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Willem Gosens, MSc; Alex J. van't Hul, PhD; Joost M. Oomen, PhD; Matthijs K. C. Hesselink, PhD; Lars B. Borghouts, PhD

■ **PURPOSE:** The primary aims of this study were (1) to evaluate whole-body mechanical efficiency (ME) in a large group of chronic obstructive pulmonary disease (COPD) patients with a wide range of degrees of illness and (2) to examine how ME in COPD is related to absolute work rate and indices of disease severity during exercise testing.

■ **METHODS:** A total of 569 patients (301 male patients; GOLD stage I: 28, GOLD stage II: 166, GOLD stage III: 265, and GOLD stage IV: 110) with chronic obstructive pulmonary disease (COPD) were included in the data analysis. Individual maximal workload (watt), peak minute ventilation ($\dot{V}_E$, L/min body temperature and pressure, saturated), and peak oxygen uptake ($\dot{V}O_2$, mL/min standard temperature and pressure, dry) were determined from a maximal incremental cycle ergometer test. Ventilatory and metabolic response parameters were collected during a constant work rate test at 75% of the individual maximal workload. From the exercise responses of the constant work rate test, the gross ME was calculated.

■ **RESULTS:** The mean whole-body gross ME was 11.0 ± 3.5% at 75% peak power. The ME declined significantly ($P < .001$) with increasing severity of the disease when measured at the same relative power. Log-transformed absolute work rate ($r = .87$, $P < .001$) was the strongest independent predictor of gross ME. Body mass was the single other variable that contributed significantly to the linear regression model.

■ **CONCLUSIONS:** Gross ME in COPD was largely predicted by the absolute work rate ($r = .87$; $P < .001$) while indices of the severity of the disease did not predict ME in COPD.

K E Y W O R D S

COPD

exercise test

mechanical efficiency

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The authors declare no conflicts of interest.

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Chronic obstructive pulmonary disease (COPD) is clinically characterized by an exertional dyspnea, fatigue, and exercise intolerance. As a consequence, patients with COPD have a reduced ability to perform activities of daily life[1] and experience impaired quality of life.[2] The underlying mechanisms of symptoms and exercise intolerance are complex, may vary from patient to patient, and are still a topic of debate.[3] Several of these mechanisms may potentially result in an increase in the metabolic demand per unit of external mechanical work, and as a consequence, negatively affect the mechanical efficiency (ME) for whole-body exercise.[4] Mechanical efficiency of an activity is defined as the ratio of external work relative to energy expenditure.[4] A diminished ME has been suggested to exacerbate the clinical impact of COPD and may result in exercise intolerance.[5] These findings have been interpreted to suggest particular strategies for rehabilitation.[5,6] Only a few studies, however, have evaluated ME in patients with COPD and reported conflicting results. Perrault et al[7] found no difference in ME during cycling ergometry between patients with moderate to severe COPD and age-matched healthy controls, despite

elevated ventilation and dynamic hyperinflation in COPD. By contrast, others have suggested a reduced net ME in patients with COPD when compared with reference values of healthy subjects.[6,8,9] However, as COPD is characterized by exercise intolerance, patients are limited to modest absolute work rates during exercise testing. Ettema et al[10] showed that absolute work rate explains approximately 90% of the gross ME in healthy subjects.[10] The low absolute work rates used in previous studies investigating ME in COPD might therefore have confounded the observation of impaired ME in these patients. Thus, we hypothesized that absolute work rate is the major determinant of gross ME during cycle ergometry in patients with COPD.

Determining the mechanisms responsible for exercise intolerance in COPD is of utmost importance to design optimal rehabilitation programs. Therefore, the primary aims of this study were (1) to evaluate whole-body ME in a large group of COPD patients with a wide range of degrees of illness and (2) to examine how ME in COPD is related to absolute work rate and indices of disease severity during exercise testing.

METHODS

Patients with COPD categorized according to the criteria set by the Global Initiative for Obstructive Lung Disease scientific committee[11] who were referred for pulmonary rehabilitation at Revant Rehabilitation Center in Breda, The Netherlands, were studied. The institutional ethical review board approved this study.

Post–bronchodilator forced expired ventilation in 1 second (FEV_1) was used to classify the patients into the appropriate GOLD stage.[11] Patients included with COPD (GOLD stages I-IV) were clinically stable. Patients had stopped smoking, were at least 40 years old, and had no evidence of cardiac disease at the time of the assessments. Exclusion criteria for this study were comorbidities that could influence the test results (ie, skeletal muscle problems) and the presence of exacerbations in the 8 weeks preceding measurements. Furthermore, all patients requiring supplemental oxygen were excluded because no metabolic measurements could be performed in the laboratory. Patients with a constant work rate performance <4 minutes during the constant work rate test (CWRT) were excluded from the test because measurement of oxygen uptake may be underestimated in these patients. Data were collected over a 4-year period (2007-2010).

Pulmonary Function

Pulmonary function measurements (spirometry, static lung volumes, and carbon monoxide transfer factor) were collected using automated equipment (MS-PFT and MS-Body, Viasys Healthcare, Höchberg, Germany) and according to recommended standards.[12] Measurements were related to reference values from Quanjer et al.[13]

Body Mass and Body Mass Index

Body mass was determined using a mechanical weight scale (model 761, Seca, Hamburg, Germany). Patients wore only underwear during the weighing. Height was measured using a wall-mounted stadiometer with individuals standing barefoot. Body mass index was calculated dividing body mass by squared height (kg/m^2).

Six-Minute Walk Distance

The 6-minute walk distance was evaluated in a gymnasium with a square track of 5 by 10 m. Patients were instructed to walk as many meters as possible in 6 minutes and were allowed to stop and rest during the test, if necessary. During the test, patients were encouraged in a standardized manner.[14]

Maximal Incremental Exercise Test

A symptom-limited exercise test was performed according to the American Thoracic Society/American College of Chest Physicians recommendations[15] on an electromagnetically braked cycle ergometer (Ergoselect 1000 LP/1000 LK, Ergoline, Bitz, Germany) to determine maximal power output. Peak minute ventilation ($\dot{V}_E$, L/min body temperature and pressure, saturated) and peak pulmonary oxygen uptake ($\dot{V}O_2$, mL/min standard temperature and pressure, dry) were measured with a breath-by-breath automated exercise metabolic system (Oxycon Pro/Delta, Viasys Healthcare, Wuerzburg, Germany). Maximal workload in watts (W_{max}) and peak $\dot{V}O_2$ were compared with the reference values from Jones et al.[16] Prior to the start of the test, spirometry was performed to be able to estimate peak $\dot{V}_E$.[17]

Constant Work Rate Test

The CWRT measurements were part of usual care at the rehabilitation center. Exercise endurance to a symptom-limited maximum was determined with a constant work rate exercise test on an electromagnetically braked cycle ergometer (Ergoselect 1000 LP/1000 LK Ergoline, Bitz, D-72475, Germany) at a work rate equal to 75% of the peak work rate attained in the earlier incremental test. Reliability and validity of this test have been shown to be good.[18,19] During testing, ventilatory and metabolic response parameters were collected with the

same metabolic cart as in the incremental exercise test (Oxycon Pro/Delta, Viasys Healthcare, Höchberg, Germany). Ventilatory responses included the measurement of inspiratory capacity (IC) at rest and at 2-minute intervals. To perform the IC maneuver, patients were instructed to make a maximal inspiration maneuver, after the end of a normal breath.[20] The maneuver ended with a normal, unforced expiration. The mean values of the last 20 seconds of metabolic and ventilatory variables of the CWRT were used for analysis to calculate the gross efficiency (GE).

Calculation of Gross ME

Mechanical efficiency is defined by the ratio of the external mechanical work in watts (W) to the metabolic energy expenditure expressed in joules per second (J/s): GE (%) = work rate [W]/energy expended [J/s] × 100% for an activity. According to Ettema et al,[10] gross ME is the most robust expression of ME. Gross efficiency is expressed as the percentage ratio of external work performed to the total energy expenditure during the cycle ergometry exercise. For the assessment of gross ME, metabolic and ventilatory variables were measured breath by breath during the CWRT performed at 75% of the maximal incremental exercise test by using a breathing mask. The abbreviated Weir equation was used to calculate the total energy expenditure during exercise from values of $\dot{V}O_2$ and carbon dioxide production ($\dot{V}CO_2$); EE = [3.9 ($\dot{V}O_2$ mL/min) + 1.1 ($\dot{V}CO_2$ mL/min)] (kcal/min).[21,22] Both total energy expenditure and external work were recalculated into kJ/min to allow the calculation of percent ME.

Statistical Analysis

Continuous data are presented as mean ± standard deviation. $P < .05$ was considered statistically significant. The mean gross ME was calculated for the population as a whole and for each GOLD stage. Differences in ME between the GOLD stages were assessed by means of 1-way analysis of variance. A Bonferroni *post hoc* test was used when appropriate, to evaluate differences between variables within groups. The maximum watts (W_{max}) data were not normally distributed; therefore, logarithmic transformation was used to normalize these. The Pearson correlation was used to calculate the degree of association between gross ME, patient characteristics, and clinical exercise characteristics. Associations > 0.2 were used in the linear regression model to assess the factors that predict gross ME. Multiple linear regression models were used with gross ME as the dependent variable, and patient characteristics and clinical exercise characteristics as independent variables. To compare our data with earlier studies, linear regression models were fitted with and without inclusion of absolute work rate as independent predictors of gross ME. SPSS version 19.0 for Windows (IBM, Chicago, IL) was used to analyze the data.

RESULTS

Five hundred sixty-nine patients (301 male) with COPD (28 GOLD stage I; 166 GOLD stage II; 265 GOLD stage III; and 110 GOLD stage IV) were included in the data analysis. All patients had a history of cigarette smoking but had quit smoking prior to inclusion in the study. Descriptive characteristics of age, gender, body mass index, pulmonary function, and GOLD stage, as well as clinical exercise data are provided in Table 1.

Mechanical Efficiency

The mean whole-body gross ME was 11.0 ± 3.5%. The gross ME declined significantly ($P < .001$) with increasing severity of the disease compared at the same *relative* workload as shown in Figure 1. There was a significant difference for ME between all GOLD stages, except between GOLD stages I and II.

Independent Predictors of Gross ME

FEV_1 ($R^2 = 0.55$; $P < .001$) was found to be the strongest independent predictor of gross ME when absolute work rate was excluded from the linear regression model explaining 31% of the variation ($R^2 = 0.31$; $P < .001$) in gross ME. Other variables that contributed to the linear regression model, as reflected by ΔR^2, were diffusing capacity of carbon monoxide and body mass (Table 2), while arterial oxygen tension at rest, residual volume, total lung capacity, and IC rest each contributed <0.02 to ΔR^2. When absolute work rate was included in the regression model, it was the strongest independent predictor of gross ME ($R^2 = 0.87$; $P < .001$). In that case, body mass was the only patient characteristic that contributed significantly to the linear regression model (Table 3).

DISCUSSION

This large-scale study demonstrated that, when patients are compared at the same *relative* workload, gross ME seemingly declines with increasing severity of disease in COPD. However, when gross ME is expressed as a function of *absolute* work rate, there is no relation between gross ME and indices of disease severity. Previous reports of a decreased ME in COPD in comparison to values in healthy controls should be interpreted in the light of these findings.

Table 1 • Patient Demographic and Clinical Characteristics

	GOLD I (n = 28)	GOLD II (n = 166)	GOLD III (n = 265)	GOLD IV (n = 110)	Total (N = 569)
Gender, male/female	14/14	73/93	144/121	70/40	301/268
Age, y	64 ± 10	63 ± 10[a]	63 ± 10[b]	60 ± 9	63 ± 9
BMI, kg/m^2	30.4 ± 6.3[c,d]	28.4 ± 5.8[a,e]	25.8 ± 5.2	24.4 ± 5.1	26.5 ± 5.7
$FEV_{1,}$ L	2.31 ± 0.70[c,d,f]	1.61 ± 0.46[a,e]	1.05 ± 0.26[b]	0.75 ± 0.17	1.22 ± 0.53
$FEV_{1,}$ % pred	87 ± 5	61 ± 8	39 ± 6	26 ± 5	45 ± 17
SVC, L	4.06 ± 1.22[c,d,f]	3.52 ± 0.95	3.42 ± 0.89	3.21 ± 0.71	3.44 ± 0.91
SVC, % pred	118 ± 16	106 ± 18	99 ± 15	86 ± 13	99 ± 18
FEV_1/VC, %	58 ± 9[c,d,f]	46 ± 9 [a,e]	32 ± 6[b]	24 ± 5	36 ± 11
TLC, L	6.68 ± 1.65[d]	6.37 ± 1.21[a,e]	7.16 ± 1.36[b]	7.89 ± 1.47	7.05 ± 1.46
TLC, % pred	113 ± 15	112 ± 17	122 ± 17	128 ± 19	120 ± 18
FRC, L	3.53 ± 1.19[c,d]	3.74 ± 0.83[a,e]	4.80 ± 1.03[b]	5.86 ± 1.34	4.63 ± 1.31
FRC, % pred	112 ± 31	124 ± 27	151 ± 28	181 ± 35	148 ± 36
RV, L	2.62 ± 0.78[c,d]	2.88 ± 0.59[a,e]	3.74 ± 0.80[b]	4.69 ± 1.15	3.62 ± 1.05
RV, % pred	118 ± 27	135 ± 31	171 ± 37	214 ± 51	166 ± 48
DL_{CO}, mMol/L/s	5.30 ± 1.46	4.74 ± 1.66	4.18 ± 6.09	3.33 ± 1.11	4.25 ± 4.34
DL_{CO}, % pred	64 ± 14	58 ± 16	46 ± 15	38 ± 12	49 ± 17
Pa_{O_2} rest, kPa	9.2 ± 0.9	9.3 ± 0.9	9.0 ± 0.9	8.7 ± 0.9	9.1 ± 0.9
Pa_{CO_2} rest, kPa	4.7 ± 0.4	5.0 ± 0.5	5.1 ± 0.6	5.5 ± 0.6	5.1 ± 0.6
6MWD, m	407 ± 111	421 ± 100[a]	406 ± 96[b]	360 ± 91	402 ± 99
6MWD, % pred	66 ± 15	68 ± 14	63 ± 13	53 ± 14	63 ± 15
W_{max}, watt	82 ± 36[c,d,f]	66 ± 35[a,e]	48 ± 25[b]	33 ± 16	52 ± 30
W_{max}, % pred	60 ± 19	51 ± 18	35 ± 15	22 ± 10	38 ± 19
Absolute work rate CWRT, W	61 ± 27[c,d,f]	50 ± 26[a,e]	36 ± 18[b]	24 ± 12	40 ± 23
Gross ME, %	13.7 ± 3.3[c,d]	12.6 ± 3.3[a,e]	10.7 ± 3.1[b]	8.7 ± 3.0	11.0 ± 3.5

Abbreviations: BMI, body mass index; CWRT, constant work rate test; DL_{CO}, diffusing capacity for carbon monoxide; FEV_1, forced expiratory volume in 1 second; FRC, functional residual capacity; Gross ME, gross whole-body mechanical efficiency; Pa_{CO_2}, arterial carbon dioxide tension; Pa_{O_2} rest, arterial oxygen tension; RV, residual capacity; SVC, slow vital capacity; TLC, total lung capacity; VC, vital capacity; W_{max}, maximal workload; 6MWD, 6-minute walk distance.

$P < .05$:

[a]Between GOLD II and GOLD IV.
[b]Between GOLD III and GOLD IV.
[c]Between GOLD I and GOLD III.
[d]Between GOLD I and GOLD IV.
[e]Between GOLD II and GOLD III.
[f]Between GOLD I and GOLD II.

It has been proposed that ME in COPD is decreased, caused by an increased energy demand of breathing.[6,23,24] If the additional ventilatory work required to overcome the increased airway resistance in COPD would significantly increase oxygen utilization of the respiratory muscles during exercise, and thereby metabolic rate,[25] ME would decline with increasing airway resistance. Another theoretical cause of impaired ME in COPD is the bioenergetic abnormalities found in skeletal muscle, such as muscle fiber type shifting from type I to II.[26] It has been suggested that the quadriceps femoris muscle in COPD patients is particularly affected,[27-29] thus impacting cycling and walking activities and possibly ME.[30]

We were able to identify a very limited number of previous, relatively small-scale studies evaluating ME in patients with COPD, which had significantly divergent conclusions. Perrault et al[7] concluded that

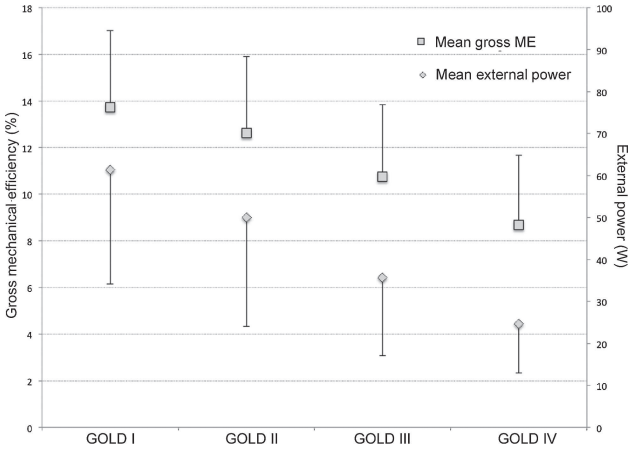

Figure 1. Mean gross mechanical efficiency calculated at the same relative workload (75% peak work rate) and the mean external power at which gross ME was calculated for patients in each GOLD stage. Abbreviations: GOLD, Global Initiative for Chronic Obstructive Lung Disease; ME, mechanical efficiency; W, watts.

ME during ergometry was not compromised in COPD but others have suggested a marked reduction.[6,9,31,32] Since gross ME during cycle ergometry is closely related to absolute work rate in healthy subjects,[10] we hypothesized that differences in absolute work rate between the assessment of ME in COPD and healthy subjects might account for the discrepancies previously reported for ME in COPD and healthy subjects.

At a relative workload of 75% W_{peak}, we observed a mean gross ME during submaximal cycling of 11.0 ± 3.5% and a significant decline in gross ME with progressing GOLD stages. The difference between GOLD stages I and II was nonsignificant, however, which could possibly be attributed to a relatively small sample in the GOLD stage I group (n = 28). The apparent relation between gross ME and disease severity was seemingly confirmed when FEV_1 was found to be the main predictor of gross ME in our regression model that included only patient characteristics (Table 2). However, when the absolute work rate during cycle ergometry was included to the model, this explained 75% of the variation in gross ME. Thus, body mass remained as the sole patient characteristic adding significantly to the model (Table 3). Therefore, ME in patients with COPD is largely explained by the absolute work rate during cycle ergometry at which ME is calculated. This is in agreement with data in healthy subjects where absolute work rate explains an even greater proportion (approximately 90%) of the variation in efficiency.[10] This difference in the strength of the relationship between gross ME and absolute work rate in patients with COPD and healthy subjects may be partially attributable to indices of disease severity in COPD, but this needs further study. Other likely candidates to explain differences in ME between studies are pedaling cadence and techniques, familiarization with the exercise, and population characteristics, since these are all known to affect ME in humans.[10,33]

In COPD, an increased severity of disease is associated with decreased exercise tolerance. In our study, this was demonstrated by the significant decline in

Table 2 • Regression Models for Gross Mechanical Efficiency in COPD (Log-Transformed Absolute Work Rate Excluded)

Dependent Variable: Gross Mechanical Efficiency in COPD	R^2	ΔR^2	β
Model 1: F_{change} (1, 508) = 222.79; $P < .05$	0.31		
Constant			
FEV_1			0.55[a]
Model 2: F_{change} (2, 507) = 131.80; $P < .05$	0.34	0.03	
Constant			
FEV_1, L			0.40[a]
DL_{CO}, mMol/L/s			0.25[a]
Model 3: F_{change} (3, 506) = 107.65; $P < .05$	0.39	0.05	
Constant			
FEV_1, L			0.43[a]
DL_{CO}, mMol/L/s			0.39[a]
Body mass, kg			−0.27[a]

Abbreviations: β, beta coefficient; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; DL_{CO}, diffusing capacity for carbon monoxide.
[a]$P < .05$.

Table 3 • Regression Models for Gross Mechanical Efficiency in COPD (Log-Transformed Absolute Work Rate Included)

Dependent Variable: Gross Mechanical Efficiency in COPD	R^2	ΔR^2	β
Model 1: F_{change} (1, 538) = 1678.47; $P < .05$	0.75		
Constant			
Log-transformed absolute work rate, W			0.87[a]
Model 2: F_{change} (2, 537) = 1150.20; $P < .05$	0.81	0.06	
Constant			
Log-transformed absolute work rate, W			0.97[a]
Body mass, kg			−0.25[a]

Abbreviations: β, beta coefficient; COPD, chronic obstructive pulmonary disease.
[a]$P < .05$.

peak work rate with increasing severity of disease (Figure 1). As a consequence, there were significant differences in absolute work rates between GOLD stages when tested at the same *relative* power. During cycling, gross ME decreases rapidly at low absolute work rates in healthy subjects. When gross ME is expressed as a function of *absolute* work rate, there is no relation between gross ME and indices of disease severity (Table 3). The impact of work rate on gross ME diminishes strongly above approximately 150 W in healthy subjects.[10] Our study suggests that this pattern of gross ME, as a function of external power, is similar in COPD (Figure 2). When we plotted our results for gross ME as a function of external power in COPD against a large set of studies reviewed by Ettema and Lorås,[10] negligible differences were found between COPD and healthy subjects (Figure 3). We therefore assume that gross ME of cycling exercise in COPD is approximately equal to gross ME in healthy subjects, at least at the low absolute work rates commonly applied in COPD. Further studies, directly comparing patients and controls, are necessary to clarify whether this assumption is correct.

Since patients with COPD are uniformly restricted to low absolute work rates during submaximal exercise caused by their exercise intolerance, the ME in these patients will be decreased, by default, when compared with ME measured at higher absolute work rates in healthy subjects. Previous studies reporting impaired ME in COPD[6,8,9,32] might have been confounded by this effect. For example, Baarends et al[6] concluded that ME in COPD was decreased compared with ME in healthy

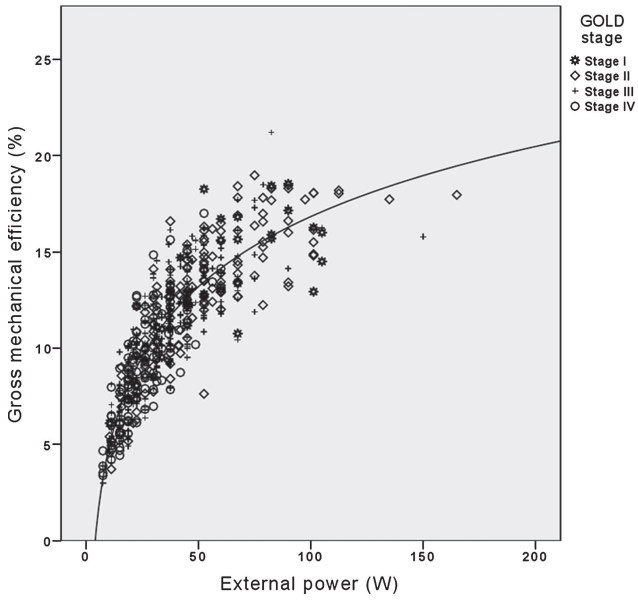

Figure 2. External power plotted against gross mechanical efficiency. $R^2 = 0.76$ (exponential function); $R = 0.87$. Abbreviations: GOLD, Global Initiative for Chronic Obstructive Lung Disease; W, watts.

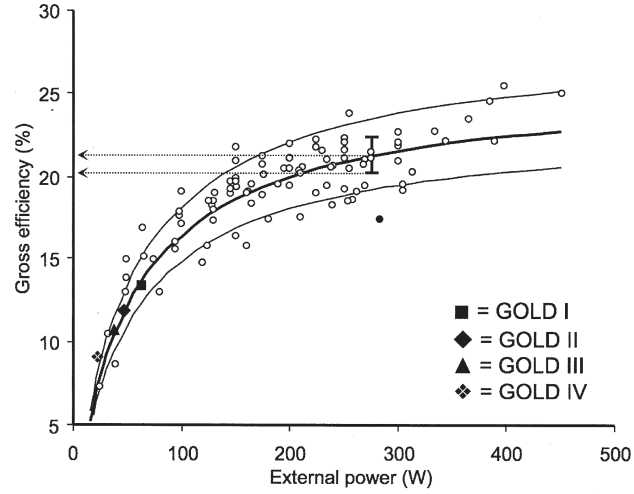

Figure 3. The figure shows an overview of data from the literature related to the quantification of efficiency. In this figure, external power is plotted against average gross ME in healthy subjects (open circles) as reviewed by Ettema et al[10] and depicts a possible measurement error of 5%. The thick, black curve is the average curve, based on the regression line from the studies included. Thinner curves indicate ranges if both metabolic rate and external power have a deviation (error) of 5% in either direction. The thick vertical error bar indicates the same range if only 1 of the measures had a 5% deviation and the horizontal arrows indicate the efficiency difference resulting from this error. The solid black circle symbol (•) represents the highest power in the study by Luhtanen et al.[29] The larger symbols (■, ♦, ▲, ❖) represent the mean gross ME in persons with COPD by GOLD stages in the present study. Abbreviations: COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ME, mechanical efficiency; W, watts.

subjects during submaximal cycling exercise.[6] However, this conclusion was based upon the comparison of their findings in COPD (a net ME of 15.5%) to a reference value in healthy subjects derived from another study (23%).[8] Although the mean absolute work rate at which ME was calculated was not reported, it can be assumed that the applied workload of 50% peak work rate in severe COPD (GOLD III) was significantly lower than that in healthy subjects calculated at the same relative workload. In an earlier study, Palange et al[8] did compare ME in COPD directly to a control group. Mechanical efficiency was again considered very low (16%) in COPD patients compared with healthy subjects (24.5%), but the absolute work rate at which ME was assessed was twice as high in healthy (50 W) subjects as in COPD patients (24 W). Similarly, Franssen et al[33] concluded that ME during cycling was decreased in COPD, although the absolute work rate at which ME was assessed was approximately 3 times higher in healthy controls (100 W) than in COPD patients (31 W). In addition, Franssen et al also concluded that arm ME, in contrast to leg ME, was relatively preserved in clinically stable COPD. The differences in absolute work rate between COPD and healthy controls in the arm exercise

experiment, however, were much smaller than in the leg exercise experiment and might therefore account for the assumedly "preserved" arm exercise ME in COPD.

In contrast, Perrault et al[7] concluded that cycling delta efficiency was not compromised in moderately severe COPD compared with healthy controls. In this study, delta ME (ie, the change in efficiency between different work rates) was calculated between relative cycling work rate of 20% versus 65% peak power. Again, patients had a significantly lower peak power than healthy controls and therefore lower absolute work rates at which delta ME was calculated. These differences in absolute work rates might have influenced the comparison of delta efficiency between COPD and healthy control subjects. Nonetheless, Perrault et al[7] found no differences in ($\dot{V}O_2$ (L/min) between COPD and healthy subjects at rest, during unloaded cycling and at the same absolute work rate of 20 W, which confirms the findings in this study.

For patients with COPD, the ability to perform large muscle mass physical activity such as cycling and walking is critical to activities of daily living. Therefore, our findings that there are no greater energy requirements in COPD patients during work of intensities comparable with activities of daily living may be used to reinforce the value of exercise for rehabilitation purposes. Furthermore, insight into the underlying mechanisms of exercise intolerance in COPD can inform decisions concerning rehabilitation strategies. The presumed attenuation of ME in patients with COPD has been used as an argument to emphasize the use of small muscle mass exercises,[32] maximal strength training of the legs,[5] and lower intensity training programs.[6] Although other (patho)physiological findings may possibly support these claims for the effectiveness of particular exercise programs in COPD patients, our study demonstrated that they are not corroborated by an altered ME.

In summary, this study demonstrates that when gross ME is expressed as a function of *absolute* work rate, there is no relation between gross ME and indices of disease severity in COPD. Further study is needed to evaluate whether gross ME, calculated at the same absolute work rate, is altered in COPD compared with healthy subjects.

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