Daily Energy Requirements in Heart Failure Patients

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Diminished body cell mass in heart failure patients contributes to poor prognosis and decreased quality of life. The level of daily energy intake needed to maintain body cell mass and optimal physiological function in heart failure patients is unknown. Thus, we examined daily energy expenditure in free-living heart failure patients to estimate daily energy requirements. Daily energy expenditure (doubly labeled water) and its components (resting and physical activity energy expenditures) were measured in 26 heart failure patients (25 men and one woman aged 69 ± 7 years) and 50 healthy controls (48 men and two women aged 69 ± 6 years). Resting energy expenditure was measured by indirect calorimetry; physical activity energy expenditure from the difference between daily and resting energy expenditure; body composition by dual-energy x-ray absorptiometry; leisure time physical activity from a questionnaire; and peak oxygen consumption ([peak $\dot{V}O_2$] n = 16 heart failure patients) from a treadmill test to exhaustion. Plasma markers of nutritional status were also considered. Daily energy expenditure was 17% lower (2,110 ± 500 *v* 2,543 ± 449 kcal/d) and physical activity energy expenditure 54% lower (333 ± 345 *v* 728 ± 374 kcal/d) in heart failure patients compared with healthy controls. Daily energy expenditure was related to physical activity energy expenditure ($r = .79$, $P < .01$), resting energy expenditure ($r = .63$, $P < .01$), leisure time physical activity ($r = .63$, $P < .01$), and peak $\dot{V}O_2$ ($r = .58$, $P < .01$) in heart failure patients. Stepwise regression analysis showed that daily energy requirements in heart failure patients were best estimated by a combination of resting energy expenditure and reported leisure time physical activity (total $R^2 = 61\%$; standard error of the estimate, ±333 kcal/d). Daily energy requirements predicted from equations derived in healthy elderly were inaccurate when applied to heart failure patients, deviating −10% to +30% from measured daily energy expenditure. We conclude that despite low levels of activity, markers of physical activity predicted daily energy needs in heart failure patients. We provide a new equation to estimate energy needs in free-living heart failure patients based on measurements of daily energy expenditure.

PATIENTS WITH HEART FAILURE often experience a depletion of fat and muscle mass,[1,2] which contributes to prolonged hospitalization,[3] increased likelihood of complications following surgical procedures,[4] and increased mortality.[5,6] Loss of body mass occurs when daily energy expenditure exceeds daily energy intake. To maintain body cell mass and optimal physiological function, daily energy intake should be maintained at a level commensurate with daily energy expenditure (ie, energy balance).

Daily energy expenditure defines the quantity of metabolizable energy intake required to maintain energy balance.[7,8] Thus, an accurate approach to determine daily energy requirements is to quantify daily energy expenditure (ie, a proxy measure of daily energy needs). The doubly labeled water technique provides a direct, integrated measure of daily energy expenditure and its components over an extended period (7 to 21 days) in an individual's free-living environment, and is therefore ideally suited to provide daily energy expenditure measurements from which daily energy requirements can be estimated. The aims of this study were (1) to examine biological determinants of daily energy expenditure in heart failure patients and (2) to develop a model to predict daily energy requirements in heart failure patients from biological markers of daily energy expenditure and compare daily energy requirements with those of the healthy elderly.

SUBJECTS AND METHODS

Subjects

Twenty-six patients (25 men and one woman) with heart failure were recruited from the Heart Failure Service of the Baltimore Veterans Affairs Medical Center and the University of Maryland Medical Center. The mean left ventricular ejection fraction was 23% ± 9% (range, 10% to 45%) as determined by radionuclide ventriculography. There were 13 patients with coronary artery disease, defined as a history of myocardial infarction or significant obstruction on a cardiac catheterization. Thirteen patients had dilated cardiomyopathy unrelated to coronary artery disease. Two patients had non–insulin-dependent diabetes mellitus and were treated with oral hypoglycemic drugs. At the time of testing, patients were hemodynamically stable and free of edema and were taking two or more of the following medications: diuretics (n = 26, 100%), vasodilators (angiotensin-converting enzyme inhibitor or hydralazine nitrates; n = 22, 85%), and digoxin (n = 23, 88%). Patients were defined by the New York Heart Association functional scale as class II (n = 9), class III (n = 12), and class IV (n = 5). Class II patients experience symptoms during heavy exercise, class III patients experience symptoms during moderate exercise (eg, walking 200 m on a flat surface), and class IV patients are symptomatic at rest. Thirteen patients (12 men and one woman) reported significant weight loss (15 ± 6 kg; range, 9 to 25) during the course of the disease.

Fifty healthy, nonsmoking elderly subjects (48 men and two women) were used as a nondiseased control group. Healthy subjects met the following criteria: (1) no symptoms or signs of heart disease or diabetes, (2) normal resting electrocardiogram, (3) normal electrocardiogram response to an exercise stress test, (4) absence of medicinal or nonmedicinal drugs that could affect cardiovascular or metabolic function, and (5) weight stability (±2 kg) within 6 months prior to

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testing. The nature, purpose, and possible risks of the study were explained to each volunteer before provision of consent. This study was approved by the Institutional Review Boards of the University of Maryland and University of Vermont.

Data from the present cohort of heart failure patients and healthy controls regarding the effect of heart failure on daily energy expenditure and its components,[9] plasma leptin concentrations,[10] and skeletal muscle mass[11] have been previously published.

Experimental Protocol

All measurements were performed during a 10-day period. On the first day, each subject received an oral dose of doubly labeled water after a baseline urine sample was obtained. On the following morning, resting energy expenditure and body composition were measured, blood was drawn, and two urine samples were collected to mark the beginning of the doubly labeled water measurement period. All subjects left the research center and resumed their daily activities (ie, free-living conditions). Ten days after the beginning of the doubly labeled water measurement period, volunteers returned to provide two urine samples and to undergo an assessment of peak oxygen consumption ($\dot{V}O_2$).

Daily Energy Expenditure

Free-living daily energy expenditure was determined over a 10-day period using the doubly labeled water technique as previously described.[9] After providing a baseline urine sample (between 12:00 noon and 4:00 PM), each subject consumed a mixed oral dose of ^2H_2O and $H_2{}^{18}O$ (0.075 and 0.15 g/kg body mass, respectively). A weighed 1:400 dilution (dose:tap water) was prepared from each subject's dose, and a sample of the tap water used for the dilution was also saved and analyzed along with each subject's urine sample set. Two urine samples were obtained the morning after dosing to mark the beginning of the measurement period and 10 days later to mark the end (all between 8:00 AM and 12:00 noon). All subjects were weight-stable and consuming a self-selected diet during the doubly labeled water measurement period. Urine samples were stored in sealed Vacutainers at −20°C until analysis in triplicate by isotope ratio mass spectrometry (Optima; Fisons Instruments, Middlewhich, Cheshire, UK) at the Biomedical Mass Spectrometry Facility at the University of Maryland. All samples were analyzed within 6 months of collection. Samples were analyzed for isotopic enrichment of ^2H_2O and $H_2{}^{18}O$ using the off-line zinc reduction procedure of Kendall and Copelan[12] and the CO_2 equilibration technique,[13] respectively. ^2H and ^{18}O enrichment of samples was expressed in delta per mil (‰). The standard deviation for 164 sets of triplicate analyses of $H_2{}^{18}O$ was 0.27‰ at a mean sample enrichment of 43.08‰. The standard deviation for 172 sets of triplicate analyses of ^2H_2O was 4.34‰ with a mean sample enrichment of 449.3‰.

The rate of carbon dioxide production was calculated using equation 2 from Speakman et al[14]:

$$rCO_2\,(\text{mold}) = 0.4554 \times N(K_o - (DSR)K_h),$$

where N is the body water pool and is equal to $[(N_0) + (N_h/DSR)]/2$, N_0 and N_h are the $H_2{}^{18}O$ and ^2H_2O dilution spaces in moles, respectively, K_o and K_h are the turnover rates of $H_2{}^{18}O$ and ^2H_2O in days, respectively, and DSR is the dilution space ratio (N_h/N_o). Turnover rates and zero time enrichment of $H_2{}^{18}O$ and ^2H_2O were determined from the slope and intercept, respectively, of the semilogarithmic plot of urinary enrichment (‰) versus time (days). Isotope dilution spaces were calculated using the equation of Coward.[15] Because the dilution space ratio of heart failure patients (1.0450 ± 0.0172) and healthy controls (1.0488 ± 0.0144) did not differ significantly from the fixed dilution space ratio of 1.0427 ± 0.0218 proposed by Speakman et al,[14] the fixed ratio of 1.0427 was used for each subject. Carbon dioxide production rates were used to calculate daily energy expenditure from equation 12 of Weir,[16] assuming a respiratory quotient of 0.85.[17]

Resting Energy Expenditure

Resting energy expenditure was measured on an outpatient basis after a 12-hour overnight fast (8:00 AM) in heart failure patients and on an inpatient basis in healthy controls. Resting energy expenditure was measured by indirect calorimetry using the ventilated-hood technique for 45 minutes (Deltatrac; Sensormedics, Yorba Linda, CA). Energy expenditure was calculated using the Weir equation.[16] Upon arrival at the hospital, heart failure patients were transported to the testing area by wheelchair and rested quietly in a dark room for 20 minutes prior to measurement.

Physical Activity Energy Expenditure

Physical activity energy expenditure was calculated based on the three-component model of daily energy expenditure: ([0.9 × daily energy expenditure] − resting energy expenditure), assuming the thermic effect of meals constitutes 10% of daily energy expenditure in older individuals.[18]

Body Composition

Fat mass and fat-free mass were measured by dual-energy x-ray absorptiometry using a DPX-L densitometer (Lunar, Madison, WI). All scans were analyzed using the Lunar Version 1.3z DPX-L extended-analysis program for body composition.

Peak $\dot{V}O_2$ and Leisure Time Physical Activity

Peak $\dot{V}O_2$ was assessed by a treadmill test to volitional fatigue using an open-circuit indirect calorimetry system. Peak $\dot{V}O_2$ was measured in 16 heart failure patients and all healthy controls. The Minnesota Leisure Time Physical Activity Questionnaire[19] was completed for each subject. The cumulative energy cost for leisure time physical activity over the past year was averaged and expressed as kilocalories per day.

Plasma Markers of Nutritional Status

The serum albumin level was measured by serum protein electrophoresis. Plasma cholesterol was assayed enzymatically. Glucose was determined using a Beckman glucose analyzer (Brea, CA).

Statistics

The mean ± SD was calculated for each variable. Differences in physical characteristics and energy expenditure between heart failure patients and healthy controls were determined using an unpaired Student's *t* test. Relationships (Pearson product-moment correlations) between variables were determined by linear regression analysis. Measures of physical activity (reported leisure time physical activity), resting energy expenditure, body composition (fat mass and fat-free mass), age, and disease severity (New York Heart Association functional class and ejection fraction) were examined as possible correlates of daily energy expenditure because of their known association with energy expenditure.[7,20] Plasma markers of nutritional status, such as albumin and glucose, which are readily available in clinical settings were examined as possible indicators of disease severity or nutritional status to explain the variation in daily energy expenditure. We used stepwise regression analysis to determine the set of variables that best predicted daily energy expenditure. Variables that had a significant bivariate relationship with daily energy expenditure were included as independent variables in the stepwise regression model: ejection fraction, fat-free mass, leisure time physical activity, and resting energy expenditure. Daily energy requirements were estimated for heart failure patients from three prediction equations previously developed in healthy elderly subjects (factorial approach, 1.75 × resting energy expenditure[21] and equations 6 and 7 from Goran and Poehlman[7]) and were compared with measured daily energy expenditure values using a paired *t* test.

RESULTS

Physical characteristics of the heart failure patients and healthy controls are shown in Table 1. Groups did not differ for age, height, body mass, fat mass, or fat-free mass. Heart failure patients reported lower ($P < .05$) leisure time physical activity and had lower ($P < .01$) peak $\dot{V}O_2$ than healthy controls. No differences in serum albumin or plasma glucose were found.

Daily energy expenditure and its components for the heart failure patients are shown in Fig 1. Heart failure patients had lower daily energy expenditure (2,110 ± 500 *v* 2,543 ± 449 kcal/d, $P < .01$) and physical activity energy expenditure (333 ± 345 *v* 728 ± 374 kcal/d) than healthy controls, respectively (data for healthy controls not shown in figure form). No difference in resting energy expenditure was found between heart failure patients (1,586 ± 281 kcal/d) and healthy controls (1,561 ± 223 kcal/d; data for healthy controls not shown in figure form). The thermic effect of meals is estimated at 10% of daily energy expenditure in both groups.

Table 2 shows correlations of daily and physical activity energy expenditure with selected independent variables. Daily energy expenditure was most strongly related to physical activity energy expenditure ($P < .01$). In addition, we found significant associations between daily energy expenditure and resting energy expenditure ($P < .01$), leisure time physical activity ($P < .01$), peak $\dot{V}O_2$ ($P < .01$), the ejection fraction ($P < .05$), and fat-free mass ($P < .05$). Daily energy expenditure was not related to New York Heart Association functional class, reported weight loss, age, or serum albumin. Physical activity energy expenditure was related to the ejection fraction and the leisure time physical activity (both $P < .01$). No relationship was found between physical activity energy expenditure and resting energy expenditure, peak $\dot{V}O_2$, fat-free mass, New York Heart Association functional class, reported weight loss, age, or serum albumin.

An equation to predict daily energy expenditure (and thus daily energy needs) in heart failure patients was derived from stepwise regression analysis (Table 3). Resting energy expenditure was the strongest predictor of daily energy expenditure, accounting for 48% (R^2) of the variation ($P < .01$). Reported leisure time physical activity explained an additional 13% (R^2) of the variation in daily energy expenditure ($P < .05$). Both predictors were positively related to daily energy expenditure. The equation generated from this model was

$$\text{daily energy expenditure (kcal/d)} = (0.919 \times \text{resting energy expenditure, kcal/d}) + (0.548 \times \text{leisure time physical activity, kcal/d}) + 481.$$

The standard error of the estimate for this equation was ±333 kcal/d.

We examined the accuracy of equations previously derived in healthy elderly subjects to predict daily energy needs in heart failure patients. The factorial equation of Roberts et al[21] overestimated ($P < .01$) daily energy needs in heart failure patients by 30% (2,745 ± 491 kcal/d) compared with measured values (2,110 ± 500 kcal/d). In the 16 heart failure patients with peak $\dot{V}O_2$ measurements, equation 6 of Goran and Poehlman[7] underestimated ($P < .05$) daily energy needs by 10% (1,949 ± 254 kcal/d) compared with measured values

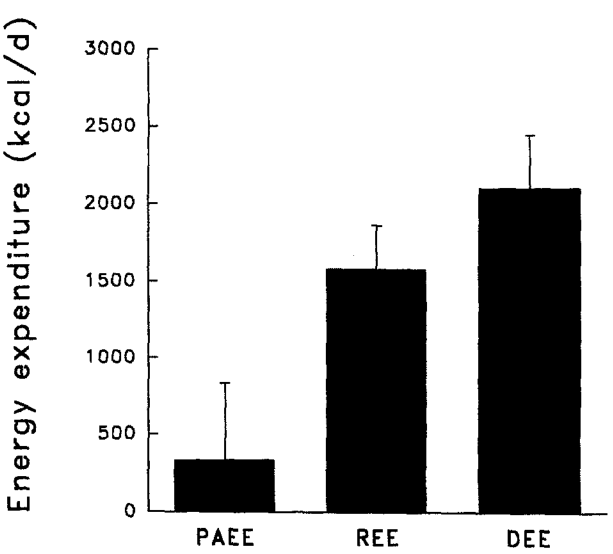

Fig 1. **Daily energy expenditure (DEE) and its components in heart failure patients. PAEE, physical activity energy expenditure; REE, resting energy expenditure.**

Table 1. Physical Characteristics of the Heart Failure Patients and Healthy Controls

Characteristic	Heart Failure Patients	Healthy Controls
No. of subjects	26	50
Age (yr)	69 ± 7	69 ± 6
Height (cm)	172 ± 8	173 ± 7
Body mass (kg)	75 ± 18	78 ± 15
Fat mass (kg)	19 ± 12	21 ± 8
Fat-free mass (kg)	55 ± 8	58 ± 9
Leisure time physical activity (kcal/d)	243 ± 371	451 ± 352*
Peak $\dot{V}O_2$ (L/min)‡	1.1 ± 0.4	1.9 ± 0.6†
Serum albumin (g/dL)	4.1 ± 0.4	4.2 ± 0.3
Plasma glucose (mg/dL)	121 ± 73	98 ± 13

*$P < .05$.
†$P < .01$.
‡$n = 16$.

Table 2. Pearson Product-Moment Correlation Coefficients for the Relationship of Daily and Physical Activity Energy Expenditure With Selected Variables

Variable	Daily Energy Expenditure	Physical Activity Energy Expenditure
Physical activity energy expenditure	.79†	—
Resting energy expenditure	.63†	.02
Leisure time physical activity	.63†	.41*
Peak $\dot{V}O_2$	.58†	.23
Ejection fraction	.44*	.47*
Fat-free mass	.41*	−.01
New York Heart Association functional class	−.33	−.24
Reported weight loss	−.26	−.16
Age	−.16	.08
Albumin	.08	.16

*$P < .05$.
†$P < .01$.

Table 3. Stepwise Regression Analysis Predicting Daily Energy Expenditure in Heart Failure Patients

Step No.	Independent Variable	R^2 (%)	SEE (kcal/d)	P
1	Resting energy expenditure	48	374	<.01
2	Leisure time physical activity	61	333	<.05

Abbreviations: SEE, standard error of the estimate; R^2, cumulative proportion of the variation accounted for by the model.

(2,170 ± 488 kcal/d). Equation 7 of Goran and Poehlman[7] more closely approximated daily energy needs, but overestimated by 6% (2,244 ± 646 kcal/d), on average, compared with measured values (2,110 ± 500 kcal/d).

DISCUSSION

To our knowledge, this is the first study to use stable isotope–derived measurements of daily energy expenditure to examine daily energy needs in free-living heart failure patients. Daily energy expenditure and thus energy needs were 17% lower in heart failure patients compared with healthy controls. Physical activity energy expenditure, not resting energy expenditure, was the strongest correlate of daily energy expenditure in heart failure patients, accounting for 61% (R^2) of individual variation. Although this strong correlation may be partially attributable to the fact that physical activity energy expenditure is calculated from daily energy expenditure, other measures of physical activity (ie, leisure time physical activity and peak $\dot{V}O_2$) were also strongly correlated with daily energy expenditure. Taken together with our previous findings in the healthy elderly,[7] these results highlight the importance of physical activity as a determinant of daily energy needs in healthy and diseased individuals.

Physical activity energy expenditure derived from the doubly labeled water method is an integrated measure of the absolute caloric cost of daily activity over a 10-day period. Because physical inactivity reflects and contributes to the decline in functional capacity characteristic of heart failure patients, it is of interest to identify factors that predict habitual physical activity in this population. We found that ejection fraction was the strongest determinant of physical activity energy expenditure, explaining 22% of the individual variation. This suggests that physical activity levels decline in heart failure patients with increasing ventricular dysfunction. However, interestingly, peak $\dot{V}O_2$, a measure of aerobic work capacity, was not related to physical activity energy expenditure. This dissociation of aerobic capacity from the energy cost of physical activity may be explained by the finding that factors unrelated to the pathophysiological syndrome of heart failure (ie, behavioral factors) may influence activity levels.[22] Further studies examining the physiological and psychological factors that determine physical activity levels in heart failure patients are needed to formulate effective interventions to increase physical activity.

Low peak $\dot{V}O_2$ is a marker of increased disease severity in heart failure patients.[23] We found a positive relationship between daily energy expenditure and peak $\dot{V}O_2$, suggesting that daily energy expenditure decreases with increasing severity of heart failure. Taken together with our previous finding that resting energy expenditure increases with increasing symptom severity,[20] these results reveal a possible scenario for the energetic adaptation to increasing disease severity in heart failure patients. With increasing severity of heart failure, the energy required to maintain basal homeostasis is increased,[20] possibly due to increased cardiac and ventilatory work.[24] However, the progression of cardiac dysfunction limits the capacity to perform physical work and decreases physical activity energy expenditure. Because the decrease in physical activity energy expenditure exceeds the increase in resting energy expenditure, the net result is a reduction in daily energy expenditure with increasing disease severity. Studies that monitor changes in daily energy expenditure and its components over time are needed to test this hypothesis.

We developed a practical equation to predict daily energy requirements in heart failure patients. We considered several physiological and disease-related variables that may predict daily energy expenditure. Resting energy expenditure and leisure time physical activity were identified as independent predictors of daily energy expenditure, and these predicted the daily energy expenditure within ± 333 kcal/d. Daily energy needs estimated from equations derived in healthy elderly subjects[7,21] deviated −10% to +30% from measured daily energy expenditure. The only equation that predicted mean daily energy expenditure with a reasonable degree of accuracy (6% overestimation, nonsignificant) was equation 7 of Goran and Poehlman.[7] The accuracy of this equation was likely due to its inclusion of resting energy expenditure and leisure time physical activity, both of which were strong predictors of daily energy expenditure in heart failure patients. Because our equation was generated in a small patient population, cross-validation studies in an independent sample of heart failure patients are needed to assess its accuracy. Furthermore, the predictive capacity of our equation may be limited to older men with heart failure, since we did not test younger patients or women. The accurate estimation and eventual prescription of daily energy requirements in heart failure patients may help to restore energy balance and offset the depletion of body energy stores. Moreover, nutritional intervention before surgery (including heart transplantation) may help to reduce postoperative morbidity and mortality, given that preoperative malnutrition is associated with a poor prognosis.[1,4]

Considerable controversy exists regarding the appropriate dilution space ratio to be used in the calculation of carbon dioxide production rates from doubly labeled water. Recent studies showed that a large proportion of the variation (60% to 100%) in the dilution space ratio among individuals was attributable to analytical error.[14,25] Thus, it has been suggested that a fixed dilution space ratio be used to limit the contribution of analytical error to variation in daily energy expenditure. However, several different dilution space ratios have been suggested in the literature. In a review of data from 161 subjects, Speakman et al[14] suggested a ratio of 1.0427. Racette et al[25] combined data from 99 subjects in their laboratory and found a dilution space ratio of 1.034, which is identical to that suggested by Coward[15] from data in 107 adults. Coward et al[26] suggested that a weighted dilution space ratio be calculated from the assumed dilution space ratio of 1.034 and each individual's measured dilution space ratio. If an assumed dilution space ratio of 1.034 is used to calculate daily energy expenditure in heart failure patients in the current study, daily energy expenditure values would be increased by 3.6%. Further studies are needed to clarify the appropriate dilution space ratio to be used in adult humans.

In conclusion, we found that daily energy needs were lower in heart failure patients compared with healthy controls. Moreover, indicators of physical activity were strong determinants of daily energy expenditure. We offer a practical equation that may be used to predict daily energy requirements in heart failure patients based on measures of resting energy expenditure and leisure time physical activity.

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