listed in the Sidebar, and a map of participating worldwide sites is shown in Figure 3.

Data Collection

The PERT Consortium® database, created in April 2018, is a robust clinical research and quality improvement database with > 200 discrete data elements per patient. Currently, data from > 3,500 patients with PE from the pre-COVID-19 era are included. Over 25 studies on PERTs have been published to date.[20-28] Prior American Heart Association and other societal position statements were spearheaded by PERT members.[29] More recent algorithms for management of acute PE have been published by the PERT Consortium® itself; these are living documents that are constantly being reviewed and updated by the Consortium. In October 2019, the PERT Consortium® hosted its 5th annual scientific session on management of acute PE with nearly 600 international attendees. More recently, PERT Consortium® has hosted several COVID-19 specific webinars, each with more than 600 attendees. In the PE world, PERT Consortium® is currently looked upon as the organization that provides the most current multidisciplinary guidance for PE management, as well as direction for quality assurance and scientific exploration that is focused on filling evidence gaps.

The COVID-19 PE registry allows physicians and other health care providers to enter data into a web-based data collection form (REDCap Cloud). Relevant COVID-19 PE elements have been identified and defined and are embedded in the new registry. This COVID-19 PE registry is open for participation to any institutional site, free of charge and regardless of current membership in the PERT Consortium®. The new COVID-19–related elements are also now nested in the existing multicenter registry of patient-level data. Data points collected include details on demographics, clinical presentation, diagnostic modalities, prognostic information, interventions, and

in-hospital and postdischarge outcomes. Reported outcomes include death, recurrent PE, bleeding, length of stay, readmission, and lab values when available. The existing multicenter registry will continue to be managed by the PERT Consortium®, in collaboration with Boston Clinical Research Institute serving as the host and data coordinating center. Importantly, both the existing and new focused registry operate with central IRB approval and waiver of consent.

Institutional Review Board

The COVID-19 PE registry is submitted as human subjects research exempt. Obtaining a non–human subjects research determination has facilitated the speed and efficiency of implementation and subsequent data collection. Data are completely deidentified and the registry complies with HIPAA (Health Insurance Portability and Accountability Act) safe harbor deidentification requirements. All steps necessary to comply with General Data Protection Regulation requirements for collecting and anonymizing personal data are being followed. Once entered, data are analyzed and observations are reported regarding clinical practice and patient outcomes in aggregate form to provide near-real-time insights to guide clinicians as they care for COVID-19 patients with PE.

Patient Population

The COVID-19 PE registry is enrolling patients with confirmed COVID-19 and confirmed or highly presumptive PE. A confirmed COVID-19 diagnosis is defined as a positive result on high-throughput sequencing or real-time reverse transcription polymerase chain reaction assay of nasal and pharyngeal swab specimens. For this registry, a PE diagnosis must be confirmed by CT, echocardiography, or MRI; although in the COVID era, a presumptive diagnosis of PE without absolute confirmation of thrombus in the pulmonary arteries by CT or MRI is possible. It is not the goal or intent of this COVID-19 PE registry to collect data indiscriminately on all COVID-19 patients; thus, patients with a known diagnosis of COVID-19 but without a confirmed or presumptive diagnosis of PE are excluded. Likewise, patients with known chronic PE but not acute PE and those with PE but without documented COVID-19 infection are excluded. However, interested sites are encouraged to join the existing main PERT PE registry and enter non-COVID PE patients into that registry. Importantly, the existing PERT PE database will provide a group of "controls" against which the COVID-positive PE patients can be compared. All central fees have been waived, and thus participation is free of charge for both the main PERT PE registry and the focused COVID-19 PE registry.

Results

The COVID-19 PE registry will enable the research committee of the PERT Consortium® to rapidly obtain information on the diagnosis, treatment, and outcomes of patients with concurrent COVID-19 and PE. To date, similar information—such as that from China, Italy, the United States, and elsewhere—are being reported from single centers.[5,10-19] The PERT Consortium® will examine this invaluable information in detail. The availability of data from a comparative cohort may provide insights into the unique aspects of PE in COVID-19. Importantly, the existing broad-based participation of the PERT Consortium®, with its large membership and infrastructure, will enable collection, analysis, and dissemination of information in a timely manner.

DISCUSSION

The PERT Consortium® recently published a consensus practice document on the care of patients with PE, which included detailed algorithms on diagnosis, treatment, and follow-up.[30] Important outcomes from the COVID-19 PE registry will include modification of those algorithms specifically targeted to COVID-19 and PE patients, as well as recommendations on how to best care for these critically ill patients. Currently, in some areas, the mortality rate of COVID-19 patients who are admitted to critical or intensive care units approaches 50%.[31] The ultimate goal of the COVID-19 PE registry is to influence prevention and treatment in concrete ways that can decrease the morbidity and mortality associated with this disease.

A potential limitation of this registry is that we are including both confirmed PE and some presumed PE patients. Use of imaging modalities can be challenging due to concerns of viral transmission; however, this limitation may also be a strength. As we learn about "real-world" management of documented and presumed PE in this challenging environment, we will also learn about the characteristics of COVID-19 and PE, including the precursors, signs, symptoms, and responses to treatment. This information will be useful to identify patients who may be at risk of developing PE and, in turn, how best to modify prevention and treatment strategies. Given that this pandemic will not be eradicated in the near future, this information is critical to the medical world.

CONCLUSION

The COVID-19 PE registry will provide expedient public reporting of aggregate data on the clinical characteristics and outcomes of patients with COVID-19 and PE in order to facilitate clinical decision-making and allocate resources. The PERT Consortium® already has successful mechanisms to quickly disseminate updates on the science of PE, including those that might emanate from analysis of COVID-19 PE registry data. These include the annual PERT scientific meeting, as well as regular national/international

webinars and other educational events that reach thousands of health care providers. The PERT Consortium® also has a robust website and provides monthly emails (entitled "PERTinent Updates"), relied upon by thousands of providers to stay current with the most important scientific discoveries in PE, as well as research and practical advice regarding optimal management of acute PE. Periodic dissemination of aggregate data from the COVID-19 PE registy to contributing centers and the clinical community at large will shape real-time decision-making and patient-level care as the pandemic evolves. Moreover, expedited publication of these data in high-impact journals will reach clinicians around the globe and positively impact patient care going forward. By leveraging existing resources to create the COVID-19 PE registry, it will be efficient, cost-effective, and scientifically powerful. ■

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