Pulmonary Embolism Response Team activation during the COVID-19 pandemic in a New York City Academic Hospital: a retrospective cohort analysis

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Abstract

Coronavirus disease 2019 (COVID-19) is associated with increased rates of deep vein thrombosis (DVT) and pulmonary embolism (PE). Pulmonary Embolism Response Teams (PERT) have previously been associated with improved outcomes. We aimed to investigate whether PERT utilization, recommendations, and outcomes for patients diagnosed with acute PE changed during the COVID-19 pandemic. This is a retrospective cohort study of all adult patients with acute PE who received care at an academic hospital system in New York City between March 1st and April 30th, 2020. These patients were compared against historic controls between March 1st and April 30th, 2019. PE severity, PERT utilization, initial management, PERT recommendations, and outcomes were compared. There were more cases of PE during the pandemic (82 vs. 59), but less PERT activations (26.8% vs. 64.4%, $p < 0.001$) despite similar markers of PE severity. PERT recommendations were similar before and during the pandemic; anticoagulation was most recommended (89.5% vs. 86.4%, $p = 0.70$). During the pandemic, those with PERT activations were more likely to be female (63.6% vs. 31.7%, $p = 0.01$), have a history of DVT/PE (22.7% vs. 1.7%, $p = 0.01$), and to be SARS-CoV-2 PCR negative (68.2% vs. 38.3% $p = 0.02$). PERT activation during the pandemic is associated with decreased length of stay (7.7 ± 7.7 vs. 13.2 ± 12.7 days, $p = 0.02$). PERT utilization decreased during the COVID-19 pandemic and its activation was associated with different biases. PERT recommendations and outcomes were similar before and during the pandemic, and led to decreased length of stay during the pandemic.

Keywords Venous thromboembolism · Pulmonary embolism · Pulmonary Embolism Response Team · COVID-19 · SARS-CoV-2

Abbreviations

BNP	Brain natriuretic peptide
CDT	Catheter-directed therapy
COVID-19	Coronavirus disease 2019
COVID era	March 1, 2020–April 30, 2020
CT-PE	Computed tomography-pulmonary embolism
DVT	Deep vein thrombosis
ESC	European Society of Cardiology
IVC	Inferior vena cava
LMWH	Low molecular weight heparin

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LOS　　　　　　　Length of stay
PE　　　　　　　　Pulmonary embolism
PERT　　　　　　 Pulmonary Embolism Response Team
PESI　　　　　　　Pulmonary Embolism Severity Index
pre-COVID era　　March 1, 2019–April 30, 2019
RT-PCR　　　　　Reverse transcription-polymerase chain reaction
RV　　　　　　　　Right ventricle
SARS-CoV-2　　　Severe acute respiratory syndrome coronavirus 2
UFH　　　　　　　Unfractionated heparin
VTE　　　　　　　Venous thromboembolism

Highlights

- We reviewed patients with acute pulmonary embolism (PE) at our institution during the COVID-19 pandemic from March 1st to April 30th, 2020.
- Of 82 cases of PE during the COVID-19 pandemic, 22 (26.8%) resulted in a Pulmonary Embolism Response Team (PERT) activation.
- PERT activations decreased during the COVID-19 pandemic.
- PERT activations were associated with a shorter length of stay.

Introduction

Mounting evidence for the associations between coronavirus disease 2019 (COVID-19), hypercoagulability, and mortality from thrombus formation have led to debate over the prevention and treatment of thrombi in this population [1]. While some institutions have used higher-intensity dosing of venous thromboembolism (VTE) chemoprophylaxis and modified treatment algorithms, there are no published guidelines recommending this change in therapy [2, 3].

Outside of COVID-19, pulmonary embolisms (PE) and VTE are common causes of cardiovascular morbidity and mortality, with high-risk (i.e. massive) PE having mortality rates of 25–65% [4–8]. Multidisciplinary Pulmonary Embolism Response Teams (PERT) help standardize and individualize complex medical decision-making. PERTs help physicians navigate the numerous treatment modalities including systemic thrombolysis, catheter-direct therapies (CDT), surgical embolectomy, and placement of inferior vena cava (IVC) filters. Evidence suggests PERTs may improve outcomes by reducing non-major bleeding, time to therapeutic anticoagulation, and mortality rates [7].

There is increasing focus of the differences between COVID-19 and non-COVID-19 VTE including incidence and changes in inflammatory makers (e.g. fibrinogen and D-dimer), coagulation panel, platelets, and thromboelastography parameters [9–11]. The COVID-19 pandemic has challenged healthcare resources and changed the practice of medicine. The effects have been widespread and have included issues such as imaging and bed availability, scarcity of blood products, and provider overextension [12–15]. Reports of healthcare providers practicing anecdotal medicine based on theories and conjecture have surfaced, leading to calls to practice "rational" care and wait for additional evidence and clinical trials before shifting patient care strategies [2, 16, 17]. PERTs provide high quality evidenced-based care in a disease where risks and benefits vary from patient to patient [7]. The impact of the COVID-19 pandemic on PERT-related outcomes is currently unknown given the lack of understanding of COVID-19-related thrombosis and evidence-based management guidelines. Presently, there are no studies examining the usage of PERT during the COVID-19 pandemic. Our study aims to see if these stressors: strain on resource allocation, seemingly higher-than expected incidence of VTE, and off-label use of anticoagulation and thrombolysis, have changed PERT activations and recommendations. Our study aims to compare PE as well as PERT activations between the pre-COVID and the COVID eras.

Methods

We performed a retrospective cohort analysis of all patients greater than or equal to 18-years-old who received emergency department or inpatient care at an academic hospital in New York City between March 1st and April 30th, 2020 (COVID era) and were found to have radiographically confirmed PE. Positive imaging studies were found via our institution's internal Venous Thromboembolism Center quality improvement database, which logs all images confirming VTE and all PERT activations. March 1st and April 30th, 2020 were chosen because of peak COVID-19-related emergency department visits. Historical controls of patients were obtained same period one-year prior (March 1st to April 30th, 2019, pre-COVID era). The Institutional Review Board at New York University Langone Health Center approved this study (#20-00501). There was no funding source for this study.

Patient charts were individually reviewed to gather variables including patient demographics, comorbidities (presence of hypertension, heart failure, diabetes mellitus, chronic lung disease, chronic kidney disease, malignancy, prior stroke, prior myocardial infarction, prior DVT or PE), and PERT activation. Parameters required to calculate a Pulmonary Embolism Severity Index (PESI) and timing of

diagnosis and PERT activation were noted. Presence of right ventricular (RV) dysfunction was identified if revealed by imaging (echocardiogram and/or CT-PE) or by elevated cardiac biomarkers including troponin or brain natriuretic peptide (BNP), as defined by our laboratory-specific cut-offs. PE risk was stratified into low, intermediate-low, intermediate-high, and high risk categories according to the European Society of Cardiology (ESC) 2019 guidelines [8]. Additional labs included severe acute respiratory disease coronavirus 2 (SARS-CoV-2) real time reverse transcription polymerase chain reaction (RT-PCR) for COVID-19. Initial management strategies (within 48 h of diagnosis) and PERT recommendations were recorded. Outcomes including death prior to discharge, bleeding, length of stay (LOS), and readmission within 30 days were compared.

Data was exported from REDCap to IBM SPSS Statistics (version 25) for analysis. Continuous variables are presented as means with standard deviations and compared using Student's unpaired t test. Categorical variables are presented as frequency and compared using Pearson's chi-squared or Fischer's exact test. Significance was assessed using two-tailed t-test with $p < 0.05$ considered significant.
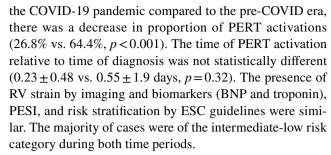
Results

During the COVID era, there were 82 patients with PE who received emergency department or inpatient care; 22 of these patients had PERT activations. Of the 82 patients, 44 patients were COVID-positive and 7 (16%) of COVID-positive patients with VTE had PERT activations. In the pre-COVID era, we identified 59 patients with emergency department visits or inpatient hospitalizations who had PE; 38 of these patients had PERT activations. We have three unique comparisons that characterize PE and PERT utilization: (1) all PEs before and during COVID era, (2) PERT and non-PERT activations pre-COVID era and COVID era, and (3) PERT and non-PERT activations during COVID era.

Comparison of PE pre-COVID era and COVID era

Patients with PE in the pre-COVID era were older (64 ± 15.3 vs. 58.1 ± 16.2 years, $p = 0.03$), more likely to have malignancy (30.5% vs. 14.6%, $p = 0.02$), and more likely to be on anticoagulation prior to admission (15.3% vs. 4.9%, $p = 0.04$) than those with PE during the COVID era. Otherwise, there were no statistically significant differences in gender, BMI, residence prior to encounter, and rates of tobacco and heavy alcohol use, and comorbidities (Supplemental Table 1).

Patients in the pre-COVID era were diagnosed with PE earlier in their hospitalization (0.97 ± 3.2 vs. 4.21 ± 7.5 days, $p = 0.001$). While there was an increase in cases of PE during

the COVID-19 pandemic compared to the pre-COVID era, there was a decrease in proportion of PERT activations (26.8% vs. 64.4%, $p < 0.001$). The time of PERT activation relative to time of diagnosis was not statistically different (0.23 ± 0.48 vs. 0.55 ± 1.9 days, $p = 0.32$). The presence of RV strain by imaging and biomarkers (BNP and troponin), PESI, and risk stratification by ESC guidelines were similar. The majority of cases were of the intermediate-low risk category during both time periods.

Most patients in both eras were initially treated with anticoagulation alone (88.1% vs. 93.9%, $p = 0.23$). In the pre-COVID era, more patients received advanced therapies, specifically catheter-directed thrombolysis (6.8% vs. 0%, $p = 0.03$) and catheter embolectomy (8.5% vs. 0%, $p = 0.01$) (Table 1). Initial anticoagulation choice differed between eras, with unfractionated heparin (UFH) being used more frequently in the pre-COVID era (69.5% vs. 50%, $p = 0.02$) and low molecular weight heparin (LMWH) used more often in the COVID era (40.2 vs. 8.5%, $p < 0.001$). Patients had shorter LOS in the pre-COVID era, especially in the intermediate-low risk group (7.2 ± 10.7 vs. 15.2 ± 13.7 days, $p = 0.004$), but were more likely to be re-admitted within 30 days (20.3% vs. 8.5% $p = 0.04$). There was no difference in deaths prior to discharge and bleeding events.

PERT activations before and during COVID era

During the pre-COVID era, 38 of the 59 new PE cases (64.4%) had a PERT activation compared to 22 of 82 (26.8%) during the COVID era. There were higher levels of serum brain natriuretic peptide (BNP) during the pre-COVID era (545 ± 1054 vs. 118.2 ± 200 pg/mL, $p = 0.04$). Otherwise, there were no significant differences in risk factors, severity indices, or PE classification (Table 2). PERT recommendations were similar, with a majority of patients being managed with anticoagulation alone (89.5% vs. 86.4%, $p = 0.70$); UFH was the most frequent choice of initial anticoagulant (78.9% vs 68.2%, $p = 0.35$).

Patients without PERT activations during the pre-COVID era were less likely to be on LMWH (9.5% vs. 48.3%, $p = 0.002$), more likely to be on a direct oral anticoagulant (28.6% vs. 6.7%, $p = 0.01$), and had a shorter LOS (5.1 ± 5.7 vs. 13.2 ± 12.7 days, $p < 0.001$), especially for those with intermediate-low risk PE. There was also a trend towards less bleeding (4.8% vs. 25%, $p = 0.057$) for those without PERT activation in the pre-COVID era.

PERT activations versus non-PERT activations in COVID era patients

There were 22 PE cases with PERT activations and 60 without during COVID era (Table 3). Patients with PERT

Table 1 Comparison of PE in the Pre-COVID and COVID era

	Pre-COVID era $n = 59$	COVID-era $n = 82$	p value
Diagnosis			
DVT, n (%)	28 (47.5)	30 (36.6)	0.2
Hospital day of diagnosis, mean (SD)	0.97 ± 3.2	4.21 ± 7.5	0.001[a]
Hospital day of PERT activation, mean (SD)	0.65 ± 1.3	1.68 ± 3.8	0.23
Delay of PERT activation, day, mean (SD)	0.23 ± 0.48	0.55 ± 1.9	0.32
PERT activated?	38 (64.4)	22 (26.8)	< 0.001[a]
Initial PERT recommendation or management, n (%)			
Anticoagulation, only	52 (88.1)	77 (93.9)	0.23
Thrombolysis (systemic)	1 (1.7)	1 (1.2)	1.00
Thrombolysis (catheter-directed)	4 (6.8)	0	0.03[a]
IVC filter	3 (5.1)	3 (3.7)	0.70
Embolectomy (surgical)	0	0	–
Embolectomy (catheter)	5 (8.5)	0	0.01[a]
Initial anticoagulant choice			
Unfractionated heparin	41 (69.5)	41 (50)	0.02[a]
Low molecular weight heparin	5 (8.5)	33 (40.2)	< 0.001[a]
Oral direct anti-Xa inhibitor	9 (15.3)	6 (7.3)	0.13
Other	0	1 (1.2)	1.00
None	4 (6.8)	1 (1.2)	0.16
Outcomes			
Death prior to discharge, n (%)	5 (8.5)	10 (12.2)	0.48
Length of stay, days, mean (SD)	6.5 ± 9.2	11.7 ± 11.7	0.004[a]
Low risk	4.5 ± 7.9	7.2 ± 8.2	0.39
Intermediate-low risk	7.2 ± 10.7	15.2 ± 13.7	0.004[a]
Intermediate-high risk	5.6 ± 3.1	8.5 ± 5.5	0.16
High risk	8.3 ± 6.5	–	–
Readmission within 30-days, n (%)	12 (20.3)	7 (8.5)	0.04[a]
Bleeding, n (%)	7 (11.9)	18 (22)	0.12

Continuous variables are presented as mean (standard deviation, SD); comparisons are performed using unpaired t-test. Categorical variables are presented as frequency; comparisons are performed using Pearson's chi-squared or Fischer's exact test. IVC, inferior vena cava

[a] $p < 0.05$ calculated by Pearson chi-squared test or Student's unpaired t test

activations were more likely to be female (63.6% vs. 31.7%, $p = 0.01$), have a history of DVT/PE (22.7% vs. 1.7%, $p = 0.01$), and to be taking anticoagulation prior to admission (13.6% vs. 1.7%, $p = 0.057$). They were also more likely to be SARS-CoV-2 RT-PCR negative (68.2% vs. 38.3% $p = 0.02$), to be diagnosed with a concurrent DVT (77.3% vs. 21.7%, $p < 0.001$), and to be diagnosed earlier during their hospitalization (1.1 ± 2.3 vs. 5.3 ± 8.4 days, $p = 0.001$). In terms of PE severity, those with PERT activations had more incidences of RV strain on imaging (54.5% vs. 18.3%, $p = 0.001$), but lower PESI (83.1 ± 26.0 vs. 103.6 ± 35.7, $p = 0.01$). There was an increased proportion of intermediate-high risk PE in those with PERT activations, but this did not reach statistical significance (28.6% vs. 13.5%, $p = 0.31$). Overall LOS was shorter with PERT activations (7.7 ± 7.7 vs. 12.2 ± 12.7 days, $p = 0.02$).

Discussion

We found that PERT activations decreased during the COVID-19 pandemic despite similar markers of risk and PE categories. The pandemic did not change PERT recommendations but did change how non-PERT PE cases were managed. This was the major hypothesis of our study, as PERT members had anecdotally felt that physicians were changing their normal medical management during the COVID era.

COVID era patients with PE were younger than prior PE patients with less known PE risk factors including malignancy. PE in the COVID era patients occurred later in patient's hospital course than pre-COVID era patients. This is interesting because all COVID era patients were placed on VTE chemoprophylaxis, unless otherwise contraindicated.

Table 2 Comparison of PERT activations before and during COVID-19 pandemic

	PERT activations			No PERT activations		
	Pre-COVID era $n=38$	COVID-era $n=22$	p value	Pre-COVID era $n=21$	COVID-era $n=60$	p value
Diagnosis						
DVT, n (%)	20 (52.6)	17 (77.3)	0.06	8 (38.1)	13 (21.7)	0.14
Hospital day of diagnosis, mean (SD)	0.45±1.33	1.1±2.3	0.20	1.9±4.9	5.3±8.4	0.03[a]
Hospital day of PERT activation, mean(SD)	0.68±1.34	1.7±3.8	0.24	–	–	–
Delay of PERT activation, day, mean (SD)	0.24±0.49	0.55±1.9	0.35	–	–	–
Severity indices						
Troponin I, admission (ng/mL)	0.119±0.206	0.281±0.670	0.32	0.068±0.143	0.234±0.707	0.37
BNP, admission (pg/mL)	545±1054	118.2±200.0	0.04[a]	125±139	168±350.2	0.69
RV strain on imaging, n (%)	14 (36.8)	12 (54.5)	0.18	3 (14.3)	11 (18.3)	1.0
Hypotension, n (%)	3 (7.9)	0	0.29	0	1 (1.7)	1.0
PESI, mean (SD)	90.5±26.1	83.1±26.0	0.30	94.2±34.8	103.6±35.7	0.30
PE severity risk, n (%)			0.10			
Low	5 (13.2)	6 (27.3)	0.19	5 (23.8)	17 (28.3)	0.69
Intermediate-low	23 (60.5)	9 (40.9)	0.18	14 (66.7)	35 (58.3)	0.50
Intermediate-high	7 (18.4)	7 (31.8)	0.34	2 (9.5)	8 (13.3)	1.0
High	3 (7.9)	0	0.29	0	0	–
Initial PERT recommendation or management n(%)						
Anticoagulation, only	34 (89.5)	19 (86.4)	0.70	18 (85.7)	58 (96.7)	0.11
Thrombolysis (systemic)	1	0	1.0	0	1	1.0
Thrombolysis (catheter-directed)	2	0	0.53	2	0	0.07
IVC filter	3	2	1.0	0	0	–
Embolectomy (surgical)	0	0	–	0	0	–
Embolectomy (catheter)	3	0	0.29	2	0	0.07
Initial anticoagulant choice						
Unfractionated heparin	30 (78.9)	15 (68.2)	0.35	11 (52.4)	26 (43.3)	0.47
Low molecular weight heparin	3 (7.9)	4 (18.2)	0.41	2 (9.5)	29 (48.3)	0.002[a]
Oral direct anti-Xa inhibitor	3 (7.9)	2 (9.1)	1.0	6 (28.6)	4 (6.7)	0.01[a]
Other	0	1 (4.5)	0.37	0	0	–
None	2 (5.3)	0	0.53	2 (9.5)	1 (1.7)	0.16
Outcomes						
Death prior to discharge, n (%)	2 (5.3)	1 (4.5)	1.0	3 (14.3)	9 (15)	1.0
Length of stay, days, mean (SD)	7.3±10.6	7.7±7.7	0.90	5.1±5.7	13.2±12.7	<0.001[a]
Low risk	1.6±0.9	4.0±3.2	0.14	7.4±10.9	8.3±9.2	0.86
Intermediate-low risk	9.1±13.1	10.6±19.8	0.77	3.9±2.9	16.4±14.3	<0.001[a]
Intermediate-high risk	5.1±3.2	7.1±4.2	0.34	7.0±2.8	9.6±6.5	0.61
High risk	8.33±6.43	–	–	–	–	–
Readmission within 30-days, n (%)	10 (26.3)	2 (9.1)	0.18	2 (9.5)	5 (8.3)	1.0
Bleeding, n (%)	6 (15.8)	3 (13.6)	1.0	1 (4.8)	15 (25)	0.057

Upper limit of normal (ULN) for brain natriuretic peptide (BNP) is 100 pg/mL. ULN for troponin is 0.04 ng/mL. *RV* right ventricle, *IVC* inferior vena cava. Continuous variables are presented as mean (standard deviation, SD); comparisons are performed using unpaired t-test. Categorical variables are presented as frequency; comparisons are performed using Pearson's chi-squared or Fischer's exact test

[a] $p<0.05$ calculated by Pearson chi-squared test or Student's unpaired t test

This supports that COVID patients may still be at increased risk to develop clots despite thromboembolism prophylaxis.

Our data corroborates that there appears to be a higher incidence of PE in patients with COVID than those without COVID. However, limitations in securing a radiographic

Table 3 Comparison of PERT and no PERT activation in patients during COVID-19 pandemic

	COVID-era		
	PERT activation	No PERT activation	*p* value
	n = 22	*n* = 60	
Diagnosis			
DVT, n (%)	17 (77.3)	13 (21.7)	< 0.001[a]
Hospital day of diagnosis, mean (SD)	1.1 ± 2.3	5.3 ± 8.4	0.001[a]
Hospital day of PERT activation, mean (SD)	1.7 ± 3.8	–	–
Delay of PERT activation, day, mean (SD)	0.55 ± 1.9	–	–
SARS-CoV-2 RT-PCR Positive	7 (31.8)	37 (61.7)	0.02[a]
Severity Indices			
Troponin I, admission (ng/mL)	0.281 ± 0.670	0.234 ± 0.707	0.8
BNP, admission (pg/mL)	118.2 ± 200.0	168 ± 350.2	0.6
RV strain on imaging, n (%)	12 (54.5)	11 (18.3)	0.001[a]
Hypotension, n (%)	0	1 (1.7)	1.0
PESI, mean (SD)	83.1 ± 26.0	103.6 ± 35.7	0.02[a]
PE severity risk, n (%)			0.16
Low	6 (27.3)	17 (28.3)	0.93
Intermediate-low	9 (40.9)	35 (58.3)	0.16
Intermediate-high	7 (31.8)	8 (13.3)	0.1
High	0	0	–
Initial PERT recommendation or management, n (%)			
Anticoagulation, only	19 (86.4)	58 (96.7)	0.12
Thrombolysis (systemic)	0	1	1.0
Thrombolysis (catheter-directed)	0	0	–
IVC filter	2	0	0.07
Embolectomy (surgical)	0	0	–
Embolectomy (catheter)	0	0	–
Initial anticoagulant choice			
Unfractionated heparin	15 (68.2)	26 (43.3)	0.046[a]
Low molecular weight heparin	4 (18.2)	29 (48.3)	0.01[a]
Oral direct anti-Xa inhibitor	2 (9.1)	4 (6.7)	0.66
Other	1 (4.5)	0	0.27
None	0	1 (1.7)	1.0
Outcomes			
Death prior to discharge, n (%)	1 (4.5)	9 (15)	0.28
Length of stay, days, mean (SD)	7.7 ± 7.7	13.2 ± 12.7	0.02[a]
Low risk	4.0 ± 3.2	8.3 ± 9.2	0.28
Intermediate-low risk	10.6 ± 19.8	16.4 ± 14.3	0.26
Intermediate-high risk	7.1 ± 4.2	9.6 ± 6.5	0.41
High risk	–	–	
Readmission within 30-days, n (%)	2 (9.1)	5 (8.3)	1.0
Bleeding, n (%)	3 (13.6)	15 (25)	0.37

Upper limit of normal (ULN) for brain natriuretic peptide (BNP) is 100 pg/mL. ULN for troponin is 0.04 ng/mL. SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2. RT-PCR, reverse transcription-polymerase chain reaction. RV, right ventricle. IVC, inferior vena cava. Continuous variables are presented as mean (standard deviation, SD); comparisons are performed using unpaired t-test. Categorical variables are presented as frequency; comparisons are performed using Pearson's chi-squared or Fischer's exact test

[a]*p* < 0.05 calculated by Pearson chi-squared test or Student's unpaired t test

COVID-19 and Pulmonary Embolism Response Team (PERT)

1. Does your patient have COVID-19 with confirmed or suspected PE and any of:

Tachycardia
Acutely worsening dyspnea
Hemoptysis
Moderate to severe chest pain
Echo with right ventricular dilation
CT-PE with signs of right heart strain
Saddle embolism or significant clot burden
Serum troponin above upper limit of normal

2. Was your patient started on empiric anticoagulation for a presumed PE (no image confirmation) and is now nearing discharge?

If yes to either, then consult PERT.

Patient with either: (1)newly diagnosed or suspected PE, or (2)receiving empiric PE treatment and being considered for discharge from the hospital

Referring team calls extension "4-PERT"

Hospital operator answers "4-PERT" and conference calls PERT members (critical care, IR, CT surgery)

Referring team presents the case to PERT. Initial feedback and preliminary plan is made.

Critical care team evaluates the patient, discusses management with referring team, and reconnects with PERT members as needed.

Fig. 1 PERT alert work flow and COVID-19 infection. *CT surgery* cardiothoracic surgery, *CT-PE* computed tomography-pulmonary embolism, *PE* pulmonary embolism, *PERT* Pulmonary Embolism Response Team, *IR* interventional radiology

diagnosis in a majority of patients with COVID due to resource allocation may skew these results. Unexpectedly, there was nearly a 40% decrease in PERT activations during the COVID era. This highlights that the PERT activation is subjective and providers can choose to practice without using the expertise of PERT. In fact, PERT activations during COVID era were predominately on female patients, those with a history of DVT/PE, those on anticoagulants prior to hospital encounter, and those who were SARS-CoV-2 RT-PCR negative. These risk factors and anticoagulant failure may have motivated providers to activate PERT. Those who were SARS-CoV-2 RT-PCR positive were less likely to have a PERT activation, another suggestion that physicians had bias when caring for these patients.

The major driver for the decrease in PERT activations, specifically on COVID-positive patients, is not explained. It is possible that there were more "critical care"-trained physicians attending during this time who did not feel extra input was needed, that there was little role for advanced therapy during this period of contagion, that there was little evidence to guide treatment for COVID-positive patients, or that the chaos of the pandemic changed physician's typical

practice. PERT recommendations were consistent before and throughout the COVID era. However, there were trends towards more use of LMWH and less CDT, though neither reached statistical significance. In cases where PERT was activated, outcomes were similar between time periods. It should be noted the PERT activations in the COVID era, were much more likely to occur on SARS-CoV-2 RT-PCR negative patients, which further supports that the presence of COVID-positivity was the main driver for the deviation in standard care rather than any other the other hypotheses listed.

During the COVID era, differences in patient characteristics between PERT and non-PERT activation gives another glimpse into the factors that motivate physicians to active PERT. While patients were well-matched by age, gender, BMI, and co-morbidities, those with PERT activation were more likely to have concurrent DVT and RV strain by imaging. The discordance between these findings and the lower PESI and lack of statistically significant differences in PE risk (by ESC guidelines) highlights the heterogeneity and difficulty in classifying submassive PE. PERT activation correlated with almost a 50% reduction in LOS and

trend towards fewer bleeding events. These are important outcomes because they may potentially relieve strain on important resources. Reduced LOS increases bed availability and the ability to accommodate increases in patient volume. Fewer bleeding events allows for conservation of scarce blood products [18]. These positive outcomes by PERT occurred without a complete understanding of the pathophysiology of COVID-19 or evidence-based management guidelines. Thus, the use of PERTs should be encouraged during future pandemics to optimize resource allocation.

There are several limitations to our study. First, there were a limited number of patients managed with therapies other than anticoagulation. This could lead to our study to be underpowered to identify differences in practice patterns in the short timeframe chosen. Second, the retrospective nature of our study and the subjective activations of PERT makes it difficult to identify and investigate provider biases. Third, our institution's convention is to generally activate PERT for radiographic-proven PE. However, obtaining radiographic evidence in all suspected cases of PE during the pandemic was unfeasible. Furthermore, many patients with COVID-19 were started empirically for PE based on D-dimer values alone. Many patients treated empirically for PE were not captured by this study, further undermining this study's ability to investigate provider biases. PERT utilization may have been helpful in cases of suspected PE to provide expert opinion regarding when to start empiric anticoagulation, when to transition to chemoprophylaxis after empiric treatment, and whether long-term anticoagulation or chemoprophylaxis is warranted at time of hospital discharge. In light of these limitations and the positive outcomes associated with PERT, we propose that other institutions consider changing their PERT guidelines to assist in cases of suspected PE (Fig. 1).

Conclusions

Patients with PE during COVID era were younger patients, had less malignancy, and developed clots later in their hospital course as compared to patients with PE in the pre-COVID era. During the COVID era, PERT activation correlated with reduction in LOS and trend towards fewer bleeding events. Medical management of PE changed during the COVID era for non-PERT patients and was associated with longer length of stay and a trend toward more bleeding. While our institutional utilization of PERT substantially decreased during the COVID era, PERT recommendations were unchanged and resulted in similar patient outcomes.

Compliance with ethical standards

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