Resting Metabolic Rate – the Applicability of Predictive Equations as an Alternative to Indirect Calorimetry

Ruheenergieumsatzbestimmung – Die Anwendbarkeit von anthropometriebasierten Formeln im Vergleich zur indirekten Kalorimetrie

Summary

- Introduction: Financial and personal costs limit the applicability of direct and indirect calorimetric resting metabolic rate (RMR) assessments during health counseling. Therefore, regression-based equations are often used in preventive settings in which their accuracy could be very limited by the impact of habitual physical activity (PA) and sedentary behavior (SB). This study analyzed the applicability of four equations and the potential of PA and SB as explanatory variables.
- > Methods: RMR of 35 non-obese men was assessed using indirect calorimetry. Harris-Benedict-, Mifflin- (factors: bodyweight, height, age), Cunningham-, and Owen equations (factor: fat free mass; FFM) were applied. PA (leisure-, commuting-, householdand work activities) and SB were assessed using a validated questionnaire.
- Results: RMR was 2061.5±537.4 kcal/day and correlated with weight, height, FFM and PA. Only age and PA correlated with RMR after adjusting for bodyweight (1.06±0.25 kcal/kg/h). Whereas all equations were associated with calorimetric RMR (p<.05), only Harris Benedict formula did not lead to a significant underestimation (-153.4±479.0 kcal/day; p>.05).
- Discussion: In our sample, Harris-Benedict was the only applicable equation. However, the accuracy of individual results was very limited. PA but not SB seems to be associated with RMR in non-obese men. PA hould be considered as an additional factor for more accurate predictive equations in preventive settings.

KEY WORDS:

Sedentary Behavior, Resting Energy Expenditure, Physical Activity

Zusammenfassung

- Einleitung: Finanzielle und personelle Kosten limitieren die Anwendbarkeit der kalorimetrischen Ruheenergieumsatz-Bestimmung (RMR) im Rahmen von Gesundheitsberatungen. Daher werden oft regressionsbasierte Formeln, deren Genauigkeit durch den starken Einfluss körperlicher Aktivität (KA) und sedentären Verhaltens (SV) eingeschränkt sein könnte, verwendet. Diese Studie analysiert die Anwendbarkeit als Alternative zur indirekten Kalorimetrie von vier populären Ruheenergieumsatz-Formeln sowie die Potentiale von KA und SV als erklärende Variablen für Unterschiede des Ruheenergieumsatzes Erwachsener mit vergleichbarer Körperzusammensetzung.
- > Methoden: Der RMR von 35 nicht-übergewichtigen Männern wurde mittels indirekter Kalorimetrie ermittelt. Die Harris-Benedict-, Mifflin- (Faktoren: Körpergewicht, Größe, Alter), Cunningham-, und Owen Formeln (Faktoren: Fettfreie Körpermasse; FFM) wurden zum Vergleich herangezogen. KA (Freizeit-, Transport-, Haushalt- und Arbeit bezogene Aktivitäten) und SV wurden mittels des IPAQ Fragebogens erfasst.
- Ergebnisse: Der RMR war 2061.5±537.4 kcal/Tag und korrelierte mit dem Körpergewicht, der Körpergröße, der FFM sowie der KA. Nur das Alter und KA korrelierten mit der RMR nach Kontrolle des Faktors Körpergewicht (1.06±0.25 kcal/kg/Stunde). Die Ergebnisse aller vier Formeln korrelierten mit der RMR (p<.05). Nur mittels Harris Benedict Formel errechnete Ergebnisse unterschätzten die RMR nicht signifikant (-153.4±479.0 kcal/Tag; p>.05).
- **Diskussion:** In der von uns untersuchten Population ist nur die Verwendung der Harris-Benedict Formel zu empfehlen. Allerdings ist auch deren Exaktheit zur Voraussage des RMR stark eingeschränkt. Eine mögliche Erklärung hierfür ist der Einfluss KA, der nicht allein durch eine KA bedingte Anpassung der Körperzusammensetzung erklärbar zu sein scheint. Der IPAQ könnte ein geeignetes Tool zur Implementierung von Aktivitätsmaßen in zukünftige Formeln zur Ruheenergieumsatzbestimmung sein.

SCHLÜSSELWÖRTER:

Sedentäres Verhalten, Grundumsatz, Körperliche Aktivität

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Introduction

Current lifestyle and diet guidelines recommend to balance caloric intake and physical activity (11). One of the most common methods to assess caloric intake is to determine resting metabolic rate (RMR) and multiply this value with an estimated physical activity level (PAL). Based on the limited availability of calorimetric chambers, indirect calorimetry via gas exchange analysis is a recommended and more often applied method to calculate a person's RMR with an acceptable error (5%) (4). However, both methods require expensive equipment, highly skilled personnel

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Table 1

Equation models for resting metabolic rate (RMR) calculation. Wt=weight in kilograms (kg); Ht=height in centimeters (cm); Age=age in years; FFM=fat free mass in kilograms (kg).

REFERENCE	EQUATION MODEL FOR RESTING METABOLIC RATE
Harris-Benedict (male) (6)	66.473 + (13.752 x Wt) + (5.003 x Ht) - (6.755 x Age)
Mifflin (14)	(9.99 x Wt) + (6.25 x Ht) – (4.92 x Age) + 5
Cunningham (3)	370 + (21.6 x FFM)
Owen (male) (15)	290 + (22.3 x FFM)

and must be carried out in the morning within fasted state. Since measurement is complicated and many practitioners don't have access to necessary equipment, a plethora of different equations, based on various populations of obese and nonobese subjects, are applied to assess RMR.

Some regressions rely on anthropometric measurements which can be assessed easily (age, bodymass and height) (6, 14). Others calculate RMR based on fat free body mass (FFM), which in this context is interpreted as a main predictor for protoplasmic tissue mass (3, 15). Likewise to calorimetric measures, the costs and efforts for valid assessment of body composition and FFM are relatively high. Recommendable methods like dilution techniques, air displacement plethysmography, dual energy X-ray absorptiometry and magnetic resonance spectroscopy or -imaging (10) are thus applied sparsely. One of the more cost effective and frequently applied methods is bio-impedance analysis (BIA) (10). However, standardized regressions for BIA based data show poor accuracy even for subjects with normal body mass index (BMI) (8). Thus, the question arises if BIAbased FFM assessment increases or decreases the accuracy of RMR calculation for individuals via predictive equations.

Based on a systematic review, Frankenfield and colleagues stated that most currently applied equations based on both, anthropometric measures and FFM, lead to significant errors even when applied to individuals matching the original population (4). Furthermore systematic under-or overestimation may occur if such equations are applied in populations with different anthropometric, behavioral or biomedical characteristics (12, 17). Therefore it is of great relevance to systematically analyze the influence of additional factors for the inter-individual variance of RMR.

Based on the current literature both, physical activity (PA) and sedentary behavior (SB) might have a great impact on RMR (18). Within one of the early studies on RMR in women Owen and colleagues indicate PA during sport and exercise as a major factor for RMR (16). In a subsequent study they analyze the accuracy of protoplasmic tissue based equations and state that, aside from FFM, additional factors may contribute to the great variance of predicted RMR found in his sample (16). They consequently develop separate equations for athletic and non-athletic women (16). Taken together, these findings already indicate that habitual PA and SB are accessible factors, which might increase explained variance of RMR via multiple pathways aside from influencing body composition. Consequently, until today multiple studies analyzed the long-term influence of regular PA and the immediate effects of an exercise bout (18). As one of the most important short-term effects, the influence of excess post-exercise oxygen consumption (EPOC) seems to be widely understood (18).

Table 2

Anthropometric measures of participants as mean \pm standard deviation and 95 percent confidence intervals.

N=35	MEAN±SD	(95% CI)
Age in years	26.3±5.4	(24.4–28.2)
Height in centimeters	181.2±6.3	(179.1–183.4)
Weight in kilograms	80.9±9.7	(77.6–84.3)
Body mass index in kilograms per squaremeter	24.6±2.2	(23.8–25.3)
Fat mass in percent	17.1±5.0	(15.4–18.9)
Fat free mass in kilograms	66.9 ±7.9	(64.1–69.7)
Physical activity in MET hours per week	126.4±98.2	(92.7–160)
Sedentary Behavior in MET hours per week	66.5±25.2	(57.8–75.2)

Contrastingly, the evidence concerning long-term effects of PA and SB remains inconclusive. This may be partly due to the currently not clearly quantifiable impact of sex age and metabolic health as potential mediating factors for the connection between long-term PA behavior and RMR (13). Aside the positive association of habitual PA with increased FFM, currently there is little information available concerning the effects of chronic PA on RMR (18). To increase the understanding, several influences, including PA intensity and SB, should be taken into account. Furthermore, since non-exercise activities during commuting, household or work may represent a large proportion of overall PA, another factor of great relevance is to assess PA not only during leisure or sporting activities.

The purposes of this study were twofold. The first purpose was to assess the applicability of common RMR calculation methods in healthy non-obese men by comparing the FFM based equations of Owen (15) and Cunningham (3) as well as the anthropometric measure based equations of Mifflin St Jeor (14) and Harris Benedict (6) with RMR values measured via indirect calorimetry (gas exchange measurement). For each of the four equations we hypothesized, that calculated RMR values show a strong correlation and no significant differences to measured RMR. The second purpose was to systematically analyze the associations of SB and PA with RMR in healthy non-obese men. To proof this research question we hypothesized, that PA and SB, assessed as MET hours per week, show a significant association with measured RMR.

Methods

Design and Subjects

For this cross sectional study healthy male participants within an age range of 18 to 40 years and a BMI range of 19.0 to 29.9 kg m-2 were recruited from the local university and community via postings in printed form and social media platforms. Healthy was defined as the absence of chronic or acute diseases. All participants read and signed an informed consent document approved by the university institutional review board. The study was approved by the Ethics Committee of the Goethe University of Frankfurt am Main, Germany and is in agreement with the Declaration of Helsinki (Version Fortaleza 2012). Participants were invited to arrive in the morning in fasted state for assessment of anthropometric measures, indirect calorimetry and bio impedance analysis. Furthermore participants were instructed to avoid exercise or other strenuous activities for 24h prior to testing.

Anthropometric Measures

Height in centimeters (cm) and bodyweight in kilograms (kg) were measured to the nearest 0.5 cm and 0.1 kg using a floor model physician stadiometer and scale. Body mass index was calculated (BMI: kg m-2). Sex and age was self reported by participants.

Indirect Calorimetry via Gas Exchange Analysis

Gas exchange analysis was conducted using a Quark CPET system (Cosmed, Fridolfing, Germany). Measurement took place in an air-conditioned room (23.5 to 24.5 degrees celsius) in a quiet setting. Gas exchange of subjects lying on their back on a cushioned surface was analyzed breath by breath for thirty minutes. Indirect calorimetry was calculated based on Oxygen consumption (VO₂) and respiratory quotient (RQ) mean values of minutes ten to thirty using the equation of Weir and colleagues: kcal min⁻¹ = VO₂ (1 min⁻¹) x [3.9 + (1.1 x RQ)] (19, 20).

Bioimpedance Analysis

BIA measurements were performed after gas exchange analysis using a standardized protocol (7). We used a tetrapolar device (Nutriguard-MS, Data Input, Darmstadt, Germany) with single frequency (50 kHz). Data was analyzed based on resistance (R), reactance (Xc) in Ohms (Ω) using the software Nutriplus (Data Input, Darmstadt, Germany).

Resting Metabolic Rate Prediction Equations

Four different equation models for RMR were applied. Two models used age, body height and weight (6, 14) and two models used FFM (3, 15). The FFM based models (3, 15) were not based on BIA analysis. Details are shown in table 1.

Physical Activity Assessment

Physical activity at present was assessed using the International Physical Activity Questionnaire (IPAQ) (2). Participants had to report mean physical activity of moderate and vigorous intensity during work, commuting, household and leisure time for the last seven days. Data was used to estimate total physical activity per week within each category by a Metabolic Equivalent of Task (MET) energy expenditure estimate (1). The weighted activity hours per week were calculated as duration x frequenca per week x MET intensity (METh week⁻¹). To produce an estimate of total physical activity METh week⁻¹ were summed across activity domains (2). Furthermore, we calculated time spend with sedentary behavior as minutes per week and subdivided PA energy expenditure achieved by moderate and vigorous intensity activities.

Statistical Analysis

Statistical analysis was conducted using SPSS 21 (IBM, Chicago, IL, USA). Significance level was set at 5% for all tests. Descriptive data are reported as mean (±standard deviation, SD) and 95% confidence intervals. Data was controlled for normality (Kolmogorov Smirnov test). Spearman bivariate correlation coefficients were used to compare predictive equations with indirect calorimetry and to analyze the association of anthropometric and physical activity data with RMR. Wilcoxon tests were used to detect systematic errors. The mean difference and the mean percentage difference were calculated to analyze accuracy of equation based RMR compared to indirect calorimetry (9). In case of significant correlation and no differences between measured and predicted RMR, Bland Altman plots were used to display limits of agreement. The relation of relevant variables with RMR was further analyzed using a multiple regression approach.

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Figure 1

Resting metabolic rate assessed using gas exchange analysis (indirect calorimetry) and four different predictive equations. Harris-Benedict-, Mifflin- (factors: bodyweight, -height, age), Cunningham-, and Owen equations (factor: fat free mass; FFM). Data is indicated as mean and 95 percent confidence interval. * indicates significant difference between indirect calorimetric and equation based values; # indicates significant correlation between indirect calorimetric and equation.



Bland Altman plot of measured RMR and predicted RMR via Harris Benedict equation. Differences on the ordinate axis are indicated as: indirect calory-metric RMR – calculated RMR.

Results

Subjects Characteristics

Anthropometric and physical activity data of participants is shown in table 2. Based on BMI fourteen participants can be defined as overweight (25.0 - <30.0) and twenty-one were in the normal range (18.5 - <25.0).

Accuracy of Equation Based Resting Metabolic Rate

Resting metabolic rate was 2061.5 ± 537.4 kcal per day (1876.9 - 2246.1 kcal/day), 1.06 ± 0.25 kcal per kilogram bodyweight per hour (0.99 - 1.15 kcal/kg/h) and 1.28 ± 0.31 kcal per kilogram FFM per hour (1.18 - 1.39 kcal/kgFFM/h) respectively. The results of comparison between equation based RMR and actual RMR measured by indirect calorimetry are presented in

Table 3

RMR via predictive equations and indirect calorimetry (calorimetric RMR) in non-obese healthy men. Values presented as mean with standard deviation (SD), 95 percent confidence intervals (95% CI) mean absolute and relative difference to measured RMR (mean±SD and 95% CI). Results of Spearman correlation and Wilcoxon test for differences between measured RMR and each predicitive equation. *=significance (p<.05).

	RMR KCAL/DAY MEAN±SD	95% CI	MEAN DIFFE- Rence Kcal/day	MEAN DIFFE- Rence %	CORRELATION r, p	WILCOXON TEST Z; P
Calorimetric RMR	2061.5±537.4	1876.9-2246.1				
Harris-Benedict (male) (6)	1908.1±153.7	1855.3-1960.9	-153.4±479.0 (-317.9-+11.2)	-0.3±30.8 (-10.9-+10.3)	0.472; 0.004*	-1.900; 0.057
Mifflin (14)	1816.5±124.5	1773.8-1859.3	-245.0±488.9 (-412.977.0)	-4.9±29.9 (-15.1-+5.4)	0.463; 0.005*	-2.686; 0.007*
Cunningham (3)	1815.5±171.6	1756.6-1874.5	-245.9±495.2 (-416.075.8)	-5.1±29.9 (-15.4-+5.2)	0.399; 0.018*	-2.670; 0.008*
Owen (male) (15)	1782.4±177.1	1721.5-1843.2	-279.1±494.0 (-449.0109.1	-6.8±29.3 (-16.9-+3.2	0.399; 0.018*	-2.997; 0.003*

table 3. All equation were significantly correlated with measured RMR (p<.05). As indicated in table 3, Harris Benedict equation showed the lowest absolute and relative mean difference to measured RMR and the results were not significantly different to measured RMR. All other equations showed significant differences to measured RMR (figure 1). Figure 2 displays Bland Altman plot including limits of agreement for Harris Benedict equation with measured RMR.

Anthropometric Factors, Physical Activity, Sedentary Behavior and Resting Metabolic Rate

Table 4 displays the association of relevant anthropometric factors and overall PA with measured RMR (kcal/day) and resting metabolic rate per kilogram bodyweight per hour (kcal/kg/h). Measured RMR was associated with weight, height, BMI, FFM and overall PA, whereas RMR adjusted for weight (kcal/kg/h) was associated with age and overall PA only. RMR adjusted for FFM (kcal/kgFFM/h) was not associated with any of the factors tested.

Weight was the strongest predictor for RMR and showed significant associations with height (r=0.640; p=0.001) BMI (r=0.814; p=0.001) and FFM (r=0.843; p=0.001). Age and PA showed no significant correlations, indicating collinearities, with any of the tested variables including FFM. Consequently, a multiple linear regressions was calculated to predict RMR based on bodyweight, age and PA.

Using the enter method we found that weight, age and overall PA explained a significant amount of the variance in the value of RMR (F(df: 3, 31)=5.25, p=0.005, R=0.580, R2=0.337, R2adjusted=0.273). The analysis of coefficients showed that weight (Beta=0.500, t(8.263)=3.338, p=0.002) significantly predict values of RMR, however predictive value of overall PA (Beta=0.239, t(0.811)=1.628, p=0.114) and age (Beta=-0.252, t(14.734)=-1.688, p=0.101) did not reach significance within this model.

At 54.6 ±24.4 percent, leisure activities (65.8 ±57.0 METh week¹) made up the largest proportion of overall PA. Commuting made up 23.3 ±24.0 percent (18.3 ±19.8 METh week⁻¹) whereas work (13.2 ±20.1%; 25.1 ±58.1 METh week⁻¹) and household (8.8 ± 10.5%; 8.1 ± 14.3 METh week⁻¹) related activity had the lowest share. Subanalysis of PA intensity revealed significant relations of moderate (3 to <6 MET) (r=.355; p=.036) and vigorous (≥6 MET) (r=.364; p=.032) PA with RMR (kcal/day). Sedentary behavior (≤1.5 MET) (r=.102; p=.559) was not related with RMR (kcal/day).

Discussion

Our results show that Harris Benedict equation was the only applicable prediction model for RMR calculation in non-obese men. Calculated values of this equation showed a significant correlation and no significant differences compared to RMR measured via indirect calorimetry. Therefore, we were able to confirm our first hypothesis for this equation. However, less than 25% percent of explained variability, the mean differences and Bland Altman Plot analysis indicate limited accuracy of this equation model to predict RMR in healthy non-obese men. Our data suggest that equation based RMR tends to underestimate RMR measured by indirect calorimetry in subjects with higher metabolic rates whereas measured RMR in subjects with lower metabolic rates seem to be overestimated. The RMR values of all other equations tested showed significant differences to measured RMR. Consequently, none of the other equations was applicable for RMR calculation in the population tested. Predictive equations using FFM, assessed with BIA, did not increase the accuracy for individual RMR calculation.

Age and questionnaire-based PA had the highest predictive value for bodyweight adjusted RMR. Therefore, we were able to confirm our second hypothesis for PA but not for SB. However, both factors did not reach significance level within a multiple regression approach and the variability of RMR values explained by PA was low even in a homogeneous sample of non-obese men.

As our data indicate, the body composition assessed with BIA did not vary to a large degree between non-obese male individuals. Further studies need to apply gold standard FFM assessments to confirm these preliminary findings. Consequently, weight had the highest predictive value for RMR, whereas FFM assessment did not lead to increased accuracy of equation models. A detailed analysis of currently applied factors revealed that age was the only measure which was significantly associated with relative RMR per kilogram bodymass (kcal/kg/h). The association of height, BMI or FFM with absolute RMR (kcal/day) in our sample could be explained by collinearity with bodyweight. These results indicate that for men within a normal to overweight BMI range accurate determination of anthropometric data is of great relevance for RMR assessment via established formulas. Contrastingly, BIA analysis seems to be obsolete for RMR prediction. However, of the four equations tested only the method of Harris-Benedict was able to predict RMR without significant underestimation.

Table 4

Correlation analysis of relevant anthropometric factors and resting metabolic rate measured with indirect calorimetry. Resting metabolic rate is indicated as kilocalories per day (KCAL/DAY), kilocalories per hour related to bodyweight (KCAL/KG/H) and kilocalories per hour related to fat free mass (KCAL/KGFFM/H). Results are indicated as Spearman correlation coefficient (r) and p value. *=significance (p<.05).

N=35	MEASURED RESTING METABOLIC RATE (R; P)			
	kcal/day	kcal/kg/h	kcal/kgFFM/h	
	-0.183	-0.383	-0.316	
Age in years	0.294	0.023*	0.064	
Height in continutors	0.349	0.132	0.103	
neight in centimeters	0.040*	0.451	0.557	
Weight in kilograme	0.443	0.030	0.093	
	0.008*	0.864	0.595	
Rody mass index in kilograms per squaremeter	0.424	0.062	0.155	
buy mass muck in knograms per squaremeter	0.011*	0.723	0.372	
Eat frag mass in kilograms	0.399	0.020	0.032	
rat ii ee iiiass iii kiiogi aliis	0.018*	0.910	0.857	
Physical activity in MET hours per wook	0.338	0.367	0.278	
Physical activity in MET nours per week	0.047*	0.030*	0.106	
Sadantary Robaviar in MET hours par wook	-0.102	-0.066	-0.122	
Seventary behavior in mET Hours per week	0.559	0.707	0.485	

Overall, our findings are in line with others indicating that equations based on bodyweight are the most suitable for RMR calculation of normal and overweight male adults (9, 12). Whereas the measured RMR values of systematic reviews (13) and previous studies (12) showed a similar range, the predictive value of the equations tested was even lower within our sample of non-obese men. As indicated in the Bland Altman Plot measured RMR showed a considerably greater variance than calculated RMR. Therefore our results underline the conclusion that equations based on anthropometric measures lead clinically relevant errors when they are applied to individuals (4) and that these individual differences may be even too large to make any current prediction formula useful for individual use (12).

In order to determine additional factors which could explain the variance of RMR and may be useful for a more accurate estimation of individual RMR, we systematically evaluate the influence of habitual weekly PA and SB. We assessed activities during work, commuting, household and leisure time as well as SB during weekend and workdays using a validated guestionnaire (5). To avoid the confounding short-term influence of PA on energy expenditure via EPOC and caloric intake, we instructed all participants to avoid exercise or other strenuous activities for 24h prior to testing and remain in the fasted state during measurements. Our findings show a linear positive association of weekly PA level with RMR. This association of overall-, moderate- and vigorous PA, as measures of time dependent energy expenditure (METh/wk), furthermore seems to be independent of the individual amount of FFM. Therefore we are able to hypothesize that habitual PA may not only influence the amount of metabolically active tissue. Based on our data we were not able to analyze mechanisms leading to PA induced long term changes of RMR. Therefore, longitudinal studies, analyzing potential changes on cellular level, are necessary. In contrast, our results provide preliminary evidence that the impact of SB on metabolic health seems not to be mediated by decreased RMR.

In order to limit the influence of confounding factors like sex or metabolic diseases (13) we analyzed a sample of 35 healthy men within a normal to overweight BMI range. Using such a standardized approach, we were able to indicate a relevant influence of overall PA level on RMR. Anyhow, a predictive equation based on this sample would not contribute in any way. We assessed PA and SB using a standardized and validated questionnaire (2). Anyhow, measuring physical activity with different scientific movement devices may strengthen future investigations in this area.

Conclusions

Taken together, assessment of overall PA level using validated questionnaires seems to be a feasible approach to estimate the impact on RMR. As our findings indicate, non-exercise PA has a large share on activity related energy expenditure and seems to be a mediating factor for RMR. Further studies could apply a standardized approach within other populations to analyze the potential influence of overall PA level. We confirm the considerable error of current estimation equations. Therefore, we cannot recommend the application of commonly known estimation equations as an alternative to indirect calorimetry to assess individual RMR in non-obese male subjects.

Conflict of Interest

The authors have no conflict of interest.

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