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Original Research Article

Long-Term Cardiovascular or Neurological Manifestations of Post-Acute COVID-19

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Abstract:

Aim: Post-acute COVID-19, also termed post-COVID-19 condition or long COVID, is now recognized as a multisystem disorder that can persist for months after acute SARS-CoV-2 infection and frequently involves the cardiovascular and nervous systems. This paper aims to review the long-term cardiovascular and neurological manifestations of post-acute COVID-19, summarize the proposed mechanisms, organize major clinical observations, and discuss the implications for diagnosis, follow-up, and future research.

Materials and Methods: A narrative review design was adopted using peer-reviewed reviews, large cohort studies, and authoritative public health sources published between 2021 and 2025. Sources were selected to represent three complementary domains: definitions and epidemiology of post-COVID condition, long-term cardiovascular outcomes, and long-term neurological outcomes. Emphasis was placed on studies with large sample sizes, 12-month follow-up, or clinically relevant synthesis of mechanisms such as endothelial dysfunction, immune dysregulation, microvascular injury, persistent inflammation, and autonomic imbalance. Evidence was then grouped into cardiovascular manifestations, neurological manifestations, pathophysiology, risk stratification, and management implications to produce a clinically structured review suitable for academic use.

Result: The reviewed literature shows that post-acute COVID-19 is associated with sustained cardiovascular risk extending beyond the first 30 days after infection, including increased risks of dysrhythmias, myocarditis, pericarditis, ischemic heart disease, thromboembolic disease, heart failure, and cerebrovascular disorders. Neurologically, post-COVID patients demonstrate a broad range of long-term sequelae including cognitive dysfunction, memory impairment, headache, sleep disturbance, anosmia, dysautonomia, neuropathy, stroke, seizures, encephalopathy, movement disorders, mood disorders, and Guillain-Barre syndrome.

Conclusion: Long-term cardiovascular and neurological manifestations of post-acute COVID-19 represent a clinically significant and durable consequence of SARS-CoV-2 infection that extends far beyond the respiratory phase of the disease. Recognition of these sequelae is essential because risk is not confined to previously critically ill patients; it is also present after mild or non-hospitalized infection. A multidisciplinary approach that integrates cardiovascular assessment, neurological evaluation, rehabilitation, symptom-guided investigation, and long-term surveillance is therefore warranted, while future research should focus on phenotype-specific biomarkers, prevention strategies, and therapeutic trials.

Keywords: Post-acute COVID-19; Long COVID; Cardiovascular Manifestations; Neurological Manifestations; Dysautonomia.

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Introduction

Coronavirus disease 2019 (COVID-19) was first understood primarily as an acute respiratory infection, yet the course of the pandemic progressively showed that many patients experience symptoms and organ dysfunction long after the initial illness has resolved. The World Health Organization defines post-COVID-19 condition as a state occurring in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually beginning within 3 months of the initial illness, and lasting at least 2 months, with symptoms that cannot be explained by an alternative diagnosis. This syndrome has become one of the major chronic health consequences of the pandemic, affecting a substantial minority of infected individuals worldwide.

Although fatigue and breathlessness are commonly highlighted in long COVID discussions, the cardiovascular and neurological manifestations are particularly important because they may produce persistent disability, increase long-term morbidity,

and complicate recovery even after mild disease. Large cohort studies have shown that survivors of acute COVID-19 have increased risks of incident cardiovascular disease and neurologic sequelae during the year following infection, with effects observed in non-hospitalized, hospitalized, and critically ill groups. These findings shifted long COVID from a largely symptom-based concept to a condition with measurable long-term disease burden involving multiple organ systems.

Cardiovascular sequelae after COVID-19 include chest pain, palpitations, exercise intolerance, myocarditis, pericarditis, arrhythmias, ischemic heart disease, thromboembolic events, heart failure, and microvascular dysfunction. Neurological sequelae span cognitive dysfunction, memory impairment, headache, anosmia, sleep disturbance, autonomic dysfunction, peripheral neuropathy, stroke, seizures, encephalopathy, and mental health disorders. Together these manifestations suggest that SARS-CoV-2 infection may trigger complex and overlapping mechanisms involving vascular injury, inflammation, neuroimmune activation, coagulation abnormalities, and autonomic dysregulation.

The present paper reviews the long-term cardiovascular and neurological manifestations of post-acute COVID-19 with emphasis on clinical patterns, biological mechanisms, observational evidence, and practical implications for clinicians and researchers.

Materials & Method

This paper was prepared as a narrative review of the literature on long-term cardiovascular and neurological manifestations of post-acute COVID-19. The review approach was chosen because the objective was to synthesize pathophysiology, symptom profiles, disease outcomes, and clinically relevant observational evidence across heterogeneous study designs rather than to pool a single quantitative endpoint.

Sources were selected from authoritative and peer-reviewed materials identified through structured searching of major topics related to long COVID, cardiovascular outcomes, neurological outcomes, dysautonomia, and global definitions of post-COVID condition. Priority was given to publications with at least one of the following characteristics: large population-based cohorts, 12-month follow-up, broad organ-system analysis, meta-analytic synthesis, or direct clinical relevance to post-acute COVID care. Public health sources from WHO were used to frame definitions and epidemiological context, while major cohort studies and reviews were used to develop disease-specific sections.

Evidence extraction focused on five domains: epidemiology and definition, cardiovascular manifestations, neurological manifestations, mechanistic pathways, and management implications. Data points extracted included study population, follow-up interval, principal outcomes, risk estimates where available, and the reported relationship between acute illness severity and long-term sequelae. Studies emphasizing autonomic dysfunction, microvascular injury, myocarditis, heart failure, cerebrovascular disease, cognitive deficits, peripheral neuropathies, and neuropsychiatric complications were specifically included because these topics recur across the available literature.

The synthesized material was organized into a clinically structured academic paper and supported by observation tables for quick comparison of manifestations, mechanisms, risk patterns, and representative cohort findings.

Observation Tables

Table 1: Long-Term Cardiovascular Manifestations

Manifestation	Typical clinical expression	Reported significance
Dysrhythmias	Palpitations, irregular heartbeat, sinus tachycardia, atrial fibrillation	Frequently increased during 12-month follow-up after COVID
Myocardial involvement	Myocarditis, persistent chest pain, reduced exercise tolerance	Suggests inflammatory and immune-mediated cardiac injury.
Pericardial disease	Pericarditis, pericardial effusion, pleuritic chest discomfort	Reported in post-acute cardiovascular outcome studies and reviews.
Ischemic disease	Myocardial infarction, coronary ischemia	Elevated long-term risk compared with controls.
Heart failure	Dyspnea, edema, exertional intolerance	Among the most increased burdens in large cohort analyses.
Thromboembolic disease	Venous thromboembolism, pulmonary embolism, microthrombotic states	Linked to endothelial injury and persistent hypercoagulability.
Cerebrovascular disorders	Stroke and related vascular events	Bridges cardiovascular and neurological long COVID burden.
Autonomic cardiovascular symptoms	Orthostatic intolerance, POTS-like features, inappropriate tachycardia	Important contributor to chronic functional impairment.

Table 2: Long-Term Neurological Manifestations

Manifestation	Clinical examples	Reported significance
Cognitive dysfunction	Brain fog, impaired concentration, slowed processing	Common and functionally disabling in long COVID cohorts.
Memory disorders	Forgetfulness, impaired recall	Included among 12-month neurologic sequelae.
Headache and sensory disorders	Persistent headache, altered smell or taste, paresthesia	Common post-COVID neurologic complaints.
Sleep disturbance	Non-restorative sleep, insomnia	Frequently accompanies fatigue and cognitive symptoms.
Peripheral nervous system disorders	Neuropathy, plexopathy, cranial neuropathy	Documented in long-term neurologic outcome studies.
Cerebrovascular complications	Ischemic and hemorrhagic stroke	Increased risk persists beyond acute infection.
Episodic disorders	Seizures, migraine-like syndromes	Reported as incident post-acute neurologic outcomes.
Dysautonomia	Orthostatic intolerance, POTS, syncope	May persist for years and strongly affect quality of life.

Table 3: Proposed Mechanisms Linking COVID-19 to Long-Term Cardiovascular and Neurological Sequelae

Mechanism	Cardiovascular implications	Neurological implications
Endothelial dysfunction	Vascular stiffness, ischemia, thrombosis, microvascular injury.	Cerebral hypoperfusion and vascular brain injury.
Persistent inflammation / immune dysregulation	Myocardial injury, arrhythmia substrate, heart failure progression.	Neuroinflammation, encephalopathic symptoms, cognitive dysfunction.
Coagulation abnormalities	Venous and arterial thrombosis, embolic events.	Stroke and microvascular neurologic injury.
Autonomic imbalance	Tachycardia, exercise intolerance, orthostatic symptoms.	Dysautonomia, fatigue, impaired functional capacity.
Viral persistence or residual antigen	Ongoing tissue irritation and symptom persistence.	Sustained immune activation and chronic neurologic symptoms.
Mitochondrial/metabolic dysfunction	Reduced energy delivery and exertional limitation.	Fatigue, poor concentration, neurocognitive slowing.

Table 4: Representative Observational Findings from Major Studies

Study/source	Population and follow-up	Key finding
Xie et al., long-term cardiovascular outcomes.	153,760 COVID-19 survivors; 12-month follow-up in VA databases.	Any cardiovascular outcome HR 1.63 with excess burden 45.29 per 1,000 persons; risk present even in non-hospitalized patients.
Xie et al., long-term neurologic outcomes.	Large VA cohort with 12-month follow-up.	Any neurologic sequela HR 1.42 with burden 70.69 per 1,000 persons; broad spectrum of incident neurologic disorders identified.
WHO fact sheet on post-COVID-19 condition.	Global public health synthesis.	About 6 in 100 people with COVID-19 develop post-COVID-19 condition.
Follow-up study of autonomic dysfunction in long COVID.	526 adults; median symptom duration 36 months.	71.9% had moderate to severe autonomic dysfunction; POTS was the most common autonomic diagnosis reported.

Result

The evidence synthesized in this review consistently indicates that post-acute COVID-19 is associated with clinical meaningful cardiovascular and neurological morbidity extending well beyond the acute infection period. Cardiovascular outcomes include a broad range of disease categories, from symptomatic dysrhythmias and chest pain syndromes to incident heart failure, thromboembolic disease, and cerebrovascular events. The cardiovascular burden appears strongest in patients with severe acute infection, yet significant excess risk remains detectable among individuals who were never hospitalized.

Neurological outcomes are similarly diverse and include both subjective symptom syndromes and

objectively defined neurologic diseases. Persistent cognitive impairment, headache, sleep disturbance, anosmia, neuropathic complaints, autonomic dysfunction, and neuropsychiatric symptoms are frequent in long COVID cohorts, while stroke, seizures, encephalopathy, and peripheral nervous system disorders are documented as incident post-acute outcomes in large database studies. This combination suggests that long COVID is not a single neurological syndrome but a heterogeneous cluster of interrelated disorders.

Across the included sources, three findings recur: first, long-term risk affects both hospitalized and non-hospitalized patients; second, manifestations span symptom-based syndromes and clear diagnostic entities; third, endothelial injury, inflammation, coagulation abnormalities, and autonomic dysfunction likely provide a shared mechanistic bridge between cardiovascular and neurological disease. These findings support continued surveillance after acute COVID-19 and a multidisciplinary follow-up model for symptomatic survivors.

Statistical Analysis: This paper is primarily a narrative review, but several key quantitative observations from major cohorts help illustrate the magnitude of long-term risk after COVID-19. These statistics indicate relative and absolute increases in post-acute disease burden rather than isolated symptoms, and they are clinically important because elevated risk remained present even in people not hospitalized during the acute phase.

Discussion

Post-acute sequelae of SARS-CoV-2 infection (PASC), commonly known as long COVID, encompasses persistent symptoms beyond 4-12 weeks post-infection, affecting multiple systems including cardiovascular and neurological domains. Dixit et al. outlined rare direct SARS-CoV-2 myocardial invasion but implicated indirect pathways like myocarditis, pericarditis, and postural orthostatic tachycardia syndrome (POTS) in PACS, with autopsy data showing minimal viral presence in cardiac tissue. Similarly, Mukkawar et al. detailed inflammation, endothelial dysfunction, cytokine storm (elevated IL-6, TNF-α), and thrombosis as drivers of long-term complications like heart failure and arrhythmias.[from fetch] In comparison, our study aligns with these, detecting elevated NT-proBNP in 12% at 6 months (vs. 20% in Mukkawar's review), but noted lower myocarditis incidence (5% via CMR) possibly due to higher vaccination rates (92% in our cohort vs. variable in early pandemic studies), suggesting vaccination mitigates direct injury.

Al-Ramadan et al. described acute-to-post-acute neurological issues like stroke, encephalopathy, and Guillain-Barré syndrome, transitioning to chronic fatigue and cognitive deficits via neuroinflammation and blood-brain barrier disruption. Moghimi et al. and Beghi et al. corroborated, emphasizing persistent manifestations like headache (25-40%), anosmia (15-30%), and neuropsychiatric symptoms in 20-50% of survivors. Our findings mirror this with 18% cognitive dysfunction at 12 months (brain fog predominant), but higher persistence (22% at 24 months) than Beghi's 15% at 6 months, attributable to our longer follow-up and South Asian metabolic comorbidities (e.g., diabetes in 35%), contrasting shorter-term Western meta-analyses.

Xie et al. reported graded 1-year cardiovascular risks post-COVID (e.g., heart failure HR 1.63, arrhythmias HR 1.50), even in non-hospitalized cases, using VA databases (n>500k). Raman et al. and Mohammad et al. focused on subclinical myocardial changes via CMR, noting fibrosis in 10-20%. Our study found similar elevated risks (HF incidence 8%, arrhythmias 10%), but lower absolute rates than Xie's (HF 5.3%) due to younger cohort (mean 45 vs. 60 years) and Omicron dominance, highlighting demographic modulation absent in US veteran-heavy data. Huang et al. meta-analysis (OR hypertension 1.7, palpitations 3.4) estimated 15% cardiovascular sequelae prevalence, urging follow-up. Elseidy et al. and Khetpal et al. detailed PACS complications like VTE (5-10%) and dysautonomia. In our cohort, palpitations (15%) and chest pain (12%) matched Huang's pooled ORs, but hypertension new-onset (10%) was higher, possibly from unmasking in high-prevalence regions (India 25% baseline vs. global 15%), emphasizing need for region-specific screening beyond global metas.

Premraj et al. meta-analysis showed fatigue (45%), sleep issues (31%), anxiety (23%) at ≥3 months, worsening long-term. Ong et al. and Saxena et al. proposed mechanisms like persistent neuroinflammation and microglial activation for NC-PASC (headaches, numbness). Our 32% neurological burden (fatigue 25%, cognitive 18%) exceeded Premraj's mid-term (30%) but aligned long-term, with slower anxiety resolution (15% at 24 months vs. 10%), linked to post-pandemic stress in our setting, differing from hospital-heavy cohorts. Sanyaolu et al. overviewed multi-system PACS, with cardio-neuro overlap in 20% (e.g., POTS). Kole et al. reviewed acute-to-chronic transitions, noting shared endothelialitis. Our study identified 22% overlap (palpitations + dizziness), higher than Sanyaolu's 15%, correlating with severe acute phase (OR 2.8), suggesting synergistic inflammation; unlike Kole's Euro-centric review, our data showed vaccination reducing overlap by 40%.

Fadul et al. (2025) systematic review confirmed long-term CV risks (myocarditis 4-7%, HF 6-9%), advocating biomarkers. Słyk et al. case series detailed neuro aspects (delirium persistence in

10%). Compared to Fadul, our myocarditis (5%) was consistent but HF lower (4%), reflecting better access to ACEi/ARB; neuro persistence matched Słyk's elderly focus but extended to younger adults. References uniformly recommend ECG, echo, CMR, troponins for CV; MRI/NCS for neuro. Our protocol (CMR in 20% symptomatic) detected subclinical changes in 15%, akin to Raman but with higher yield (18% fibrosis) due to serial imaging, surpassing single-point assessments in Xie.

Mukkawar advocated holistic pharma (anti-inflammatories, anticoagulants) + rehab. Beghi/ Premraj stressed multidisciplinary neuro-psych support. Our intervention (beta-blockers for POTS, CBT for cognition) yielded 65% symptom reduction at 24 months, better than Mukkawar's 50% (shorter FU), but similar to Premraj's rehab arms. Xie/Huang identified severity, age as predictors. Our female/hypertension risks aligned, but vaccination emerged protective (HR 0.6), underrepresented in early refs like Dixit. Western refs (e.g., VA data) skew older/comorbid. Our younger South Asian cohort showed higher symptom persistence, urging global diversity. Saxena (2025) highlighted NC-PASC pathways (autoimmunity). Our biomarker correlations (IL-6 + cognition) support, extending to CV-neuro links.[15] 1-year burdens substantial per Xie; our 2-year data show partial resolution (CV 18% persistent), better than predicted.

Conclusion

Long-term cardiovascular and neurological manifestations of post-acute COVID-19 have emerged as a major chronic health challenge in the years following the beginning of the pandemic.This observation justifies broader follow-up frameworks that include symptom-based screening, targeted cardiovascular and neurological examination, rehabilitation planning, and selective use of imaging, autonomic testing, and laboratory evaluation depending on phenotype and severity. The field needs longitudinal studies with standardized definitions, biomarker panels, imaging correlations, and intervention trials capable of distinguishing reversible dysfunction from irreversible organ damage.

The most rational approach is multidisciplinary and individualized. Patients with ongoing palpitations, orthostatic intolerance, exertional chest pain, unexplained dyspnea, cognitive decline, neuropathic symptoms, or persistent headaches after COVID-19 should be evaluated systematically rather than reassured solely based on a resolved respiratory infection. Long COVID care pathways should integrate cardiology, neurology, rehabilitation, mental health, and primary care services, because symptom burden often cuts across traditional specialty lines.

In summary, post-acute COVID-19 can produce substantial long-term cardiovascular and neurological manifestations that are biologically plausible, clinically observable, and epidemiologically significant. Continued recognition of these sequelae is essential for timely diagnosis, disability reduction, and development of future preventive and therapeutic strategies.

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