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Original article

Energy expenditure in women and men with COPD

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SUMMARY

Background: Many patients with chronic obstructive pulmonary disease (COPD) lose weight. Successful nutritional intervention is vital, thus assessment of energy requirement is required. The aim of this study was to present an improved possibility to assess energy requirement in patients with COPD.
Methods: Pub Med search was conducted for all the studies reporting total energy expenditure (TEE) measured by doubly labeled water (DLW) method in patients with COPD. Four studies were identified, whereof three were conducted in Sweden. The present analysis is based on these three studies of which the data was acquired.
Results: There was a large variation in resting metabolic rate (RMR) and TEE. Body mass index decreased significantly with increase in disease severity ($p < .001$), and correlated significantly to forced expiratory volume in 1 s (FEV_1) % predicted ($r = .627$, $p < .001$). FEV_1% predicted had a significant correlation with RMR/kg body weight (BW)/day ($r = -.503$, $p = .001$), RMR/kg fat-free mass (FFM)/day ($r = .338$, $p = .031$), and TEE/kg FFM/day ($r = .671$, $p < .001$). Compared to men, women had a lower RMR and TEE/kg BW/day ($p < .001$ respectively $p = .002$), and higher RMR and TEE/kg FFM/day ($p = .080$ respectively $p = .005$). The correlates of: RMR/kg BW were gender and FEV1% predicted; of TEE/kg BW the correlates were age and gender, and of TEE/kg FFM the correlates were age and FEV1% predicted.
Conclusion: In this study, we have presented a possibility to assess energy requirement per kg BW/day and per kg FFM/day in patients with COPD in clinical settings. However, gender, age, and disease severity must be considered.

1. Introduction

A gradual and significant weight loss occurs in a considerable number of patients with chronic obstructive pulmonary disease (COPD) during the natural course of their illness [1,2]. The prevalence of weight loss in COPD has been reported in the range 25–50% [3], and can be a result of an inadequate energy intake, increased resting metabolic rate (RMR) [4], and/or increased activity energy expenditure (AEE) [5]. Low body-weight (BW), loss of BW, low body mass index (BMI) or fat-free mass index (FFMI) in patients with COPD has been related to osteoporosis, reduced performance, higher acute exacerbation, and increased morbidity and mortality [6–9].

Since many patients with COPD lose BW, nutritional intervention is important, thus assessment of energy requirement is necessary. Assessment of energy requirements in patients with chronic disease is often based on prediction equations of resting metabolic rate (RMR) and theoretical factors covering disease specific and physical activity effects on energy requirements [10]. These methods do however often provide inaccurate assessments [11,12], as patients with COPD of different disease severity may show large individual variation in RMR, total daily energy expenditure (TEE), and physical activity level (PAL) [13–15]. There is consequently a need for objective assessment of energy requirement in patients with COPD of different disease severity since it is important to give individual nutritional treatment [16].

Abbreviations: AEE, Activity energy expenditure; BMI, Body mass index; BW, Body-weight; COPD, Chronic obstructive pulmonary disease; DLW, Doubly labeled water; FFM, Fat-free mass; FFMI, Fat-free mass index; PAL, Physical activity level; RMR, Resting metabolic rate; TEE, Total daily energy expenditure.

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When a person is in weight equilibrium, TEE is equal to energy expenditure and thus can be used to assess energy requirement. The doubly labeled water method (DLW) is the "Gold Standard" for assessment of TEE. This method is demanding regarding laboratory availability, significant technical expertise required, high costs and patient compliance with regards to collecting urine samples. Consequently, the application of DLW method has been restricted in patients with COPD resulting in relatively few studies with moderately-sized COPD populations [5,15,17,18]. For the clinical purpose, it is important to know the TEE per kg BW or fat-free mass (FFM) in COPD patients so that the given nutritional treatment can be more individualized. To our knowledge, till date, only one study in COPD patients has shown TEE/kg BW/day or TEE/kg FFM/day measured by DLW [15]. A compilation of data from complementary studies is an attractive approach to increase the understanding of TEE and energy requirement in patients with COPD. Therefore, our aim was to present an improved possibility to assess energy requirement in patients with COPD based on compilation of all available data on TEE measured by DLW in this group of patients.

2. Material and methods

2.1. Study design

We searched Pub Med for all the studies reporting TEE measured by DLW method in patients with COPD. Mesh terms used were: energy expenditure and COPD; doubly labeled water and COPD; energy expenditure and DLW and COPD. Four studies were identified [5,15,17,18]. Three studies were conducted in Sweden, two in Gothenburg and one with the lead author in Umeå, and the present study is based on these three studies. The studies are referred to in chronological order as study-1 [15], study-2 [18], and study-3 [17]. The lead author Frode Slinde in studies-1 and 2 was contacted for data sharing, and the required raw data was acquired. All relevant data from study 1–3 were collected for analysis. As regards to the fourth study [5], at present, these data have not become available to be included in the present analysis.

2.2. Subjects

Study-1 included ten patients (five women and five men) with BMI $\leq$ 20 kg/m^2, and study-2 comprised of 15 patients (ten women and five men) with BMI < 21 kg/m^2. All patients in studies 1 and 2 had severe and stable COPD with forced volume in 1 s (FEV_1) < 50% predicted using the criteria from The European Respiratory Society [19]. In study-3, 19 women with stable COPD, GOLD 2–3 (FEV_1% predicted <80–30%) [20], and BMI 18.5–30 kg/m^2 were included. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria was used to define the disease severity [20]. All the three studies had more or less similar exclusion criteria namely, oxygen therapy, diabetes, thyroid dysfunction, cancer (studies 1–3), myopathic disease (study-3), and heart failure and (studies 1 & 2).

Therefore, the present study includes 44 patients (34 women and ten men) with stable COPD, FEV1 < 80% predicted, and BMI $\leq$ 30 kg/m^2.

2.3. Pulmonary function tests

In study-1 & 2, the pulmonary tests were performed using a Vitalograph spirometer (Selefa, Buckingham, Ireland) before and 15 min after inhalation of 1 mg terbutaline. In study-3, all the patients had COPD diagnosed by clinical investigation as well as post-bronchodilator spirometry with FEV_1/FVC < 0.7 prior to their inclusion in the study. For the study purpose, dynamic and static pulmonary function tests were performed (Jaeger, MasterScreen Body and MasterScreen PFT; CareFusion, Höchberg, Germany). In the present study, GOLD spirometry criteria was used to define disease severity [20]: GOLD 2 (moderate), 50% $\leq$ FEV1 < 80% of predicted values; GOLD 3 (severe), 30% $\leq$ FEV1 < 50% of predicted values; GOLD 4, (very severe), FEV1 < 30% of predicted values.

2.4. Body composition

Body-weight was measured with patients wearing light clothing to the nearest 0.1 kg, using a digital scale. The height was measured to the nearest 0.5–1 cm using a horizontal headboard with an attached wall-mounted metric scale. BMI was then calculated based on these measurements (BW in kg/height in m^2). Body composition was measured by dual energy X-ray absorptiometry (DXA) using a total body scanner in study-1 and 2 (Lunar Prodigy, GE Lunar Corp, Madison, USA), and in study 3 (Lunar Prodigy, version 13.31; Scanex Medical Systems, Helsingborg, Sweden). FFMI was calculated as FFM in kg/height in m^2.

The BMI cut-off for defining underweight was <22.5 kg/m^2 [21], and for FFMI, the cut-off for depletion was $\leq$15 (women) or $\leq$16 (men) kg/m^2 [3].

2.5. Energy expenditure

2.5.1. Resting metabolic rate

The RMR was measured by indirect calorimetry using a ventilated hood system in all the three studies. In Study-1 & 3 Deltatrac™ II Metabolic Monitor (Datex, Helsinki, Finland) was used, and in study-2 the equipment used was a Medical Graphics Corp. cardio pulmonary exercise system CPX (Medical Graphics Corporation, Minneapolis, USA). In all the measurements manufactures instructions for gas mixture calibration and room temperature were followed. Patients arrived on the test day in a fasting state, and the RMR of each patient was measured for 20–30 min after the patients had rested in a supine position for 30 min.

The RMR/kg BW/day (daily RMR, kJ/BW, kg), and RMR/kg FFM/day (daily RMR, kJ/FFM, kg) were calculated.

2.5.2. Total daily energy expenditure

The TEE was measured using the DLW method as described earlier [15,17,18]. The analysis of the DLW in all the three studies were conducted in the same laboratory. The DLW method involves administering a dose of stable isotopes of deuterium (^{2}H) and oxygen-18 (^{18}O), and subsequently measuring the rates of elimination of these isotopes from the body over time in urine samples. Urine samples were analyzed in triplicate using a Finnigan MAT Delta Plus Isotope-Ratio Mass Spectrometer (ThermoFinnigan, Uppsala, Sweden). The relationship between pool size deuterium (N_D) and pool size oxygen-18 (N_O) was used as a quality measurement. The acceptable range of this relationship (N_D/N_O) has been proposed by the International Atomic Energy Agency to be between 1.015 and 1.060 [22], and the range in the present study was 1.018–1.048. The respiratory quotient was set at 0.85 for calculations of the energy equivalence of CO_2 produced [23].

The TEE/kg BW/day (daily TEE, kJ/BW, kg), and TEE/kg FFM/day (daily TEE, kJ/FFM, kg) were calculated.

2.5.3. Activity energy expenditure and physical activity level

In the present study, AEE was defined as the energy expenditure for all the movements that were performed daily. The AEE was

Table 1
Patient characteristics of women and men with COPD.

	Present study			Study 1, 2003			Study 2, 2006			Study 3, 2013		
	N	Mean ± SD	Min-Max	N	Mean ± SD	Min-Max	N	Mean ± SD	Min-Max	N	Mean ± SD	Min-Max
Age, years	44	66.0 ± 7.5	47.0–80.0	10	63.0 ± 7.9	47–72	15	64.0 ± 8.0	53–74	19	69.2 ± 6.0	59.7–80.0
Women, n (%)	34 (77)			5 (50)			10 (67)			19 (100)		
FEV1, % predicted value	41	42.6 ± 16.7	19–78	10	30.8 ± 10.6	19–46	15	34.9 ± 9.4	20–49	16	56.0 ± 15.0	30–78
Disease severity, n (%)												
GOLD 2, 50% ≤ FEV1< 80% predicted	10 (24)			none			none			10 (62)		
GOLD 3, 30% ≤ FEV1<50% predicted	21 (52)			5 (50)			10 (67)			6 (38)		
GOLD 4, <30% predicted	10 (24)			5 (50)			5 (33)			none		
BMI, kg/m^2	44	21.4 ± 3.8	13.5–30.0	10	18.7 ± 1.2	16.8–20.6	15	19.1 ± 1.9	13.5–21.2	19	24.5 ± 3.5	18.5–30.0
FFMI, kg/m^2	44	14.4 ± 1.7	11.4–19.0	10	14.7 ± 2.2	11.4–17.2	15	14.7 ± 1.8	12.6–19.0	19	12.6 ± 1.3	10.3–16.0
Pack-years		NA			NA			NA		19	27.7 ± 9.0	14–42
Arterial pCO_2, kPa	41	5.2 ± 0.56	4.3–6.7	10	5.2 ± 0.58	4.5–6.2	15	5.2 ± 0.55	4.5–6.3	16	5.2 ± 0.6	4.3–6.7
Arterial pO_2, kPa	41	9.7 ± 2.2	4.4–18.4	10	9.3 ± 2.1	5.6–13.3	15	9.6 ± 1.4	8.1–12.6	16	10.2 ± 2.9	4.4–18.4
O_2 saturation		NA			NA		11	94.2 ± 2.0	91–98	19	96.3 ± 3.1	87–100
RMR, kJ/day	44	5039 ± 834	3617–7464	10	5580 ± 1214	3787–7467	15	5013 ± 644	4058–6276	19	4768 ± 601	3617–6248
TEE, kJ/day	44	7920 ± 1348	5197–11,075	10	8294 ± 1938	5197–11,075	15	7612 ± 1198	5313–10,173	19	7967 ± 1090	5318–10,258
AEE, kJ/day	44	2884 ± 847	723–4594	10	2715 ± 984	723–3611	15	2599 ± 850	1045–4148	19	3199 ± 693	1701–4594
PAL	44	1.58 ± .18	1.15–2.09	10	1.49 ± 0.17	1.15–1.80	15	1.52 ± 0.18	1.24–1.90	19	1.67 ± 0.15	1.46–2.09

FEV1, Forced expiratory volume in 1 s; BMI, body mass index; FFMI, fat-free mass index; NA, not available; RMR, resting metabolic rate; TEE, total energy expenditure; AEE, activity energy expenditure; PAL, physical activity level.

calculated as the difference between TEE and RMR (AEE = TEE − RMR), and PAL as TEE/RMR.

2.6. Statistics

The data were analyzed using the statistical program SPSS version 24.0 (Statistical Package for the Social Sciences; IBM Corporation, Armonk, NY, USA). Descriptive statistics, such as means, standard deviations, and minimum and maximum values, were used. To compare the means between women and men, independent *t*-tests were performed, and analysis of variance was used when means were compared by disease severity. We studied the correlation between the two variables using Pearson's correlation analysis. Multiple linear regression analysis was used to identify correlates of outcome measures of RMR, TEE, and AEE carried out in separate models. The covariates in each analysis were age, gender, FEV_1% predicted and FFM. The level of significance was set at 0.05.

3. Results

3.1. Patient characteristics

The patient characteristics are shown in Table 1. Seventy-six % of the patients had severe/very severe COPD. The proportion of patients with GOLD 2, 3 and 4 in women was 32%, 52%, and 16% respectively, and in men, 50% had GOLD 3 and 50% GOLD 4. The

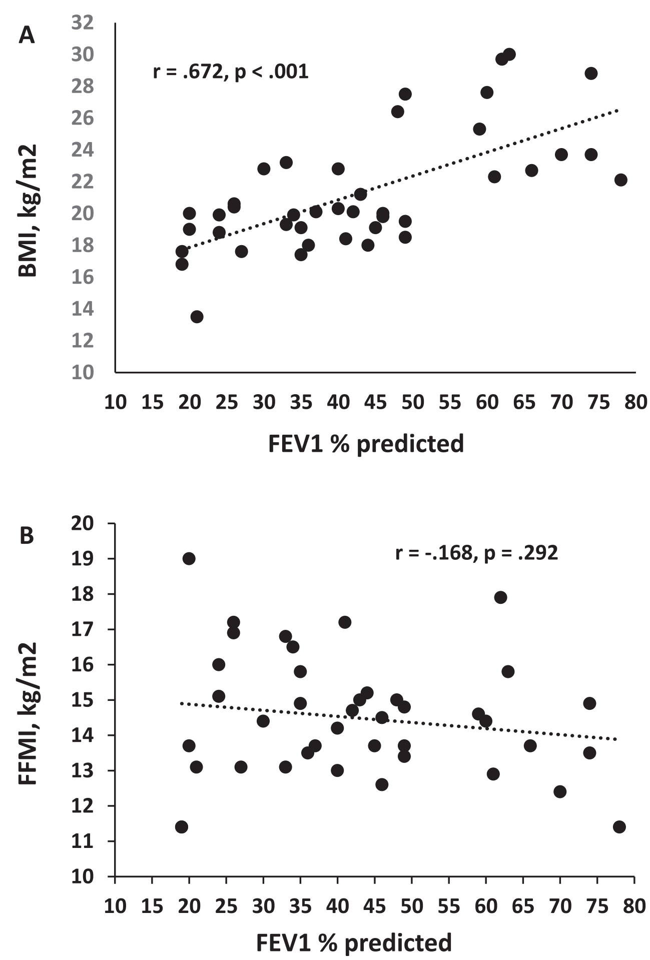

Fig. 1. Correlation between Forced Expiratory Volume in 1 s (FEV_1) % of predicted value and (A) BMI, kg/m^2, and (B) Fat-free mass index (FFMI), kg/m^2.

mean BMI and FFMI were low compared to reference values. Fifty % of the patients had BMI and FFMI less than the reference values, 27% had BMI ≥22.5 kg/m^2 and low FFMI, 18% had low BMI and normal FFMI, and 5% had normal BMI and FFMI. The RMR, TEE, AEE and PAL varied among the patients (Table 1).

The RMR and TEE had a significant association with FFM ($r = .820$, $p < .001$ respectively $r = .706$, $p < .001$), and FFMI ($r = .687$, $p < .001$ respectively $r = .673$, $p < .001$). BMI was significantly correlated to FEV1% predicted (Fig. 1). The PAL was significantly correlated to FEV1% predicted and BMI of the patients (Fig. 2). The calculated RMR, TEE and AEE per kg BW and kg FFM is shown in Table 2. There was a large variation in RMR, TEE, and AEE per kg BW, and per kg FFM.

3.2. Energy expenditure stratified by gender

Table 3 shows patient characteristics and energy expenditure stratified by gender. In the present analysis, the women had higher FEV_1% predicted and BMI than men ($p < .001$ respectively $p = .001$), and lower FFMI ($p < .001$). Compared to men, women had a lower RMR and TEE/kg BW/day ($p < .001$ respectively $p = .002$), and higher RMR and TEE/kg FFM/day ($p = .080$ respectively $p = .005$). Percent of FFM (mean ± SD) was 64 ± 9.3% in women, and 87 ± 5.7% in men, and this difference was associated with male sex ($\beta = 23.4$; 95% CI, 17.1 to 29.7; $p < .001$).

3.3. Energy expenditure stratified by disease severity

BMI in this study decreased significantly with increase in disease severity ($p < .001$) (Table 3). Patients with GOLD 3 and GOLD 4 had significantly higher RMR/kg BW/day and lower TEE- and AEE/kg FFM/day than patients with GOLD 2. Comparing by disease

Table 2
Resting metabolic rate, total energy expenditure, and activity energy expenditure measured by indirect calorimetry and doubly labeled water in 44 patients with COPD.

	Mean ± SD	Min-Max
RMR, kJ/kg BW/day	89 ± 16.6	62–135
RMR, kJ/kg FFM/day	130 ± 15.0	108–192
TEE, kJ/kg BW/day	139 ± 22.7	98–201
TEE, kJ/kg FFM/day	204 ± 29.6	142–318
AEE, kJ/kg BW/day	50 ± 13.4	15–75
AEE, kJ/kg FFM/day	75 ± 22.8	22–125

RMR, resting metabolic rate; BW, body-weight; FFM, fat-free mass; TEE, total energy expenditure; AEE, activity energy expenditure.

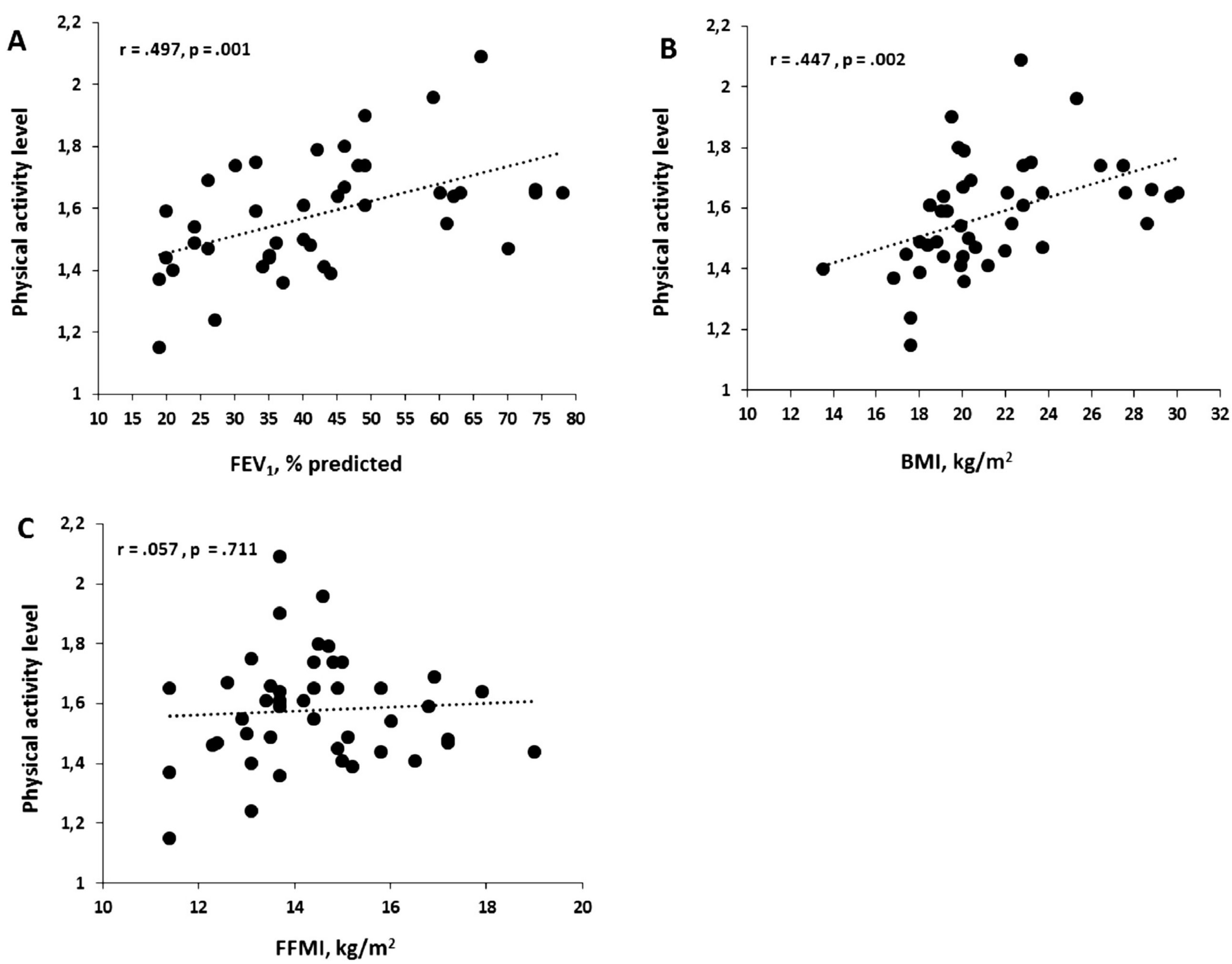

Fig. 2. Correlation between physical activity level and (A) Forced Expiratory Volume in 1 s (FEV_1) % of predicted value, (B) BMI, kg/m^2, and (C) Fat-free mass index (FFMI), kg/m^2.

Table 3
Patient characteristics, and energy expenditure in patients with COPD stratified by gender and by disease severity.

	Stratified by gender[a]			Stratified by disease severity[a]					
	Women N = 34	Men N = 10	P value	GOLD 2 N = 10	GOLD 3 N = 21	GOLD 4 N = 10	Gold 2 vs 3 P value	Gold 2 vs 4 P value	Gold 3 vs 4 P value
Age, years	67 ± 7.3	63 ± 7.8	.200	70.2 ± 7.5	64.7 ± 7.1	64.2 ± 8.3	.150	.185	.982
FEV1, % predicted value[b]	46.6 ± 16.9[c]	30.4 ± 8.3	<.001	67 ± 6.8	41 ± 6.1	23 ± 3.1	<.001	<.001	<.001
BMI, kg/m^2	22.1 ± 3.8	18.7 ± 2.1	.001	25.6 ± 3.2	20.5 ± 2.6	18.4 ± 2.2	<.001	<.001	.115
FFMI, kg/m^2	13.9 ± 1.3	16.3 ± 1.6	<.001	14.1 ± 1.8	14.6 ± 1.3	14.7 ± 2.6	.821	.767	.976
RMR, kJ/day	4727 ± 526	6087 ± 851	<.001	4862 ± 787	5025 ± 786	5326 ± 1066	.875	.458	.638
TEE, kJ/day	7591 ± 1176	9041 ± 1343	.002	8233 ± 1366	7949 ± 976	7735 ± 2054	.857	.706	.916
AEE, kJ/day	2864 ± 900	2955 ± 672	.770	3370 ± 834.9	2923 ± 617.4	2409 ± 1125.5	.338	.032	.242
PAL	1.61 ± .19	1.49 ± .10	.063	1.70 ± .19	1.59 ± .16	1.44 ± .16	.253	.004	.050
RMR, kJ/kg BW/day	84 ± 14.0	107 ± 12.1	<.001	76 ± 10.8	91 ± 17.4	99 ± 9.1	.020	.002	.522
RMR, kJ/kg FFM/day	132 ± 15.5	123 ± 10.7	.080	137 ± 22.4	127 ± 9.9	125 ± 14.2	.219	.242	.89
TEE, kJ/kg BW/day	134 ± 20.9	158 ± 18.3	.002	128 ± 20.0	144 ± 20.5	143 ± 23.3	.169	.363	.78
TEE, kJ/kg FFM/day	211 ± 29.0	182 ± 19.2	.005	232 ± 36.5	201 ± 14.5	180 ± 26.2	.007	<.001	.088
AEE, kJ/kg BW/day	50 ± 14.3	52 ± 10.3	.708	52 ± 13.5	53 ± 10.5	44 ± 17.3	.987	.324	.212
AEE, kJ/kg FFM/day	79 ± 23.3	59 ± 12.6	.015	94 ± 22.3	74 ± 16.5	55 ± 21.1	.025	<.001	.028

FEV1, Forced expiratory volume in 1 s; BMI, body mass index; FFMI, fat-free mass index; RMR, resting metabolic rate; TEE, total energy expenditure; AEE, activity energy expenditure; PAL, physical activity level; BW, body-weight; FFM, fat-free mass.
[a] Data are represented as mean ± SD.
[b] N = 41.
[c] N = 31.

severity, % of FFM (mean ± SD) in patients with GOLD 2 was significantly lower than GOLD 3 (55.5 ± 5.0% vs 71.9 ± 11.0%, p < .001), and GOLD 4 (55.5 ± 5.0% vs 79.9 ± 10.5%, p < .001).

3.4. Energy expenditure and lung function

The correlation between energy expenditure and FEV_1% predicted is shown in Fig. 3. FEV_1% predicted had a significant correlation with RMR/kg BW/day (r = −.503, p = .001), RMR/kg FFM/day (r = .338, p = .031), TEE/kg FFM/day (r = .671, p < .001), and AEE/kg FFM/day (r = .641, p < .001).

3.5. Correlates of energy expenditure

Multiple linear regression analysis performed separately revealed that FFM was independently correlated to RMR (β = 82.97, 95% CI, 49.7 to 116.2, p < .001), and TEE (β = 164.30, 95% CI, 113.1 to 215.5, p < .001) after adjusting for age, gender, and FEV1% predicted. In the separate analysis, RMR/kg BW/day respectively TEE/kg BW/day continued to be significantly lower in women than men after adjustment for age, FEV1% predicted and FFM (Table 4). The increase in age correlated independently with lower TEE/kg BW/day, TEE/kg FFM/day, AEE/kg BW/day, and AEE/kg FFM/day. FEV1% predicted had an independent negative association with RMR/kg BW/day, and correlated positively with TEE/kg FFM/day, AEE/kg BW/day, and AEE/kg FFM/day after adjusting for age, gender and FFM (Table 4).

4. Discussion

In the present study we have presented energy expenditure per kg body-weight and per kg fat-free mass measured by the Gold Standard DLW method in patients with COPD that may be applied for assessment of energy requirement in clinical settings. BMI had a strong positive correlation with FEV1% predicted. The FFM was strongly correlated with both RMR and TEE. The RMR- and TEE/kg BW/day correlated inversely with FEV1% predicted indicating an increase in energy expenditure as lung function worsens in COPD. There was a large individual variation in RMR, TEE, AEE and PAL. The correlates of: RMR/kg BW were gender and FEV1% predicted; of TEE/kg BW the correlates were age and gender, and of TEE/kg FFM the correlates were age and FEV1% predicted.

In the first ever DLW study conducted in patients with COPD by Baarends et al. [5], the average RMR, TEE, and AEE were higher than in the present study. Although the age, BMI, and FEV1% predicted did not differ much between the Baarend's study and the present report, the difference in energy expenditure can be attributed partly to the gender and body composition of the participants. In the former study [5], all participants were men, whereas, in the present study most were women. No data on FFM was presented in the Baarend's study, whereas, we found that the FFM continued to be significantly correlated with RMR and TEE after adjusting for age, gender and FEV1% predicted. It has become more evident that FFM is the primary determinant of RMR [24]. The effect of FFM on RMR depends on factors such as its quantity and metabolic activity, which might be influenced by race, gender, physical activity, functional- and health status. Furthermore, our results suggest that the BMI increases with better lung function. Large population-based studies have shown that BMI is not only related to disease severity in COPD but also have suggested that low BMI is a risk factor for developing COPD [25,26].

Exploring the gender differences, women in the present study had a significantly lower energy expenditure despite having a higher FEV1% predicted, BMI, and PAL than men. Further, the RMR- and TEE/kg BW were significantly lower, and TEE/kg FFM was higher in women than in men. These differences can be attributed partly to a higher FFM and a lower lung function in men and gender differences. There are reports suggesting that the relationship between energy intake and energy expenditure is different in men and women [27]. The reason for these gender differences in energy metabolism is not known; however, it may relate to sex steroids, differences in insulin resistance, or metabolic effects of other hormones such as leptin [27]. Further, the difference in energy expended by the vital organs such as the brain, heart, liver, kidneys, etc. which have a high metabolic rate may also influence the energy expenditure [28].

The TEE decreased, whereas RMR increased, with increased disease severity in the studied COPD patients, suggesting that with disease progression patients with COPD decrease their physical activity. A finding further strengthened by a significant positive correlation between PAL and FEV1% predicted, indicating that the PAL in COPD patients decreased with disease severity. In a controlled trial, patients with COPD had a normal TEE despite an elevated RMR, and it was concluded that COPD patients reduce

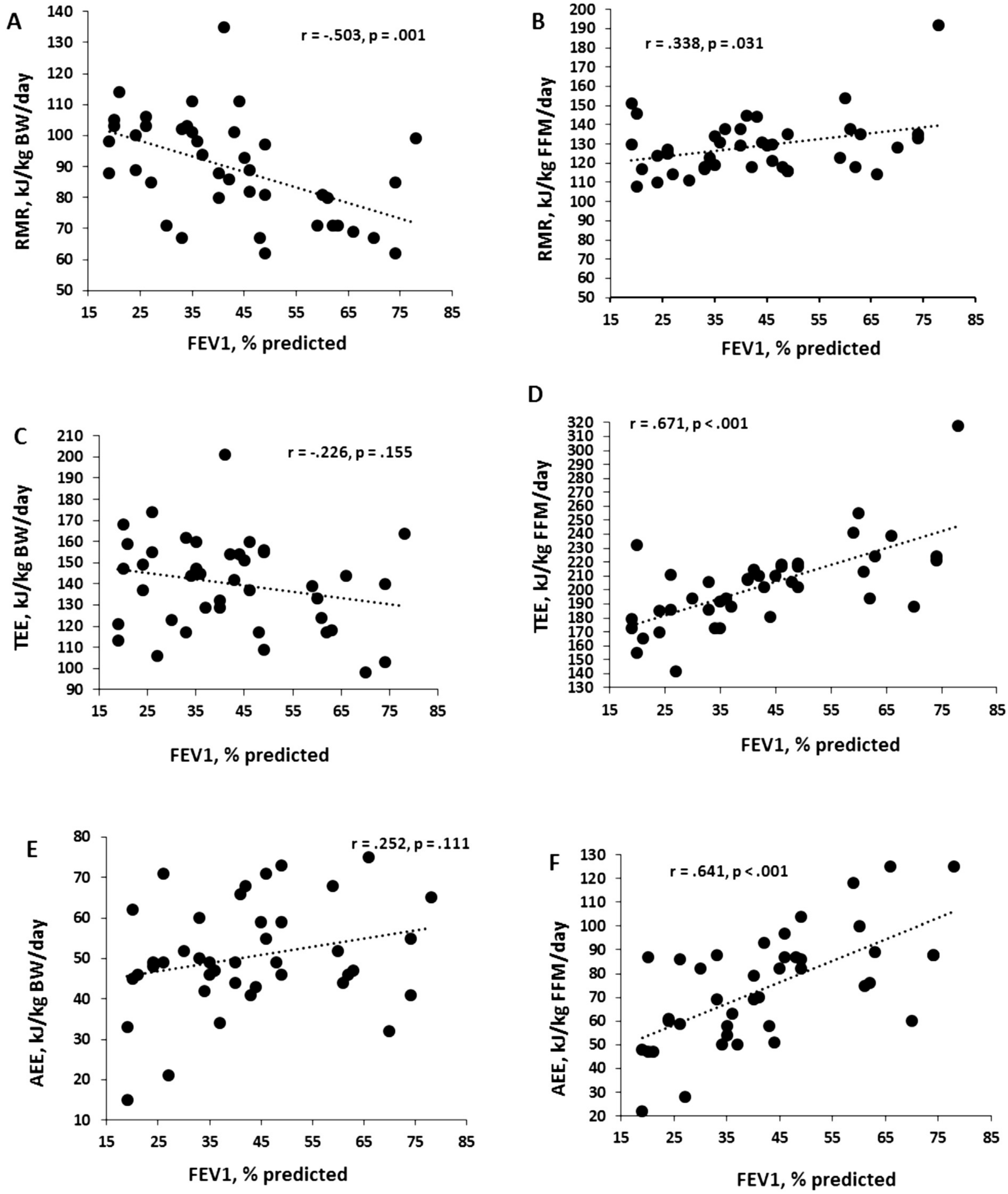

Fig. 3. Correlation between FEV1% predicted and (A) RMR, kJ/kg BW/day; (B) RMR, kJ/kg FFM/day; (C) TEE, kJ/kg BW/day; (D) TEE, kJ/kg FFM/day; (E) AEE, kJ/kg BW/day; (F) AEE, kJ/kg FFM/day.

their PAL [29]. Furthermore, physical activity measured as PAL, steps/day, or time spent in moderate physical activity (>3 METS) has been shown to decrease as disease severity increases [30]. Reduced physical activity in patients with COPD has been associated with higher values of systemic inflammation and left cardiac dysfunction [30]. Further, we found that the FEV_1% predicted correlated significantly with different measures of energy expenditure suggesting an increase in RMR- and TEE/kg BW with a decrease in FEV_1% predicted values. The increased RMR and TEE has been shown to be associated with disease severity and can partly be contributed to an increase in the energy cost of breathing [31,32]. Other possible reasons can be the bronchodilation medication, hypoxia and systemic inflammation [32].

This study has both strengths and limitations. The strengths are that the RMR and TEE are measured with Gold Standard methods; the analysis of the DLW was conducted in the same laboratory; the patients included had stable COPD, as the majority of COPD patients are in that state at any given point of time. A limitation is that

Table 4
Multiple regression analysis of correlates of measures of RMR, TEE, and AEE in patients with COPD.

	RMR, kJ/kg BW/day β coefficient (95% CI)[a]	RMR, kJ/kg FFM/day β coefficient (95% CI)[a]	TEE, kJ/kg BW/day β coefficient (95% CI)[a]	TEE, kJ/kg FFM/day β coefficient (95% CI)[a]	AEE, kJ/kg BW/day β coefficient (95% CI)[a]	AEE, kJ/kg FFM/day β coefficient (95% CI)[a]
Age, years	−.180 (−.72 to .36)	−.180 (−.77 to .41)	−.923 (−1.7 to −.13)*	−1.094 (−2.0 to −.19)*	−.745 (−1.3 to−.23)*	−.913 (−1.7 to −.18)*
Gender (women vs men)	26.45 (11.5 to 41.4)**	10.819 (−5.6 to 27.2)	27.282 (5.0 to 49.4)*	−2.132 (−27.4 to 23.2)	.772 (−13.5 to 15.0)	−12.948 (−33.5 to 7.6)
FEV1, % predicted	−.298 (−.57 to −.03)*	.250 (−.05 to .54)	.033 (−.37 to .43)	1.154 (.70 to 1.6)***	.332 (.08 to .59)**	.909 (.54 to 1.3)***
FFM, kg	−.679 (−1.53 to .17)	−1.209 (-2.1 to -.28)*	−.410 (−1.7 to .85)	−.856 (−2.3 to .58)	.269 (−.54 to 1.1)	.349 (−.82 to 1.5)
R^2	.48	.27	.34	.58	.29	.52

*P < .05.
**P < .01.
***P < .001.
RMR, resting metabolic rate; TEE, total energy expenditure; AEE, activity energy expenditure; BW, body-weight; FFM, fat-free mass; FEV1, Forced expiratory volume in 1 second.
[a] Refers to unstandardized coefficients of the independent variables in the linear regression model with RMR, TEE, and AEE as the dependent variables.

different devices were used for measuring pulmonary function, and body composition. It has been reported that using different DXA devices may result in 1–7% variation in body composition measures [33]. The patients included in this study are a selected group with regards to gender, BMI, and FEV_1% predicted. The distribution of gender across the range of COPD severity was not uniform. Data from larger COPD populations would, therefore, be beneficial, and would be a valuable addition to further studies. So far the complexity and costs associated with DLW based studies have largely led to moderately sized COPD populations to be included. Rabinovich et al. conducted a DLW study in 80 patients with COPD [14]. The aim of the study was to validate physical activity monitors, and the TEE data measured by DLW was not presented.

The current findings of energy expenditure are shown by BW and FFM with the aim of applying these findings for the assessment of energy requirement, both in the primary health care and in hospitals. Body weight measurements are much more common in primary health care as well as in hospital setting than measuring body composition, although body composition measures are desirable and provide information about proportions of FFM, fat-mass, and bone mineral content [34]. Energy metabolism is a complex process, which can be affected by many factors. This process is even more complicated in patients with chronic disease such as COPD. There is a considerable individual variation in energy expenditure and requirements. In Sweden, evidence-based National clinical guidelines for the treatment of patients with COPD are available [35]. The guidelines include issues with malnutrition, nutritional treatment, assessment of energy requirement, and recommend 146–167 kJ/kg BW/day. Compared with the results of the current analysis, the national recommendations for energy requirements are higher, and lack gender differentiation, although, we found gender differences in energy expenditure. Besides, age and FEV_1% predicted were correlated with energy expenditure. Therefore, when applying the current findings in clinical settings, gender, age, and disease severity of the individual COPD patient need to be considered, and it is imperative to follow-up the patient when nutritional treatment is given.

5. Conclusion

In this study, an improved possibility to assess energy requirement in patients with COPD in clinical settings is suggested. We have presented energy requirement as RMR and TEE per kg BW/day and per kg FFM/day in patients with COPD. However, gender, age, and disease severity must be considered as these variables have an association with the energy expenditure. There is a need to establish detailed guidelines and recommendations for energy requirements in COPD. Further studies measuring energy expenditure with DLW in patients with COPD that include a larger population of women and men in all GOLD stages are warranted.

Conflict of interest

None of the authors have any personal or financial conflicts of interest to report.

Author declaration

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

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