OPEN ACCESS

ISSN: 2835-9496

Palacios-Castrillo R (2024): 427
DOI: 10.47991/2835-9496/AJCMR-135

Research Article

American Journal of Clinical and Medical Research

Long Covid Syndrome due to Natural Viral Infection (NSITV) or ModRNA Vaccines (VSITV) are Primarily a Spike Protein-Induced Thrombotic Vasculopathy Linked to a Hyper Immune-inflammatory Response

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Citation: Palacios-Castrillo R (2024) Long Covid Syndrome due to Natural Viral Infection (NSITV) or ModRNA Vaccines (VSITV) are Primarily a Spike Protein-Induced Thrombotic Vasculopathy Linked to a Hyper Immune-inflammatory Response. Ameri J Clin Med Re: AJCMR-135.

Received Date: 08 June, 2024; **Accepted Date:** 14 June, 2024; **Published Date:** 19 June, 2024

Abstract

Long COVID, characterized by persistent symptoms following SARS-CoV-2 infection, poses significant challenges in understanding its underlying pathophysiology and effective management. Here, we propose mechanisms and potential treatments for Long COVID, focusing on thrombotic vasculopathy associated with hyperimmune-inflammatory responses triggered by persistent spike protein expression. We also introduce the terms "NSITV" (Natural Spike-Induced Thrombotic Vasculopathy) and "VSITV" (Vaccine Spike-Induced Thrombotic Vasculopathy) to describe Long COVID pathogenesis resulting from wild-type or ModRNA- encoded recombinant spike protein exposure. Importantly, most Long COVID patients have been both infected with the virus and ModRNA vaccinated, experiencing persistent expression of recombinant and natural spike proteins. Understanding NSITV and VSITV as multifaceted thrombotic vasculopathy highlights the importance of tailored therapeutic strategies. Future research should explore aggressive treatment approaches, such as the one suggested here, to alleviate symptoms and improve outcomes in patients with Long COVID.

Keywords: *ModRNA Vaccines, Long Covid, Thrombotic vasculopathy, Spike protein pathology.*

Introduction

Long COVID is a debilitating multisystem disease that causes significant disability [1]. The World Health Organization [2] defines long-term coronavirus infection as a disease where a possible or confirmed infection with SARS-CoV-2 occurs, symptoms appear within three months, and persist for an extended duration. The diagnosis requires symptoms lasting at least 2-4 months and confirmation of the case, with no alternatives available for diagnosis. The SARSCoV-2 coronavirus has affected over 200 million people worldwide, with most cases categorized as "mild" [3,4], and approximately one-third of these cases exhibiting no discernible symptoms [5,6]. Additionally, a significant rise in the incidence of long-COVID disease-like symptoms (VSITV) has been observed after 4,444 doses of SARSCoV-2 vaccination, especially with ModRNA-based vaccines [7-11].

In long COVID patients, an average of 56 symptoms occur, affecting nine different body systems [1]. The most common symptoms include fatigue, cognitive impairment, shortness of breath, exercise intolerance, post-exercise symptom exacerbation (PESE), sleep disorders, and myalgia [1,3,12-14]. With such a broad definition, Long COVID likely represents a complex pathological condition [10-12]. Estimates of the long-term prevalence of COVID-19 vary [3,13,15-19], but a study in Scotland found that the long-term prevalence rates are comparable to those of cancer (2.5%), chronic kidney disease (3.2%), chronic obstructive pulmonary disease (2.3%), and stroke (2.2%) [20-22]. Two meta-analyses concluded that 43–45% of patients experience persistent symptoms post the acute phase of COVID-19 [3,13]. Follow-up studies suggest that 85% of the patients symptomatic at 2 months post-infection remained symptomatic 1 year later [23]. Similarly, symptom resolution after 90 days seems to be uncommon [24], resulting in disability among the previously employed population [1]. Consequently, the economic costs in the UK alone are estimated to reach up to US$25 billion [25].

Although vaccination offers modest benefits in acute COVID-19 cases, it may increase the likelihood of developing long-term COVID-19. Likewise, studies indicate that reinfection with SARS-CoV-2 virus can lead to severe outcomes regardless of vaccination status, particularly as many countries scale back public health measures [26,27]. This trend further escalates the prevalence of Long COVID [28–31]. Moreover, both the severity and spectrum of adverse reactions to ModRNA-based vaccines are increasing, ranging from sudden death to myocarditis and endocarditis in previously healthy individuals, including athletes. The affected organs and tissues are also expanding to include pericarditis, venous and arterial thrombosis, meningoencephalopathy, peripheral neuropathy, systemic inflammatory syndromes such as Still's syndrome, gastrointestinal syndromes, and infertility due to orchitis (resulting in decreased spermatocyte production) and premature ovarian failure due to oophoritis-induced infertility, respectively. The scope of affected tissues and organs is extensive (Refer to the report “Frequency and affiliation of adverse reactions to COVID-19 vaccines reported to European Union and US pharmacovigilance systems.”). Therefore, it is evident that this pertains to a significant portion of long-term

immunizations, and Long COVID and VSITV cases are not expected to decrease over time, imposing substantial financial burdens on an already productive workforce.

Understanding the pathophysiology of Long COVID and VSITV is crucial. In this article, we posit that both Long COVID(NSIVT) and side effects of ModRNA vaccination (VSITV) involve sustained and prolonged expression of the spike protein in various body tissues and organs. This persistent expression may trigger coagulopathy, microvasculitis, and endothelitis, serving as the primary drivers, and potentially exacerbating or alleviating other common pathologies in Long COVID, such as a B cell activation disorder, autonomic dysfunction, and sudden death due to arrhythmias and myocardial infarctions. Given increasing reports on this subject, we hypothesize that the persistence of the spike protein is a critical component of persistent vascular coagulopathy within NSIVT and VSITV. We are exploring various therapeutic targets for the management of coagulopathy, endothelitis, and vasculitis, and we believe that early intervention, particularly with anticoagulants, antiplatelets, corticosteroids, and rapamycin/everolimus combinations, will provide significant relief to many patients.

To draw attention to these therapeutic objectives, we propose to refer to Long Covid caused by viral infection "natural spike protein-induced thrombotic vasculopathy" (NSITV) and renaming the side effect of ModRRNA vaccines to "vaccine spike protein-induced thrombotic vasculopathy" (VSITV), which primarily stems from the intermittent and persistent cellular expression of the spike protein. These concepts require urgent consideration, particularly as the world endeavors to coexist with the coronavirus.

Vaccines Based on ModRNA Platforms. The foundations that support VSITV, based on ModRNA:

1. Following vaccine administration, ModRNA disseminates in various tissues, prompting cells to express the Spike protein encoded by the ModRNA in diverse organs and tissues.
2. Spike protein expression in cells can persist longer than initially anticipated, extending for months or even years.
3. The widespread and prolonged expression of spike protein in various organs and tissues remains unpredictable and uncontrollable with Pfizer and Moderna ModRNA-based vaccines.
4. Similar to any foreign protein or antigen expressed in cells, the spike protein triggers an immune response mediated by antibodies and T-lymphocytes, resulting in the destruction of spike protein-producing cells and subsequent systemic inflammation.
5. Spike protein expression induced by ModRNA vaccines in endothelial cells renders them susceptible to destruction, inflammation, and dysfunction, potentially leading to vasculitis and coagulopathy characterized by microthrombosis and platelet hyperactivation. These effects may stem from abnormal spike protein expression in the endothelium, the immune response to the spike protein, or both mechanisms.
6. The immune response against the spike protein persists as long as cells continue to produce it. Prolonged presence of spike protein prolongs immune-mediated inflammation, leading to chronic tissue and organ damage.
7. Administration of booster doses of ModRNA vaccines elicits stronger, faster, and longer immune responses, accompanied by increased spike protein expression in cells, thereby heightening the risk of tissue and organ destruction and damage.

The Foundations Supporting Long COVID-19

Endothelial cells play crucial roles in vascular homeostasis and hemostasis, regulating vascular tone, blood flow, fibrinolysis, and platelet aggregation [32-35]. Acute COVID-19 primarily affects the vascular endothelium, leading to microcirculatory thrombotic vasculitis [33,34,36-43]. SARS-CoV-2 spike proteins facilitate viral binding to target cells by binding to Angiotensin-Converting Enzyme 2 (ACE2), initiating intracellular viral replication [42,44,45]. ACE2, present in various tissues including the vasculature, serves as an entry point for SARS-CoV-2, allowing widespread dissemination throughout the body, including across the blood-brain barrier [33,34,37,39,42,46-48]. Entry of SARS-CoV-2 into endothelial cells decreases ACE2 expression, promoting a proinflammatory and prothrombotic environment [34,49-51]. Endothelial injury may result from direct SARS-CoV-2 infection, leading to endothelial cell apoptosis and endothelitis, followed by systemic immuno-inflammatory responses [33,34,37,39,49,51,52].

Spike proteins alter the structure of beta and gamma fibrinogen, complement C3, and prothrombin, fostering the development of larger and more resistant blood clots. Spike proteins can initiate clot formation independent of thrombin and platelets, penetrate the blood brain barrier and cause long term neuronal inflammation and damage [39], microvascular hemostasis destabilization, thrombosis, platelet activation, and endothelial dysfunction. Endothelial dysfunction leads to impaired vascular tone and a prothrombotic state [32,34,35,37,39,43,49-60,61-78].

Post-mortem examination of critically ill COVID-19 patients reveals generalized coagulopathy, with a significantly higher prevalence of alveolar-capillary microthrombi compared to influenza A [62]. Additionally, microclot burden in acute COVID-19 patients is notably higher regardless of disease severity, suggesting a chronic sequela following COVID-19 [39,40].

Thrombi can develop from inflammation, potentially triggering cytokine storms. SARSCoV-2 or ModRNA Spike proteins activate platelets and the complement system, leading to endothelial dysfunction. The resulting pro - inflammatory environment may induce immunothrombosis, particularly affecting the microvasculature. Furthermore, the S1 subunit of the spike protein can directly interact with platelets and fibrin, contributing to microclot formation. These microclots, resistant to fibrinolysis, play a central role in the pathogenesis of NSITV and VSITV.

Various mechanisms have been proposed to explain Long COVID, including Mast Cell Activation Syndrome (MCAS), neuroinflammation, viral reactivation, persistence of SARS-CoV-2 and/or spike protein, autoimmunity, and gut dysbiosis [9,79-81]. Many patients may experience a combination of these pathologies, interacting with each other.

Capillary Occlusion

Human capillaries typically have diameters ranging from 5 to 10 μm, allowing for continuous circulation of red blood cells due to their flexible structure [82,83]. However, microclots in Long COVID patients vary in diameter from 5 to 200 μm, posing a risk of capillary blockage [82,83]. This can lead to ischemia-reperfusion injury at the microvascular level, explaining the exacerbation of post-exercise symptoms (PESE) observed in 75-89% of patients. PESE can be objectively demonstrated through daily cardiopulmonary exercise testing and prolongs subsequent recovery [1,83-87]. Additionally, microvascular occlusion may manifest as symptoms such as chest pain, attributable to microvascular ischemia [88,89].

Several studies on Long COVID patients have provided evidence of capillary occlusion and systemic vascular changes, including decreased sublingual and retinal blood vessel density, and the presence of fibrin clots in skin and muscle capillaries [88-98]. Compensatory angiogenesis observed in severe acute COVID-19 patients further supports the notion of capillary occlusion by microclots [99].

Microthrombosis in Long COVID patients was first reported by Pretorius et al. [40], who observed the persist ent presence of fibrinolysis-resistant microthrombosis in the blood capillaries, accompanied by increased platelet activation and dysregulated hemostatic function. These microthrombi are visible in platelet-depleted plasma samples after centrifugation and were also observed in patients with acute COVID-19 infection [82]. Another study, analyzing post-mortem data from 325 patients who died after ModRNA-based vaccine administration, found that 53% of VSITV-related deaths were cardiovascular-related, with additional cases related to blood, respiratory, and multiorgan-system issues [82]. Of the 4,444 individuals vaccinated with ModRNA-based vaccines, 240 deaths were directly attributed to vaccination.

Furthermore, the presence of coagulopathy in Long COVID patients extends beyond typical symptoms and is associated with an increased risk of cardiovascular disease, including ischemic heart disease and myocardial inflammation, following acute COVID-19 infection, ModRNA vaccination, or both [100-103]. Thrombotic vasculopathy persists in some individuals, with microclots detected more than 23 months after SARS-CoV-2 infection and/or ModRNA vaccination [82,103-109]. Additionally, Long COVID patients exhibit sustained elevation in circulating thrombogenic spike protein S1 subunit levels compared to those who have recovered from COVID-19 infection [67,110-112]. Analysis of microthrombi associated with COVID-19 has revealed the presence of spike protein (but not full-length SARS-CoV-2 virus) and inflammatory markers within the clot. Clot lysis may perpetuate clot formation and platelet activation by releasing entrapped spike proteins and inflammatory proteins, creating a vicious cycle. The retention of inflammatory proteins may also explain why many NSITV and VSITV patients have normal test results for inflammatory markers such as C-reactive protein and D-dimers [58, 66, 113-114].

Platelet hyperactivation and endothelitis

Platelet enactment and endothelitis are imperative highlights related with microcoagulation in Long COVID and VSITV [43]. Markers of endothelial harm have been related to expanded symptomatology and less work out resilience in long Covid patients [103,105,107,109,115-121]; indeed, hyperactivated platelets amplify and maintain endothelitis [116], contributing to the development and maintenance of Long COVID [82,104,108,122,123]. Moreover, Long COVID patients, who encounter more cognitive disability, display higher levels of cerebral hypoperfusion [124] and neuroinflammation [125], with plasma inflammatory markers in plasma consistent with endothelitis [118,126,127].

Since endothelial dysfunction is a precursor to atherosclerosis, this complications could manifest in the coming decades in Long Covid patients [128]. Capillary impediment caused by microthrombi or endotheliitis can lead to defective systemic oxygen extraction [43,129-133]. Long COVID patients may have higher blood lactate concentrations at rest and amid work out and lower anaerobic edges [130]. The diminished maximal oxygen utilization (VO2 max) in Long Covid patients is due to the restriction of fringe oxygen supply due to deficient oxygen extraction at the capillary level [130-133], coming about in diminished physical condition. [134]. Thus, deficient oxygen extraction has been related with impaired work out in Long COVID patients, together with plasma markers suggestive of endothelitis [133].

These observations are radiologically backed by magnetic resonance imaging utilizing xenon, which demonstrates impeded lung gas transmission in Long Covid patients due to microthrombi, decreased work out resilience and increased blood desaturation [135-137]. CT-pulmonary angiography for assessing capillary thrombosis and perfusion may be less sensitive [138], than Ventilation/perfusion scans and single photon emission computed tomography (CT) [138-140]. Taken together, these observations document the presence of microcoagulation and further suggest that the wide assortment of symptoms in Long Covid patients are due to multiorgan tissue hypoxia [129,131-133,136].

Other consequences of multiorgan Tissue Hypoxia

Beyond the central problem of tissue hypoxia resulting from thrombotic vasculitis, there are other consequences of persistent endothelial inflammation. Patients with Long COVID are at significantly elevated risk (HR > 80) of dysautonomia [79]. Some symptoms, such as postural tachycardia, may be partly explained by coagulopathy, particularly early in disease progression [80]. The autonomic nervous system innervates the walls of blood vessels to regulate vascular tone [32]. Sympathetic and parasympathetic fibers innervate the muscular layer of the vessels, while only parasympathetic fibers innervate the endothelial layer, making parasympathetic fibers more susceptible to the consequences of endothelial inflammation [32]. Nerve ischemia has been proposed as an etiology [9]. The resulting dysautonomia, where sympathetic function predominates, occurs in the moderate to severe range in two-thirds of Long COVID patients, independent of the initial severity of the infection [32,141], and is associated with exercise intolerance [142].

An important consequence of post-COVID-19 dysautonomia is Postural Orthostatic Tachycardia Syndrome (POTS) [143]. The etiology of POTS is multifactorial, involving endothelial disease [144], hyperactive platelets [145,146], tissue hypoxia [147], immunothrombosis [146], and increased sympathetic activation

[144,147-149]. POTS causes abnormal cerebral blood flow and oxygenation [150,151], consistent with the target organ consequences of thrombotic vasculitis in Long COVID, and contributes to a variety of common Long COVID symptoms such as fatigue, tremors, and dizziness [152]. Predominant sympathetic activation can produce symptoms that are often misdiagnosed as anxiety [153-155].

ACE2 downregulation and tissue hypoxia can reduce serotonin synthesis [156,157], while overactive platelets (which store serotonin) can cause serotonin depletion [113]. Therefore, anxiety and depression in some patients may be a consequence of coagulopathy and dysautonomia [158]. More cases of POTS have been observed after SARS-CoV-2 infection and, less frequently, after vaccination [143,159].

It is increasingly recognized that Long COVID symptoms, diagnoses, and pathophysiology may also be triggered by SARS-CoV-2 vaccination in some patients [7,8,10,11], where the persistence of the spike protein has been documented [7-9]. With the same diseases occurring after both vaccination and infection, we suggest that the persistence of the spike protein (rather than the whole virus) may lead to Long COVID, POTS, and VSITV pathology. The spike protein alone has been shown to induce microclotting in vitro [36], and some individuals vaccinated with an ModRNA-based vaccine develop thrombotic vasculitis similar to that seen in Long COVID-19. This offers crucial insight into the etiology of Long COVID-19 and VSITV. Supporting this, and in line with the evidence for Long COVID, several cases of post COVID-19 vaccine retinal vascular occlusion have been reported, attributed to Susac syndrome (an autoimmune endotheliopathy) and microthrombi, with potential links to hyperviscosity syndrome [160].

Mast Cell Activation Syndrome (MCAS) appears to play an important role in both Long COVID and Postural Orthostatic Tachycardia Syndrome (POTS). Mast cells, found in the vasculature, are involved in inflammation, hemostasis, and endothelial cell activation. Their degranulation may contribute to immunological and thrombotic outcomes in COVID-19. Furthermore, platelet activation and ischemia-reperfusion can stimulate mast cell degranulation. Several mast cell mediators, such as heparin, tryptase, and VEGF, are directly involved in coagulopathy.

Thus, MCAS may be a direct consequence of persistent coagulopathy, even if activation was initiated through the spike protein. The persistence of the spike protein may be a chronic trigger of MCAS. Although MCAS appears to be a co-pathology in some Long COVID patients, addressing the coagulopathy could have a dual benefit by reducing inappropriate and harmful mast cell activation as well as mitigating thrombogenesis.

Current evidence suggests that both Long COVID and Vaccine-Induced Spike Protein Thrombotic Vasculitis (VSITV) are primarily coagulopathies and vasculopathies causing multisystem symptoms due to systemic tissue hypoxia. The clinical similarity with other coagulopathic diseases, such as antiphospholipid syndrome, also supports this idea.

Thus, it is likely that Long COVID and VSITV are, in many cases, Spike Protein-Induced Thrombotic Vasculitis (SITV). Therefore, the use of the terms NSITV and VSITV is proposed to describe these disorders, as they are more descriptive of the proposed mechanism and primary pathology. This helps focus attention on early therapeutic interventions to prevent chronic complications and also distinguishes these conditions from other pathologies that may predominate in some patients.

Importantly, this proposal is supported by current evidence, but research on Long COVID and VSITV is ongoing [161-168]. Further studies are needed to fully understand their pathophysiology and develop effective therapeutic approaches.

Potential Treatments

Therapeutic efforts for Long COVID have predominantly focused on rehabilitation and psychological therapy [169], perhaps due to the perception that Long COVID patients are recovering from acute COVID-19 rather than suffering from a continuing pathology. Considering this pathology, such treatments can be harmful due to Post-Exertional Symptom Exacerbation (PESE) [1,87,170]. In fact, rehabilitation is largely ineffective in improving Long COVID symptoms [169]. We maintain that Long COVID patients (those with NSITV) will not be ready for rehabilitation until the underlying disease and its complications have been effectively treated.

Treatment targets for NSITV and VSITV include microclots, hyperactive platelets, and endothelitis. It is proposed that treating this multifaceted inflammatory coagulopathy with a single drug will be insufficient. A combination of anticoagulant, steroidal anti-inflammatory, and antiplatelet drugs will be required to achieve synergistic and superior results [81,114,156]. Early intervention is recommended [43,114,156].

Anticoagulants In acute cases of COVID-19, favorable outcomes have been hypothesized and achieved when coagulopathy is addressed [38,171,172]. NICE recommends anticoagulants in certain circumstances [173]. In a case series of Long COVID patients, early treatment with apixaban 5 mg B.I.D. (with aspirin, clopidogrel, and a proton pump inhibitor) for $\geq$ 1 month resulted in symptomatic resolution in all 24 patients [81]. Symptomatic improvement was also correlated with a reduction in microclots and hyperactive platelets. Another case series (n=91) of anticoagulant/antiplatelet therapy showed that between 74% and 87% of patients reported an improvement in nine key symptoms and a concurrent reduction in microclots, although there was an increase in gastrointestinal bleeding [80]. Since Long COVID microclots are resistant to fibrinolysis [36,69,78], dabigatran may be superior, as it increases clot susceptibility to fibrinolysis more than other anticoagulants [174,175].

Heparin inhibits the binding of the spike protein to ACE2, giving it both antiviral and anticoagulant properties [60,176-178]. Heparin has been effectively used to treat conditions such as prolonged COVID-related perfusion defects [139] and microclots in the context of pulmonary embolism [179]. Additionally, obstetric patients (n=291) with Long COVID who received enoxaparin antepartum through six weeks postpartum reported ongoing symptoms of Long COVID less frequently than those who did not [180].

Antiplatelet Drugs

The targets of antiplatelet therapy are hyperactive platelets and endothelitis. Emerging evidence suggests a unique role for P2Y12 inhibitors (e.g., ticagrelor, clopidogrel) that attenuate the interaction between platelets and endothelial cells, thus reducing

platelet activation, endothelitis, and endothelial clot formation more effectively than aspirin [58,116]. In hospitalized patients with acute COVID-19, favorable outcomes, such as reduced mortality, have been observed with antiplatelet drugs, with increased survival seen with dual antiplatelet therapy without a higher risk of bleeding [181,182]. Improved perfusion has also been noted with tirofiban, along with aspirin, clopidogrel, and prophylactic doses of anticoagulants [183]. In a randomized controlled trial, hospitalized patients receiving aspirin had similar 28-day mortality rates compared to standard care but experienced a slightly shorter hospital stay and a higher proportion of patients discharged alive within 28 days [184].

For Long COVID, obstetric patients taking aspirin 325 mg/day reported symptomatic improvement compared with those who did not [180]. In a case series of 24 Long COVID patients, aspirin was shown to reduce hyperactive platelets as a single agent but required the addition of apixaban and clopidogrel to reduce microclots [81]. Similar findings were reported in a larger case series (n=91), showing reduced platelet activation after anticoagulation with dual antiplatelet agents [80]. Considering the emerging evidence of Long COVID-like vaccine reactions, aspirin has been explored as a method to reduce vaccine-induced acute endothelitis [185].

mTORC1 Inhibitors

A drug that should be considered is rapamycin or everolimus, mTORC1 inhibitors with excellent anti-inflammatory effects on endothelial cells in addition to their immunosuppressive effects. These drugs have shown very good results in conditions such as Takayasu vasculitis, kidney transplant rejections, graft vs. host disease, and in preventing endothelial and myocyte proliferation in coronary stents.

It is the author's opinion that the most reasonable treatment for severe NSITV and severe/serious VSITV, considering the importance of thrombotic vasculitis in its pathogenesis, includes a combination of steroidal anti-inflammatories (deflazacort doses of 15 to 30 mg/day, prednisolone 10-20 mg/day), anticoagulants (apixaban 5-10 mg/day, dabigatran 110-150 mg/day), antiplatelet drugs (clopidogrel 75 mg BID, ticagrelor 60-90 mg/ day), and rapamycin 1 mg BID or everolimus 10 mg/ day. In cases of mild to moderate NSITV and VSITV, low doses of s t eroidal ant i - inflammator y drugs, anticoagulants, and antiplatelet drugs should be considered. If no improvement is observed, rapamycin or everolimus should be considered.

Patients with NSITV and VSITV experiencing symptoms of anxiety and depression may benefit from the antidepressant sertraline. This drug also has additional antiplatelet and endothelial protective properties. Moreover, sertraline binds to the S1 subunit of the spike protein, blocking its interaction with ACE2, which may be important considering the growing evidence of spike protein persistence in NSITV and VSITV [7-9,186-201].

Discussion and Conclusion

A growing body of evidence supports that NSITV and VSITV are primarily endothelial and immuno-coagulopathic diseases initiated by the persistent SPIKE expression in cells following infection or the use of ModRNA platform-based vaccines. We propose the use of the terms NSITV and VSITV, as they accurately describe the pathophysiology of post-COVID-19 and post-vaccination presentations, and help focus attention on early therapeutic interventions targeting microclots, hyperactive platelets, and endothelitis. This multifaceted coagulopathy requires synergistic polypharmacy to achieve symptomatic resolution. Thromboelastography can be utilized to mitigate the risk of bleeding.

Our perspective does not deny the need to identify and treat other common pathologies in Long COVID and VSITV but highlights how thrombotic vasculitis can cause, exacerbate, and interact with other conditions. Future research should investigate the efficacy of aggressive anticoagulation, antiplatelet therapy (particularly early), and the use of Rapamycin/Everolimus after COVID-19 infection or post-ModRNA vaccine sequelae to treat NSITV and VSITV.

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