Normalized metabolic stress for $^{31}$P-MR spectroscopy studies of human skeletal muscle: MVC vs. muscle volume

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Fowler, M. D., T. W. Ryschon, R. E. Wysong, C. A. Combs, and R. S. Balaban. Normalized metabolic stress for $^{31}$P-MR spectroscopy studies of human skeletal muscle: MVC vs. muscle volume. J. Appl. Physiol. 83(3): 875–883, 1997.—A critical requirement of submaximal exercise tests is the comparability of workload and associated metabolic stress between subjects. In this study, $^{31}$P-magnetic resonance spectroscopy was used to estimate metabolic strain in the soleus muscle during dynamic, submaximal plantar flexion in which target torque was 10 and 15% of a maximal voluntary contraction (MVC). In 10 healthy, normally active adults, ($PCr + P_i)/PCr$ and the torque produced, indicating that metabolic strain was increasing rather than achieving constancy as a function of MVC. These findings provide new insight into the design of dynamic muscle contraction protocols aimed at detecting metabolic differences between subjects of different body size but having similar blood flow capacity and mitochondrial volume per unit of muscle.

maximal voluntary contraction; soleus; magnetic resonance imaging; 4 tesla; creatine phosphate; adenosine 5′-triphosphate; phosphorus-31 magnetic resonance spectroscopy

SKELETAL MUSCLE ENERGETICS has been extensively studied by using $^{31}$P-magnetic resonance ($^{31}$P-MR) spectroscopy coupled with isometric, eccentric, and concentric muscle actions in subjects who are physically conditioned (15, 16, 20, 26), have disease (13, 14, 25, 29), or are sedentary (15, 26, 28). In general, these studies examine metabolic changes (i.e., metabolic strain) with metabolic stress associated with a given workload. Most of these studies have used exercise parameters that increase mechanical load on the muscle group until exhaustion or fatigue occurs (maximal protocols) (13, 20, 30). An alternative approach prescribes exercise as a percentage of an assumed maximal ATP synthesis rate ($Q_{max}$) in an attempt to scale metabolic stress or demand to the maximal metabolic capacity (3, 4, 14). In these submaximal steady-state exercise protocols, the ATP synthesis rate matches the rate of ATP hydrolysis needed for muscle contraction, resulting in a constant ATP level in the muscle. Advantages of steady-state protocols include a greater specificity to oxidative ATP synthesis, a reduction in the influence of fatigue mechanisms associated with maximal contraction protocols, and better subject compliance. Moreover, submaximal exercise is routinely used in activities of daily living.

To achieve the same relative work intensity and subsequent metabolic stress in subjects of different body sizes, the power performed in steady-state protocols must be normalized between individuals. We define a normalized metabolic stress as

$$Q/Q_{max} \times E$$

where $Q$ is the power performed (J/s), $E$ represents mechanochemical efficiency, $Q_{max}$ is the maximum metabolic power (J/s). From Eq. 1, a measure of the $Q_{max}$ and $E$ is required to properly normalize the metabolic stress on a given muscle. In general, the efficiency for a given muscle action is assumed to be constant. Thus a measure of $Q_{max}$ is all that is required. There have been several approaches to determine the $Q_{max}$ to normalize metabolic stress in studies of human muscle.

One of the most common strategies for normalizing metabolic stress is the force generated during a maximal voluntary contraction (MVC). The MVC is often used because it is a relatively easy measurement to obtain. MVC as an estimate of $Q_{max}$ assumes that individuals are highly compliant, that all muscle fibers are activated by voluntary effort, and that no antagonistic muscles contract concurrently to reduce overall force output. These assumptions are controversial for most human subjects (2, 6, 19, 22).

An alternative approach for determining $Q_{max}$ in individuals of different body size is to assume that the activated muscle volume is an approximation of $Q_{max}$ (5). This assumption requires that the amount of mitochondria per cubic centimeter of muscle and the supporting intermediary metabolism are constant, that the activated muscle can be identified and consistently stimulated, and that blood flow does not limit submaximal metabolic rates. Although volume and $Q_{max}$ have been estimated by lean body mass and cross-sectional area (CSA), absolute three-dimensional volume measurements should provide a more accurate means of estimating muscle volume and related $Q_{max}$.

To compare the use of MVC and muscle volume as measures of $Q_{max}$, a measure of metabolic stress independent of muscle mechanics is necessary. In response to a metabolic stress, a change or strain occurs in the energy metabolism of the muscle. Because the major source of energy in the cell is the free energy of ATP hydrolysis, we are defining the metabolic strain as the percent change in ATP free energy or the related

http://www.jap.org
(PCr + Pi)/PCr ratio, where PCr is phosphocreatine. It has been shown that this metabolic strain is linearly related to the metabolic stress in several systems over moderate workloads (11, 18).

In this study, metabolic strain or changes in (PCr + Pi)/PCr were used to evaluate different methods of normalizing the metabolic stress in a series of individuals undergoing different levels of submaximal plantar flexion. $^{31}$P nuclear magnetic resonance (NMR) was used to continuously monitor the metabolic strain. $^1$H magnetic resonance imaging (MRI) was used to determine NMR coil placements as well as muscle volume. Muscle mechanics were controlled and monitored by using a specially designed dynamometer (23). Volume, MVC, and CSA were evaluated as methods of normalizing a given workload to $Q_{\text{max}}$. Identification of a morphometric or functional variable that can be used to normalize metabolic stress is likely to increase the sensitivity and clinical usefulness of $^{31}$P-MR for studying metabolic consequences associated with age, pathology, and conditioning.

MATERIAL AND METHODS

Subjects. Informed consent was obtained from 16 subjects between the ages of 29 and 53 yr (8 men and 8 women) as prescribed by the Institutional Review Board of the National Heart, Lung, and Blood Institute at the National Institutes of Health. Before participation in the study, all subjects completed medical history and physical activity questionnaires to identify the presence of medical conditions, recent leg injuries, or previous surgical implants that would contraindicate MRI, $^{31}$P-MR spectroscopy, or leg exercise. By report, all subjects engaged in <4 h of aerobic activities per week.

NMR spectroscopy. All NMR and MRI experiments were conducted using a 55-cm (clear)-bore 4-T superconducting magnet (Oxford Magnetics, Oxford, UK) customized with resonant-imaging gradients (Advance NMR, Boston, MA). Spectroscopy and imaging experiments were conducted by using a GE/Bruker Omega console and a GE Signa (5.0) console (GE Medical Systems, Milwaukee, WI), respectively.

$^{31}$P-MR spectra were acquired from the soleus muscle by using a 2.5-cm dual-tuned ($^1$H and $^{31}$P) coil, as previously described (23). The flat surface coil is affixed to an adjustable platform that can be moved in three dimensions relative to the overlying leg. In all subjects, the center of the coil was positioned against the soleus muscle at a point between and caudal to the insertion of the medial and lateral gastrocnemius muscles on the Achilles sheath (estimated by palpation and visual estimation based on anatomic expectations). On most subjects, this point was 10–14 cm above the plantar surface of the foot. The localization of the coil was confirmed by using $^1$H-MRI. A padded and contoured shelf was positioned under the cephalid portion of the calf to support the leg and to prevent local muscular compression and reduction of perfusion.

The magnetic field was optimized by manual adjustment of the room temperature shims by using the $^1$H free-induction decay (resulting PCr line width < 20 Hz). During the control period, a fully relaxed $^{31}$P-MR spectrum was collected at a rate of 0.05 spectrum/s (10-kHz sweep width, 2 K points, 300-ms pulse width, 1-kW amplifier, 1 transient/spectrum) to determine the saturation factors for the more rapidly collected spectrum during the exercise protocol. Throughout the exercise protocol, spectra were collected at a rate of 1.3 spectra/s (10-kHz sweep width, 300-ms pulse width; 4 transients/spectrum) continuously during 10 min of rest, 5 min of exercise, and 5 min of recovery for each exercise trial. Spectra were block averaged to 1 spectrum/min for most analysis. Spectra were processed by using a linear baseline correction, zero filling to 4K points, exponential multiplication with 20-Hz line broadening, and fast Fourier transformation with zero and first-order phase correction. Integration of $PCr$ and $Pi$ peak areas was performed by using Omega software. Integration limits were determined by eye and held constant through a given experiment, and pH was determined from the frequency shift of $Pi$ relative to $PCr$ (26).

Metabolic steady state, a critical requirement of the study design, was defined as a <10% decrease in PCr peak area between the fourth and fifth minute of exercise and a <0.05 decrease in pH during the entire test.

Free intracellular ADP concentration ([ADP]) was calculated by using the equilibrium constant for the creatine kinase reaction, as previously described (11), using a Michaelis constant ($K_m$) of 1.66 × 10$^8$ and a total creatine of 42.5 mM.

$^1$H-MRI. Muscle volume experiments were conducted within 7 days after collection of $^{31}$P-MR spectra by using a homebuilt $^1$H quadrature "birdcage" coil. Axial images of the right lower extremity were obtained every 0.5 cm from the knee to the ankle by using a multislice spoiled-gradient echo sequence [1-cm slice thickness, 11-ms echo time (TE), 15° flip angle, 50-ms repetition time (TR), 20-cm field of view (FOV), number of acquisitions (NA) = 2, and 512 × 512 resolution].

Multislice gradient-echo recalled echo images (15–25 slices) were collected to map out the sensitive region of the dual-tuned 2.5-cm surface coil [3-mm slice thickness, 2.5-mm slice separation, 9-ms TE, 100-ms TR, ~10° flip angle (surface coil excitation), 15–20 cm FOV, NA = 3, and 256 × 128 resolution]. The entire sensitive volume of the coil was covered to assure the localization of the coil.

Image processing. Axial images were processed on Sun Workstations by using a routine written in Interactive Data Language (Research Systems, Boulder, CO). A region of interest (ROI) encompassing the entire plantar flexor (PF) compartment (including all muscles, connective tissue, and vessels) was manually drawn for each slice (Fig. 1). The PF volume for each slice was calculated by multiplying the ROI area (PF CSA) by 1.5 cm (0.5-cm slice thickness and 1-cm slice separation). Total PF volume was calculated as the sum of individual slice volumes from the tibial tuberosity to near the ankle. Accuracy of the measurements was assessed by calculating the volume of a phantom of known volume. The phantom was a tapering glass bottle of approximately the same volume as the lower leg. The coefficient of variation (SD/mean × 100) was calculated for the volume determination of both the phantom and a human leg. All image processing was completed by a single investigator (M. D. Fowler) to eliminate interobserver bias.

Dynamometer. Dynamic concentric plantar flexion was performed by using a custom leg dynamometer incorporating a foot-pedal module mounted on a standard patient-transport bed, as described previously (23). Briefly, the subject was placed on the bed in a supine position with the right leg fully extended. The right foot was secured by using nylon straps attached to the foot pedal with axis of rotation around the ankle. Additional straps were placed 4–5 cm above and below the knee to prevent movement of the thigh and lower leg relative to the dynamometer platform. A broad, contoured foam shelf was positioned below the right calf to support the lower leg.

The dynamometer foot pedal is coupled through a low-friction point to a 6.0-kW (peak power) direct-current servomotor (Glentek, El Segundo, CA). The pedal is attached to a
crank arm mounted on the motor driveshaft by an aluminum-fiberglass tube. This arrangement allows translation of the rotation of the motor driveshaft to rotation of the foot pedal around the ankle joint. An integrated analog-to-digital converter was used to sample torque and pedal position as a function of time at a rate of 10 Hz. The subject received real-time feedback of torque from a vertical bar graph mounted at eye level in the magnet.

Leg exercise. After the position of the surface coil was confirmed, the magnetic field was shimmed. A fully relaxed 31P-MR spectrum was collected at rest. The leg exercise portion of the protocol was then initiated. After the range of motion of an individual was determined, MVC was determined by the peak torque attained during 3–5 maximal effort plantar flexions. Each maximal effort was 3–5 s in duration and was accompanied by vigorous verbal encouragement. Submaximal exercise testing with continuous collection of 31P-MR data was started after 15 min of rest. Each subject performed trials of 10 and 15% MVC concentric plantar flexion separated by 10–15 min of recovery. During the effort portion of each pedal stroke, the pedal rotation was constrained to 30°/s. After the stroke, the pedal was returned to the starting position at 240°/s. In all trials, ankle rotation was limited to 30° (5° dorsiflexion and 25° plantar flexion). All subjects included in the analysis reached a metabolic steady state at each workload. The average tension time integral (TTI) for each stroke was calculated as the sum of sampled torque values during an effort stroke divided by the number of samples in that stroke. Average power per stroke was calculated for the final minute of each period of exercise as the product of pedal velocity (radi/s) and instantaneous torque.

Data analysis. All data are reported as means ± SD when normal distributions were determined. All statistics were performed by using SigmaStat (San Rafael, CA). Comparisons between parameter conditions were made via analysis of variance with the Student-Newman-Keuls test for multiple comparisons where necessary. The relationships between morphometric and functional measures and inverse phosphorylation potential, (PCr + P_i)/PCr, were determined from

![Fig. 1. Plantar flexor volume measurement. Single subject's set of images from tibial tuberosity (top left) to near ankle (bottom right) with plantar flexor compartment defined for each image. Images are collected with a volume coil. Imaging parameters are presented in MATERIALS AND METHODS.](image-url)
linear regression analysis and the Pearson correlation coefficient. A significance level of $P < 0.05$ was selected.

RESULTS

Subject characteristics and compliance. Of the 16 subjects, six did not achieve a metabolic steady state in the last minute of exercise in one of the exercise trials and were excluded from further analysis. Characteristics of the included subjects are shown in Table 1. There is an approximate twofold range in the weight, MVC, CSA, and PF volume among individuals in the group.

To test the ability of our imaging sequences and segmentation programs to accurately measure volumes on the order of the human lower leg, studies were conducted on a simple phantom. Five repeated measures (including placement of the phantom, separate image acquisitions, segmentation, and processing) of a 1.057-liter phantom resulted in a volume estimate of $1.031 \pm 0.025$ liters (2.4% coefficient of variation from the known volume). To evaluate the precision of these measurements in the human leg, repeated processing (5) of one subject resulted in a volume estimate of $0.558 \pm 0.025$ liter (4.4% coefficient of variation).

With regard to subject compliance during the protocols, torque output is plotted vs. time for a representative 10-s period during the 10 and 15% MVC exercise trials in Fig. 2. The target torque is indicated by dotted lines for each exercise. Subjects were generally unable to produce a sharp increase or decrease in torque output, resulting in the slow on-off kinetics of the torque tracings. Torque output averaged $78 \pm 14$ and $82 \pm 9$% of target output for 10 and 15% MVC, respectively.

Surface coil. An example of a surface coil localization image series is shown in Fig. 3. The entire sensitive volume of the surface coil is presented in this multislice study. The major muscle observed is the soleus, with some contributions from deeper muscle groups. The gastrocnemius muscle was completely excluded with this coil placement. Similar images were collected for each subject to ensure the anatomy and placement of the coil.

Typical 1-min spectra are shown in Fig. 4. The rest and last-minute exercise spectra at 10 and 15% MVC had a PCr signal-to-noise (peak-to-peak) ratio of 163, 113, and 104, respectively. Table 2 shows the $(PCr + Pi)/PCr$, [ADP], intracellular pH, and ATP concentration ([ATP]) during the last minute of rest and the last minute of exercise at 10 and 15% MVC, respectively. There was a significant difference in the $(PCr + Pi)/PCr$ and calculated [ADP] between rest and the end of each exercise trial and between the end of the 10 and 15% MVC exercise trials. No significant changes were detected in [ATP] or pH. No significant change in the chemical shift of the ATP $\beta$-phosphate was observed throughout the protocol, suggesting no change in the intracellular free Mg$^{2+}$ concentration ([Mg$^{2+}$]) (24). From the pH and chemical shift difference between the $\alpha$- and $\beta$-ATP, the mean intracellular free Mg$^{2+}$ was estimated to be $\sim0.6$ mM, similar to previous studies (24).

Metabolic strain relative to percent MVC, PF CSA, and PF volume. Figure 5 shows that power normalized to the volume of the PF compartment had a high positive correlation with $(PCr + Pi)/PCr$ at the end of exercise ($r = 0.89$, $P < 0.001$), indicating that the ratio of power-to-muscle volume and metabolic strain are linearly related. A significant but lower correlation was found between power normalized to CSA and $(PCr + Pi)/PCr$ ($r = 0.78$, $P < 0.001$).

Figure 7 shows the positive correlation between mechanical power (in W) and $(PCr + Pi)/PCr$ at both 10 and 15% of MVC. This plot indicates that subjects with

### Table 1. Variability of subject characteristics

<table>
<thead>
<tr>
<th>Subject Characteristics</th>
<th>Values</th>
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<tbody>
<tr>
<td>Gender</td>
<td>7 women/3 men</td>
</tr>
<tr>
<td>Age, yr</td>
<td>40 ± 9 (28–52)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>63.9 ± 11.7 (46.4–79.5)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>162.7 ± 8.8 (149.9–177.5)</td>
</tr>
<tr>
<td>MVC, N·m</td>
<td>82.2 ± 26.6 (52.2–126.7)</td>
</tr>
<tr>
<td>Cross-sectional volume PF, cm$^2$</td>
<td>53.2 ± 10.4 (38.7–74.6)</td>
</tr>
<tr>
<td>Volume PF, liter</td>
<td>0.87 ± 0.18 (0.60–1.23)</td>
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Values are presented as means ± SD, with ranges in parentheses. MVC, maximal voluntary contraction; PF, plantar flexor.
larger MVC had larger metabolic strains associated with the given percentage of MVC. If selection of power as a function of MVC had produced comparable metabolic strain, the regression line should have had a slope of zero for each exercise trial. These data suggest that a percentage of MVC did not provide a normalized metabolic stress.

**DISCUSSION**

In the present study, the relationships between muscle morphometrics, power, and metabolic strain were investigated to find the most appropriate strategy of normalizing submaximal workloads for use in steady-state dynamic muscle ergometry. We sought an approach of
assigning load parameters that would achieve metabolic stress and resulting strain in a given muscle group that would be comparable between subjects. In this study, the same percent MVC did not result in comparable metabolic strain between subjects spanning a twofold range in muscle mass. Power output normalized to muscle volume showed the highest correlation, with indexes of metabolic strain compared with MVC or CSA. Muscle volume was better than CSA as an estimate of muscle mass, probably because of the variation in muscle shape and difficulty in finding the maximal CSA slice. These data suggest that muscle volume is a good estimate of Q\text{max} and provides a

Table 2. $^{31}$P-nuclear magnetic resonance parameters as a function of 10 and 15% MVC

<table>
<thead>
<tr>
<th></th>
<th>(PCr + P)/PCr</th>
<th>[ADP], µm</th>
<th>pH</th>
<th>[ATP]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.10</td>
<td>4.5 ± 1.7</td>
<td>7.02 ± 0.03</td>
<td>100</td>
</tr>
<tr>
<td>10% MVC</td>
<td>1.24*</td>
<td>18.0 ± 4.4*</td>
<td>7.02 ± 0.04</td>
<td>97.1 ± 11.2</td>
</tr>
<tr>
<td>15% MVC</td>
<td>1.37†</td>
<td>28.4 ± 7.6†</td>
<td>7.00 ± 0.06</td>
<td>105 ± 12.0</td>
</tr>
</tbody>
</table>

Values are means ± SD and as median, 25%, and 75%-quartiles for phosphocreatine (PCr). [ADP], ADP concentration calculated as discussed in MATERIALS AND METHODS. [ATP], ATP concentration values normalized to control value. *P < 0.05 vs. rest; and †P < 0.05 vs. 10% MVC.
measure to generate comparable metabolic stress between individuals.

We sought a twofold range in age, weight, MVC, PF CSA, and PF volume to optimize the dynamic range of the absolute values of torque output in a similarly active group of adults. Subjects that were able to achieve a metabolic steady state demonstrated inaccuracy of adhering to the torque target, reaching only 79 and 83% of the target TTI for 10 and 15% MVC, respectively. The difficulty in achieving target torque may reflect limitations in neurological activation of muscle contraction (2), an excessively intense target power output, or noncompliance. We selected mechanical parameters for exercise that were anticipated to be within the ability of all subjects. An effort-stroke contraction speed of 30°/s was selected to replicate the muscle contraction speed of a walking gait of ~3 miles/h (assuming a 3-ft. stride length). A rapid speed of 240°/s was selected to ensure that individuals did not try to “help” the automatically returning foot pedal back to the original position. We had found in previous experiments, using return velocities of 30–60°/s, that individuals fatigue their dorsiflexor muscles before challenging the PF muscle group because of inadvertent attempts to assist the foot pedal in returning to the starting position. These compliance issues demonstrate the importance of measuring work performed during an experiment rather than assuming 100% subject compliance.

On the basis of phantom calibrations and repeated measures on a human leg, MRI muscle volume measurements were apparently accurate and precise. However, some limitations of this method should be pointed out. Beginning the calculation of PF volume at the tibial tuberosity gave a reproducible starting point in all individuals. An end point was more difficult, because a precise anatomic end point for the PF compartment could not be determined. Errors related to the failure to identify this terminus of the muscle would be small, because the contribution of each slice in this region of the PF compartment to the overall PF volume was typically <1%slice. The accuracy of this method for measuring muscle volume could be increased by increasing the spatial resolution with reduced slice thickness and slice separation. However, this approach would dramatically increase the number of images to be processed (from the current average of 25), a scenario more tenable once automated multislice image segmentation is available.

The most accurate and precise measurements of muscle metabolic strain associated with work and morphometry are likely to come from single-muscle models composed of one fiber type. The complex architecture and enervation of coactive muscles around joints in the human body precludes mechanical isolation of most muscles. In addition, the phenotypic and metabolic heterogeneity of human skeletal muscle has been well described (12). Nonetheless, the soleus muscle is more uniform in fiber type (type I) than any of the other large, accessible muscles of the human body (12). The type I fiber composition of the soleus also improved the chances of maintaining a metabolic steady required for this study. For these reasons, the measurement of metabolic strain was made principally from the soleus in this complex muscle action.

In the PF compartment, all muscles are capable of participating in plantar flexion; thus the entire PF compartment was used to estimate Q_max. Estimating the fraction of observed plantar flexion power attributable to any single muscle in this compartment has proven difficult. Furthermore, the stability of a contribution during a sustained bout of submaximal dynamic activity is unclear. Although electromyogram methods and T2-weighted MRI have been used to estimate mechanical activation (1, 7, 8, 21), these methods have limitations in sensitivity and specificity. This is especially true for the water T2 measures, where a complete biophysical description of the exercise-induced water proton-relaxation changes has not been established. Using a nonfatiguing, steady-state paradigm, we have assumed that the soleus muscle contributes a constant fraction of the power. Support for this contention comes from several observations. First, a linear relation between volume-normalized power and soleus metabolic strain was observed among different individuals. This suggests that the contribution of the soleus muscle was similar among individuals. In addition, glycogen depletion is primarily confined to type I fibers during isometric plantar flexion action of <20% MVC (9).
Because the soleus is predominantly type I, it is unlikely that very active recruitment of type II fibers (both within the soleus and in other muscles of the PF compartment) would occur in submaximal exercise. Finally, time-dependent activation or recruitment of other muscle groups or fibers was eliminated in this study, because only those individuals who maintained a metabolic steady state were included. A metabolic steady state implies that activation was constant in these individuals. It should be stressed that the metabolic strain measured in this study was only for the soleus muscle group and did not represent the total metabolic strain of the lower leg muscle groups.

There are several critical assumptions in using muscle volume as an estimate of \( Q_{\text{max}} \). First, the blood flow capacity per liter of muscle does not become rate limiting for metabolism. No evidence of demand ischemia was observed in these studies. That is, \( pH \) was unchanged and a metabolic steady state was achieved at these submaximal workloads. The use of moderate workloads minimizes the possibility of blood flow limitations as well as improved subject compliance. Second, the mitochondrial volume per liter of muscle and the supporting intermediary metabolism must be the same between index and control groups. This may be a serious limitation in muscle myopathies, some drug treatments, or genetically linked conditions. Third, the degree of muscle activation, for any given muscle group analyzed, must be the same in the exercise protocol. In the present study, a linear correlation was observed between muscle workload and soleus metabolic strain, suggesting that consistent soleus activation was achieved. This may not be the case in other exercise protocols or patient populations. If these assumptions do not hold, then the use of muscle volume as an estimate of \( Q_{\text{max}} \) in these protocols may be inappropriate.

Conclusions

These data suggest that normalizing power to muscle volume will result in a similar metabolic stress and strain between different individuals performing submaximal dynamic work. This approach was superior to the use of percentage of MVC or CSA as normalizing parameters. This strategy of power normalization can be used to study populations with either enhanced or impaired muscle performance, provided that the assumptions discussed are adequately addressed when selecting a control group. Normalizing metabolic stress by using muscle volume may improve the sensitivity of clinical studies using \(^{31}\)P-MR spectroscopy to detect alterations in the relationship between work and metabolism.

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REFERENCES


