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ORIGINAL RESEARCH

Post-COVID-19 Condition and Pulmonary Embolism

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Purpose: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes post-acute sequelae of coronavirus disease 2019 (COVID-19), including pulmonary vasculopathy, increasing thrombotic risk. Screening and treating survivors are essential to reduce associated disabilities. We aim to investigate the clinical characteristics of patients with post-COVID-19 condition and pulmonary embolism, as well as their health-related quality of life one year after COVID-19 diagnosis.

Patients and Methods: In our study, we analyzed nine cases of post-COVID-19 condition and pulmonary embolism in a tertiary hospital in Taiwan. Patient characteristics, including age, sex, symptoms, and outcomes, were recorded. One year post-diagnosis, patients underwent follow-up with lab tests, chest X-rays, electrocardiograms, and health-related quality of life (HRQOL) assessments using the EuroQoL 5-Dimension 5-Level (EQ-5D-5L) tool.

Results: Post-COVID-19 condition with pulmonary embolism predominantly affects females. Common symptoms include breathlessness and chest pain, and a lung perfusion scan may be useful for diagnosis. The one-year follow-up of five patients mainly showed normal lab results and no active lung lesions. The mean EQ-5D score was 0.928 ± 0.119, and the EQ visual analogue scale (EQ-VAS) was 85.00 ± 11.18. Pain/discomfort was the most reported issue.

Conclusion: This research reveals that post-COVID-19 condition with pulmonary embolism affects a significant number of women and those with preexisting conditions like cancer or diabetes. Symptoms overlap also complicates diagnosis. Although many lab results were normal, the elevated risk of pulmonary embolism persists. Lower utility scores and increased anxiety highlight the need for targeted interventions and mental health support. Our study underscores the importance of monitoring pulmonary embolism in patients after COVID-19 infection, given the significant impact on post-COVID-19 condition and overall health outcomes.

Keywords: SARS-CoV-2, health related quality of life, pulmonary vasculopathy, EQ-5D

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection leads to post-acute sequelae of coronavirus disease 2019 (COVID-19), affecting various organ systems.[1] Despite the official conclusion of the pandemic, particularly due to its long-term effects, the global outbreaks have provided deeper insights into the pathogenesis of SARS-CoV-2, revealing a specific pulmonary vascular disorder that persists beyond the acute phase of infection. COVID-19 has been shown to increase the risk of thrombotic diseases in both venous and arterial circulation, with numerous cases of severe acute pulmonary embolism reported.[2] The prevalence of pulmonary embolism in hospitalized COVID-19 patients has been estimated to be as high as 16.5%, significantly higher than in non-COVID-19 patients.[3] This increased risk is thought to persist even after the acute phase of the illness, contributing to the burden of post-COVID-19 condition.

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The pathophysiology underlying this increased thrombotic risk is multifaceted. The confirmed presence of SARS-CoV-2 in endothelial cells suggests that both direct viral effects and indirect effects from perivascular inflammation and coagulopathy play roles in the development of pulmonary vasculopathy in COVID-19. This endothelial dysfunction, combined with systemic inflammation and alterations in the coagulation cascade, creates a prothrombotic state that can persist even after viral clearance.[4] While the acute management of COVID-19-associated thrombosis has been widely studied, there remains a significant gap in our understanding of the long-term outcomes and quality of life impact for patients who develop pulmonary embolism as a post-acute sequela of COVID-19. The chronic nature of post-COVID-19 condition, coupled with the potential long-term effects of pulmonary embolism, may significantly impact patients' overall health and well-being.

Given these concerns, it is crucial to screen, diagnose, treat, and monitor the pulmonary vasculopathy of COVID-19 survivors to reduce the burden of associated disability. This study aims to investigate the clinical characteristics, laboratory findings, and health-related quality of life outcomes in patients with post-COVID-19 condition and pulmonary embolism. By providing insights into the long-term sequelae of this condition, we hope to inform clinical management strategies and improve patient outcomes.

Materials and Methods

Study Population

This retrospective study analyzed cases of post-COVID-19 condition with pulmonary embolism managed at a tertiary hospital in Taiwan from 2020 to 2023, following approval from the Institutional Review Board. Patients were included if they had a confirmed SARS-CoV-2 infection by reverse transcription polymerase chain reaction (RT-PCR), met the World Health Organization (WHO) definition of post-COVID-19 condition, and had pulmonary embolism confirmed by computed tomography (CT) angiography or lung perfusion scan. At least two authors independently reviewed each patient's electronic medical record, extracting data on demographics, underlying medical conditions, COVID-19-related information, symptoms of post-COVID-19 condition, laboratory data, pulmonary embolism diagnostic method, follow-up frequency, and mortality.

Follow-Up

One year after the initial COVID-19 diagnosis, surviving patients underwent a comprehensive follow-up assessment. This included laboratory tests (complete blood count, liver and kidney function tests, cardiac markers, D-dimer), chest X-ray, electrocardiogram (ECG), and a health-related quality of life (HRQOL) assessment. HRQOL was measured using the EuroQoL 5-Dimension 5-Level (EQ-5D-5L) tool, a standardized instrument validated for use in Taiwan. The EQ-5D-5L consists of a descriptive system assessing five health dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) on five levels of severity, and a visual analogue scale (EQ-VAS) ranging from 0 to 100.[5] We used the Taiwan value set and scoring algorithm to calculate utility scores, where 1 indicates perfect health and −1 represents a state worse than death.[6]

Data Analysis

We calculated descriptive statistics for all variables, using frequencies and percentages for categorical data, and median and range for continuous variables due to the small sample size and potential non-normal distribution. For EQ-5D-5L utility scores and EQ-VAS scores, we calculated mean and standard deviation. This comprehensive approach allowed us to characterize the clinical features, long-term outcomes, and quality of life impact of post-COVID-19 pulmonary embolism in our patient cohort.

Results

Patient Characteristics and Initial Presentation

Our study included nine patients diagnosed with post-COVID-19 condition and pulmonary embolism (Table 1, Supplement Table 1). The median age was 61 years (range: 32–81), with a slight female predominance (5/9, 56%). Underlying conditions were common, with three patients (33%) having pre-existing solid or hematological malignancies, three (33%) with diabetes mellitus, one (11%) with thyroid goiter, and one (11%) with rheumatoid arthritis.

Table 1 Characteristics of Patients with Post-COVID-19 Condition and Pulmonary Embolism (n=9)

Part A: Demographic and Clinical Characteristics	
Characteristic	**Value**
Age, median (range), years	61 (32–81)
Sex, n (%)	
Female	5 (56%)
Male	4 (44%)
Underlying conditions, n (%)	
Cancer	3 (33%)
Diabetes mellitus	3 (33%)
Other	3 (33%)
Post-COVID-19 condition symptoms, n (%)	
Breathlessness	6 (67%)
Malaise	4 (44%)
Chest tightness/pain	4 (44%)
Other	7 (78%)
COVID-19 related information	
Hospitalization, n (%)	2 (22%)
Antiviral treatment, n (%)	5 (56%)
Pulmonary embolism diagnostic tool, n (%)	
CT angiography	5 (56%)
Lung perfusion scan	4 (44%)
Outpatient follow-up in 6 months, median (range)	10 (3–23)
1-year mortality, n (%)	3 (33%)

Part B: Laboratory Findings (at diagnosis)		
Parameter	**Median (Range)**	**Normal Range**
White blood cell count (/μL)	7800 (4600–8840)	4000–11000
Neutrophil (%)	62.8 (46.3–75.0)	40–75
Lymphocyte (%)	28.6 (13.0–41.8)	20–45
Eosinophil (%)	1.2 (0–5.2)	0–6
Hemoglobin (g/dL)	13.8 (12.7–15.5)	12–16
Platelet (10^3/μL)	269 (154–326)	150–450
C-reactive protein (mg/dL)	0.3 (0.1–11.7)	< 0.5
Alanine aminotransferase (U/L)	23 (14–54)	0–50
Creatinine (mg/dL)	0.95 (0.61–1.54)	0.6–1.3
D-dimer (mg/L FEU)	0.7 (0.2–22.0)	< 0.5

Abbreviations: CT, Computed Tomography; FEU, Fibrinogen Equivalent Units.

All patients experienced at least two post-COVID-19 condition symptoms. Breathlessness was the most prevalent (6/9, 67%), followed by malaise (4/9, 44%) and chest tightness or pain (4/9, 44%). Other symptoms were reported in 78% of patients, highlighting the diverse clinical presentation of this condition.

COVID-19 Management and Pulmonary Embolism Diagnosis

Most patients (7/9, 78%) were managed on an outpatient basis, with only two patients (22%) requiring hospitalization. Antiviral treatment was administered to five patients (56%), with three receiving nirmatrelvir/ritonavir and two receiving remdesivir. Pulmonary embolism was diagnosed through CT angiography in five patients (56%) and pulmonary perfusion scan in four patients (44%).

Laboratory Findings

At initial diagnosis, most patients had laboratory values within normal ranges, including white blood cell count (median: 7800/μL, range: 4600–8840), platelet count (median: 269 x 10^3/μL, range: 154–326), and hemoglobin (median: 13.8 g/dL, range: 12.7–15.5). However, D-dimer levels were notably elevated in some patients (median: 0.7 mg/L FEU, range: 0.2–22.0), consistent with the thrombotic nature of their condition.

Follow-Up and Outcomes

The median number of outpatient follow-up visits within 6 months after COVID-19 diagnosis was 10 (range: 3–23), indicating the need for close monitoring of these patients. Notably, three patients (33%) died within one year of diagnosis, underscoring the potential severity of this condition.

One-Year Follow-Up

Five patients completed the one-year follow-up assessment (Table 2, Supplement Table 2). Their median age was 59 years (range: 37–71), with three females (60%) and two males. Laboratory findings at this time point were largely within normal ranges, suggesting resolution of acute inflammation and organ dysfunction. Follow-up chest X-rays showed no active lung lesions in all five patients, and electrocardiograms consistently demonstrated sinus rhythm, indicating cardiac stability.

Table 2 One-Year Follow-Up of Patients with Post-COVID-19 Condition and Pulmonary Embolism (n=5)

Parameter	Median (Range)	Normal Range
Hematology		
White blood cell count (/μL)	6480 (3640–9400)	4000–11000
Hemoglobin (g/dL)	13.0 (12.7–15.6)	12–16
Platelet (10^3/μL)	262 (172–348)	150–450
Inflammation markers		
C-reactive protein (mg/dL)	0.1 (0.1–0.8)	< 0.5
Procalcitonin (ng/mL)	0.03 (0.02–0.37)	< 0.5
Liver function		
Alanine aminotransferase (U/L)	18 (13–43)	0–50
Aspartate aminotransferase (U/L)	16 (13–44)	0–50
Total bilirubin (mg/dL)	0.64 (0.40–0.91)	0.3–1.2
Kidney function		
Creatinine (mg/dL)	0.72 (0.58–1.22)	0.6–1.3
Cardiac markers		
Creatine kinase (U/L)	90 (48–110)	30–200
Troponin-T (ng/L)	3.77 (3.21–10.68)	< 14
Coagulation		
D-dimer (mg/L FEU)	0.38 (0.23–1.03)	< 0.5
Imaging results	n (%)	
No active lung lesion on chest X-ray	5 (100%)	
Sinus rhythm on ECG	5 (100%)	
Quality of life measures	Mean ± SD (Range)	
EQ-5D-5L index	0.928 ± 0.119 (0.7261–1.0000)	
EQ-VAS	85.00 ± 11.18 (70–100)	

Abbreviations: ECG, Electrocardiogram; EQ-5D-5L, EuroQoL 5-Dimension 5-Level; EQ-VAS, EuroQoL Visual Analogue Scale; FEU, Fibrinogen Equivalent Units; SD, Standard Deviation.

Health-Related Quality of Life

The mean EQ-5D index score (utility score) at one year was 0.928 ± 0.119, and the mean EQ-VAS was 85.00 ± 11.18. These scores, while generally good, suggest some persistent impact on quality of life compared to population norms. The most commonly reported issues were pain/discomfort (40% of patients), followed by anxiety/depression (20%) and problems with usual activities (20%). A moderate, positive association was found between EQ-5D utility and EQ-VAS scores (correlation coefficient: 0.686), indicating consistency between the two measures of health-related quality of life.

These findings highlight the complex and potentially long-lasting effects of post-COVID-19 condition with pulmonary embolism, emphasizing the need for comprehensive long-term follow-up and support for affected patients.

Discussion

Our study provides valuable insights into the clinical characteristics and long-term outcomes of patients with post-COVID-19 condition and pulmonary embolism. Several key findings warrant further discussion.

Firstly, we observed a female predominance (56%) among affected patients, consistent with previous studies linking post-COVID-19 condition to female sex.[7] Notably, 40% of the female patients were of reproductive age (18–44 years), highlighting the need for targeted interventions and patient education for this demographic.[8] This gender disparity in post-COVID-19 outcomes underscores the importance of considering sex-specific factors in both research and clinical management.

The high prevalence of comorbidities, particularly cancer (33%) and diabetes mellitus (33%), among our cohort is noteworthy. Both COVID-19 and cancer are established risk factors for thrombosis, and cancer patients face higher mortality rates following COVID-19 hospitalization.[9,10] Furthermore, pulmonary embolism was more frequent in patients who had persisted post-COVID-19 symptoms, and the psychological distress may also be associated with silent impairment in myocardial systolic functions and chest conformation.[11,12] The co-occurrence of these conditions may create a perfect storm for thromboembolic complications. Similarly, the link between diabetes, COVID-19, and thromboembolism is well-documented, with emerging evidence suggesting bidirectional relationships between post-COVID-19 condition, insulin resistance, and new-onset diabetes. These findings emphasize the need for vigilant monitoring and aggressive management of these high-risk groups.

Among the nine patients diagnosed with pulmonary embolism and post-COVID-19 condition, three (33%) had preexisting diabetes mellitus. Patients with diabetes and COVID-19 pneumonia have an increased risk of thromboembolism, which is linked to worse clinical outcomes.[13] Additionally, people with diabetes face a higher risk of post-COVID-19 condition.[14] Furthermore, post-COVID-19 condition is linked to insulin resistance, and pulmonary embolism was linked to the onset of diabetes mellitus in COVID-19 patients.[15,16] Therefore, targeted interventions should be intensified.

Among our patients diagnosed with post-COVID-19 condition and pulmonary embolism, the most common symptoms were shortness of breath and chest tightness. Although the typical symptoms of pulmonary embolism are chest pain, dyspnea, hemoptysis, tachypnea, and tachycardia, the diagnosis of pulmonary embolism can be challenging because the signs and symptoms are often nonspecific and overlap those of post-COVID-19 condition. As a result, pulmonary embolism may be underestimated in patients with post-COVID-19 condition. In our study, four (44%) patients were diagnosed with pulmonary embolism through a pulmonary perfusion scan. For COVID-19 patients, lung perfusion imaging serves as a straightforward and useful tool. It helps enhance the understanding of the natural progression of thromboembolic events in COVID-19, and also aids in distinguishing between hemodynamic consequences and functional limitations caused by deconditioning and dysfunctional breathing.[17]

On the other hand, most patients had normal ranges of blood cell counts, as well as cardiac enzyme, liver and renal function. This was similar to a previous study, where no specific laboratory tests for the diagnosis of post-COVID-19 condition were identified.[18] Most patients had d-dimer levels within normal ranges at the 1-year follow-up. Although previous studies showed that the risk of pulmonary embolism returned to baseline levels or below from 12 weeks to 1 year after SARS-CoV-2 infection, there is still evidence that the risk of pulmonary embolism remains higher in hospitalized COVID-19 patients 3 years after infection.[1,19] More caution should be taken with these patients.

Lastly, in our study, the utility score was lower (0.928) than that of the general population. This finding aligns with recent EQ-5D studies from India, China, the USA, Iran, and Switzerland, which also reported lower utility values compared to the general population.[20] An interesting observation is that men had higher utility scores than women, which corroborates with other studies showing a link between gender and the severity of illness.[20] In all EQ-5D domains, most of our participants reported fewer problems with mobility and self-care. Our study also found that a small number of patients experienced more pain/discomfort and anxiety or depression, similar to those affected by SARS and MERS.[21,22] Furthermore, our findings are consistent with previous research showing that women were more anxious than men about COVID-19.[23] Another study found that reducing anxiety and depression in individuals leads to a significant improvement in quality of life.[24] Increased caution is necessary when dealing with these patients.

Conclusion

This research reveals that post-COVID-19 condition with pulmonary embolism disproportionately affects women and individuals with preexisting conditions such as cancer or diabetes. The symptom overlap between post-COVID-19 condition and pulmonary embolism complicates diagnosis, emphasizing the value of tools like lung perfusion scans. While many laboratory results normalize over time, the risk of pulmonary embolism may persist, necessitating ongoing vigilance. Lower quality of life scores, particularly in domains of pain/discomfort and anxiety/depression, highlight the need for comprehensive, long-term care including mental health support.

Our findings underscore the importance of tailored monitoring and management strategies for pulmonary embolism in post-COVID-19 patients, given its significant impact on overall health outcomes. Future research should focus on larger, multicenter studies to validate these findings and explore targeted interventions to improve outcomes in this vulnerable population.

Ethics Approval

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Taichung Veterans General Hospital (approval number: CE23164A-1). All the participants signed the informed consent form.

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Disclosure

The authors report no conflicts of interest in this work.

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