

Characterising the Blood Pressure Response to Physical Counterpressure Manoeuvres Using Surface Electromyography in Adults with Long Covid

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Abstract

Objective: Orthostatic intolerance (OI) is common in Long Covid. Physical counterpressure manoeuvres (PCM) may improve OI in other disorders. We characterised the blood pressure-rising effect of PCM using surface electromyography (sEMG) and investigated its association with fatigue in adults with Long Covid. Methods: Participants performed an active stand with beat-to-beat hemodynamic monitoring and sEMG of both thighs, including PCM at 3-minutes post-stand. Multivariable linear regression investigated the association between change in systolic blood pressure (SBP) and change in normalised root mean square (RMS) of sEMG amplitude, controlling for confounders including the Chalder Fatigue Scale (CFQ). Results: In 90 participants (mean age 46), mean SBP rise with PCM was 13.7 (SD 9.0) mmHg. In regression, SBP change was significantly, directly associated with change in RMS sEMG ($\beta=0.25$, 95% CI 0.07–0.43, $P=0.007$); however, CFQ was not significant. Discussion/Conclusion: PCM measured by sEMG augmented SBP without the influence of fatigue.

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Structured Abstract— Objective: Orthostatic intolerance (OI) is common in Long Covid. Physical counterpressure manoeuvres (PCM) may improve OI in other disorders. We characterised the blood pressure-rising effect of PCM using surface electromyography (sEMG) and investigated its association with fatigue in adults with Long Covid. Methods: Participants performed an active stand with beat-to-beat hemodynamic monitoring and sEMG of both thighs, including PCM at 3-minutes post-stand. Multivariable linear regression investigated the association between change in systolic blood pressure (SBP) and change in normalised root mean square (RMS) of sEMG amplitude, controlling for confounders including the Chalder Fatigue Scale (CFQ). Results: In 90 participants (mean age 46), mean SBP rise with PCM was 13.7 (SD 9.0) mmHg. In regression, SBP change was significantly, directly associated with change in RMS sEMG ($\beta=0.25$, 95% CI 0.07–0.43, $P=0.007$); however, CFQ was not significant. Discussion/Conclusion: PCM measured by sEMG augmented SBP without the influence of fatigue.

Index Terms— Long Covid, surface EMG, blood pressure, physical counterpressure manoeuvres, fatigue

Clinical and Translational Impact Statement— The blood pressure-rising effect of physical counterpressure manoeuvres after an active stand can be measured by surface electromyography (sEMG). In adults with Long Covid, this was not influenced by fatigue.

I. INTRODUCTION AND HEALTHCARE NEED¹

Post COVID-19 condition or ‘Long Covid’ is defined by the World Health Organisation as ongoing symptoms for at least 2 months in an individual usually 3 months post confirmed or probable SARS CoV-2 infection [1]. A recent meta-analysis estimated the global Long Covid prevalence to be at 43%, and given its high symptom burden and morbidity it is increasingly recognised worldwide as an emerging health burden [2].

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Orthostatic intolerance (OI) is one of the frequently reported symptoms of Long Covid [3]. Concern has been raised that Long Covid could be associated with autonomic nervous system dysfunction [4] and consequent increased risk of orthostatic hypotension (OH), which is an excessive blood pressure drop on standing that can resolve or persist post-stand [5].

However, OI may have non-OH aetiologies [7] and it has been previously shown that complaints of OI may not be associated with OH in adults reporting Long Covid symptoms [8]. Physical counterpressure manoeuvres (PCM) such as lower limb muscle tensing have been recommended in patients at risk of vasovagal syncope and OH for some time [9], and a number of studies have illustrated their effectiveness in improving orthostatic tolerance [10], [11]. Whilst leg muscle or buttock clenching have been recommended for combatting symptomatic OH [12], these manoeuvres may also help conditions where OI is not associated with OH (e.g., postural orthostatic tachycardia syndrome) [13].

The relationship between neuromuscular fatigue and muscular weakness is also known to be heterogeneous [14]. Hypothetically, the experience of general fatigue in an adult with Long Covid could result in the weakening of the ‘muscle pump’ and hence reduce the PCM-driven rise in blood pressure. A challenge is that no clinical practice guidelines currently exist as to how to non-invasively

measure the blood pressure-rising effect of PCM, including in adults with Long Covid fatigue. Surface electromyography (sEMG) is a long-established, yet under-utilised method of objectively and non-invasively studying muscle activation [15]. With the appropriate biomedical signal processing, sEMG can provide useful evidence of muscle activation in both the time and frequency domains [16]. Yet, sEMG has not previously been used for the modelling of the ‘muscle pump’ in PCM. Hence, the aim of this study was to characterise the blood pressure-rising effect of PCM after an active stand test using surface electromyography (sEMG) and investigate its association with self-reported fatigue in adults with Long Covid.

II. METHODS

A. Setting and Cohort Description

This cross-sectional observational study was conducted on a cohort of adult participants recruited for the TROPIC (Technology Assisted Solutions for the Recognition Of Objective Physiological Indicators of Post-Coronavirus-19 Fatigue) investigation at Trinity College Dublin and St. James’s Hospital Dublin, Ireland. The study received full ethical approval from St James’s Hospital/Tallaght University Hospital Joint Research Ethics Committee (Submission Number: 104: TROPIC; Approval Date: 4 May 2021) and participants provided explicit, informed and voluntary consent. Full details of the cohort have been described elsewhere [17] and the methodologies of the assessment have been previously reported in detail [18].

B. Assessment Protocol

As part of a wider bespoke multimodal clinical assessment protocol, participants underwent a lying-to-standing orthostatic test (active stand) with non-invasive beat-to-beat blood pressure monitoring using digital artery photoplethysmography (Finapres® NOVA, Finapres Medical Systems, Amsterdam, The Netherlands) and sEMG monitoring of the rectus femoris and vastus lateralis muscles bilaterally (SHIMMER®, Shimmer Sensing, Dublin, Ireland). Prior to standing, participants lay supine for a period of 10 minutes, during the first 5 minutes of which they were asked to perform a ten-second prompted maximum bilateral quadriceps contraction (‘squeeze both thighs as hard as you can for 10 seconds’). After the supine rest, and a 5-second countdown, participants were asked to stand, unaided, as quickly as possible, and beat-to-beat hemodynamic parameters including systolic blood pressure (SBP) were monitored for 3 minutes, following which participants were asked to perform another ten-second prompted maximum bilateral quadriceps contraction. After the active stand test participants went on to perform two further prompted maximum bilateral quadriceps contractions, one supine at 5 minutes post active stand, one upright at 20 minutes post, as part of a head-up tilt test. These contractions were used only for normalisation purposes in this study.

	β	95% Conf. Interval for β		P
		Lower	Upper	
Change in mean RMS sEMG	0.25	0.07	0.007	0.007
Age	-0.19	-0.39	0.063	0.063
Sex	-0.28	-0.48	0.006	0.006
Days post-acute COVID-19 illness	-0.08	-0.28	0.414	0.414
CFQ score	-0.16	-0.36	0.117	0.117
On antihypertensives	-0.00	-0.19	0.984	0.984

Table 1. Multivariable linear regression investigating the association between SBP change (dependent variable) and change in RMS sEMG amplitude of the four channels, controlling for possible confounders. B: standardised regression coefficient; CFQ: Chalder Fatigue Scale.

C. Signal Processing

The raw data collected from the assessments were processed in R version 4.0.5 using RStudio 1.4.1106 (Boston, MA). The beat-to-beat SBP signals, expressed as mmHg, were interpolated at 5Hz following best practice [19]. The baseline SBP was established as the mean during a 10-second standing resting period, from 20 seconds to 10 seconds before the second prompted thigh muscle contraction. In addition, a 10-second section of the SBP data was extracted for each participant during the second prompted maximum quadriceps contraction, immediately after the 3-minute stand. The mean SBP gain was defined as the mean SBP during the 10-second quadriceps contraction post-stand, minus the mean of the baseline (standing resting) SBP.

The sEMG recordings of the thigh muscles during the post-stand 10-second maximum voluntary contraction were extracted for both the left and right thighs, resulting in four channels for each participant, i.e. left rectus femoris (L1), left vastus lateralis (L2), right rectus femoris (R1) and right vastus lateralis (R2). A 10-second section of the sEMG recordings, from 20 seconds to 10 seconds before the first squeeze during the supine period, was extracted as the sEMG baseline. The supine period was chosen in order to reduce movement artifact in the signal. sEMG gain was defined as sEMG during the 10-second quadriceps contraction post-stand, minus the baseline.

All sEMG signals were band passed between 20Hz and 500Hz to filter out baseline noise and movement artifacts. They were then normalised with the maximum voluntary contraction, which was established during the first two seconds of each of the four voluntary maximum thigh muscle contractions implemented throughout the assessment. As suggested by previous investigations [20], [21], the amplitude of the sEMG signals was assessed by computing the Root Mean Square (RMS), which was computed over both the post-stand 10-second muscle contraction and the baseline periods for all four channels.

D. Data Visualisation

RStudio 1.4.1106 (Boston, MA) was used to generate a visualisation of the mean SBP and sEMG activity that are aligned at the start of the prompted maximum bilateral quadriceps contraction across all participants. A duration of

20 seconds, consisting of 10 seconds prior to and during the 10-second squeeze, was included in the plot. The normalised sEMG signals were rectified and averaged (mean $\pm$ SD) over the same period for all four channels. A marker section that indicates the time at which participants were given the command to start and finish squeezing the thigh muscle was included in the visualisation plot.

E. Statistical Analysis

Descriptive, bivariate and regression analyses were conducted with Stata 15.1 (Statacorp, Texas, USA). Descriptive statistics were presented as either: count and percentage, mean and standard deviation (SD) or median and interquartile range (IQR). Pearson's correlation was performed to assess the correlation between the change in SBP and the change in RMS sEMG activity. Multivariable linear regression was performed to investigate the association between the change in SBP and the change in mean RMS sEMG activity while adjusting for age (in years), sex (0: male; 1: female), number of days post-acute COVID-19 illness, fatigue score on the Chalder Fatigue Scale (CFQ) and being on any antihypertensive medication (0: no; 1: yes). To aid comparison of effect sizes between variables, regression coefficients were standardised to their respective standard deviations. Normality of the residuals was checked with normal quantile plots, standardised normal probability plots and the skewness-kurtosis test for normality. The level of statistical significance was defined as $P < 0.05$ throughout.

III. RESULTS

In total, 108 participants were recruited to the study with complete data for the present analysis available for 90 (83.3%) participants. In terms of missing data: 8 participants were missing sEMG data, 6 were missing CFQ data and 4 were missing time post Covid. The mean age of participants was 46.0 years (SD 9.6, range 25-67), 71.1% ($n = 64$) were female, the mean number of days post-acute COVID-19 illness was 368.8 (SD 160.2), median CFQ score was 26 (IQR 13), and 21.1% ($n = 19$) were taking antihypertensive medication.

Figure 1 shows the visualisation of mean SBP and sEMG activity of all 90 participants, 10 seconds before and during the 10-second prompted maximum bilateral quadriceps contraction. Whilst the maximum sEMG activity was reached during the first two seconds of the voluntary maximum thigh muscle contractions in all four channels, the maximum SBP occurred at the end of the muscle squeezes.

Participants had on average a 13.7 (SD 9.0) mmHg mean SBP gain over 10 seconds from voluntary maximum thigh muscle contractions with a change in mean RMS of the sEMG signal of 0.12 (SD 0.034) mV. The change in mean RMS sEMG activity was significantly positively correlated with mean SBP gain ($r = 0.27$, $P < 0.05$).

In the multivariable linear regression model (Table 1), change in mean RMS sEMG activity was significantly and independently associated with mean SBP gain ($\beta = 0.25$, 95% CI 0.07–0.43, $P = 0.007$) controlling for age, sex,

number of days post-acute COVID-19 illness, CFQ score and being on anti-hypertensive medication. Among the controlling variables, only sex was independently associated with mean SBP gain, with female sex being associated with lower mean SBP gain ($\beta = -0.28$, 95% CI -0.48 – -0.08, $P = 0.006$). CFQ was not significant in the model.

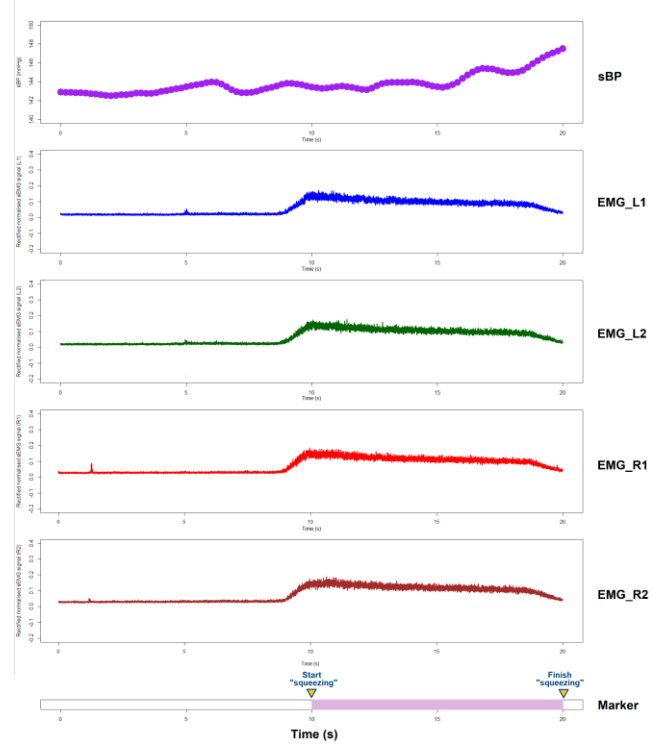


Figure 1. Mean SBP and sEMG activity (left rectus femoris [L1], left vastus lateralis [L2], right rectus femoris [R1] and right vastus lateralis [R2]) of all 90 participants, 10 seconds before and during the 10-second prompted maximum bilateral quadriceps contraction ('squeeze both thighs as hard as you can for 10 seconds'). The normalised sEMG signals were rectified and averaged (mean $\pm$ SD) over the same period for all four channels.

IV. DISCUSSION

The aim of this study was to characterise the blood pressure-rising effect of physical counterpressure manoeuvres (PCM) using non-invasive sEMG and investigate its association with self-reported fatigue in adults with Long Covid. We found that the PCM-driven muscle pump, as captured by RMS sEMG activity in 4 thigh channels during a 10-second maximum voluntary squeeze, was significantly and directly associated with the magnitude of the rise in systolic blood pressure (SBP) even when adjusting for potential confounders. A data visualisation showed that whilst the maximum RMS sEMG activity was reached during the first two seconds of the voluntary maximum thigh muscle contractions in all four channels, the maximum mean SBP occurred at the end of the muscle squeezes. In keeping with the fact that women have lower muscle mass than men [22], female sex was independently associated with lower mean SBP gain. Our multivariable model demonstrated that self-reported fatigue as measured by the CFQ was not significantly associated with mean SBP gain, indicating that in our Long

Covid sample the experience of general fatigue did not suppress the PCM-driven muscle pump function. In other conditions such as autonomic failure, syncope and initial orthostatic hypotension, PCM (without EMG monitoring) have also been shown to be effective at increasing blood pressure. Van Lieshout et al. [23] studied leg-crossing in 7 patients with autonomic failure resulting in orthostatic hypotension and found that it allowed all the participants to stand for more than 10 minutes whereas previously they were limited to less than this, and they had a mean blood pressure rise of 13 mmHg from standing baseline, compared to 1 mmHg in the control group. Ten Harkel et al. [24] also found a mean increase of 13 mmHg from standing baseline with leg crossing in 7 autonomic failure patients. Krediet et al. [25] studied PCM by leg-crossing during tilt-table testing in 21 patients with recurrent syncope and found an average rise in blood pressure of 41 mmHg from standing baseline, with resolution of light-headedness symptoms in patients and none losing consciousness during the tilt test after they had performed PCM. Krediet et al. [26] also studied PCM by lower body muscle tensing in 13 patients with initial orthostatic hypotension finding an increased mean arterial pressure of 19mmHg after standing from squatting when using PCM and fewer symptoms of initial orthostatic hypotension. To the best of our knowledge, our study is the first time PCM have been studied in Long Covid.

Furthermore, we showed a significant correlation between change in RMS sEMG activity and the magnitude of the blood pressure response to PCM. This is in agreement with Mitchell et al. [27] and Schibye et al. [28] who studied the blood pressure response to isometric exercise of lower limbs with sEMG. They found a correlation between sEMG activity and blood pressure increase when force was held constant. In our study, the effect size of the association between change in RMS sEMG activity and SBP gain was mild ($r = 0.27$), which is in keeping with physiological knowledge that other factors such as autonomic nervous system response with splanchnic vasoconstriction are also involved in blood pressure rise during PCM [29].

We found that the magnitude of the blood pressure rise was significantly associated with the change in RMS sEMG activity when adjusted for age, days post-acute COVID-19 illness and antihypertensive medication. The independence of our main finding from these factors is important because of their clinical plausibility as potential confounders. For example, older age (which almost reached statistical significance in our model: $P=0.063$) is known to be associated with increased risk of sarcopenia [30]. Time post-acute COVID-19 might have also played a role in view of our previous finding on this same cohort that longer time since COVID-19 was independently predictive of better performance in a cardiopulmonary exercise test [31]. Moreover, the presence of antihypertensive medication may well have altered the blood pressure response to PCM, especially considering the possibility that orthostatic hypotension may be more pronounced in those treated with antihypertensives [32]. However, in a previous report of this same cohort we noted that symptoms of orthostatic intolerance post-stand were neither related to orthostatic

hypotension nor to antihypertensives [8]. Hence, whilst clearly evidencing a PCM-muscle pump effect, our present results do not necessarily indicate an PCM avenue for treating orthostatic intolerance in Long Covid.

There are several important limitations to our study. Given non-random recruitment of the participants, findings are not necessarily generalisable to the wider Long Covid or the general population. The limitation of not having a control group is also clear: whilst we evidence that the PCM muscle pump is not suppressed in Long Covid, without a control group we cannot comment whether the observed muscle pump effect is similar, or lower, than in normal controls. In addition, and as noted previously [8], COVID-19 status was self-reported, and we did not have access to PCR verification or antibody tests for confirmation of COVID-19 status. Analogously, the CFQ is also liable to self-report bias.

Surface EMG faces a number of challenges, especially in assessing a clinical cohort. Skin preparation, electrode positions and electrical interference from other medical electrical devices are common problems. Normalisation of sEMG signals in an untrained clinical population can also be problematic [33]. We normalised according to the PCM of interest rather than participants performing an exercise against a fixed resistance and so there may have been additional variability and error in our sEMG measurements. Furthermore, inadvertent movement of participants during the baseline resting stage may have affected the delta between rest and muscle squeezing possibly reducing the effect between sEMG activity and SBP change. Despite the protocol requirement of a motionless finger during the hemodynamic measurement, and the 5-second signal averaging, patient movement artifacts may have also affected the non-invasive beat-to-beat finger blood pressure acquisition with NOVA®.

V. FUTURE DIRECTIONS AND POTENTIAL HEALTHCARE IMPACT

Surface EMG remains underutilised in clinical practice [15] and as demonstrated in this study, it could provide a non-invasive, easy to implement method for clinicians to measure the effectiveness of PCM and the resulting blood pressure gains. Biofeedback showing blood pressure tracings to patients has been used previously to help improved efficacy of PCM [34]. This could be expanded with the use of surface EMG biofeedback to allow patients to see their own level of muscle effort. This could be effective in training patients how best to perform lower body muscle tensing and help them identify which specific muscles are being activated. With the help of a physiotherapist or specialist they could then work on improving their muscle contractions. Whether this will help treat orthostatic intolerance in Long Covid or not, requires further investigation. In any case, sEMG could also be used in a clinical setting to understand the effects of age, sarcopenia and other medical conditions on the performance of PCM and the resultant effect on blood pressure, in Long Covid and other conditions, this way

gaining better insight into the pathophysiology involved.

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