Anaerobic and aerobic relative contribution to total energy release during supramaximal effort in patients with left ventricular dysfunction

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Mezzani A, Corrà U, Andriani C, Giordano A, Colombo R, Giannuzzi P. Anaerobic and aerobic relative contribution to total energy release during supramaximal effort in patients with left ventricular dysfunction. J Appl Physiol 104: 97–102, 2008. First published October 4, 2007; doi:10.1152/japplphysiol.00608.2007.—Energetic metabolism during effort is impaired in patients with left ventricular dysfunction (Dysf), but data have been lacking up to now on the relative anaerobic vs. aerobic contribution to total energy release during supramaximal effort. Recently, the maximal accumulated oxygen deficit (MAOD) has been shown to be measurable in Dysf patients, making it possible to evaluate the anaerobic/aerobic interaction under conditions of maximal stress of both anaerobic and aerobic metabolic pathways in this population. Nineteen Dysf patients and 17 normal patients (N) underwent one ramp cardiopulmonary, three moderate-intensity constant-power, and three supramaximal constant-power (1- to 2-min, 2- to 3-min, and 3- to 4-min duration) exercise tests. MAOD was the difference between accumulated O2 demand (accO2dem; estimated from the moderate-intensity O2 uptake/watt relationship) and uptake during supramaximal tests. Percent anaerobic (%Anaer) and aerobic (%Aer) energetic release were [(MAOD/accO2dem) x 100] and 100 – %Anaer, respectively. MAOD did not vary between 1–2, 2–3, and 3–4 min supramaximal tests, whereas accO2dem increased significantly with and was linearly related to test duration in both Dysf and N. Consequently, %Anaer and %Aer decreased and increased, respectively, with increasing test duration but did not differ between Dysf and N in 1–2 min, 2–3 min, and 3–4 min tests. Our study demonstrates a similar relative anaerobic vs. aerobic contribution to total energy release during supramaximal effort in Dysf and N. This finding indicates that energetic metabolism during supramaximal exercise is exercise tolerance independent and that relative anaerobic vs. aerobic contribution in this effort domain remains the same within the physiology- or pathology-induced limits to individual peak exercise performance.

EXERCISE ENERGETIC METABOLISM is impaired in patients with left ventricular dysfunction in both cardiac and skeletal muscle (4, 19). Aerobic energy release at peak exercise (Vo2peak) is classically reduced (2), and its evaluation has become part of the routine clinical assessment of these patients, since the degree of its reduction is a strong prognostic marker (15). On the contrary, anaerobic metabolic pathways have received less attention. In patients with left ventricular dysfunction, anaerobic energetic release during exercise has been evaluated only in effort intensity domains below Vo2peak (10, 20, 25, 27), but no data are available on the anaerobic energetic yield during supramaximal effort, i.e., above Vo2peak, which would describe the true anaerobic metabolism energetic potential. More importantly, a simultaneous evaluation of maximal activation of both anaerobic and aerobic systems would examine the anaerobic/aerobic interaction under conditions of maximal stress.

We recently proposed the maximal accumulated oxygen deficit (MAOD) as a descriptor of the maximal amount of energy obtainable from anaerobic metabolism in stable chronic heart failure patients (20) and demonstrated the safety of its determination in this population. This makes it possible to directly measure maximal anaerobic energy release in the effort supramaximal domain, i.e., at powers evolving by definition Vo2peak (34), offering for the first time the possibility to simultaneously evaluate the maximal activation of both anaerobic and aerobic metabolic systems and obtain a complete and coherent description of exercise energetic metabolism in patients with left ventricular dysfunction.

The aim of the present study was thus to apply the above-mentioned findings to the evaluation of the relative anaerobic vs. aerobic contribution to total energy release during supramaximal effort in patients with symptomatic and asymptomatic left ventricular dysfunction and to compare it with that of an age-matched group of normal subjects to gain new insight into left ventricular dysfunction exercise pathophysiology.

METHODS

Study population. We studied 19 male patients with left ventricular dysfunction (Dysf) and 17 normal male subjects. Patients were selected according to the following criteria: 1) history of ischemic or idiopathic dilated cardiomyopathy with or without symptoms and clinical episodes of heart failure; 2) echocardiographic left ventricular ejection fraction of ≤40%; 3) cardiopulmonary exercise test (CPX) stopped for fatigue and/or dyspnea with ventilatory anaerobic threshold (VAT) identification and peak respiratory exchange ratio of ≥1.10; 4) absence of angina and/or instrumentally inducible myocardial ischemia and/or evidence of complex ventricular arrhythmias; 5) stable medications with no exacerbation of symptoms or need for intravenous inotropic support in the 6 mo before assessment. Thirteen Dysf had a history of chronic heart failure (New York Heart Association class I–II), whereas the remaining six did not. All patients underwent an echocardiographic evaluation within 5 ± 2 days of the baseline CPX. Recruitment criteria for normal subjects (N) were 1) no history of cardiac or noncardiac disease; 2) normal resting ECG; 3) CPX stopped for fatigue and/or dyspnea with VAT identification and peak respiratory exchange ratio of ≥1.10.

The protocol was approved by the Central Ethics Committee of the S. Maugeri Foundation, and informed, written consent was obtained from all participants in the study.

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Anthropometric evaluation. Three skinfold thicknesses were measured in all subjects according to standard procedures (8) by means of a Lafayette caliper. The skinfold sites used were chest, abdomen, and thigh. Body density was calculated using the Jackson-Pollock prediction equations for white male adults (24), and percent body fat was determined by the Siri formula (24).

Ergometric evaluation. All subjects underwent 1) a baseline ramp CPX for VO2peak and VAT assessment; 2) three moderate-intensity constant-power exercise tests for determination of the VO2/power relationship; 3) three supramaximal constant-power exercise tests for MAOD measurement. The terms “moderate-intensity” and “supramaximal” are to be intended as lower than VAT power and higher than peak power reached at CPX, respectively. All tests were performed on a bicycle ergometer (Ergometrics 800S; Sensormedics, Yorba Linda, CA).

Ramp CPX. After a 2-min unloaded cycling warm-up period, a ramp protocol of 10 or 15 W/min (Dysf) and 15 or 20 W/min (N) was started, and participants were encouraged to exercise until exhaustion. Respiratory gas exchange measurements were obtained breath by breath using a computerized metabolic cart (Vmax29; Sensormedics). VO2peak was the mean oxygen uptake (VO2) value observed during the last 30 s of the exercise period. Predicted maximal VO2 was determined by using a sex-, age-, and protocol-specific formula outlined by Wasserman (32), and VAT was estimated by the V-slope and/or MAOD measurement. The terms “moderate-intensity” and “supramaximal” are to be intended as lower than VAT power and higher than peak power reached at CPX, respectively. All tests were performed on a bicycle ergometer (Ergometrics 800S; Sensormedics, Yorba Linda, CA).

Supramaximal constant-power exercise tests. During the 2 wk following performance of moderate-intensity tests, all subjects underwent three supramaximal constant-power exercise tests with respiratory gas exchange measurement at powers equal to 30%, 60%, and 90% of the VAT power. Tests were performed in a random sequence on separate days. After a 3-min resting baseline period, subjects started pedalling at the established power, which was maintained for 10 min at a pedalling rate of 60 revolutions/min (rpm).

Supramaximal constant-power exercise tests. During the 2 wk following performance of moderate-intensity tests, all subjects underwent three supramaximal constant-power exercise tests with respiratory gas exchange measurement, in which the power was adjusted to cause exhaustion in ~1–2 min, 2–3 min, and 3–4 min on the basis of previous data from our laboratory (19). After a 4-min warm-up at an intensity of 30% peak power at baseline CPX and a 2-min rest period, subjects attained a pedaling rate of 60 rpm within 20 s, and then the established power was applied. Verbal motivation was provided by the experimenters, and the test ended when patients or subjects were unable to maintain 50 rpm. Tests were performed in random order and separated by a rest period of at least 48 h.

Data analysis. Slope and intercept of the VO2/power relationship were determined for each subject by calculating the regression of the estimated VO2 (estVO2) was determined. Assuming oxygen demand to be constant during the exercise period, MAOD was then calculated as the difference between the accumulated oxygen demand and the measured accumulated oxygen uptake as follows (20):

\[
\text{MAOD (mL/kg)} = \left[\text{estVO2/60} \cdot T \right] - \left(\sum_{i=1}^{n} \text{measVO2/60} \cdot T\right)
\]

where estVO2 is expressed in milliliters per kilogram per minute, T is test duration expressed in seconds, n is the number of 10-s periods composing the exercise phase, measVO2 is the VO2 mean value for each 10-s period expressed in milliliters per kilogram per minute, and t is equal to 10 s. Because patients and subjects did not reach exhaustion at precise 10-s intervals, the measVO2 of the last 10-s interval of the exercise period (i.e., that containing the residual exercise seconds) was divided by 60 and then multiplied by the number of residual seconds, and the result was added to measured accumulated VO2.

Percent anaerobic (%Anaer) and aerobic (%Aer) contributions to total energy release were then calculated as follows:

\[
\%\text{Anaer} = \frac{\text{MAOD}/[(\text{estVO2/60}) \cdot T]}{100} \quad (2)
\]

\[
\%\text{Aer} = 100 - \%\text{Anaer} \quad (3)
\]

Brain-natriuretic peptide level evaluation. At the beginning of the study protocol, in all Dysf patients, a blood sample was collected by venipuncture into EDTA tubes, kept at room temperature, and analyzed within 15 min of the draw time. Before analysis, each tube was turned upside down several times to ensure homogeneity. Brain-natriuretic peptide (BNP) was measured by using a fluorescence immunoassay for the quantitative determination of BNP in whole blood and plasma specimens (Triage BNP Test; Biosite, San Diego, CA).

Statistics. Unpaired t-tests were used to compare the means of quantitative variables. Linear regression and Pearson’s product-moment coefficients were used to determine the correlation between measured variables. The level of statistical significance was set at a two-tailed P value of ≤0.05. For t-tests evaluating differences between %Anaer and %Aer mean values of Dysf and N at different supramaximal test durations, the smallest difference physiologically worth detecting was considered to be 25%; accordingly, for such an effect size and a two-tailed α value = 0.05, a sample size of at least 15 subjects for each of the two study groups was required to yield a statistical power of >80%. The StatView 5.0.1. (SAS Institute, Cary, NC) and Power And Precision 2 (Biosoft, Englewood, NJ) software packages were used for statistical calculations.

RESULTS

Demographic, clinical, and ergometric characteristics. Study groups were well matched as to age, weight, body mass index, and lean body mass values (Table 1). All Dysf patients showed severely dysfunctioning and dilated left ventricles, and all were on β-blockers and ACE inhibitors (Table 1).

At baseline CPX, Dysf had VO2 and power mean values lower than N, both at VAT and peak effort; however, VAT VO2 expressed as a percentage of VO2peak did not differ between the two groups (Table 2). VO2peak of Dysf expressed as a percentage of age- and sex-predicted maximum indicated a reduced aerobic power, whereas that of N was very close to 100% of

Table 1. Demographic and clinical characteristics

<table>
<thead>
<tr>
<th>Dysf</th>
<th>N</th>
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<tbody>
<tr>
<td>n</td>
<td>19</td>
</tr>
<tr>
<td>Age, yr</td>
<td>66±5</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>77±9</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.5±2</td>
</tr>
<tr>
<td>Lean body mass, kg</td>
<td>60±7</td>
</tr>
<tr>
<td>NYHA class</td>
<td>2.1±0.5</td>
</tr>
<tr>
<td>LVFE, %</td>
<td>27±10</td>
</tr>
<tr>
<td>LVEDV, ml/m²</td>
<td>126±50</td>
</tr>
<tr>
<td>β-blockers, n (%)</td>
<td>19 (100)</td>
</tr>
<tr>
<td>ACE-inhibitors, n (%)</td>
<td>19 (100)</td>
</tr>
<tr>
<td>BNP, pg/ml</td>
<td>175±75</td>
</tr>
</tbody>
</table>

Values are means ± SD, number, or percentage. Dysf, patients with left ventricular dysfunction; N, normal subjects; BMI, body mass index; NYHA, New York Heart Association; LVFE, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; ACE, angiotensin-converting enzyme; BNP, brain natriuretic peptide.
EFFORT ENERGY RELEASE IN LEFT VENTRICULAR DYSFUNCTION

Table 2. Ergometric characteristics

<table>
<thead>
<tr>
<th></th>
<th>Dysf</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak power, W</td>
<td>105±13*</td>
<td>181±19</td>
</tr>
<tr>
<td>Peak VO2 ml/min</td>
<td>1,302±154*</td>
<td>2,444±155</td>
</tr>
<tr>
<td>Peak VO2, ml·kg⁻¹·min⁻¹</td>
<td>17·1±2·2*</td>
<td>28±5·4</td>
</tr>
<tr>
<td>%Predicted VO2max</td>
<td>62±9*</td>
<td>102±14</td>
</tr>
<tr>
<td>Peak VO2, ml·kg⁻¹·min⁻¹</td>
<td>1,490±192*</td>
<td>2,850±183</td>
</tr>
<tr>
<td>Peak RER</td>
<td>1·14±0·03</td>
<td>1·17±0·04</td>
</tr>
<tr>
<td>Peak VE, l/min</td>
<td>56±16*</td>
<td>85±13</td>
</tr>
<tr>
<td>Peak HR, beats/min</td>
<td>127±15†</td>
<td>161±20</td>
</tr>
<tr>
<td>Peak SBP, mmHg</td>
<td>155±24†</td>
<td>203±23</td>
</tr>
<tr>
<td>VAT power, W</td>
<td>55±15*</td>
<td>82±17</td>
</tr>
<tr>
<td>VAT VO2, ml·kg⁻¹·min⁻¹</td>
<td>10·2±1·5†</td>
<td>15·9±4</td>
</tr>
<tr>
<td>VAT VO2%</td>
<td>59±8</td>
<td>56±5</td>
</tr>
</tbody>
</table>

Values are means ± SD. VO2, oxygen uptake; VO2max, maximal VO2; VO2peak, peak VO2; CO2 uptake; RER, respiratory exchange ratio; VE, ventilation; HR, heart rate; SBP, systolic blood pressure; VAT, ventilatory anaerobic threshold; VAT VO2%, VO2 at VAT as percentage of peak VO2. *P < 0.005 vs. N. †P < 0.001 vs. N.

predicted (Table 2). Ventilation, heart rate, and systolic blood pressure mean values at peak effort were significantly lower in Dysf than in N, whereas peak respiratory exchange ratio did not differ between the two groups (Table 2).

Relative anaerobic and aerobic contribution to total energy release during supramaximal effort. Mean peak power was significantly lower in Dysf than N for each supramaximal test duration, and corresponded to 145 ± 20%, 124 ± 15%, and 110 ± 10% of peak power at baseline CPX for 1–2 min, 2–3 min, and 3–4 min supramaximal tests, respectively (Table 3). Mean durations of 1–2 min, 2–3 min, and 3–4 min supramaximal tests in the total study population were 93 ± 15, 139 ± 19, and 216 ± 40 s, respectively, with no differences between Dysf and N.

MAOD, i.e., anaerobic contribution to total energy release, and accumulated oxygen demand mean values were significantly lower in Dysf than N for each supramaximal test duration; however, MAOD did not vary with increasing duration of supramaximal tests in the two groups, whereas accumulated oxygen demand did increase significantly (Table 3). Accordingly, %Anaer and %Aer decreased and increased, respectively, with increasing test duration (Fig. 1). Of note, accumulated oxygen demand was linearly related to test duration in both Dysf and N (r = 0·72 and 0·91, respectively; both P < 0·001); as a consequence, %Anaer and %Aer did not differ between Dysf and N for each test duration considered (45 ± 8% vs. 45 ± 9% at 1–2 min test, 35 ± 10% vs. 32 ± 11% at 2–3 min test, and 23 ± 9% vs. 25 ± 11% at 3–4 min test for %Anaer; Fig. 1). The same was true also for %Anaer and %Aer mean values in symptomatic and asymptomatic Dysf patients (44 ± 3% vs. 47 ± 5% at 1–2 min test, 32 ± 8% vs. 38 ± 10% at 2–3 min test, and 23 ± 7% vs. 26 ± 9% at 3–4 min test for %Anaer).

Since MAOD values did not differ with increasing supramaximal test duration in both groups, the mean MAOD value of the three tests (meanMAOD) was calculated for each participant in the study. MeanMAOD correlated significantly with VO2peak (Fig. 2), VAT VO2, and percent of predicted maximal VO2 values in the total study population (r values between 0·74 and 0·77; all P < 0·0001). Moreover, no relationship was found between both meanMAOD and VO2peak values and those of blood natriuretic peptide levels in the Dysf group (r = 0·24 and 0·41, respectively; both P > 0·20).

DISCUSSION

The main finding of this study is that relative anaerobic vs. aerobic contribution to total energy release during comparable relative supramaximal effort is similar in patients with symptomatic and asymptomatic left ventricular dysfunction and...
When VO₂ on-kinetics descriptors are normalized for VO₂peak absolute, exercise intensities are considered (10, 20, 27) or subjects. On the contrary, when matched relative, rather than energetic release (17).

evaluation allows a reasonable estimate of anaerobic energy demand (as expressed by slower VO₂ on-kinetics and/or larger oxygen deficit) than normal subjects when matched absolute workloads are considered (10, 20, 25, 27). This is expected when considering that, in this case, patients are working at a higher percentage of their VO₂peak (and possibly at a lower delta VO₂/delta power) than normal subjects. On the contrary, when matched relative, rather than absolute, exercise intensities are considered (10, 20, 27) or when VO₂ on-kinetics descriptors are normalized for VO₂peak values (25), a similar anaerobic contribution in patients and normal subjects is evident. However, in the moderate-intensity domain, determination of the relative anaerobic contribution to total energy release is strictly protocol dependent, since, by definition, no fatigue is expected to occur and exercise duration is set by operators, i.e., the longer the exercise duration the lower the relative anaerobic energetic release, whereas in the high/very high domain the appearance of the VO₂ slow component makes a precise definition of oxygen deficit impossible (34). Conversely, during supramaximal effort, the relative anaerobic contribution to total energy yield is unequivocally measurable since exercise duration (and thus accumulated energy demand) has a finite value, and MAOD evaluation allows a reasonable estimate of anaerobic energetic release (17).

This study evaluated for the first time such parameters during supramaximal effort in patients with left ventricular dysfunction, revealing that the relative anaerobic vs. aerobic contribution to total energetic yield is similar to that of normal subjects at comparable relative effort intensities, notwithstanding significantly different absolute workloads. Such a finding is matched to that of similar times to exhaustion at comparable effort relative intensities in the two groups, which strengthens still further the concept of a similar anaerobic vs. aerobic energetic contribution in Dysf and N. Moreover, %Anaer and %Aer values were strikingly close to those reported in normal subjects for similar test durations, obtained by fitting data from over 30 studies using various methods for anaerobic vs. aerobic contribution determination (7). Interestingly, the same results were obtained when symptomatic and asymptomatic Dysf patients were compared; this is of note, considering that asymptomatic Dysf patients have usually been found to have a physiological and metabolic response to effort very close to that of normal subjects (9).

Pathophysiological correlates. A tendency toward a higher reliance than normal subjects on anaerobic energetic metabolism during effort is classically described in patients with left ventricular dysfunction, as witnessed by a more rapid depletion of PCR stores and the development of higher intracellular acidosis (14, 16, 37), a reduced aerobic enzyme activity together with reduced mitochondrial volume (5, 21, 29), and the shift to a higher percentage of type II fibers and myosin heavy chains (26, 31) with respect to normal subjects. Our whole body metabolic data do not fit with this picture, showing a normal-like relative anaerobic vs. aerobic energetic yield in both symptomatic and asymptomatic patients with left ventricular dysfunction during supramaximal effort. This apparent contradiction may be due to several reasons. Indeed, authors who used magnetic resonance spectroscopy for metabolic analyses evaluated patients and controls at matched absolute workloads, thus with patients working at a higher percentage of their peak exercise capacity. On the other hand, histological studies may suffer from limitations such as high interindividual muscle fiber-type proportion and enzyme activity composition variability (28), large overlap in enzyme activity levels between fast and slow skeletal muscle fibers (23), and existence of hybrid fibers, i.e., containing three or more myosin heavy chain isoforms (23), which may complicate inferences from biopptic studies dealing with energetic metabolism. In addition, several lines of evidence suggest the possibility of a maintained relative aerobic energetic yield in patients with left ventricular dysfunction. First, phase II of VO₂ on-kinetics, which reflects normal-like relative anaerobic vs. aerobic energetic yield in both symptomatic and asymptomatic Dysf patients have usually been found to have a physiological and metabolic response to effort very close to that of normal subjects (9).

Relative anaerobic and aerobic contribution to total energy release. The contribution of anaerobic metabolism to exercise energetic needs has been evaluated in patients with left ventricular dysfunction in the effort moderate- and high-/very high-intensity domains (10, 20, 25, 27). Available data indicate that patients with left ventricular dysfunction have a higher anaerobic energetic yield (as expressed by slower VO₂ on-kinetics and/or larger oxygen deficit) than normal subjects when matched absolute workloads are considered (10, 20, 25, 27). This is expected when considering that, in this case, patients are working at a higher percentage of their VO₂peak (and possibly at a lower delta VO₂/delta power) than normal subjects. On the contrary, when matched relative, rather than absolute, exercise intensities are considered (10, 20, 27) or when VO₂ on-kinetics descriptors are normalized for VO₂peak values (25), a similar anaerobic contribution in patients and normal subjects is evident. However, in the moderate-intensity domain, determination of the relative anaerobic contribution to total energy release is strictly protocol dependent, since, by definition, no fatigue is expected to occur and exercise duration is set by operators, i.e., the longer the exercise duration the lower the relative anaerobic energetic release, whereas in the high/very high domain the appearance of the VO₂ slow component makes a precise definition of oxygen deficit impossible (34). Conversely, during supramaximal effort, the relative anaerobic contribution to total energy yield is unequivocally measurable since exercise duration (and thus accumulated energy demand) has a finite value, and MAOD evaluation allows a reasonable estimate of anaerobic energetic release (17).

This study evaluated for the first time such parameters during supramaximal effort in patients with left ventricular dysfunction, revealing that the relative anaerobic vs. aerobic contribution to total energetic yield is similar to that of normal subjects at comparable relative effort intensities, notwithstanding significantly different absolute workloads. Such a finding is matched to that of similar times to exhaustion at comparable effort relative intensities in the two groups, which strengthens still further the concept of a similar anaerobic vs. aerobic energetic contribution in Dysf and N. Moreover, %Anaer and %Aer values were strikingly close to those reported in normal subjects for similar test durations, obtained by fitting data from over 30 studies using various methods for anaerobic vs. aerobic contribution determination (7). Interestingly, the same results were obtained when symptomatic and asymptomatic Dysf patients were compared; this is of note, considering that asymptomatic Dysf patients have usually been found to have a physiological and metabolic response to effort very close to that of normal subjects (9).
fast phenotype transition. Finally, MAOD and \( V_{O2\text{peak}} \) have been proposed to be strictly related (34), as confirmed in vivo both in normal subjects and patients with left ventricular dysfunction in this and a previous study from our laboratory (20), underlining that anaerobic and aerobic metabolic contributions can be considered as separate entities but as closely linked and coordinated energetic systems (3).

As a whole, these findings provide a rational basis to the preserved proportionality between anaerobic and aerobic energetic contributions during supramaximal effort observed in our patients, at least at the disease stages evaluated in this study. Such a constancy of the relative anaerobic/aerobic energy release, observed in this and other papers over the whole range of effort intensity domains, can be seen as a basal and inherent characteristic of human metabolism during transitions from lower to higher energy demand levels, revealing a similar response to relatively similar metabolic “error signals” (13) within the physiology- or pathology-induced limits to individual exercise tolerance. Moreover, the finding of a preserved anaerobic/aerobic energy release ratio in Dysf patients argues for a coordinated adaptation of energetic metabolic pathways to the disease pathophysiological picture (12). Finally, the influence of neurohormonal factors on the relative anaerobic and aerobic energetic yield during effort in Dysf patients remains to be determined, even if the absence of a significant influence of neurohormonal factors on the relative anaerobic to the disease pathophysiological picture (12). Finally, the influence of neurohormonal factors on the relative anaerobic and aerobic energetic yield during effort in Dysf patients remains to be determined, even if the absence of a significant relationship between both MAOD and \( V_{O2\text{peak}} \) and BNP levels seems to exclude a link between neurohormonal activation and energetic metabolism during effort, at least at the disease stages evaluated in this paper.

The extrapolation of the below-anaerobic threshold \( V_{O2/W} \) relationship to the supramaximal domain of effort used in this study for MAOD determination may be questioned, since the appearance of a \( V_{O2} \) slow component during a constant-power exercise above anaerobic threshold would alter the \( V_{O2/W} \) relationship, projecting the \( V_{O2} \) steady-state value (when attainable) at values higher than expected according to the below-anaerobic threshold \( V_{O2/W} \) relationship (33). However, it has been shown that, at supramaximal powers such as those evaluated in this study, test duration is too short to let the slow component appear or be detectable (11, 22, 33–35), which lends support to the methodology we used for MAOD determination.

In conclusion, this study demonstrates the existence of a similar relative anaerobic vs. aerobic metabolism contribution to total energy release during supramaximal effort in patients with symptomatic and asymptomatic left ventricular dysfunction and normal subjects. Such a behavior seems to describe an inherent characteristic of the anaerobic/aerobic interaction during effort in humans within the physiology- or pathology-induced limits to individual exercise tolerance. Further data are needed to confirm the whole body energetic picture described in this study, which could be substantiated by taking into consideration patients with pathologies other than left ventricular dysfunction in which a reduced exercise tolerance is part of the clinical picture.

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