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Energy expenditure in chronic obstructive pulmonary disease – evaluation of simple measures

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Running title: Energy expenditure in COPD

ABSTRACT

Background & Objectives: Almost 50% of all COPD patients become underweight. One possible reason for nutritional treatment to fail could be miscalculation of patients' energy requirements. The aim of this study was therefore to evaluate simple measures that may be used to assess the energy requirement of COPD patients.

Subjects & Methods: This cross-sectional evaluation study includes 68 COPD patients (42 women). Resting metabolic rate (RMR) was assessed by indirect calorimetry while total energy expenditure was assessed by a 7-day monitoring using the ActiReg. Simple measures to evaluate was body weight (kg) multiplied by 125 kJ (30 kcal), predicted RMR multiplied by 1.7 and two simple questionnaires.

Results: Mean physical activity level (PAL) from the ActiReg was 1.46. Calculation of energy expenditure multiplying body weight with 125 kJ resulted in a total energy expenditure (TEE) of 8614 kJ compared to ActiReg 8317 kJ (p=0.10). To multiply predicted RMR by 1.7 resulted in a statistically significant overestimation of 1335 kJ (p<0.01). Both questionnaires showed a clear "dose-response" regarding PAL from ActiReg in the different activity categories.

Conclusion: This study shows that simple measures of energy expenditure could, on group level, assess COPD patient's energy needs. However, for individual assessment of energy need, more thorough procedures are necessary.

Trial registration: ClinicalTrials.gov NCT01179178

Key words: Physical activity, malnutrition, energy requirements, ActiReg

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is one of the leading causes of death in Sweden as well as in many other countries (Hoyert et al. 2006; WHO 2008; Socialstyrelsen 2010). Almost 50% of all COPD patients become underweight and several studies have shown that a low body mass index (BMI) or body composition with low fat-free mass index (FFMI), is a major mortality risk factor (Gray-Donald et al. 1996; Schols et al. 1998; Slinde et al. 2005; Hitzl et al. 2010). Studies aiming at improving the nutritional situation in malnourished patients with COPD have shown variable results (Sridhar et al. 1994; Slinde et al. 2002; Creutzberg et al. 2003; Weekes et al. 2009). In addition to recurrent illness and loss of appetite, miscalculation of patients' energy requirements could be one possible reason for nutritional treatment to fail.

In previous studies we demonstrated a great variation in total energy expenditure among underweight patients with COPD (Slinde et al. 2003; Slinde et al. 2006). Doubly labelled water (DLW) is considered to be the gold-standard for assessment of total energy expenditure (IAEA 2009) but is too complicated and expensive to be performed in clinical praxis. We have previously presented an activity monitor, ActiReg, to be valid to assess energy expenditure in COPD (Arvidsson et al. 2006). This is an easier and less expensive method compared to DLW. However, it is a cumbersome system for the clinical practitioner to use, and the probability to incorporate the system into clinical practice is low.

In this paper we therefore evaluate very simple measures which could be used to assess the energy requirement of COPD patients.

PATIENTS AND METHODS

The Regional Ethical Review Board, Gothenburg, Sweden previously approved the procedures used in the study. The patients were informed of the nature and purpose of the study and written informed consent was given.

Patients

The patients in the study were recruited from the out-patient unit at the Department of Respiratory Medicine, Sahlgrenska University Hospital, Göteborg, Sweden.

The inclusion criteria were: diagnosis of COPD, smoking history of > 10 pack years (number of years smoking > one pack (n=20) cigarettes per day), age over 45 yrs, a spirometry test performed during the 12 last months showing a FEV₁/FVC ratio less than 0.7, FEV 1.0 < 60% of predicted normal. The exclusion criteria were inability to perform investigations without oxygen supply, inability to contribute at the investigations, other severe diseases such as malignancy in an unstable phase, chronic heart failure, metabolic disease or renal failure.

Study design

This cross-sectional evaluation study comprised of one visit at the hospital and one week of activity monitoring in free-living conditions. For the study visit the patient had to be fasting during 12 hours before arrival to the hospital.

Anthropometric measurements

Height was measured to the nearest 0.5 cm using a horizontal headboard with an attached wall-mounted metric rule. Patients were weighed without shoes in underwear on a digital balance to the nearest 0.1 kg (Weighcare, Newhaven, England). BMI was calculated as weight (kg) divided by height² (m).

Pulmonary function tests

Spirometry was performed on a Spirometer SensorMedics model 922, (SensorMedics Co, Palm Springs,USA). Prediction normal values according to the European Respiratory Society equations (Quanjer et al. 1993) were used.

Resting Metabolic Rate (RMR)

RMR was measured by indirect calorimetry using a ventilated-hood system. The equipment used was a DeltatracTM II Metabolic Monitor (Datex, Helsinki, Finland). Before each measurement, the equipment was calibrated with gas mixtures of known O₂ and CO₂ contents according to the manufacturer's instructions. All subjects were measured after an overnight fast. After a 30 min rest in the supine position, RMR was measured during 30 min when the subjects were awake. The measurements were performed in an environmental temperature between 22-23° C. The presented mean RMR for each patient was based on the last 25 min of the measurement. RMR was also calculated using the WHO equations(FAO/WHO/UNU 1985).

Total energy expenditure - measured

During the first seven days following the study visit, an ActiReg® was used to monitor physical activity in the patients. The ActiReg is using combined recordings of body position and motion to measure physical activity (Hustvedt et al. 2004) and consists of two pairs of position and motion sensors connected by cables to a storage unit fixed to a waist belt. ActiReg has been shown to have good validity in patients with severe COPD (Arvidsson, Slinde et al. 2006). Sensors were attached by medical tape to the chest and the right thigh and the patients were requested to use ActiReg continuously during seven days, except during night and during bathing or taking a shower. The results were analysed in the computer

program ActiCalc that enables calculation of the total daily energy expenditure, based on the measured RMR.

Total energy expenditure - calculated

Two different, in the clinic often used, calculations were performed; body weight (kg) multiplied by 125 kJ (30 kcal) and predicted RMR multiplied by 1.7, as shown to be characteristic for patients with COPD by Baarends et al (Baarends et al. 1997).

Total energy expenditure - based on questionnaires

Two different questionnaires were used in the study. In the first questionnaire (Q1) (Sonn et al. 1993), the patient was asked to circle the description which most properly describe her physical activity (PA). The patient can describe her PA from one of six alternatives from one ("hardly any PA at all") to six ("hard exercise regularly and several times per week, the physical effort is large, such as running and skiing").

The second questionnaire (Q2) (Saltin et al. 1968) consists of two questions. Question one concerns occupational work or housekeeping ("how much do you physically move and exert yourself at work or during housekeeping") and the patient can describe her PA from one of five alternatives from zero ("not working, no housekeeping") to four ("I have a heavy manual work, lifts heavy objects and physically exerts myself much. Examples are lumberjack, dock worker, stone mason, farm worker, fishing using heavy equipment, heavy construction work"). Question two concerns leisure time activities and the patient was asked to choose the category corresponding to her own physical activity. The patient can describe her leisure time PA from one of four alternatives from one ("Sedentary leisure time. I mostly take up reading, embroidery, TV, cinema or other sedentary activities during my leisure time") to four

("Regular hard exercise or competitive sport. I go in for hard exercise and competitions in running, orienteering, skiing, swimming, soccer, handball etc regularly and at least four times a week"). The score from the first question was added to the second question giving possible results from one (not working, no housekeeping and sedentary leisure time) to eight (heavy manual work and hard exercise or competitive sport).

Separately for each questionnaire, a mean value of PAL from ActiReg was assessed from the individuals having answered the same activity category. Total energy expenditure based on each questionnaire was then calculated as predicted RMR (WHO) multiplied by the mean PAL for the different activity categories from the questionnaires.

Statistical analysis

All results are presented as mean (SD). Gender differences were studied using Student's *t*-test while comparison between methods were studied using paired *t*-tests and Bland-Altman analysis (Bland et al. 1986). Statistical analysis of the different activity categories in the questionnaire was done using ANOVA with Tukey's post hoc test.

RESULTS

Sixty-eight patients (42 females and 26 males) completed all measurements. Females had statistical significantly lower body weight and height (table 1). No statistical significant differences between genders were found in BMI or pulmonary function. Calculated RMR from WHO equations did not significantly differ from measured RMR (p=0.88) (table 2). Mean physical activity level (PAL) from the ActiReg was 1.46 (table 2). Calculation of energy expenditure multiplying body weight with 125 kJ resulted in a total energy expenditure (TEE) of 8614 kJ compared to ActiReg 8317 kJ (p=0.10). To multiply predicted RMR by 1.7 resulted in a statistically significant overestimation of 1335 kJ (p<0.01) (table 2).

Figure 1 presents the individual results. Panel A shows that calculated RMR differed ± 1000 kJ from the measured RMR. Calculation of energy expenditure multiplying body weight with 125 kJ differed ± 4000 kJ from the measured TEE and when multiplying predicted RMR by 1.7 most often results in an overestimation of TEE with up to 4000 kJ.

From questionnaire one (Q1), a clear "dose-response" could be shown regarding PAL from ActiReg in the different activity categories (table 3). None of the patients graded themselves to category five or six. The patients that answered category three or four, had a statistical significantly higher PAL from ActiReg compared to the patients in category one or two. No significant differences were found between categories one and two, or between categories four and five.

From questionnaire two (Q2), also a clear "dose-response" could be shown regarding PAL from ActiReg in the different activity categories (table 4). One patient graded herself to category six while none of the patients graded themselves to category seven or eight. The

patients that answered category three, four or five, had a statistical significantly higher PAL from ActiReg compared to the patients in category one. No significant differences were found between the other categories.

Calculated energy expenditure from Q1 did not statistically significant differ from measured TEE by ActiReg (p=0.76) (table 5). This was also the case with Q2 (p=0.87) (table 5). Figure 2 shows that both questionnaires however overestimate TEE in patients with low TEE and underestimates TEE in patients with high TEE.

DISCUSSION

Overall, the very simple measures used to assess the energy expenditure in COPD patients in this study, corresponded well to the patient's energy expenditure, at group level. The only measure not fitting this group well was the 1.7 times RMR since the patients showed not to have such high physical activity level. The questionnaires evaluated in this study performed surprisingly well. However, none of the methods met up to the standards required for assessment of energy expenditure at an individual level. This did not though come as a surprise. We have in earlier studies shown, both in COPD patients (Slinde, Ellegård et al. 2003), and in adolescents (Slinde et al. 2003), that simple measures of physical activity have a low precision in predicting energy expenditure. A comprehensive review of the literature also concluded that care must be taken when using questionnaires to quantify amount of physical activity in COPD (Pitta et al. 2006).

Hence, if a more accurate estimate of energy requirement in COPD is demanded in clinical practice, with the aim of improving outcomes of nutritional treatment, we are referred to subjective assessments of the physical activity levels. But before doing that, an accurate measure of the patients RMR is also necessary. In the clinic, the most accurate way of assessing RMR is by using indirect calorimetry. At least in Sweden, the access of indirect calorimeters for this purpose is very limited. Most of clinicians are referred to prediction equations. We have recently presented a validated disease specific prediction equation for RMR in underweight patients with COPD (Nordenson et al. 2010) which could be used in underweight patients. In the current study the widespread equations from WHO are used, showing quite some variation in precision at individual level. The perfect prediction does not exist, and probably never will. For the clinician this is important information to take this into account when planning nutritional treatment.

A limitation of the study is that the patients' "true" energy requirement is not known. The requirement of energy does not necessary equal the energy expenditure. Especially in cases of underweight or overweight, the actual energy expenditure could be higher or lower than the energy requirement. However, a measure of the energy expenditure is the current standard method to estimate energy requirements.

Following a proper estimation of RMR, subjective assessment of the individuals physical activity level could be done. A number of activity monitors are currently available. Which to select for use in the clinic calls for consideration of the validity, reliability, user-friendliness and cost of the method (Pitta, Troosters et al. 2006). Still, disease-specific validation studies for many of the activity monitors are lacking. At the end of the day, new methods need to be implemented in the health care practice. Routinely use of activity monitors in nutritional treatment of COPD probably would enhance health outcomes for the patients. When scientists built the evidence base, both healthcare professionals and healthcare organisations need to be active in the process of implementing new evidence-based methodology in routine practice.

To conclude, this study shows that very simple measures of energy expenditure could, on group level, assess COPD patient's energy needs. However, for individual nutritional treatment, more thorough procedures are necessary.

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CONFLICT OF INTEREST STATEMENT

None of the authors have any conflicts of interest.

STATEMENT OF AUTHORSHIP

FS designed the study, conducted the research, analyzed data and wrote the paper, AMG designed the study, conducted the research and wrote the paper, US wrote the paper, LH and SL designed the study and wrote the paper.

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Figure legends

Figure 1. Bland Altman plots of Panel A) measured vs. predicted RMR, Panel B) measured TEE vs. TEE calculated as 125 kJ * BW, and Panel C) measured TEE vs. TEE calculated as RMR * 1.7

Figure 2. Bland Altman plots of Panel A) measured TEE vs. calculated TEE from Q1, PanelB) measured TEE vs. calculated TEE from Q2

	Females (n=42)	Males (n=26)	р
Age (years)	64 (7)	66 (6)	0.19
Body weight (kg)	63.2 (12.9)	78.0 (20.7)	0.0023
Body height (m)	1.62 (0.09)	1.75 (0.07)	< 0.001
BMI (kg/m ²)	23.7 (4.4)	25.3 (5.5)	0.23
FEV ₁ (% predicted)	44 (15)	41 (16)	0.39
FEV%	43 (9)	41 (10)	0.31

Table 1. Description of the patients, n=68 (mean (SD)).

 FEV_1 = Forced expiratory volume in 1 second

RMR, measured (kJ)	5663 (1172)
RMR, calculated (kJ)	5678 (943)
TEE, measured by ActiReg (kJ)	8317 (2255)
PAL, measured by ActiReg	1.46 (0.19)
TEE, 125 kJ * BW (kJ)	8614 (2219)
TEE, calculated BMR * 1.7	9652 (1602)**

Table 2. Resting and total energy expenditure, n=68 (mean (SD)).

p<0.01 compared to TEE measured by ActiReg

RMR=resting metabolic rate; TEE=total energy expenditure;

PAL=physical activity level; BW=body weight

	Mean PAL from ActiReg
Category 1 (n=4)	1.24
Category 2 (n=26)	1.38
Category 3 (n=35)	1.52* ^a
Category 4 (n=4)	1.65* ^a
Category 5 (n=0)	-
Category 6 (n=0)	-

Table 3. Mean PAL from ActiReg for each category in Q1, n=68 (mean (SD)).

*p<0.05 compared to category 1 ^ap<0.05 compared to category 2

PAL=physical activity level

	Mean PAL from ActiReg
Category 1 (n=5)	1.22
Category 2 (n=19)	1.39
Category 3 (n=8)	1.51*
Category 4 (n=32)	1.51*
Category 5 (n=5)	1.61*
Category 6 (n=1)	1.44
Category 7 (n=0)	-
Category 8 (n=0)	-

Table 4. Mean PAL from ActiReg for each category in Q2, n=68 (mean (SD)).

*p<0.05 compared to category 1

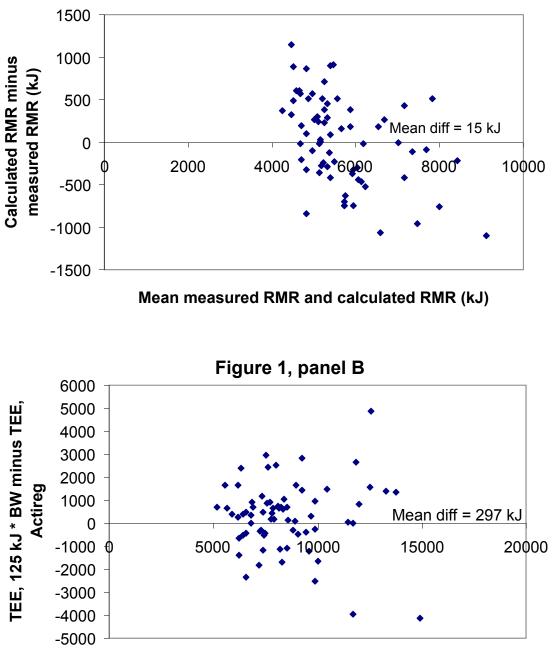
PAL=physical activity level

Table 5. Calculated energy expenditure from Q1 and Q2 compared to energy expenditurefrom ActiReg, n=68 (mean (SD)).

TEE, measured by ActiReg (kJ)	8317 (2255)
TEE, calculated from Q1 (kJ)	8272 (1412)
TEE, calculated from Q2 (kJ)	8324 (1484)

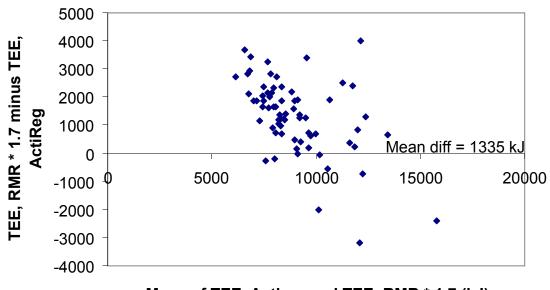
TEE=total energy expenditure

Figure 1, panel A



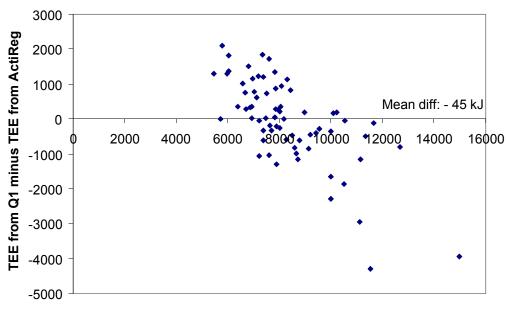
Mean TEE, ActiReg and TEE, 125 kJ * BW (kJ)

Figure 1, panel C



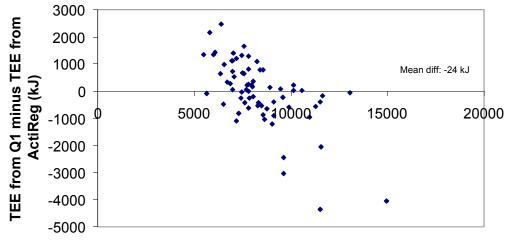
Mean of TEE, Actireg and TEE, RMR * 1.7 (kJ)

Figure 2, panel A



Mean TEE from ActiReg and Q1 (kJ)

Figure 2, panel B



Mean TEE from ActiReg and Q2 (kJ)