CLINICAL RESEARCH STUDY

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People with Long COVID and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Exhibit Similarly Impaired Vascular Function

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ABSTRACT

BACKGROUND: This study aimed to compare flow-mediated dilation values between individuals with long COVID, individuals with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), and healthy age-matched controls to assess the potential implications for clinical management and long-term health outcomes.

METHODS: A case-case-control approach was employed, and flow-mediated dilation measurements were obtained from 51 participants (17 long COVID patients, 17 ME/CFS patients, and 17 healthy age-matched controls). Flow-mediated dilation values were analyzed using 1-way analysis of variance for between-group comparisons.

RESULTS: Results revealed significantly impaired endothelial function in both long COVID and ME/CFS groups compared with healthy age-matched controls as determined by maximum % brachial artery diameter post-occlusion compared with pre-occlusion resting diameter (6.99 ± 4.33% and 6.60 ± 3.48% vs 11.30 ± 4.44%, respectively, both $P < .05$). Notably, there was no difference in flow-mediated dilation between long COVID and ME/CFS groups ($P = .949$), despite significantly longer illness duration in the ME/CFS group (ME/CFS: 16 ± 11.15 years vs long COVID: 1.36 ± 0.51 years, $P < .0001$).

CONCLUSION: The study demonstrates that both long COVID and ME/CFS patients exhibit similarly impaired endothelial function, indicating potential vascular involvement in the pathogenesis of these post-viral illnesses. The significant reduction in flow-mediated dilation values suggests an increased cardiovascular risk in these populations, warranting careful monitoring and the development of targeted interventions to improve endothelial function and mitigate long-term health implications.

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KEYWORDS: Chronic fatigue syndrome; Flow-mediated dilation; Long COVID; Myalgic encephalomyelitis

INTRODUCTION

Following a viral infection, individuals may experience post-viral illness, which is characterized by prolonged feelings of unwellness and fatigue.[1−3] Post-viral illnesses exhibit various symptoms,[4−7] involving cardiovascular, respiratory, neurological, and musculoskeletal systems, significantly impacting the quality of life and functional capacity of affected individuals.[1] The term "long COVID" has gained prominence over the past 3 years, as it refers to persistent symptoms lasting over 12 weeks after the acute phase of COVID-19 infection, drawing attention to post-viral fatigue. Long COVID shares similarities with myalgic encephalomyelitis (ME), chronic fatigue syndrome (CFS), or ME/CFS,[8] conditions that have been known in the medical literature for decades,[9] with several overlapping symptoms.[8,10,11] Myalgic encephalomyelitis/chronic fatigue syndrome and long COVID are debilitating conditions characterized by post-

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exertional malaise, fatigue, cognitive impairments, and pain, for which there is currently no known cure or definitive treatment.[12–14] Interestingly, both long COVID and ME/CFS are associated with vascular effects, which may drive some of the persistent symptoms experienced.[15–19] A dominantly proposed mechanism concerning post-viral syndromes involves vascular damage and endothelial dysfunction-driven inflammatory response, leading to microclots which block capillaries, leading to hypoxic tissues.[20–22] This may well be a mechanistic pathway responsible for symptoms including fatigue, cognitive impairment, and pain.[23]

CLINICAL SIGNIFICANCE

- Long COVID and myalgic encephalomyelitis/chronic fatigue syndrome groups exhibit similarly impaired endothelial function compared with healthy age-matched controls, as determined by flow-mediated dilation, despite significantly longer illness duration in the myalgic encephalomyelitis/chronic fatigue syndrome group.
- The findings indicate potential vascular involvement in the pathogenesis of both conditions.
- Impaired endothelial function suggests an increased cardiovascular risk, warranting careful monitoring and the development of targeted interventions to improve endothelial function and mitigate long-term health implications.

Endothelial dysfunction, characterized by impaired nitric oxide bioavailability and altered vascular reactivity, is a key hallmark of various cardiovascular and metabolic disorders,[24,25] and can be quantified using flow-mediated dilation. This technique involves measuring the diameter of an artery before and after a period of occlusion with an inflation cuff.[26] Upon deflation, blood flow is elevated downstream through the artery causing arterial dilation. This elevation in blood flow causes shear stress across the endothelium, which stimulates endothelial nitric oxide synthase (eNOS) activity, resulting in nitric oxide (NO) production and release, subsequently causing vasodilation as the smooth muscle relaxes.[27] Therefore, flow-mediated dilation is an indirect measure of NO bioavailability.[27] Reduced flow-mediated dilation has been associated with increased cardiovascular risk, including hypertension, atherosclerosis, and endothelial dysfunction.[24] Investigating flow-mediated dilation in individuals living with post-viral illnesses may provide valuable insights into potential vascular abnormalities and their relevance to the persistent symptoms experienced by these individuals. In this way, theories suggest that vascular damage and subsequent dysfunction may play a leading role in long COVID,[15] and reduced flow-mediated dilation has been observed in this population (8.2% vs 10.3%).[18] Similarly, ME/CFS patients had markedly reduced flow-mediated dilation compared with healthy controls (5.1% vs 8.2%).[17]

Although vascular function impairments have been reported in people with long COVID[18] and people with ME/CFS,[17] these 2 patient groups have never been compared directly in the same study. This could be of interest as long COVID is a relatively new condition, and therefore it could be speculated that people with ME/CFS would have poorer vascular function as they have been suffering from the post-viral illness longer, therefore experiencing the multi-systems disease and deconditioning for a longer time.[28]

Given the considerable overlap with long COVID and ME/CFS, we sought to examine flow-mediated dilation, compared with healthy controls. The objective of this case-control study was to investigate the effects of long COVID and ME/CFS on vascular function. The study compared flow-mediated dilation between individuals with long COVID or ME/CFS and age-matched healthy controls. By unravelling the link between vascular health and post-viral illnesses, our study aimed to provide a deeper understanding of the underlying pathophysiology of these debilitating conditions.

METHODS

Participants

Fifty-one participants (long COVID, n = 17 ME/CFS, n = 17; and healthy controls, n = 17, Table) were recruited for this study via social media advertisement. Participants attended a one-off visit to the Cardiovascular Imaging laboratory at the University of the West of Scotland, Lanarkshire, between March 2022 and January 2023. This study was carried out in accordance with the Declaration of Helsinki and approved by the University of the West of Scotland Institutional Ethics Committee (Approval number:17449). Written informed consent was obtained from all participants prior to study commencement. Descriptive statistics for participants are shown in Table, and further described in the results section.

Sample size was calculated based on clinically meaningful changes in flow-mediated dilation from previous literature.[29] The effect size of persistent symptoms following COVID 19 infection, in terms of flow-mediated dilation, is large (Cohen’s d = 1.08). To achieve 90% statistical power, with an alpha level of 0.05, 17 participants were required per group. To allow for 20% attrition, 20 participants were recruited to each group.

Participant Characteristics

Height, which was recorded in centimeters, was measured using a wall-mounted stadiometer (SECA, CE0123, Hamburg, Germany). Participants were required to remove their shoes and stand in the anatomical position keeping a straight back and ensuring their heels were in contact with the floor. The body mass of each participant was recorded using electronic scales (SECA 876, CE0123, Germany). Participants wore minimal clothing (shorts and t-shirt where

Table Descriptive Data of Participants

Variable	Group	Mean	SD	ANOVA *P* Value for Effect of Group
Age (years)	LC (n = 21)	47.52	9.60	.8084 (LC vs ME)
	ME/CFS (n = 20)	49.7	9.78	.9005 (LC vs controls)
	Control (n = 20)	49.05	13.77	.9816 (ME vs controls)
Height (cm)	LC (n = 21)	168	9.925	.9735 (LC vs ME)
	ME/CFS (n = 20)	168.7	9.464	.6643 (LC vs controls)
	Control (n = 20)	170.6	8.874	.8007 (ME vs controls)
Body mass (kg)	LC (n = 21)	97.04	23.04	.2720 (LC vs ME)
	ME/CFS (n = 20)	86.79	23.9	.0006 (LC vs controls)***
	Control (n = 20)	70.93	15.04	.0531 (ME vs controls)
BMI (kg·m^2)	LC (n = 21)	34.19	6.14	.4058 (LC vs ME)
	ME/CFS (n = 20)	31.49	9.21	<.0001 (LC vs controls)****
	Control (n = 20)	24.23	3.62	.0033 (ME vs controls)**
Systolic |blood pressure (mmHg)	LC (n = 21)	140	19	<.0001 (LC vs ME)***
	ME/CFS (n = 20)	102	33	<.0001 (LC vs controls)***
	Control (n = 20)	94	40	.2958 (ME vs controls)
Diastolic blood pressure (mmHg)	LC (n = 21)	95	15	.9503 (LC vs ME)
	ME/CFS (n = 20)	87	12	.0928 (LC vs controls)
	Control (n = 20)	77	8	.0501 (ME vs controls)
Resting heart rate (bpm)	LC (n = 21)	80	14	.3882 (LC vs ME)
	ME/CFS (n = 20)	82	19	.3191 (LC vs controls)
	Control (n = 20)	65	10	.0215 (ME vs controls)*

ANOVA = analysis of variance; BMI = body mass index; LC = long COVID; ME = myalgic encephalomyelitis; ME/CFS = myalgic encephalomyelitis/chronic fatigue syndrome; SD = standard deviation.

*$P < .05$.

**$P < .01$.

***$P < .001$.

****$P < .0001$.

possible), and body mass was recorded in kilograms. Body composition determination was conducted in accordance with the International Society for the Assessment of Kinanthropometry. Each participant's body mass index (BMI) was then calculated (BMI = kg/m^2) from the body composition values. Resting blood pressure (BP) of participants was measured using an automated sphygmomanometer (Omron, the Netherlands), in accordance with the International Society of Hypertension (ISH) protocol. The participant was seated, and the BP cuff was secured on their left arm, a few centimeters above the elbow crease. The machine was then initialized, and the cuff inflated to 200 mmHg and subsequently deflated to 0 mmHg. This process was repeated 3 times and recorded. A 1-minute rest period between repetitions was used, deemed optimal for BP accuracy.

Flow-Mediated Dilation Measurement

Ultrasound examinations were performed in a semi-darkened room, with participants supine. Vascular reactive function was measured using flow-mediated dilation of the brachial artery, using a high-resolution 12 MHz linear ultrasound transducer (Siemens, Erlangen, Germany) and rapid cuff inflators. This protocol required imaging of a short non-branching segment of the brachial artery proximal to the antecubital fossa, using duplex sonography. The dominant limb was comfortably extended in a horizontal position to allow consistent imaging of the brachial artery. A segment of the brachial artery above the antecubital crease was imaged in the longitudinal plane, ensuring the lumen diameter was maximized and the light-dark contrast optimized to provide clear visualization of the double lines of Pignoli. After 1 minute of baseline data incorporating brachial artery diameter and doppler flow was collected, a pressure cuff around the upper forearm was inflated to suprasystolic pressure (180 mmHg), using a rapid cuff inflator (Hockanson, Washington) for 5 minutes. Subsequently, the cuff was deflated, and 5 minutes of post-deflation diameters and Doppler flow data was recorded in accordance with expert-consensus guidelines.[26]

Flow-Mediated Dilation Calculation

All scans were recorded in the internal memory of the ultrasound equipment, exported to universal serial bus devices, and transferred to the core laboratory computer. Video files were condensed to 10 frames per second (fps) using MediaCoder 0.8.65 video analysis software (Microsoft Corporation, Armonk, NY). An automatic edge detection system (Brachial Analyzer, Vascular Tools 5, Medical Imaging Applications LLC, Coralville, Iowa), was used to calculate flow-mediated dilation, taken as the maximal percentage increase in diameter above baseline (mean of measures obtained during the first minute). Scans were rejected in cases where there was poor quality or instability of the images due to inconsistency of clear artery borders and anatomical markers.

Statistical Analysis

All data were assessed for normal distribution and homogeneity of variance. Data were analyzed using jamovi (version 2.3.21, Sydney, Australia) and figures were created using GraphPad Prism (version 9.4.1, GraphPad Software, Boston, Mass). To assess the differences dependent variables, Welch's 1-way analyses of variance (ANOVA) were performed. The relation between percent flow-mediated dilation and vessel diameter was assessed by linear regression, for vessel size alone and then with adjustment for age, BMI, diastolic and systolic BP, and resting heart rate. Pearson's correlations were used to assess the relationship between flow-mediated dilation values and baseline diameter, age, BMI, systolic BP, diastolic BP, and resting heart rate. Effect size for paired comparisons was conducted using Cohen's d whereby the difference in means between 2 samples was divided by the pooled standard deviation (SD). Thresholds of 0.2, 0.5, and 0.8 for small, moderate, and large effects were used for Cohen's d.[30] Thresholds of 0-0.29, 0.3-0.49, and ≥0.5 for small, moderate, and large effects were used to interpret Pearson's correlation coefficients. Data are presented without subjective terminology, and alpha levels are reported as exact *P* values, without dichotomous interpretation of "significant" or "non-significant" as advised by the American Statistical Association.[31] Data are presented as mean ± SD. For bar graphs, individual data points are presented as recommended by Drummond and Vowler.[32,33]

RESULTS

Descriptive participant parameters are displayed in Table. Illness duration of the long COVID group was 1.36 ± 0.51 years and ME/CFS was 16 ± 11.15 years ($P < .0001$). Pairwise differences between long COVID, ME/CFS, and controls for age and height were trivial to small ($P > .67$, d < 0.31). Long COVID participants were heavier than ME/CFS ($P = .272$, d = 0.55; medium effect) and controls ($P < .001$, d = 2.10; large effect). Myalgic encephalomyelitis/chronic fatigue syndrome participants were heavier than controls ($P = .053$, d = 0.80; large effect). As a result of the differences in body mass, long COVID participants had a higher BMI than ME/CFS ($P = .406$, d = 0.39; small effect) and controls ($P < .001$, d = 2.56; large effect). Myalgic encephalomyelitis/chronic fatigue syndrome participants were heavier than controls ($P = .003$, d = 1.44; large effect). Long COVID participants had higher diastolic BP than ME/CFS ($P < .001$, d = 1.41; large effect) and controls ($P < .001$, d = 1.47; large effect). The ME/CFS group had higher diastolic BP than controls ($P = .296$, d = 0.22; small effect). Systolic BP was not different between long COVID and ME/CFS ($P = .950$, d = 0.09; trivial effect), whereas controls had lower systolic BP than long COVID ($P = .093$, d = 1.50; large effect) and ME/CFS groups ($P = .050$, d = 0.65; medium effect). Resting heart rate was not different between long COVID and ME/CFS groups ($P = .970$, d = 0.12; trivial effect), whereas controls had lower resting heart rate than long COVID ($P < .001$, d = 1.23; large effect) and ME/CFS cohorts ($P = .005$, d = 1.12; medium effect).

After rejecting the poor-quality scans, 51 flow-mediated dilation videos were analyzed (long COVID n = 17, 13 females, 4 males, ME/CFS n = 17, 10 females, 7 males, controls n = 17, 10 females, 7 males). Baseline diameter of brachial artery (long COVID: 0.43 ± 0.11 cm, ME/CFS: 0.40 ± 0.05 cm, and controls: 0.40 ± 0.08 cm) was similar across groups (long COVID vs ME/CFS $P = 0.683$ Cohen's d = 0.137, long COVID vs control $P = 0.828$, Cohen's d = -0.076, and ME/CFS vs control $P = 0.863$, Cohen's d = 0.137) (Figure A). The maximum diameter of vessels was 0.464 ± 0.12 cm, 0.428 ± 0.05 cm, and 0.440 ± 0.08 cm in long COVID, ME/CFS, and controls, respectively.

Analysis of variance and post-hoc tests revealed between group difference for flow-mediated dilation of long COVID

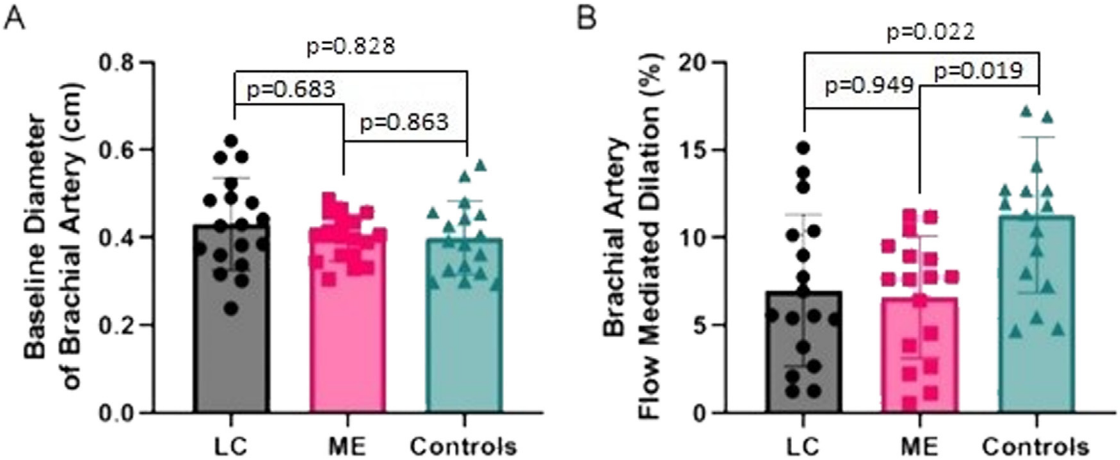

Figure (**A**) Baseline diameter of brachial artery (cm) and (**B**) percentage change of brachial artery diameter upon cuff deflation in relation to baseline diameter. Data presented are mean ± standard deviation, with individual data points displayed. Long COVID (LC; n =17, 13 females, 4 males), myalgic encephalomyelitis/chronic fatigue syndrome, (ME; n = 17, 10 females, 7 males), controls (n = 17, 10 females, 7 males).

vs controls (6.99 ± 4.33% vs 11.30 ± 4.44%, P = .022, Cohen's d = 0.98); and for ME/CFS vs controls (6.60 ± 3.48% vs 11.30 ± 4.44%, P = .019, Cohen's d = 1.18). There was no between group difference for long COVID vs ME/CFS (6.99 ± 4.33% vs 11.30 ± 4.44%, P = 0.949, Cohen's d = 0.983). The R^2 value revealed a small effect of flow-mediated dilation between groups (R^2 = 0.22). Flow-mediated dilation data are displayed in Figure B.

Pearson's correlations revealed no relationship between flow-mediated dilation values and age (r = -0.179, P = .21), BMI (r = -0.097, P = .50), systolic BP (r = -0.045, P = .75), diastolic BP (r = -0.191, P = .18), or heart rate (r = -0.072, P = .62). However, there was a moderate Pearson's correlation coefficient between flow-mediated dilation and baseline diameter (r = -0.324, P = .02).

DISCUSSION

The objective of this study was to compare flow-mediated dilation between individuals with long COVID, ME/CFS, and healthy age-matched controls. The main findings from this case-case-control study show that long COVID and ME/CFS both have similarly impaired endothelial function, as determined by lower flow-mediated dilation values compared with healthy age-matched controls (Figure 1). This has significant implications for both the clinical management and long-term health outcomes of individuals living with long COVID and ME/CFS, including clinical assessment, management, and treatment of endothelial dysfunction to prevent subsequent cardiovascular disease progression.[34,35] Understanding the potential vascular contributions to persistent symptoms can guide the development of targeted interventions aimed at improving endothelial function and mitigating the burden of post-viral illnesses.

Flow-mediated dilation is a clinically meaningful measurement and has prognostic value for cardiovascular events.[34] A meta-analysis of 35 studies found every 1% increase in flow-mediated dilation associated with a 12% reduced risk for cardiovascular events, with even higher risk reductions in disease populations.[34] Remarkably, cardiovascular disease risk was halved for those in high vs low flow-mediated dilation categories.[35] Previous studies have observed lower flow-mediated dilation in long COVID vs healthy controls (8.2% vs 10.3%).[18] Similarly, another previous study found ME/CFS patients had markedly reduced flow-mediated dilation compared with healthy controls (5.1% vs 8.2%).[17] The current findings show that, in comparison to controls, long COVID and ME/CFS groups had similar flow-mediated dilation values, which were significantly lower than controls (6.99 ± 4.33% and 6.60 ± 3.48% vs 11.30 ± 4.44%, respectively) and may be indicative of ~50% increased cardiovascular risk.[34,35] This highlights the need for individuals with post-viral illnesses to be carefully monitored for cardiovascular risk and potentially prescribed treatments to lower risk.

It is worth noting that the large spread of the data shows that some individuals in long COVID and ME/CFS groups had very severely impaired endothelial function, whereas others had comparable flow-mediated dilation to that of the controls. This suggests possibly different disease trajectories and symptomology among individuals with post-viral illnesses, which is yet to be explored. This is emphasized by the divergent symptoms experienced by people with ME/CFS and long COVID.[1,8,36] The lack of uniform symptomology must be considered when contemplating personalized medicine treatment options, as data presented herein suggest endothelial dysfunction may not be ubiquitous in post-viral conditions.[37]

Although flow-mediated dilation impairments have been reported in people with long COVID[18] and people with ME/CFS,[17] these 2 patient groups have never had flow-mediated dilation compared directly in the same study. It would have seemed reasonable *a priori* to hypothesize that people with ME/CFS would have poorer vascular function than people with long COVID, due to post-viral illness duration, and multi-system deconditioning for longer (which is known to reduce flow-mediated dilation).[28] However, the current study opposes this contention as long COVID and ME/CFS groups exhibited similar flow-mediated dilation values despite significantly different illness duration (ME/CFS: 16±11.15 years vs long COVID: 1.36± 0.51 years, P < .0001). Therefore, the impairment in flow-mediated dilation in the current study is unlikely due to deconditioning. It is more likely that endothelial damage is experienced in the early post-viral phase, without further reduction in flow-mediated dilation after this initial diminution.

Although endothelial dysfunction may be a consequence of post-viral illnesses, vascular damage and subsequent dysfunction may play a leading role in development of the conditions and their persistent symptoms.[15] It has been well established that the SARS-CoV-2 virus enters eukaryotic cells via the angiotensin-converting enzyme-2 receptor.[38] Because the vascular endothelium possesses angiotensin-converting enzyme-2 receptors, vascular damage and endothelial dysfunction is likely caused by the virus.[39,40] This damage subsequently drives an inflammatory response, stimulating microclot formation within the blood due to hyperactivation of platelets, subsequently blocking capillaries from delivering oxygen and nutrients to local tissues.[20–22] This is a highly plausible mechanistic pathway that could explain several symptoms of long COVID including fatigue, cognitive impairment, and pain.[23] As ME/CFS is likely to have a similar disease etiology to long COVID, endothelial damage and formation of microclots[22] may also explain, at least partly, ME/CFS development and symptomology. Notably, a study utilizing hyperemia index to determine endothelial function found that a subset of both long COVID and ME/CFS groups had endothelial dysfunction compared with healthy controls.[20] This observation occurred alongside significantly reduced serum angiotensin-2 and elevated circulating endothelin-1.[20] Reduced levels of angiotensin-2 may reflect high shear stress due to chronic inflammation or endothelial damage.[41] Endothelin-1 plays a key role in vasoconstriction and elevated levels are an aggravating factor for hypertension and cardiovascular disease states.[42] Therefore, there is clear evidence for cardiovascular risk within both long COVID and ME/CFS.[17,18,20] Promisingly, treatment to resolve mircoclots has successfully reduced symptoms, including fatigue, within long COVID sufferers.[43] However, controlled clinical trials are still required to confirm initial findings and further research is required within ME/CFS populations.

The current study found no relationship between flow-mediated dilation and age (r = -0.179, *P* = .21), BMI (r = -0.097, *P* = .50), systolic BP (r = -0.045, *P* = .75), diastolic BP (r = -0.191, *P* = .18) or heart rate (r = -0.072, *P* = .62). In contrast, a large study investigating flow-mediated dilation reference intervals (n = 5362) found that age was strongly associated with flow-mediated dilation.[44] Perhaps larger participant numbers were required to confirm this effect in the current study. Furthermore, previous studies have found that obesity has an association with flow-mediated dilation.[45] In the current study, BMI was high in both ME/CFS and long COVID groups (34.19 ± 6.14 kg·m^2 and 31.49 ± 9.21 kg/m2, respectively) compared with the control group (24.23 ± 3.62 kg/m2). This may explain the lack of interactions between BMI and flow-mediated dilation in this study and highlights the requirement for further investigation in BMI-matched individuals. Similarly, previous studies have found flow-mediated dilation to relate to systolic and diastolic BP in healthy individuals[44] which is in contrast to the findings in this study. There is no clear explanation for this divergence, warranting further investigation and potential explanations for these differences.

Limitations

This study has certain limitations that necessitate acknowledgment. Firstly, the findings may not be readily applicable to the broader population of individuals with long COVID, especially those who are unable to visit a laboratory, such as those severely affected by the condition. It is important to note that our experimental methods constrained participation to individuals who could travel to our laboratory, navigate stairs or lifts, and undergo the testing process. This approach was not entirely inclusive for people with long COVID and ME/CFS, considering that according to the National Institute for Health and Care Excellence, approximately 25% of individuals with ME/CFS are bedbound or housebound,[46] making it impossible for them to visit a laboratory. As a result, the extent of vascular function deficits observed in this study likely underestimates the true effect due to the inherent recruitment bias.

Expert-consensus guidelines for flow-mediated dilation acquisition were followed where possible.[26] As such, baseline diameter was presented. Baseline diameter is the biggest determinant of flow-mediated dilation and has a strong negative correlation with flow-mediated dilation.[26,44] The current study also found a correlation between flow-mediated dilation and baseline diameter (r = -0.324, *P* = .02). To reduce participant burden, participants were not advised to fast before the test as recommended.[26] Hence, there is potential for confounding effect of dietary intake immediately prior to the flow-mediated dilation acquisition.

CONCLUSION

Both long COVID and ME/CFS display notable impairment in endothelial function, evidenced by lower flow-mediated dilation values compared with the age-matched control group. Flow-mediated dilation has prognostic value for cardiovascular events, highlighting the importance of monitoring individuals with long COVID and ME/CFS for cardiovascular risk.[34,35] The large variability in flow-mediated dilation values within the long COVID and ME/CFS groups suggests the presence of different disease trajectories and etiological mechanisms among individuals with post-viral illnesses, emphasizing the need for individualized care.[37] This study provides valuable insights into the vascular implications of long COVID and ME/CFS, contributing to a growing body of knowledge that can aid healthcare professionals in monitoring and managing these conditions effectively. Findings strongly agree with a potential link between endothelial dysfunction,[39,40] microclot formation,[20−22] and persistent symptoms,[23] opening avenues for targeted interventions and providing hope for improved outcomes for those with post-viral illnesses. Further research in this area is essential to refine our understanding and develop evidence-based therapeutic approaches to address the long-term consequences of these conditions.

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