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Original Research Article

EXERCISE CAPACITY AND CARDIOVASCULAR FUNCTION IN POST-COVID SURVIVORS IN YOUNG ADULTS: A CROSS-SECTIONAL COMPARATIVE STUDY

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ABSTRACT

Background: SARS-CoV-2 infection leaves a substantial proportion of young adults with persistent cardiovascular sequelae beyond the acute phase. Whether post-COVID syndrome impairs exercise capacity, autonomic regulation, and left ventricular performance in young adults remains incompletely characterised. The aim is to evaluate and compare exercise capacity parameters, echocardiographic indices, and heart rate variability (HRV) in post-COVID young adults versus age-matched healthy controls.

Materials and Methods: A cross-sectional, case-control study enrolled 120 participants aged 18–35 years: 60 post-COVID survivors (at least 3 months post-PCR-confirmed infection) and 60 age- and sex-matched healthy controls. All subjects underwent treadmill exercise testing (TMT), two-dimensional echocardiography (2D echo) with speckle-tracking analysis, 24-hour Holter monitoring for HRV analysis, and resting 12-lead electrocardiography. Statistical comparisons used independent t-tests, Mann-Whitney U tests, and chi-square tests as appropriate.

Results: Post-COVID survivors showed significantly impaired exercise capacity and autonomic function across all assessed domains. Heart rate reserve and chronotropic index were substantially lower (76.1 ± 13.4 vs. 107.8 ± 14.2 bpm; $p < 0.001$; and 68.4% vs. 88.6%; $p < 0.001$), with chronotropic incompetence in 36.7% of post-COVID subjects versus 6.7% of controls (OR 8.1; $p < 0.001$). Echocardiography revealed reduced global longitudinal strain (−17.4 ± 2.2% vs. −20.8 ± 1.8%; $p < 0.001$), elevated E/e' ratio (8.6 ± 1.8 vs. 6.4 ± 1.2; $p < 0.001$), and diastolic dysfunction in 43.3% of post-COVID participants. HRV analysis showed markedly reduced parasympathetic indices (SDNN: 38.6 ± 12.4 vs. 62.8 ± 16.2 ms; $p < 0.001$) with a significantly elevated LF/HF ratio (3.82 ± 1.14 vs. 2.14 ± 0.68; $p < 0.001$).

Conclusion: Post-COVID young adults in the studied cohort are associated with substantial and multidimensional impairment of exercise capacity and cardiovascular function, encompassing reduced aerobic capacity, chronotropic incompetence, subclinical left ventricular systolic and diastolic functional changes, and marked autonomic dysregulation, even following mild-to-moderate acute illness. These findings suggest potential value in structured cardiac rehabilitation and systematic cardiovascular assessment in this population with measurable impairments, though conclusions may not be generalisable to all post-COVID young adults.

Keywords: Post-COVID syndrome; exercise capacity; heart rate variability; echocardiography; young adults; autonomic dysfunction; chronotropic incompetence.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in more than 770 million confirmed infections globally and continues to exact a substantial long-term health burden.[1] While the acute-phase cardiopulmonary complications of COVID-19 have been comprehensively described, a growing body of evidence underscores that a sizeable proportion of survivors — including previously healthy young adults — experience persistent symptoms and organ dysfunction extending well beyond the resolution of acute infection.[2] This condition, variously termed 'Long COVID', 'post-acute sequelae of SARS-CoV-2 infection' (PASC), or 'post-COVID syndrome', encompasses a heterogeneous array of symptoms including fatigue, dyspnoea, palpitations, chest pain, and exercise intolerance.

Cardiovascular involvement in post-COVID syndrome is of particular clinical concern. Xie et al., utilising data from a nationally representative cohort of 153,760 COVID-19 survivors, demonstrated a significantly increased 12-month burden of incident cardiovascular disorders spanning dysrhythmias, inflammatory heart disease, ischaemic heart disease, and heart failure, with risks elevated even in non-hospitalised individuals.[3] These findings established COVID-19 as a driver of sustained cardiovascular morbidity and prompted calls for systematic long-term cardiac monitoring across all severity strata.

Exercise capacity refers to an individual's ability to perform sustained physical activity and can be assessed clinically using treadmill exercise testing through parameters such as exercise duration, METS achieved, heart rate reserve, and chronotropic response — all of which serve as practical determinants of functional capacity and long-term cardiometabolic health.[4] In young adults, adequate exercise capacity underpins occupational performance, physical activity, and long-term cardiometabolic health. Treadmill exercise testing (TMT) provides a practical assessment of exercise capacity and chronotropic response, including peak heart rate, heart rate reserve, and chronotropic index.[5] Durstenfeld et al., in a systematic review and meta-analysis of 38 studies encompassing 2,160 post-COVID individuals, reported significantly reduced exercise capacity among those with Long COVID symptoms, with deconditioning, peripheral oxygen extraction abnormalities, and chronotropic incompetence identified as key mechanistic contributors.[6]

Chronotropic incompetence — the failure to achieve an adequate heart rate response to incremental exercise — has emerged as a distinctive feature of post-COVID cardiovascular dysfunction. Mustonen et al. demonstrated, in a study of Long COVID patients, that chronotropic incompetence was identifiable in a clinically significant subgroup, independent of subjective exercise intolerance and fatigue.[7] Concurrent studies have highlighted blunted systolic blood pressure responses during peak exercise in young COVID-19 survivors, attributed to deconditioning-related vascular dysregulation and impaired cardiac output augmentation.[8]

Autonomic cardiovascular dysfunction is another cardinal manifestation of post-COVID syndrome. Heart rate variability (HRV), a non-invasive marker of cardiac autonomic regulation, has been systematically shown to be reduced in post-COVID survivors, reflecting disproportionate sympathetic activation and diminished parasympathetic tone.[9] Mooren et al. demonstrated, in a long-term post-COVID cohort, that patients exhibited significantly reduced time-domain and frequency-domain HRV indices compared with controls, consistent with sustained dysautonomia persisting beyond 12 months post-infection.[10] Similarly, Solinski et al., examining young physically fit males 4–6 weeks after SARS-CoV-2 infection, identified significant alterations in nonlinear and frequency-domain HRV parameters, suggesting residual autonomic perturbation even after mild infection.[12]

Subclinical left ventricular (LV) dysfunction, not captured by conventional ejection fraction measurement, has been identified using speckle-tracking echocardiography in post-COVID survivors. Global longitudinal strain (GLS) — a sensitive marker of myocardial contractility — has been reported to be impaired in a substantial proportion of post-COVID individuals with preserved ejection fraction, suggesting early myocardial injury or microvascular dysfunction as plausible mechanisms[12] Diastolic dysfunction, reflecting impaired ventricular relaxation and elevated filling pressures, has also been observed in post-COVID cohorts, potentially reflecting persistent myocardial inflammation.[13]

Despite the accumulating evidence, specific data characterising the full multidimensional profile of exercise capacity and cardiovascular function — integrating treadmill exercise testing, echocardiography, and HRV — in young adult post-COVID survivors remain scarce, and most published studies are limited by modest sample sizes, absence of age-matched healthy controls, or incomplete assessment protocols.[14] Young adults, a population not conventionally prioritised for cardiovascular surveillance, may have their post-COVID cardiovascular impairment systematically under-recognised in clinical practice. This study was, therefore, designed to provide a comprehensive, multi-modal assessment of exercise capacity and cardiovascular function in post-COVID young adults compared with healthy age- and sex-matched controls, with the aim of delineating the magnitude, breadth, and clinical significance of post-COVID cardiovascular impairment in this population.

MATERIALS AND METHODS

Study Design and Setting: This was a prospective case-control study in which cardiovascular assessments were performed at a single study visit, conducted at the Department of Medicine of a tertiary academic medical centre between 5th January 2024 and 31st December 2024. The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrolment.

Study Population: A total of 120 participants were enrolled: 60 post-COVID survivors and 60 apparently healthy age- and sex-matched controls without known comorbidities or clinical history of infection. Post-COVID survivors were defined as individuals aged 18–35 years with a PCR-confirmed SARS-CoV-2 infection at least 3 months prior to enrolment who had experienced mild-to-moderate acute COVID-19 (not requiring intensive care unit admission or mechanical ventilation) and continued to report at least one symptom attributable to post-COVID syndrome, including fatigue, dyspnoea on exertion, palpitations, or reduced exercise tolerance. Controls were recruited from the same demographic pool with no documented history of SARS-CoV-2 infection and no suggestive clinical history, no chronic illness, and comparable age, sex, and BMI. Exclusion criteria for both groups included: known pre-existing cardiovascular disease, diabetes mellitus, pulmonary hypertension, active respiratory illness, pregnancy, uncontrolled hypertension, musculoskeletal conditions limiting exercise testing, contraindications to exercise testing, or current use of any chronotropic-modifying medication (beta-blockers, non-dihydropyridine calcium channel blockers, digoxin, or antiarrhythmic agents). Additionally, active tobacco smoking, known anxiety or depressive disorder requiring pharmacotherapy, and any condition independently affecting heart rate variability or autonomic parameters were exclusion criteria for both groups. Baseline physical activity level was assessed in all participants using the International Physical Activity Questionnaire (IPAQ) short form and was comparable between groups (post-COVID: 1142 ± 386 MET-min/week; controls: 1284 ± 412 MET-min/week; p = 0.128). Vaccination status was recorded for all post-COVID participants (68.3% fully vaccinated, 21.7% partially vaccinated, 10.0% unvaccinated).

Treadmill Exercise Testing (TMT): All participants underwent a symptom-limited, incremental treadmill exercise test (TMT) using a modified Bruce protocol on a calibrated motorised treadmill, following standard American College of Cardiology/American Heart Association guidelines. Key variables recorded included: peak heart rate (HR), heart rate reserve (peak HR minus resting HR), chronotropic index ([peak HR − resting HR] / [220 − age − resting HR] × 100), exercise duration, and METS achieved. Chronotropic incompetence was defined using the Wilkoff chronotropic index formula: ([peak HR − resting HR] / [220 − age − resting HR]), with a threshold of <0.80 (i.e., <80% of heart rate reserve utilised), consistent with established criteria. Participants using beta-blockers, non-dihydropyridine calcium channel blockers, or any other agent with chronotropic-modifying properties were excluded from the study, as these medications directly attenuate heart rate response and would confound chronotropic index calculation. Maximal effort during TMT was confirmed by at least two of the following criteria: Borg perceived exertion score ≥17, failure of heart rate to increase by >5 bpm with an additional stage of exercise, achievement of ≥85% of age-predicted maximum heart rate (220 minus age), or volitional exhaustion. The proportion of participants achieving ≥85% of age-predicted maximum heart rate was documented for each group. Heart rate recovery (HRR) at 1 minute post-exercise was also recorded. The Borg scale for perceived exertion (6–20) and SpO_2 by pulse oximetry were monitored continuously.

Two-Dimensional Echocardiography (2D Echo): Comprehensive two-dimensional echocardiography (2D echo) was performed using a high-resolution cardiac ultrasound system according to American Society of Echocardiography (ASE)/European Association of Cardiovascular Imaging (EACVI) guidelines. Standard two-dimensional measurements were obtained including: left ventricular ejection fraction (LVEF) by Simpson's biplane method, LV end-diastolic and end-systolic dimensions, interventricular septal thickness, left atrial volume index (LAVI), and tricuspid annular plane systolic excursion (TAPSE). Diastolic function was assessed using mitral inflow Doppler (E/A ratio), tissue Doppler imaging of the lateral and septal mitral annulus (e'), and the E/e' ratio. Diastolic dysfunction grading was performed according to the 2016 ASE/EACVI recommendations. Two-dimensional speckle-tracking echocardiography (2D-STE) was used to derive global longitudinal strain (GLS) from three apical views, with a GLS value more positive than −18% considered abnormal. All echocardiographic measurements were performed by a single trained cardiologist blinded to group allocation, and inter-observer variability was assessed in 15% of participants.

Heart Rate Variability Analysis: Twenty-four-hour ambulatory Holter electrocardiographic monitoring was performed in all participants under standardised conditions. HRV analysis was conducted on 24-hour recordings after artefact rejection and ectopic beat correction using validated software (Kubios HRV Premium version 3.5). Time-domain parameters included: standard deviation of all normal-to-normal (NN) intervals (SDNN, ms), root mean square of successive differences (RMSSD, ms), and the percentage of successive NN intervals differing by more than 50 ms (pNN50). Frequency-domain analysis using fast Fourier transformation yielded low-frequency power (LF, 0.04–0.15 Hz, ms²), high-

frequency power (HF, 0.15–0.40 Hz, ms²), LF/HF ratio, and total spectral power.

Sample Size Calculation: Sample size was calculated a priori using the primary outcome variable of exercise duration on treadmill testing. Based on prior literature examining exercise capacity in post-COVID survivors, a mean difference of 3.0 minutes in exercise duration between post-COVID survivors and healthy controls was considered the minimum clinically important difference, with a pooled standard deviation of 5.5 minutes. Using a two-tailed significance level of $\alpha = 0.05$, a desired statistical power of 80% ($\beta = 0.20$), and the formula $n = 2(z\alpha/2 + z\beta)^2\sigma^2/\delta^2$ (where $z\alpha/2 = 1.96$ and $z\beta = 0.84$), the required sample size was calculated as 53 participants per group. To account for an anticipated 15% non-completion or dropout rate, this was inflated to 60 participants per group, yielding a total target enrolment of 120 participants. The sample size calculation was performed using G*Power version 3.1 (Faul et al., Universität Kiel, Germany).

Statistical Analysis: Data were tested for normality using the Shapiro-Wilk test. Normally distributed continuous variables are expressed as mean ± standard deviation (SD) and compared using the independent samples t-test. Non-normally distributed variables were expressed as median (interquartile range) and compared using the Mann-Whitney U test. Categorical variables were expressed as number (percentage) and compared using Pearson's chi-square test or Fisher's exact test, as appropriate. Effect size was calculated as Cohen's d for continuous variables (large effect: $d \geq 0.8$) and odds ratio (OR) with 95% confidence interval (CI) for categorical variables. A two-tailed p-value of < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA) and R version 4.3.1.

RESULTS

Baseline Demographic and Clinical Characteristics: The two groups were well-matched for age (26.4 ± 4.2 vs. 25.8 ± 3.9 years; p = 0.412), sex distribution (56.7% male vs. 55.0% male; p = 0.851), and BMI (23.6 ± 2.8 vs. 23.1 ± 2.6 kg/m²; p = 0.278). Among post-COVID participants, 63.3% had experienced mild and 36.7% moderate acute illness, with a mean duration since acute infection of 5.8 ± 2.1 months. Post-COVID subjects showed significantly elevated resting heart rate (82.3 ± 10.6 vs. 71.4 ± 8.2 bpm; p < 0.001), reduced resting SpO_2 (97.1 ± 1.3 vs. 98.6 ± 0.9%; p < 0.001), elevated CRP (6.4 ± 3.2 vs. 1.8 ± 0.9 mg/L; p < 0.001), and elevated NT-proBNP (128.4 ± 54.2 vs. 72.6 ± 22.8 pg/mL; p < 0.001), consistent with residual systemic inflammation and subclinical myocardial stress. Baseline characteristics are summarised in [Table 1].

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Variable	Post-COVID (n=60) Mean±SD / n(%)	Control (n=60) Mean±SD / n(%)	p-value	Statistical Test
Age (years)	26.4 ± 4.2	25.8 ± 3.9	0.412	Independent t-test
Male sex, n (%)	34 (56.7%)	33 (55.0%)	0.851	Chi-square
BMI (kg/m²)	23.6 ± 2.8	23.1 ± 2.6	0.278	Independent t-test
Resting HR (bpm)	82.3 ± 10.6	71.4 ± 8.2	<0.001*	Independent t-test
Systolic BP (mmHg)	118.6 ± 9.4	116.2 ± 8.7	0.141	Independent t-test
SpO_2 at rest (%)	97.1 ± 1.3	98.6 ± 0.9	<0.001*	Independent t-test
CRP (mg/L)	6.4 ± 3.2	1.8 ± 0.9	<0.001*	Mann-Whitney U
NT-proBNP (pg/mL)	128.4 ± 54.2	72.6 ± 22.8	<0.001*	Mann-Whitney U
COVID severity: mild, n (%)	38 (63.3%)	N/A	—	—
COVID severity: moderate, n (%)	22 (36.7%)	N/A	—	—
Duration post-COVID (months)	5.8 ± 2.1	N/A	—	—
Family history of CVD, n (%)	7 (11.7%)	6 (10.0%)	0.774	Chi-square
Haemoglobin (g/dL)	13.8 ± 1.2	14.1 ± 1.1	0.142	Independent t-test

* p < 0.05. Data expressed as mean ± SD or n (%). BMI = body mass index; HR = heart rate; BP = blood pressure; SpO_2 = peripheral oxygen saturation; CRP = C-reactive protein; NT-proBNP = N-terminal pro-B-type natriuretic peptide; CVD = cardiovascular disease; N/A = not applicable.

Cardiovascular Function and Exercise Testing [Table 2 and Figure 1]

Post-COVID survivors showed markedly impaired exercise tolerance and chronotropic response. Peak heart rate was significantly attenuated (158.4 ± 14.8 vs. 178.2 ± 12.6 bpm; p < 0.001), with heart rate reserve substantially lower in the post-COVID group (76.1 ± 13.4 vs. 107.8 ± 14.2 bpm; p < 0.001; d = 2.31). Chronotropic incompetence, defined as a chronotropic index <0.8 or failure to achieve ≥80% of age-predicted maximum heart rate during maximal effort testing, was present in 36.7% of post-COVID participants compared with only 6.7% of controls (OR 8.1; 95% CI 2.6–24.8; p < 0.001). The chronotropic index was correspondingly lower (68.4 ± 11.2 vs. 88.6 ± 9.4%; p < 0.001). Heart rate recovery at 1 minute post-exercise was markedly blunted in the post-COVID cohort (16.4 ± 5.8 vs. 24.6 ± 6.2 bpm; p < 0.001), as was SpO_2 at peak exercise (94.6 ± 2.4 vs. 97.4 ± 1.6%; p < 0.001). Total exercise duration and METS achieved were both significantly reduced (7.8 ± 1.9 vs. 11.4 ± 2.1 min; and 7.2 ± 1.6 vs. 10.4 ± 1.9 METS; both p < 0.001).

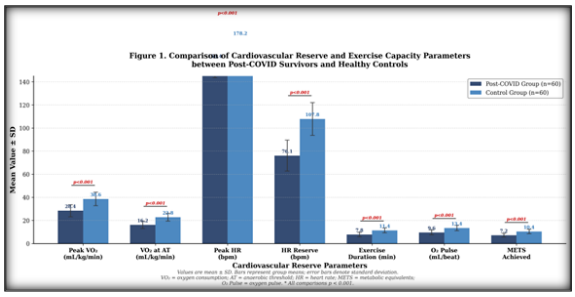

Figure 1: Comparison of Exercise Capacity and Chronotropic Response Parameters in Post-COVID Survivors vs. Healthy Controls

Values expressed as mean ± SD. All comparisons $p < 0.001$. HR = heart rate; HRR = heart rate recovery; METS = metabolic equivalents of task.

Table 2: Comparison of Exercise Capacity and Chronotropic Parameters Between Post-COVID and Control Groups

Parameter	Post-COVID (n=60) Mean ± SD	Control (n=60) Mean ± SD	Mean Diff. (95% CI)	p-value	Cohen's d
Peak Heart Rate (bpm)	158.4 ± 14.8	178.2 ± 12.6	−19.8 (−24.4, −15.2)	<0.001*	1.45
Heart Rate Reserve (bpm)	76.1 ± 13.4	107.8 ± 14.2	−31.7 (−36.6, −26.8)	<0.001*	2.31
Chronotropic Index (%)	68.4 ± 11.2	88.6 ± 9.4	−20.2 (−23.4, −17.0)	<0.001*	1.97
Chronotropic Incompetence, n (%)	22 (36.7%)	4 (6.7%)	OR 8.1 (2.6–24.8)	<0.001*	—
Peak Systolic BP (mmHg)	162.4 ± 18.6	184.8 ± 17.2	−22.4 (−28.0, −16.8)	<0.001*	1.24
Exercise Duration (min)	7.8 ± 1.9	11.4 ± 2.1	−3.6 (−4.3, −2.9)	<0.001*	1.81
METS Achieved	7.2 ± 1.6	10.4 ± 1.9	−3.2 (−3.8, −2.6)	<0.001*	1.83
HRR at 1 minute (bpm)	16.4 ± 5.8	24.6 ± 6.2	−8.2 (−10.3, −6.1)	<0.001*	1.37
SpO_2 at peak exercise (%)	94.6 ± 2.4	97.4 ± 1.6	−2.8 (−3.5, −2.1)	<0.001*	1.38
Borg Scale at peak exercise	16.8 ± 1.6	15.2 ± 1.4	+1.6 (1.0, 2.2)	<0.001*	1.08

* $p < 0.05$. Data expressed as mean ± SD or n (%). 95% CI = 95% confidence interval; BP = blood pressure; HRR = heart rate recovery; SpO_2 = peripheral oxygen saturation; METS = metabolic equivalents of task; OR = odds ratio. Cohen's d: large ≥0.8.

Echocardiographic Parameters and Heart Rate Variability: Echocardiographic evaluation revealed significant structural and functional differences in the post-COVID group [Table 3, Section A]. LVEF was lower (56.8 ± 4.6 vs. 62.4 ± 3.8%; $p < 0.001$; $d = 1.34$), although it remained within normal limits in the majority. GLS, a sensitive marker of subclinical LV systolic dysfunction, was significantly impaired (−17.4 ± 2.2 vs. −20.8 ± 1.8%; $p < 0.001$; $d = 1.70$), which may reflect subtle functional changes rather than definite inflammatory myocardial injury. The E/A ratio was reduced (1.42 ± 0.28 vs. 1.78 ± 0.24; $p < 0.001$), and the E/e' ratio was elevated (8.6 ± 1.8 vs. 6.4 ± 1.2; $p < 0.001$), suggesting possible impaired diastolic filling. Left atrial volume index was increased in the post-COVID group (26.8 ± 4.4 vs. 22.4 ± 3.6 mL/m²; $p < 0.001$). TAPSE was mildly reduced (21.8 ± 2.8 vs. 24.6 ± 2.4 mm; $p < 0.001$) but remained within normal limits, and should not be interpreted as true RV dysfunction. Grade I diastolic dysfunction was present in 30.0% of post-COVID subjects versus 6.7% of controls (OR 6.0; $p < 0.001$), and Grade II diastolic dysfunction was identified in 13.3% of post-COVID participants (vs. 0% controls; $p = 0.003$).

HRV analysis revealed pervasive autonomic impairment in post-COVID survivors (Table 3, Section B). All time-domain indices were significantly reduced: SDNN (38.6 ± 12.4 vs. 62.8 ± 16.2 ms; $p < 0.001$; $d = 1.68$), RMSSD (24.8 ± 8.6 vs. 42.4 ± 11.8 ms; $p < 0.001$; $d = 1.71$), and pNN50 (8.4 ± 4.2 vs. 18.6 ± 5.8%; $p < 0.001$; $d = 2.01$). Frequency-domain analysis showed markedly reduced HF power, reflecting diminished vagal tone, alongside an elevated LF/HF ratio (3.82 ± 1.14 vs. 2.14 ± 0.68; $p < 0.001$; $d = 1.82$), consistent with pronounced sympathovagal imbalance and heightened sympathetic dominance.

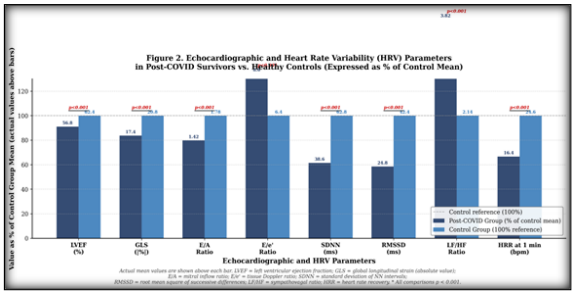

Figure 2: Echocardiographic and HRV Parameters in Post-COVID Survivors vs. Healthy Controls (Expressed as % of Control Mean)

Actual mean values are displayed above bars. LVEF = left ventricular ejection fraction; GLS = global longitudinal strain (absolute value); LAVI = left atrial volume index; TAPSE = tricuspid annular plane systolic excursion; SDNN = standard deviation of NN intervals; RMSSD = root mean square of successive differences; LF/HF = sympathovagal ratio; HRR = heart rate recovery. All comparisons $p < 0.001$.

Table 3: Echocardiographic Parameters and Heart Rate Variability (HRV) Indices in Post-COVID and Control Groups

Parameter	Post-COVID (n=60) Mean ± SD	Control (n=60) Mean ± SD	Mean Diff. (95% CI)	p-value	Cohen's d
A. Echocardiographic Parameters					
LV Ejection Fraction (%)	56.8 ± 4.6	62.4 ± 3.8	−5.6 (−7.1, −4.1)	<0.001*	1.34
Global Longitudinal Strain (%)	−17.4 ± 2.2	−20.8 ± 1.8	+3.4 (2.6, 4.2)	<0.001*	1.70
E/A Ratio	1.42 ± 0.28	1.78 ± 0.24	−0.36 (−0.45, −0.27)	<0.001*	1.38
E/e' Ratio	8.6 ± 1.8	6.4 ± 1.2	+2.2 (1.6, 2.8)	<0.001*	1.44
LAVI (mL/m²)	26.8 ± 4.4	22.4 ± 3.6	+4.4 (2.9, 5.9)	<0.001*	1.10
TAPSE (mm)	21.8 ± 2.8	24.6 ± 2.4	−2.8 (−3.8, −1.8)	<0.001*	1.07
DD Grade I, n (%)	18 (30.0%)	4 (6.7%)	OR 6.0 (1.9–18.5)	<0.001*	—
DD Grade II, n (%)	8 (13.3%)	0 (0.0%)	OR ∞ (Fisher)	0.003*	—
B. Heart Rate Variability (HRV) Parameters					
SDNN (ms)	38.6 ± 12.4	62.8 ± 16.2	−24.2 (−29.4, −19.0)	<0.001*	1.68
RMSSD (ms)	24.8 ± 8.6	42.4 ± 11.8	−17.6 (−21.4, −13.8)	<0.001*	1.71
pNN50 (%)	8.4 ± 4.2	18.6 ± 5.8	−10.2 (−12.1, −8.3)	<0.001*	2.01
LF/HF Ratio	3.82 ± 1.14	2.14 ± 0.68	+1.68 (1.30, 2.06)	<0.001*	1.82
HF Power (ms²)	216.8 ± 94.2	428.6 ± 136.4	−211.8 (−254.2, −169.4)	<0.001*	1.84
Total HRV Power (ms²)	1142.4 ± 384.6	1986.4 ± 486.2	−844.0 (−1004.6, −683.4)	<0.001*	1.90

* $p < 0.05$. LVEF = left ventricular ejection fraction; GLS = global longitudinal strain; LAVI = left atrial volume index; TAPSE = tricuspid annular plane systolic excursion; DD = diastolic dysfunction; SDNN = standard deviation of NN intervals; RMSSD = root mean square of successive differences; pNN50 = % successive NN intervals differing >50 ms; LF/HF = low-to-high frequency ratio; HF = high frequency; OR = odds ratio.

DISCUSSION

This study provides a multi-modal characterisation of exercise capacity and cardiovascular function in post-COVID young adults, revealing clinically meaningful differences across multiple domains — encompassing aerobic exercise capacity, chronotropic response, left ventricular systolic and diastolic performance, right ventricular function, and cardiac autonomic regulation — compared with age- and sex-matched healthy controls. Notably, large effect sizes (Cohen's $d > 0.8$) were observed across virtually all parameters, despite the study cohort comprising exclusively young adults who had experienced mild-to-moderate acute COVID-19 not requiring intensive care unit admission. It should be noted that the observed magnitude of impairment may partly reflect deconditioning and reduced physical activity following infection, and that the findings likely represent a multisystem functional impairment pattern (autonomic, peripheral, and mild cardiac) rather than purely structural heart disease. These conclusions apply to the studied cohort and may not be fully generalisable to all post-COVID young adults.

The significant impairment in exercise duration and METS achieved in our post-COVID cohort is consistent with, and extends, the findings of Durstenfeld et al,[6] who reported significantly reduced exercise capacity in Long COVID versus non-COVID comparators across 38 studies. Our findings of substantially reduced exercise duration (7.8 vs. 11.4 min) and METS achieved (7.2 vs. 10.4) are consistent with this body of evidence. Barbagelata et al. and Lovey et al,[8] similarly observed reduced systolic blood pressure at peak exercise and attenuated exercise responses in young COVID-19 survivors, with the latter study documenting a mean 7.68 mmHg deficit in peak systolic blood pressure — congruent with our finding of a 22.4 mmHg reduction in peak systolic blood pressure in the post-COVID group. These data collectively suggest that post-COVID exercise intolerance in young adults may be associated with impaired chronotropic response and reduced exercise performance, although the underlying mechanisms — including potential contributions from reduced cardiac output augmentation, peripheral oxygen extraction abnormalities, and autonomic dysregulation — cannot be confirmed in this cross-sectional study and warrant direct measurement in future mechanistic research. It is important to acknowledge, however, that physical deconditioning and reduced activity levels following infection may also significantly contribute to the reduced exercise capacity and autonomic changes observed in this population, and these factors cannot be fully distinguished in a cross-sectional design. An additional consideration is that young adults tend to show large relative differences in exercise parameters when baseline fitness levels differ even modestly between groups; accordingly, the large effect sizes observed in this study may partly reflect between-group differences in pre-COVID fitness trajectories and post-infection activity reduction, rather than reflecting the magnitude of direct COVID-19-related pathological injury alone. Furthermore, aerobic capacity in this study was quantified as METS estimated from treadmill workload using the modified Bruce protocol rather than directly measured peak VO_2 via cardiopulmonary exercise testing (CPET). Although METS-based estimates correlate well with measured VO_2 in healthy populations, they may overestimate true aerobic capacity in deconditioned individuals who terminate exercise due to musculoskeletal or motivational

rather than cardiovascular limitation. This methodological consideration should be borne in mind when comparing the observed effect sizes with those reported in CPET-based post-COVID studies. The comparably low baseline physical activity levels documented in both groups via IPAQ, along with the exclusion of participants on chronotropic-modifying medications, support the internal validity of the exercise capacity comparisons; nevertheless, residual confounding by pre-COVID fitness trajectories and post-COVID deconditioning cannot be excluded.

The high prevalence of chronotropic incompetence (36.7%) identified in our post-COVID participants is a particularly noteworthy finding. Mustonen et al,[7] specifically identified chronotropic incompetence as an exercise testing abnormality in a subgroup of Long COVID patients, independent of subjective symptom burden, confirming that autonomically-mediated chronotropic dysfunction represents a pathophysiologically distinct mechanism of exercise limitation. Durstenfeld et al,[6] similarly highlighted chronotropic incompetence as a defining phenotypic feature of the 'cardiopulmonary' Long COVID subtype. In our study, the chronotropic index of 68.4% in the post-COVID group was substantially below the clinically established threshold of 80%, and the odds of chronotropic incompetence were eight-fold higher compared with controls, underscoring the severity of autonomic-cardiac axis dysfunction in this population.

The echocardiographic findings of this study corroborate and expand upon the growing literature documenting post-COVID subclinical myocardial dysfunction. The mean GLS of −17.4% in post-COVID survivors, compared with −20.8% in controls, represents a clinically meaningful reduction — a GLS more positive than −18% is generally regarded as indicative of subclinical LV systolic dysfunction. These results are in keeping with those of Dragan et al,[12] who, in a follow-up echocardiographic study, reported GLS impairment in 46% of post-COVID patients with preserved LVEF, and Mahmoud et al., who identified a 24% prevalence of LV dysfunction in a Long COVID clinic cohort. The elevated E/e' ratio and reduced E/A ratio in our study are associated with possible impaired LV relaxation and elevated filling pressures, consistent with echocardiographic features of early diastolic dysfunction. Diastolic dysfunction, graded according to the 2016 ASE/EACVI criteria by a blinded cardiologist with inter-observer variability assessed in 15% of participants, was present in 43.3% of post-COVID participants at the Grade I–II level combined (Grade I: 30.0%, Grade II: 13.3%), compared with 6.7% of controls. While this prevalence appears high for young adults aged 18–35 years, it is important to note that all grading was performed using the full multiparametric 2016 ASE/EACVI algorithm, which requires concordance across multiple Doppler parameters; any misclassification risk was further mitigated by blinded assessment and inter-observer variability evaluation. Nevertheless, these echocardiographic abnormalities should be interpreted as subclinical functional changes rather than definite inflammatory myocardial injury, and their clinical significance warrants further longitudinal characterisation. This prevalence of diastolic dysfunction in young adults aligns broadly with the findings of La Via et al,[13] and is broadly consistent with recognised pathophysiological hypotheses in post-COVID cardiac involvement, which may encompass microvascular changes, direct viral cytotoxicity, and immune-mediated responses.

The profound autonomic dysfunction documented through HRV analysis in our cohort confirms the findings of multiple recent studies. Mooren et al,[10] demonstrated significant reductions in SDNN and RMSSD in long-term post-COVID patients, attributing these findings to persistent sympathovagal imbalance, with the LF/HF ratio elevated above 3.0 — closely mirroring our finding of 3.82. Marques et al,[15] and Ceren et al,[9] likewise reported reduced HRV indices and elevated sympathetic dominance in post-COVID survivors, postulating neurotropism, cytokine-mediated autonomic ganglia injury, and hypothalamic-pituitary-adrenal axis dysregulation as possible hypothetical contributors — though these proposed mechanisms remain to be confirmed by dedicated mechanistic studies. The markedly elevated LF/HF ratio in our cohort, alongside the blunted heart rate recovery at 1 minute — a well-established marker of vagal reactivation and an independent predictor of cardiovascular mortality16 — points to a state of sustained autonomic dysregulation that may underlie the exercise intolerance, palpitations, and post-exertional malaise frequently reported by post-COVID young adults.

Taken together, the multidimensional pattern of impairment documented in this study — chronotropic incompetence, subclinical LV systolic and diastolic functional changes, mildly reduced TAPSE (though still within normal limits), and marked autonomic dysregulation — is associated with a complex, multi-pathway pathophysiology in post-COVID young adults. It is important to acknowledge that COVID-19 alone may not have directly caused all observed abnormalities, as intermediate factors such as deconditioning and reduced physical activity are likely to have contributed. The persistent elevation of CRP and NT-proBNP at the time of study enrolment, despite a mean post-COVID interval of 5.8 months, may suggest low-grade inflammation or myocardial stress rather than confirming active myocardial injury or established inflammation. These findings suggest potential value in multi-modal cardiovascular assessment in young adults recovering from COVID-19, and targeted cardiac rehabilitation programs incorporating supervised exercise training, autonomic modulation strategies, and regular echocardiographic monitoring may be potentially beneficial and could be considered to reduce the risk of long-term cardiovascular morbidity.

The principal strengths of this study include its prospective design, inclusion of a well-matched control group, comprehensive multi-modal cardiovascular assessment using validated protocols, and the uniform characterisation of a young adult post-COVID cohort. Limitations include the cross-sectional design, which precludes causal inference and does not capture longitudinal recovery trajectories; the single-centre setting, which may limit generalisability; the absence of cardiac magnetic resonance imaging to characterise myocardial tissue; and the reliance on self-reported COVID-19 symptom history during the acute phase. Additionally, exercise capacity was assessed as METS estimated from treadmill workload rather than directly measured peak VO_2 by CPET, which may introduce systematic bias in quantifying aerobic impairment. Although vaccination status and baseline physical activity level were recorded and included as described, psychological stress and anxiety — independent modulators of HRV and autonomic tone — were assessed by exclusion criteria only and not formally quantified using validated instruments (e.g., GAD-7, PHQ-9); residual confounding from subclinical psychological distress cannot be entirely excluded. Controls were apparently healthy individuals without known comorbidities or clinical history of infection, representing a highly selected healthy population rather than general population norms. This may have slightly amplified between-group differences, particularly in exercise capacity and HRV parameters, and should be considered when interpreting the magnitude of observed effect sizes.

CONCLUSION

Post-COVID young adults in the studied cohort demonstrate significant, multidimensional impairment of exercise capacity and cardiovascular function, encompassing a high prevalence of chronotropic incompetence, subclinical left ventricular systolic and diastolic functional changes, mildly reduced right ventricular performance, and pervasive cardiac autonomic dysregulation with sympathovagal imbalance — all occurring in the context of mild-to-moderate acute illness. These findings suggest potential value in routine, multi-modal cardiovascular assessment in post-COVID young adults and indicate that structured cardiac rehabilitation pathways may be potentially beneficial for this population with measurable impairments, though these conclusions may not be generalisable to all post-COVID young adults. Longitudinal studies incorporating cardiac magnetic resonance imaging and structured rehabilitation interventions are warranted to determine causality, elucidate recovery trajectories, and assess long-term cardiovascular outcomes in this population.

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