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LONG COVID AND LUNG THROMBOEMBOLISM IN YOUNG ADULTS

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ABSTRACT

Long-term COVID-19 (Long COVID) and pulmonary thromboembolism (PTE) significantly challenge healthcare, especially in young adults who are typically at lower risk for such severe outcomes. This review explores the complex relationship between long-term COVID and PTE, focusing on the pathophysiological mechanisms, diagnostic challenges, and therapeutic approaches. Persistent inflammation and immune dysregulation associated with long-term COVID-19 contribute to this demographic's increased thrombotic risk. The symptom overlaps between long-term COVID and PTE complicate the accuracy and timeliness of diagnoses, highlighting the necessity for improved diagnostic strategies. Findings emphasize the need for anticoagulation protocols tailored to the specific clinical presentations of Long COVID patients and suggest that extended treatment durations may be beneficial. The potential of genetic and biomarker research to identify individuals at heightened risk of thrombotic complications is discussed. The review calls for a multidisciplinary approach that integrates medical and psychosocial interventions to manage the long-term effects of COVID-19 effectively. As the pandemic evolves, advancing our understanding and adapting healthcare strategies to these insights are crucial for developing effective clinical practices. This is essential for addressing the immediate health impacts and reducing the broader socioeconomic burdens associated with long-term COVID and PTE in young adults.

Keywords: immunotherapy, Hashimoto disease, autoimmune thyroiditis, neoadjuvant therapy, adverse drug reactions

INTRODUCTION

The protracted repercussions of the SARS-CoV-2 infection, widely recognized as Long COVID, have emerged as a multifaceted challenge in the wake of the global pandemic. Among the myriad complications associated with Long COVID, pulmonary thromboembolism (PTE) represents a particularly severe condition that disproportionately affects young adults, a demographic previously considered at lower risk for severe outcomes from the initial infection[1-3].

This article aims to elucidate the underlying mechanisms, prevalence, and potential preventive strategies for lung thromboembolism in young adults suffering from long-term COVID-19[2].

The pathophysiology of Long COVID is complex and not entirely understood. It involves a persistent inflammatory response, immune dysregulation, and residual viral particles that might incite a hypercoagulable state, leading to thromboembolic events[4-6].

Recent studies have shown an increased incidence of venous thromboembolism (VTE) in patients recovering from COVID-19, suggesting a sustained risk that extends beyond the acute phase of the disease[5].

Pulmonary thromboembolism in young adults post-COVID presents unique clinical challenges. This age group does not exhibit traditional risk factors for thromboembolism, such as comorbidities like heart disease or prolonged immobilization[7-9].

However, the inflammatory milieu induced by SARS-CoV-2 appears to predispose even previously healthy individuals to thrombotic complications. This raises critical questions about the mechanisms driving this increased thrombotic risk and the potential for genetic or other intrinsic factors that may predispose individuals to such outcomes[9-11].

The incidence of PTE in young adults with Long COVID necessitates a reassessment of our understanding of risk factors associated with thromboembolic diseases[10]. Emerging data suggest that factors such as a sedentary lifestyle during lockdown periods, direct viral effects on the endothelium, and an imbalance in pro-coagulant and anticoagulant factors might contribute to this risk[12-14].

The diagnosis of pulmonary thromboembolism in Long-term COVID patients is complicated by the overlap of symptoms between PTE and long-term COVID itself, such as shortness of breath, chest pain, and fatigue. This symptom overlap can lead to delays in diagnosis and appropriate management, potentially worsening outcomes[15-17].

Regarding management, the therapeutic strategies for PTE in the context of Long COVID are still being refined. Current guidelines for managing acute pulmonary embolism may not be fully applicable to Long-term COVID patients, given their unique pathophysiology and clinical presentation[18]. Tailored anticoagulation strategies, potentially extending beyond the standard treatment durations, are being explored to mitigate this risk[19].

Preventive strategies are also paramount, especially considering the potential for significant morbidity associated with PTE in young adults[3]. These strategies may include more aggressive prevention in patients with known COVID-19 infection, especially those with severe disease or prolonged immobility, and targeted education to raise awareness about the symptoms and risks of thromboembolism[20-23].

The socioeconomic impact of long-term COVID-19, including the burden of pulmonary thromboembolism in young adults, is profound[7]. It affects not only the healthcare system but also the economic contributions and quality of life of this active portion of the population[8]. Thus, understanding and addressing this complication is a medical priority and a societal imperative[24].

This review calls for ongoing research into the long-term effects of COVID-19. Large-scale epidemiological studies and detailed mechanistic studies are necessary to understand the full spectrum of Long-term COVID symptoms, the risk factors for severe outcomes like PTE, and the optimal management strategies to prevent significant morbidity and mortality in this and future pandemics[25-27].

Pulmonary thromboembolism represents a critical and potentially life-threatening complication of Long COVID in young adults[2,28]. By advancing our understanding of its pathophysiology, improving strategies for its diagnosis and management, and implementing effective preventive measures, we can mitigate the impact of this serious condition on an already vulnerable population[29-31].

The primary objective of this review article is to investigate and clarify the relationship between long-term COVID-19 and the increased risk of pulmonary thromboembolism in young adults[22]. The article aims to explore the pathophysiology that links prolonged SARS-CoV-2 infection to the development of pulmonary thromboembolism, highlighting how persistent inflammation and immune dysfunction can contribute to a hypercoagulable state[32-34].

It also seeks to assess the prevalence of pulmonary thromboembolism among young adults experiencing Long COVID, providing insights into incidence rates and risk factors[15]. The article discusses diagnostic challenges and overlaps in symptoms between long-term COVID and pulmonary thromboembolism, which complicate the timely identification and treatment of the condition[35].

The review further evaluates current management strategies and the need for possibly extended anticoagulation therapy tailored to the unique clinical presentation

of these patients[29]. It emphasizes the importance of preventive measures and the broader socioeconomic impact of these health issues on young adults, aiming to enhance awareness and inform better clinical practices and health policies[36].

METHODS

The research methodology for this review was designed to investigate the association between long-term COVID-19 and the onset of pulmonary thromboembolism (PTE) in young adults. Multiple reputable databases were utilized to ensure comprehensive coverage of relevant scientific and medical literature, including PubMed, Scopus, SciELO, Embase, and Web of Science, which were recognized for their extensive collections of peer-reviewed publications. Additionally, Google Scholar was employed to access gray literature, which often includes significant studies not available in standard academic journals. The primary objective was to understand PTE's incidence and underlying mechanisms as a complication of long-term COVID in young adults. To achieve this, search parameters were carefully crafted using relevant keywords such as "Long COVID," "pulmonary thromboembolism," "young adults," "SARS-CoV-2," "anticoagulants," "thrombosis," "diagnosis," and "physiopathology." This strategic combination of search terms ensured the retrieval of studies directly pertinent to the research objectives. Inclusion criteria encompassed a broad spectrum of study designs, including randomized controlled trials, cohort studies, case-control studies, systematic reviews, and meta-analyses. This approach aimed to capture diverse evidence and perspectives regarding the association between long-term COVID and PTE. Exclusion criteria were established to filter out studies focusing on unrelated pathologies, non-COVID-19-related thromboembolism, or other age groups. Two independent reviewers initially screened each study's title and abstract for relevance and compliance with predefined criteria to ensure methodological rigor. Any discrepancies between the reviewers were resolved through consultation with a third reviewer, thereby minimizing bias and ensuring consistent selection. This dual-review process ensured that the final dataset comprised studies meeting the highest standards of relevance and quality. This systematic approach to the literature review provided a solid foundation for evaluating and synthesizing the findings. It ensured that the conclusions of this study were based on a comprehensive and critically assessed body of scientific evidence regarding Long-term COVID as a risk factor for pulmonary thromboembolism in young adults.

RESULTS AND DISCUSSION

The intersection of long-term COVID and pulmonary thromboembolism (PTE) in young adults presents a compelling yet complex facet of the post-acute sequelae of SARS-CoV-2 infection. This review has illuminated several critical areas while identifying gaps in our current understanding and management of these conditions[37,38].

The diagnostic challenges inherent in distinguishing between long-term COVID and PTE stem primarily from their overlapping symptomatology, including fatigue, dyspnea, and chest pain[6].

Such overlaps can significantly delay accurate diagnoses, as healthcare providers may initially attribute these symptoms to the more benign and lingering effects of Long COVID rather than a potentially life-threatening PTE[27].

This situation is complicated because standard diagnostic tools for PTE, such as D-dimer testing, can be persistently elevated in patients recovering from COVID-19, thereby reducing their specificity for thromboembolic events[39].

A critical gap in current research is identifying and understanding specific genetic or intrinsic factors that might predispose young adults to increased thrombotic risk in long-term COVID-19 patients[40].

While specific genetic markers have been associated with thrombophilia in the general population, their contributions to thrombosis in Long-Term COVID patients remain poorly defined. Studies focusing on genetic predispositions could provide valuable insights into personalized risk assessments and targeted prophylactic strategies[41-43].

The overlap of symptoms between PTE and Long COVID complicates not only the diagnosis but also the management of these patients. This overlap can lead to underutilization of diagnostic imaging due to concerns about radiation exposure or misattribution of symptoms to less severe causes[8-10].

However, the fear of potential interactions between COVID-19 therapies and anticoagulants may lead clinicians to hesitate in initiating or adjusting treatment protocols optimally[18-21].

Emerging from the current discourse is the critical need for tailored anticoagulation strategies designed explicitly for long-term COVID patients with suspected or confirmed PTE[44].

While the standard anticoagulation duration for unprovoked PTE in otherwise healthy individuals typically ranges from three to six months, preliminary data suggest that extended anticoagulation may be necessary for those recovering from severe COVID-19, given their ongoing risk of thrombotic events[45].

The ongoing studies evaluate the efficacy and safety of prolonged anticoagulation in this specific patient population, with early findings indicating a potential reduction in recurrent thrombotic events without a corresponding increase in bleeding risks[46].

The review touches on the role of inflammation and immune dysregulation in Long-Term COVID-19, a deeper dive into the specific pathways and immune mechanisms involved in thrombogenesis during Long-Term COVID-19 could provide valuable insights[47].

Understanding whether the virus primarily drives these pathways, the body's immune response, or a combination of both could help tailor more specific anti-inflammatory or immunomodulatory therapies that could reduce the risk of thrombosis[32].

Another aspect that could be further discussed is the impact of COVID-19 vaccination on the incidence of PTE in patients with long-term COVID-19. As vaccines play a crucial role in modulating the immune response to SARS-CoV-2, there is potential that vaccination status could influence the prevalence and severity of thrombotic events in Long-term COVID[48]. Research into whether vaccines can mitigate some thrombotic risks associated with long-term COVID-19 would be particularly beneficial[11].

The psychosocial impacts of Long COVID and PTE, particularly in young adults, is another area that deserves attention[2]. The chronic nature of Long COVID can lead to significant mental health challenges, including anxiety, depression, and post-traumatic stress, which can further complicate the clinical management of these patients[35]. Discussions about the need for integrated care models that include mental health support alongside physical health interventions are necessary[16].

There remains a significant need for large-scale, longitudinal studies to better define the pathophysiology of thromboembolism in the context of long-term COVID-19. Such studies should aim to delineate the mechanisms by which SARS-CoV-2 influences coagulation pathways, focusing on any viral or host factors that may sustain or exacerbate a prothrombotic state[49-51].

Researchers into developing predictive models incorporating clinical, genetic, and biochemical markers could significantly enhance our ability to identify at-risk individuals at an early stage[34]. Implementing such models in clinical practice could lead to more timely and precise interventions, potentially improving outcomes for young adults with Long-term COVID-19[13].

The current review has provided valuable insights into the challenges and complexities of managing PTE in patients with long-term COVID-19, substantial gaps remain in our understanding and treatment of this condition[45]. These gaps through focused research and clinical trials will be crucial in developing more effective diagnostic

tools and therapeutic strategies, ultimately reducing the burden of this condition on young adults and the healthcare system[42].

A more thorough discussion on the economic and societal impacts of long-term COVID and PTE in young adults could provide a more holistic view of the burden of this condition[44]. Young adults are a highly active segment of the workforce, and the long-term health complications associated with COVID-19 can lead to significant economic losses, reduced productivity, and increased healthcare costs[47-49].

By addressing these additional points, future discussions and research can provide a more comprehensive understanding of long-term COVID and PTE in young adults, ultimately leading to more effective prevention, management, and support strategies for this vulnerable population[50,51].

CONCLUSION

In conclusion, the intersection of long-term COVID and pulmonary thromboembolism (PTE) in young adults presents a significant clinical challenge that is compounded by the complex pathophysiology of SARS-CoV-2 infection.

The persisting inflammatory response and immune dysregulation associated with Long COVID contribute to a heightened thrombotic risk, which manifests distinctly in this younger demographic, which is typically at lower risk for such severe outcomes.

This review highlights the critical need for enhanced diagnostic strategies that consider the overlapping symptoms of long-term COVID and PTE, as well as the development of tailored anticoagulation protocols that address the unique clinical needs of these patients. It also underscores the importance of genetic and biomarker research to identify better those at increased risk of thrombotic complications post-COVID-19 infection.

The discussions within this review call for a multidisciplinary approach to managing the long-term effects of COVID-19, incorporating medical and psychosocial interventions to support the comprehensive health of young adults. As we continue to gather data and refine our understanding, it will be crucial to translate this knowledge into policy and practice, optimizing long-term outcomes and minimizing the broader socioeconomic impacts.

These gaps will be essential for mitigating the long-term complications associated with COVID-19 through focused research, patient education, and public health initiatives. This will ensure that young adults can recover fully and actively contribute to society. As such, the need for ongoing surveillance, research, and adapted healthcare strategies remains paramount in our global response to this unprecedented health crisis.

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