

Impact and role of pulmonary embolism response teams in venous thromboembolism associated with COVID-19

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ABSTRACT

Venous thromboembolism associated with COVID-19, particularly acute pulmonary embolism, may represent a challenging and complex clinical scenario. The benefits of having a multidisciplinary pulmonary embolism response team (PERT) can be important during such a pandemic. The aim of PERT in the care of such patients is to provide fast, appropriate, multidisciplinary, team-based approach, with the common goal to tailor the best therapeutic decision making, prioritizing always optimal patient care, especially given lack of evidence-based clinical practice guidelines in the setting of COVID-19, which potentially confers a significant prothrombotic state. Herein, we would like to briefly emphasize the importance and potential critical role of PERT in the care of patients in which these two devastating illnesses are present together.

INTRODUCTION

According to the Centers for Disease Control and Prevention, estimates suggest that 300,000–600,000 people are affected annually by venous thromboembolism (VTE). There is evidence that suggests these numbers have been increasing over the past decade and now even more since COVID-19 emerged from Wuhan, China, in November 2019.¹

Infection with SARS-CoV-2 causes a prothrombotic state resulting in higher risk of developing VTE.² The incidence of pulmonary embolism (PE) in hospitalized patients with COVID-19 has been reported from 1.9% up to 8.9% in acutely medically ill patients affected with COVID-19 hospitalized in a medical ward section; cumulative incidence of VTE in critically ill patients has ranged from 12.6% up to 30.0% in some retrospective studies.^{3–5}

RATIONALE OF PULMONARY EMBOLISM RESPONSE TEAMS (PERTS)

PERTs were initially instituted at Massachusetts General Hospital in 2012.⁶ PERTs have been designed to facilitate, in a multidisciplinary fashion, the best decision-making and optimal care in regard to diagnostic and therapeutic

strategies for complex cases of VTE, particularly acute PE, with the goal of improving quality of care, outcomes, and survival. PERTs are integrated by experienced physicians in diverse medical and surgical specialties like pulmonology, cardiology, critical care, hematology, thrombosis, and vascular medicine, leveraging and supporting each other; however, the number of PERT members may vary, depending on each academic institution/hospital.^{7–9}

PERTs can be activated by any clinician, from any area of the hospital (eg, from the emergency department, the operating room, or the medical floor), even from an outside remote hospital, as soon as the clinician encounters a patient with complex acute PE, with the purpose of reaching a final decision by consensus in an expedited time after the PERT consultation has been activated. There are a wide variety of therapeutic alternatives available to PERTs that range from anticoagulation, systemic thrombolysis, catheter-directed therapies, surgical pulmonary embolectomy (SPE), and advanced cardiopulmonary support like extracorporeal membrane oxygenation (ECMO); however, these technological therapeutic advances may be contingent and dependent on specific resources and infrastructure available for a given hospital, having the ability to deliver an effective, rapid, and most appropriate therapeutic approach for a given complex acute PE.^{10 11}

WHAT IS THE ROLE OF PERT IN THE ERA OF COVID-19 AND WHICH PATIENTS MAY BENEFIT THE MOST?

We strongly believe that PERTs play an important role in patients with COVID-19 in which the diagnosis of VTE, particularly significant complex acute PE, represents a priority to diagnose and is high in the differential diagnosis. Given the complex interplay between COVID-19 and acute PE, which is still an incompletely understood and evolving phenomena, PERT members could aid in the clinical decision making while performing fast,



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appropriate risk stratification, diagnosis, and therapeutic strategies in these extremely sick patients.

Key aspects like patient clinical characteristics, mode of onset/presentation, specific risk factors for VTE, pertinent medical history, like previous VTE event, biomarkers like D-dimer, troponins, brain natriuretic peptide, as well as imaging modalities when available, alongside the abrupt onset of cardiopulmonary deterioration (eg, worsening refractory hypoxemia and/or rapid progressive hemodynamic compromise), which is out of proportion to the COVID-19 pulmonary involvement, require further in-depth exploration for a superimposed complex acute PE, triggering a prompt PERT consultation. PERT members can expedite initial diagnostic and management recommendations, and in most instances, if no contraindication exists, initiation of full therapeutic anticoagulation should be instituted while ongoing further investigation is performed for definitive diagnosis of acute PE.

PERT must assist and address important issues in the setting of complex acute PE complicating COVID-19. Specifically, they should

1. Determine which patients should undergo rapid, safe, and appropriate further diagnostic and risk stratification, when complex acute PE is highly likely in hospitalized patients with moderate to severe pneumonic COVID-19.
2. Determine which is the best and safest diagnostic tool for a given patient with possible VTE, and in which such diagnostic tool used will be effective and with minimal exposure to personnel, to avoid transmissibility and infectibility of SARS-COV 2 (eg, use of computed tomographic angiography of the chest in hemodynamic stable patients in the medical floor vs bedside transthoracic echocardiography or lower extremity venous Doppler studies in very labile unstable patients in the intensive care unit, receiving vasopressor support and mechanical ventilatory support).
3. Determine which patients may benefit from potential empirical full therapeutic anticoagulation therapies while confirmation of acute PE is established.
4. In patients with rapidly progressive cardiopulmonary deterioration, PERTs must screen and carefully and thoroughly review indications and contraindications of the potential use of advanced reperfusion strategies like systemic thrombolysis, catheter-directed therapies or, in extreme cases, if emergent surgical pulmonary embolectomy (SPE) will be needed.
5. PERT members always need to balance the benefit versus risk of such advanced therapies, determining which subset of patients with complex acute PE meets criteria for the aforementioned while also taking into consideration minimal exposure of healthcare personnel while applying such therapies, with the goal to reduce potential transmissibility of COVID-19. Afterwards, deciding by consensus within the PERT members, rapid mobilization of resources within the academic hospital must be initiated to provide the desired therapeutic modality.
6. PERTs must decide which patients need to be transferred to a hospital or facility with a higher level of care, in case such therapeutic modality is not available in their institutions (eg, need of ECMO or 24/7 on-call cardiothoracic surgeon with expertise in SPE).

7. PERT should further aid and facilitate smooth transfer of care in patients with concomitant COVID-19 and acute PE, providing recommendations of type of anticoagulation, length of therapy, and prompt follow-up in a designated thrombosis/vascular medicine or postacute PE multidisciplinary clinic, once discharged from the hospital.

Recently, the National PERT Consortium published a useful and informative position statement document, focusing on the important role of PERT in the diagnosis and therapies of acute PE, emphasizing the importance, the perks, and benefits of having a team-based, multidisciplinary approach like PERT, which can provide the most optimal patient care of complex acute VTE during the COVID-19 pandemic.¹²

IMPACT OF PERT IN VTE ASSOCIATED WITH COVID-19

Kwok and colleagues performed an interesting descriptive retrospective comparative analysis of PERT in the pre-COVID-19 and during the COVID-19 era; PERT activations decreased significantly during the pandemic (26% vs 68%, $p < 0.001$); was used more commonly in those who were SARS-COV 2 negative (68.2% vs 38.3%, $p = 0.02$); however, during the pandemic, in patients with and without COVID-19, when activated PERT was associated with decreased length of stay (7.7 ± 7.7 vs 13.2 ± 12.7 days, $p = 0.02$).¹³

Due to the lack of robust evidence-based data with regard to the potential impact of PERT during COVID-19, the National PERT Consortium created the COVID-19/Acute PE Registry, with the objective to characterize and identify different diagnostic and therapeutic patterns, as well as to generate knowledge regarding short-term and long-term outcomes of patients with VTE associated with COVID-19, particularly complex acute PE (<https://pertconsortium.org/covid-19-and-pe-registry/>).¹⁴ Such real-world data will generate valuable information and knowledge, with implications for diagnostic and therapeutic decision-making, with the aim of enhancing hard outcomes and survival in affected patients with these two potentially fatal entities present together.^{12 14}

CONCLUDING REMARKS AND FUTURE DIRECTIONS

Because difficult decisions are made in complex case scenarios of VTE in the challenging era of COVID-19, without the support of solid evidence-based data available, PERT definitively can be of aid and extremely helpful while carefully and thoroughly analyzing and individualizing on a case-by-case basis every unique complex VTE scenarios encountered in hospitalized patients with pneumonic COVID-19.

PERTs are currently playing and will continue to play a pivotal role in such challenging clinical decisions for the busy clinician, and this is a call to action to clinicians and researchers that fight against VTE to mitigate these two deadly diseases with the support of PERT.¹⁵ We are convinced and certain that, as the PERT model and process continue to evolve during these unprecedented times, and with more robust evidence-based data available from the COVID-19/Acute PE Registry, the adoption of PERT will shift the paradigm in the care of complex acute

PE by perfecting and pursuing excellence in such care, not only in the USA but also globally, with the ultimate goal of improving outcomes and quality of life, and minimizing morbidity and mortality of VTE during the COVID-19 pandemic.

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