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Effect of altering breathing frequency on maximum voluntary ventilation in healthy adults

Eric V. Neufeld[1], Brett A. Dolezal[1*], William Speier[2] and Christopher B. Cooper[1]

Abstract

Background: Compared to other pulmonary function tests, there is a lack of standardization regarding how a maximum voluntary ventilation (MVV) maneuver is performed. Specifically, little is known about the variation in breathing frequency (f_R) and its potential impact on the accuracy of test results. This study examines the effect of several preselected values for f_R and one self-selected f_R (f_{Rself}) on MVV.

Methods: Ten participants performed MVV maneuvers at various f_R values, ranging from 50 to 130 breaths·min^{-1} in 10 breaths·min^{-1} intervals and at one f_{Rself}. Three identical trials with 2-min rest periods were conducted at each f_R, and the sequence in which f_R was tested was randomized. Ventilation and related parameters were measured directly by gas exchange analysis via a metabolic measurement system.

Results: A third-order polynomial regression analysis showed that MVV = − 0.0001(f_R)^3 + 0.0258(f_R)^2–1.38(f_R) + 96.9 at preselected f_R and increased up to approximately 100 breaths·min^{-1} ($r^2 = 0.982$, $P < 0.001$). Paired *t*-tests indicated that average MVV values obtained at all preselected f_R values, but not f_{Rself}, were significantly lower than the average maximum value across all participants. A linear regression analysis revealed that tidal volume (V_T) = − 2.63(MVV) + 300.4 at preselected f_R ($r^2 = 0.846$, $P < 0.001$); however, this inverse relationship between V_T and MVV did not remain true for the self-selected f_R. The V_T obtained at this f_R (90.9 ± 19.1% of maximum) was significantly greater than the V_T associated with the most similar MVV value (at a preselected f_R of 100 breaths·min^{-1}, 62.0 ± 10.4% of maximum; 95% confidence interval of difference: (17.5, 40.4%), $P < 0.001$).

Conclusions: This study demonstrates the shortcomings of the current lack of standardization in MVV testing and establishes data-driven recommendations for optimal f_R. The true MVV was obtained with a self-selected f_R (mean ± SD: 69.9 ± 22.3 breaths·min^{-1}) or within a preselected f_R range of 110–120 breaths·min^{-1}. Until a comprehensive reference equation is established, it is advised that MVV be measured directly using these guidelines. If an individual is unable to perform or performs the maneuver poorly at a self-selected f_R, ventilating within a mandated f_R range of 110–120 breaths·min^{-1} may also be acceptable.

Keywords: Pulmonary function test, Standardization, Breathing frequency, Exercise testing, Ventilatory reserve, Maximal exercise ventilation, Forced expiratory volume in 1 s

* Correspondence: BDolezal@mednet.ucla.edu
[1]Exercise Physiology Research Laboratory, Departments of Medicine and Physiology, David Geffen School of Medicine at UCLA, 10833 Le Conte Avenue, 37-131 CHS Building, Los Angeles, CA 90095, USA
Full list of author information is available at the end of the article

Background

Formerly referred to as maximum breathing capacity, maximum voluntary ventilation (MVV) is a pulmonary function test (PFT) that measures the maximum amount of air a person can inhale and then exhale with voluntary effort. The test is measured in liters per minute ($L{\cdot}min^{-1}$), but data is only collected for 12–15 s and then extrapolated to 1 m in order avoid prolonged hyperventilation by the participant. While the test has been used less over the recent decades due to its fewer applications than the forced expiratory volume in 1 s (FEV_1), MVV still possesses clinical utility. Performing the maneuver is contingent on several factors, including respiratory system mechanics (obstructive or restrictive) and ventilatory muscle endurance. Therefore, the test provides a broad assessment of respiratory system function [1]. Abnormal MVV results are valuable in evaluating various neuromuscular disorders [2–4] and predicting the risk for postoperative complications [1, 5]. MVV also remains useful in cardiopulmonary exercise testing as a measure of ventilatory capacity, especially in determining an individual's ventilatory reserve—the difference between MVV and maximal exercise ventilation ($\dot{V}_{Emax}$)—which aids in the diagnosis and differentiation of pulmonary and cardiovascular diseases [6–10].

What primarily distinguishes MVV from other PFTs, however, is the lack of standardization regarding how the maneuver is performed. A major component of the test is breathing frequency (f_R), but little consensus exists on precisely what f_R or range of f_R values yield optimal results. The majority of both past and current research that employed MVV does not provide the frequency at which participants ventilated as part of the methodology [11–13]. Moreover, the few studies that do provide this information offer diverging suggestions. One of the earliest investigations on this matter concluded that ventilating at 70 $breaths{\cdot}min^{-1}$ maximized MVV [14]. A later study utilized an f_R range of 60–120 $breaths{\cdot}min^{-1}$ [15] while another argued against accepting results obtained with a frequency of less than 65 $breaths{\cdot}min^{-1}$ [16]. A third investigation suggested a narrower window of 70–110 $breaths{\cdot}min^{-1}$ [17]. The American Thoracic Society/European Respiratory Society (ATS/ERS) Task Force offered perhaps the most widely accepted range of 90–110 $breaths{\cdot}min^{-1}$ with an ideal rate of approximately 90 $breaths{\cdot}min^{-1}$, but also declared that no specific f_R can be mandated due to a lack of research on the topic [18].

The limited evidence supporting an ideal f_R range is problematic. Considering both the diagnostic and prognostic value of MVV, as well as its ability to assess participant compliance during pulmonary function testing [19], inaccurate results due to poor standardization may have substantial clinical implications. Consequently, it is imperative that the variety of current guidelines be evaluated. The aim of this investigation, therefore, was to determine whether there is an optimal f_R at which the MVV maneuver ought to be performed, i.e., to consistently provide the highest outcome value. This was accomplished by conducting MVV tests at a wide range of f_R utilizing a repeated-measures design. In addition to examining preselected f_R, this study also explored the effect of a self-selected f_R (f_{Rself}). Given that synchronizing breathing frequency to a rhythm-keeping device at a preset rate may feel unnatural or interfere with performance, we hypothesized that participants would maximize MVV by ventilating at a f_R uniquely self-selected by each individual rather than breathing within a predetermined range.

Methods

Study design

Ten healthy, non-smoking adults (six men) were recruited from the University of California, Los Angeles (UCLA) community to participate in this study. Nine were undergraduate students aged 18–22 years old and one was a 46 year-old university employee (height 1.72 ± 0.13 m; mass 67.1 ± 16.3 kg). The UCLA Institutional Review Board approved this study, and all participants provided informed consent prior to enrollment.

Each participant performed MVV maneuvers using nine different preselected f_Rs ranging from 50 to 130 $breaths{\cdot}min^{-1}$ in increments of 10 $breaths{\cdot}min^{-1}$ as measured by a metronome. Additionally, all participants performed a maneuver using f_{Rself}. In this condition, subjects performed the test without the aid of a metronome, and were instead instructed to breathe as rapidly and deeply as possible without inducing significant discomfort. The resulting frequency was then recorded. For each frequency, including f_{Rself}, participants performed three trials for a total of 30 tests (10 per day with 2-min rest between each) over three consecutive days to allow for adequate recovery. To limit order and practice effects, a random number generator determined the sequence in which f_R was tested for each participant.

Data acquisition

All data were obtained using a metabolic measurement system (Oxycon Pro™; CareFusion, Yorba Linda, CA) that underwent volume and gas composition calibrations prior to each testing session. All tests occurred in a laboratory setting where the ambient temperature and humidity were measured and entered into the system before calibration. The volume calibration was done mechanically with known volumes of air, while the composition calibration was performed using ambient air and a gas tank of 16% O2, 4% CO2 to encompass the range found in normal exhaled air. Participants were seated upright in a stationary chair, wore a nose clip, and breathed through a mouthpiece that connected to the metabolic cart. Participants were also instructed to refrain from eating or engaging in vigorous exercise at least before testing.

Prior to performing the first MVV maneuver, slow vital capacity (SVC) was measured using the same system. Participants were instructed to inhale as much air as possible in a single breath and then exhale, completely emptying the lungs. This value was obtained to compare the ratio of the tidal volume (V_T) during MVV to SVC. In addition, participants took normal breaths to establish a baseline respiratory exchange ratio, which was used as a metabolic indicator to determine when a participant had achieved sufficient rest between trials. Once this value had been established, MVV testing began. For each trial, participants were instructed to maximize ventilation by inhaling and exhaling as deeply as possible for 12 s. As frequent vigorous respiration can cause dry mouth, water was provided if requested between tests. During trials defined by a preselected f_R, participants listened to a corresponding preset tempo from a metronome and timed their breaths accordingly. In between each beat, both an inhalation and an exhalation were performed. During the trials associated with f_{Rself}, no metronome was used— participants freely maximized breathing while the metabolic cart recorded f_R, the value of which was blinded until after a maneuver was completed. In addition to f_R and MVV, which were recorded and analyzed for all trials, breath-by-breath measurements of V_T and partial pressure of end-tidal CO_2 (PETCO$_2$) were also obtained for all maneuvers except those at the preselected f_R of 130 breaths·min^{-1} (f_{R130}) (Table 1).

Statistical analysis

Data for each subject were scaled relative to the maximum value recorded during preselected f_R and reported as the mean ± standard deviation (SD) for all variables. Sample size was estimated from a combination of pilot testing and preliminary power calculations based on an alpha level of 0.05 and a beta level of 0.20 [20]. As suggested by the ATS/ERS Task Force [18], only the test that resulted in the highest MVV out of the three trials per f_R was used for data analysis. The overall effect of f_R was tested using repeated-measures analysis of variance (ANOVA); comparisons were made between the outcome value at every f_R and the maximum value using paired *t*-tests. The average MVV values were found across subjects for each f_R, and the relationship between these values and the corresponding f_R and V_T were analyzed using polynomial regression. The statistics were calculated in MATLAB (version 8.6.0; MathWorks, Inc., Natick, MA) and significance was determined using an alpha level of 0.05.

Results

All ten participants successfully performed three trials at all ten f_R values. As demonstrated in Fig. 1, a third-order polynomial regression analysis showed that $MVV = -0.0001(f_R)^3 + 0.0258(f_R)^2 - 1.38(f_R) + 96.9$ at preselected f_R and increased up to approximately 100 breaths·min^{-1} ($r^2 = 0.982$, $P < 0.001$). A paired *t*-test

Table 1 Outcome variables (scaled and absolute values)

f_R	MVV		V_T		$P_{ET}CO_2$
(breaths·min^{-1})	(%)	(L·min^{-1})	(%)	(L)	(mmHg)
50	76.2 ± 9.9*†	125.1 ± 45.3	99.1 ± 1.6	2.4 ± 0.9	15.3 ± 2.0
60	81.7 ± 13.9†	131.4 ± 52.0	88.4 ± 9.0†	2.2 ± 0.8	15.0 ± 3.3
70	84.3 ± 11.9†	134.1 ± 47.2	78.5 ± 5.4†	1.9 ± 0.7	14.5 ± 2.9
80	87.5 ± 8.3†	139.4 ± 50.2	72.1 ± 12.3*†	1.7 ± 0.6	14.2 ± 2.7
90	91.4 ± 5.9†	144.1 ± 49.6	67.7 ± 11.5*†	1.6 ± 0.5	13.3 ± 2.1
100	93.3 ± 3.7†	147.6 ± 51.5	62.0 ± 10.4*†	1.5 ± 0.5†	14.2 ± 2.7
110	92.2 ± 9.5†	144.9 ± 48.4	51.9 ± 19.9*†	1.3 ± 0.6	13.6 ± 2.2
120	90.2 ± 10.2†	144.7 ± 58.3	50.5 ± 10.3*†	1.2 ± 0.5	13.0 ± 2.4
130	81.0 ± 11.4†	129.6 ± 52.1	n/a[b]	n/a[b]	n/a[b]
Self-Selected (69.9 ± 22.3)	91.1 ± 16.5	144.8 ± 59.4	90.9 ± 19.1	2.1 ± 0.7	13.7 ± 2.0
Maximum[a]	–	157.7 ± 52.5	–	2.4 ± 0.9	17.1 ± 2.5

Values are presented as mean ± SD both 1) scaled as a percentage of the maximum and 2) absolute. Statistical analysis was performed only on scaled values
All values are reported as the percent of the maximum value obtained using preselected f_R values
Abbreviations: f_R breathing frequency, *MVV* maximum voluntary ventilation, V_T tidal volume, *PETCO$_2$* partial pressure of end-tidal CO2
**P* < 0.05 when compared to self-selected f_R
†*P* < 0.05 when compared to maximum
[a]Highest value obtained across all f_R values for every participant
[b]Values were missing from data collection

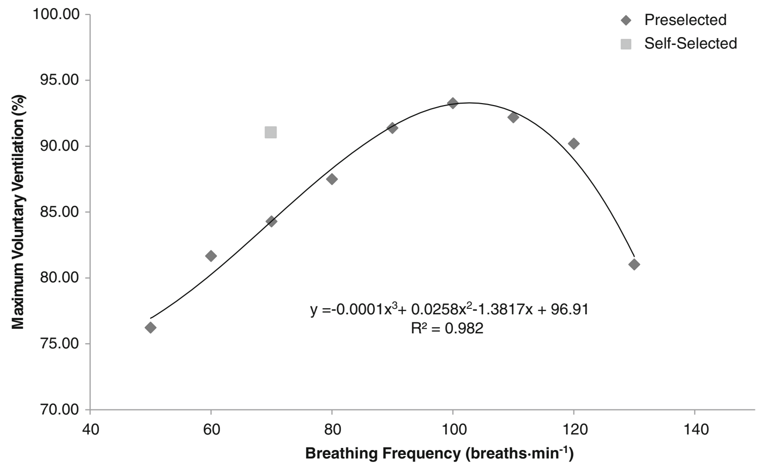

Fig. 1 Relationship between the average maximum voluntary ventilation (MVV) across subjects and average breathing frequency (fR). MVV values are presented as a percentage (%) of the maximum. A polynomial regression analysis of the preselected fRs yielded a third-order relationship ($R^2 = 0.982$, $P < 0.001$)

revealed that the MVV value obtained at an average f_{Rself} of 69.9 ± 22.3 breaths·min^{-1} (91.1 ± 16.5% of maximum) was not significantly different from the value measured at the roughly equivalent preselected f_{R70} (84.3 ± 11.9% of maximum; 95% confidence interval of difference: (− 2.7, 16.3%), $P = 0.190$). When the MVV values at all f_{R} values were compared to the average maximum value for all subjects, a repeated-measures ANOVA showed a significant effect of f_{R} on MVV ($P < 0.001$). Further statistical analysis showed that results obtained at every preselected f_{R} were significantly lower than this maximum value, but those measured at f_{Rself} were not (Table 1). If multiple comparisons are controlled for using a Bonferroni correction, all preselected f_{R} values other than f_{R110} and f_{R120} remain significantly different from the maximum.

As demonstrated in Fig. 2, a linear regression analysis revealed that $V_T = -2.63(\mathrm{MVV}) + 300.4$ at preselected f_{R} ($r^2 = 0.846$, $P < 0.001$). This steadily decreasing trend in V_T was observed as the preselected f_{R} and MVV

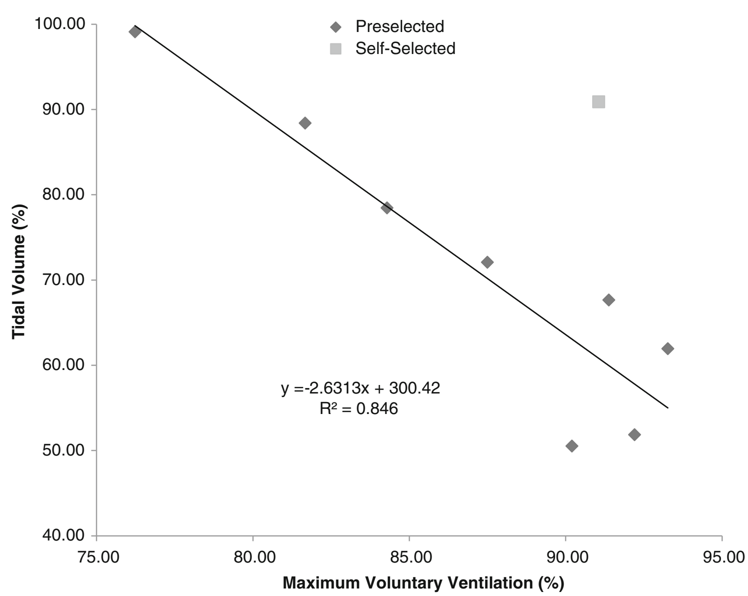

Fig. 2 Relationship between the average tidal volume (V_T) across subjects and the average maximum voluntary ventilation (MVV). V_T and MVV values are presented as a percentage (%) of their respective maxima. A linear regression analysis revealed a significant decreasing trend for the preselected breathing frequencies ($R^2 = 0.846$, $P < 0.001$)

increased, but paired *t*-tests showed that this inverse relationship did not remain true for f_{Rself}. The V_T obtained at this f_R (90.9 ± 19.1% of maximum) was significantly greater than the V_T associated with the most similar MVV value (at f_{R100}, 62.0 ± 10.4% of maximum; 95% confidence interval of difference: (17.5, 40.4%), $P < 0.001$). By contrast, none of the $PETCO_2$ data measured at the preselected f_R differed significantly from that of f_{Rself}, and all were significantly less than the average $PETCO_2$ maximum.

Discussion

Our study, to the best of our knowledge, is the first that examines the effect of altering f_R on MVV. After testing preselected f_R values ranging from 50 to 130 breaths·min^{-1} as dictated by a metronome and one self-selected f_R by each participant, we found that trials conducted at 90–120 breaths·min^{-1}, and the self-selected rate were equally successful at maximizing MVV. This result differed from our hypothesis where we predicted that only f_{Rself} would yield the highest MVV. When compared to the aforementioned guidelines for optimizing MVV of 60–120, 70–110, and 90–110 breaths·min^{-1} suggested by Dillard et al. (1993) [15], Morris (1976) [17], and the ATS/ERS Task Force [18] respectively, our findings disagreed with the first and second recommendations but closely resembled the third. However, our data do not support the ATS/ERS Task Force's recommended goal of 90 breaths·min^{-1}. Considering that participants maximized MVV by breathing at $f_{R90-120}$ and f_{Rself}, we recommend choosing either of these approaches rather than aiming for a single value of f_R. Furthermore, because maximal values were obtained at f_{Rself}, our data suggest that no rhythm-keeping instrument or preselected f_R range may be necessary at all.

Interestingly, while the trials defined by a f_{R70} yielded a significantly lower MVV than the mean maximum for all subjects, they were not statistically different than the MVV value obtained at f_{Rself} (69.9 ± 22.3 breaths·min^{-1}, nearly equivalent to 70 breaths·min^{-1}). This is likely explained by the variance, which suggests that while breathing at a self-selected rate may increase the likelihood of achieving one's true MVV, this chosen rate may not be equal among all individuals. Another noteworthy observation stemmed from the differences in V_T measured at the preselected and self-selected f_R. When plotted against MVV, V_T steadily decreased at the preselected f_R values. This was unsurprising considering that MVV values were greater at higher f_R and as f_R increases, the tidal volume may decrease in order to sustain the faster rate. However, it is also possible that during exercise, increased intra-thoracic pressure and work of breathing can permit concomitant increases in f_R and V_T. Interestingly, the data showed that the V_T associated with the MVV value obtained at f_{Rself} deviated from the trend observed at the preselected f_R values—it was significantly greater than its most similar preselected counterpart (obtained at f_{R100}). This suggests that when breathing at a self-selected rate, individuals are more likely to utilize an optimal combination of slower deep breaths and faster shallower breaths to maximize MVV. Additionally, matching the rate of one's breathing to a metronome or other rhythm-keeping instrument can feel distracting and unnatural to the participant, especially compared to ventilating at a natural rate during an assessment of $\dot{V}_{Emax}$, which may decrease the likelihood of an accurate measurement [1, 21].

Unlike MVV and V_T, there were no significant relationships observed between f_R and $PETCO_2$. This is somewhat unexpected as $PETCO_2$ is known to decrease as the ventilation increases. The lack of this trend in the data may be partially explained by the missing values associated with f_{R130}. It also is plausible that the inverse relationship between f_R and $PETCO_2$ is not evident until the rate of ventilation is much greater than what was tested in this study. Moreover, it is important to note that the missing values for V_T at f_{R130} may not have fit the strong, negative linear correlation demonstrated in Fig. 2. Due to the sharp decrease in MVV from f_{R120} to f_{R130}, it is unlikely that the corresponding reduction in V_T would have been of the same magnitude; however, it is also improbable that this single data pair would have rendered the aforementioned relationship between V_T and MVV non-significant.

Regarded as one of the most long-standing PFTs, equations developed to predict MVV from more widely applicable parameters, such as FEV, have existed since the mid-twentieth century. The most common and simplistic of these include $MVV = FEV_1 \times 35$ [22]; $FEV_1 \times 37.5$ [23]; and $FEV_1 \times 40$ [24]. And while some still prefer to utilize these equations over a direct assessment, substantial evidence has highlighted the limitations of such practice. These along with many similar reference equations fail to account for a number of physical characteristics that have been shown to influence MVV. The most predominant of these include height, sex, and age [25, 26]. Studies have shown that individuals who smoke [27], suffer from cystic fibrosis [28], and women who are pregnant [29] also exhibit MVV values that deviate from height-, sex- and age-matched controls. Furthermore, a growing body of literature suggests that current reference equations for MVV and other PFTs fail to account for ethnic and socioeconomic disparities in addition to ignoring the trend of increasing racial diversity [30, 31]. Investigations have derived specific prediction equations based on ethnicity, such as in Brazilian [11], Chinese [13], Filipino [32], and African-American adolescent [12] populations, but all possess significant mathematical differences from one another. The recurring shortcoming of these equations is their lack of cohesion—no comprehensive equation exists that successfully incorporates all of the aforementioned variables. As a result, a number of studies have argued that MVV is best measured directly [19, 28, 33].

It is important to note that the results from this investigation possess similar limitations to those outlined above, including a homogenous participant cohort and the inability to account for differences in physical characteristics due to a small sample size. Further research ought to examine whether a self-selected f_R is as accurate and more efficient than a preselected range of f_R in a larger, more heterogeneous population. Future investigations should also explore other methods to standardize the assessment of MVV, for instance, an optimal test duration and the feasibility of a definitive reference equation. Until then, we advise that participants perform the maneuver preferably at a self-selected f_R or within a preselected range of 90–120 breaths·min^{-1}.

Conclusion

Although not as prominent as in decades past, MVV remains a clinically relevant PFT whose outcomes are valuable in cardiopulmonary exercise testing and aid in the diagnosis of various neuromuscular, cardiovascular, and pulmonary diseases. This study demonstrates the shortcomings of the current lack of standardization in MVV testing and establishes data-driven recommendations for optimal f_R. While classic literature has previously investigated this topic, the antiquity of these works warrants modern research. Furthermore, what these studies suggest as an optimal measurement technique has been overlooked or forgotten in the current guidelines. Our paper therefore contributes a new and much-needed focus on an evidence-based approach to selecting the optimal f_R for MVV measurement. We recommend that participants perform an MVV maneuver at a self-selected f_R as it maximizes the likelihood of an accurate measurement by optimizing a combination of slower deep breaths and faster shallower breaths, eliminates the necessity to synchronize breaths to a rhythm-keeping device, and more closely resembles the procedure to obtain $\dot{V}_{Emax}$. If an individual is unable to perform or performs the maneuver poorly at a self-selected f_R, ventilating within a mandated f_R range of 110–120 breaths·min^{-1} may also be acceptable.

Abbreviations

ATS/ERS: American Thoracic Society/European Respiratory Society; FEV_1: Forced expiratory volume in 1 s; F_R: Breathing frequency; f_{Rself}: Self-selected breathing frequency; f_{RX}: Preselected breathing frequency of X breaths·min^{-1}; MVV: Maximum voluntary ventilation; $PETCO_2$: Partial pressure of end-tidal CO_2; PFT: Pulmonary function test; SD: Standard deviation; SVC: Slow vital capacity; UCLA: University of California, Los Angeles; $\dot{V}_{Emax}$: Maximal exercise ventilation; V_T: Tidal volume

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Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authors' contributions

All authors made substantial contributions to this study and manuscript. The study was conceived and designed by BAD and CBC. EVN and WS collected and analyzed the data. EVN, BAD, WS, and CBC composed significant portions of the manuscript and made crucial edits. All authors also read and approved the final version of the manuscript.

Ethics approval and consent to participate

This study was approved by the UCLA Institutional Review Board. All participants provided informed consent prior to enrollment.

Competing interests

The authors declare that they have no competing interests.

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Author details

[1]Exercise Physiology Research Laboratory, Departments of Medicine and Physiology, David Geffen School of Medicine at UCLA, 10833 Le Conte Avenue, 37-131 CHS Building, Los Angeles, CA 90095, USA. [2]Medical Imaging Informatics, Department of Radiology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA.

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