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Clinical determinants of resting metabolic rate in geriatric outpatients

Suey S.Y. Yeung[a,b], Esmee M. Reijnierse[b], Marijke C. Trappenburg[c,d], Carel G.M. Meskers[e], Andrea B. Maier[a,b,*]

[a] Department of Human Movement Sciences, @AgeAmsterdam, Faculty of Behavioural and Movement Sciences, Amsterdam Movement Sciences, Vrije Universiteit, Amsterdam, the Netherlands
[b] Department of Medicine and Aged Care, @AgeMelbourne, The Royal Melbourne Hospital, The University of Melbourne, Victoria, Australia
[c] Department of Internal Medicine, Section of Gerontology and Geriatrics, Amsterdam UMC, Vrije Universiteit, Amsterdam, the Netherlands
[d] Department of Internal Medicine, Amstelland Hospital, Amstelveen, the Netherlands
[e] Department of Rehabilitation Medicine, Amsterdam UMC, Vrije Universiteit, Amsterdam, the Netherlands

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ABSTRACT

Purpose: Accurate estimation of the energy requirements including resting metabolic rate (RMR) is important for optimal nutritional care, yet its clinical determinants are unknown. This study examined the associations between clinical determinants of the Comprehensive Geriatric Assessment (CGA) domains with RMR among geriatric outpatients.

Materials & methods: Data were retrieved from cohorts of community-dwelling older adults (n = 84, 54 female) referring to geriatrics outpatient mobility clinics in both Amsterdam, The Netherlands and Melbourne, Australia. Determinants within domains of the CGA included diseases (number, type and severity of diseases, polypharmacy), nutrition (body weight, body mass index, absolute and relative skeletal muscle mass, fat-free mass and fat mass, risk of malnutrition), physical function (handgrip strength, Short Physical Performance Battery, Timed Up & Go), cognition (Mini-Mental State Examination), psychological wellbeing (Geriatric Depression Scale) and blood pressure. RMR was objectively measured using indirect calorimetry with a canopy hood. Association between the clinical determinants with standardized RMR (country and sex-specific z-score) were analysed with linear regression adjusted for age, sex and body weight.

Results: Determinants within the nutritional domain were associated with RMR; body weight showed the strongest association with RMR. Significant associations between determinants within the nutritional domain with RMR disappeared after further adjustment for body weight. None of the other domains were associated with RMR.

Conclusions: Body weight is the strongest clinical determinant of RMR and should be taken into account when estimating RMR in geriatric care.

1. Introduction

To maintain a desirable body weight and optimize geriatric nutritional care, accurate estimation of individual energy requirements is a prerequisite. Resting metabolic rate (RMR), the energy required to maintain body functions at rest, accounts for 60 %–70 % of daily energy requirements (Manini, 2010). In clinical practice, RMR is usually estimated by predictive equations, which were derived from healthy populations and do not account for body composition and diseases (Harris & Benedict, 1918; Schofield, 1985).

Some studies support the need to take body composition and diseases into account when estimating RMR. Fat-free mass (FFM) has been shown to be a predominant determinant of RMR in healthy adults (Cunningham, 1980; Manini, 2010; Nelson, Weinsier, Long, & Schutz, 1992). Independent of age, sex and body composition, the number of diseases was found to be positively associated with RMR in community-dwelling older adults (Fabbri et al., 2015). The severity of diseases was positively associated with RMR among older adults with heart failure (Obisesan et al., 1996) and rheumatoid arthritis (Arshad, Rashid, & Benjamin, 2007; Binymin, Herrick, Carlson, & Hopkins, 2011). Individuals with a metabolic demanding disease, such as congestive heart failure, cancer, chronic obstructive pulmonary disease (COPD) or Parkinson's disease, have been shown to have higher RMR compared to healthy controls (Levi, Cox, Lugon, Hodkinson, & Tomkins, 1990;

* Corresponding author at: Department of Human Movement Sciences, @Age, Faculty of Behavioural and Movement Sciences, Amsterdam Movement Sciences, Vrije Universiteit, V.d. Boechorststraat 7-9, 1081 BT, Amsterdam, the Netherlands.
E-mail address: a.b.maier@vu.nl (A.B. Maier).

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Nguyen, Batterham, & Edwards, 2016; Poehlman, Scheffers, Gottlieb, Fisher, & Vaitekevicius, 1994; Sergi et al., 2006). The Comprehensive Geriatric Assessment (CGA) is a multi-dimensional, inter-disciplinary diagnostic process for older adults to assess a range of health domains which have been shown to influence the patients' quality of life and health outcomes such as diseases, nutrition, physical function, cognition and psychological wellbeing and blood pressure (Pilotto et al., 2017). Therewith, the CGA could provide clinical determinants of RMR.

The aim of this study was to examine the associations between clinical determinants within domains of the CGA with objectively measured RMR among geriatric outpatients. We hypothesized that body composition and diseases are more strongly associated with RMR than other clinical determinants among geriatric outpatients.

2. Materials & methods

2.1. Setting

Data were derived from the SHAPE cohort which includes community-dwelling older adults with mobility problems referred to geriatric outpatient clinics in Amsterdam (June 2015 to June 2016) and Melbourne (December 2017 and January 2019). No exclusion criteria were applied; inclusion was based on written consent obtained from the outpatients or their next of kin for use of their medical information and completion of a full nutritional assessment, which is not a routine practice for outpatients who had normal nutritional status as screened by the Mini-Nutritional Assessment (MNA). A CGA was completed by a multidisciplinary team as routine care in the outpatient clinics. The CGA included questionnaires and measurements of diseases, nutrition, physical function, cognition and psychological wellbeing and blood pressure.

2.2. Ethics

The SHAPE cohort in Amsterdam and Melbourne was approved by the local medical ethical committees. The study was conducted in accordance with the ethical standards laid down in the Declaration of Helsinki of 1975 and its later amendments.

2.3. Geriatric outpatient characteristics & clinical determinants

Data on age, sex and independent living was collected from medical records. The number, type and severity of diseases were ascertained by physicians. Physicians were instructed to document all diseases and their severity of each of the 14 organ systems as classified in the Cumulative Illness Rating Scale (CIRS) (Miller et al., 1992). The severity of diseases was rated as 0 (no problem affecting that system) to 4 (extremely severe problem). Supplementary Table S1 shows a list of diseases present in our sample of geriatric outpatients, these included common diseases such as hypertension, osteoarthritis, osteoporosis, cataracts, depression, diabetes, cancer, COPD, chronic kidney disease, rheumatoid arthritis, Parkinson's disease and heart failure. In the case of several diseases within the same organ system, only the most severe was scored. The total score was defined as the sum of scores in all organ systems (maximum 56 points) and the severity index was defined as the total score divided by the number of systems with a score > 0. Presence of metabolic demanding diseases (yes/no) was defined as having at least one of the following diseases: cancer (Nguyen et al., 2016), COPD (Ramires et al., 2012; Sergi et al., 2006), chronic kidney disease (CKD) (Ikizler et al., 2002; Utaka et al., 2005), rheumatoid arthritis (Arshad et al., 2007; Binymin et al., 2011), Parkinson's disease (Kistner, Lhommee, & Krack, 2014) and heart failure (Poehlman et al., 1994). Information regarding the number of medications was extracted from medical records. Polypharmacy was defined as having five or more medications (Masnoon, Shakib, Kalisch-Ellett, & Caughey, 2017).

Anthropometric measurements were performed to assess standing height to the nearest 0.1 cm, body weight to the nearest 0.1 kg and body mass index (BMI) in kg/m^2. Absolute (kg) and relative (%) skeletal muscle mass (SMM), fat-free mass (FFM) and fat mass (FM) was measured using a direct segmental multi-frequency bioelectrical impedance analysis (DSM-BIA, Amsterdam: In-Body 720, Biospace Co., Ltd, Seoul, Korea; Melbourne: In-Body 770; Biospace Co., Ltd, Seoul, Korea). The DSM-BIA has been shown to be a valid tool to measure total body and segmental body composition with excellent agreements between DSM-BIA and dual-energy X-ray absorptiometry (DEXA) (Ling et al., 2011). The full Mini-Nutritional Assessment (MNA) consists of 18 questions and was used to assess the nutritional status of older adults (Guigoz, Vellas, & Garry, 1996).

Handgrip strength was measured using the JAMAR hand dynamometer (Sammons Preston, Inc., Bolingbrook, IL, USA). Three trials were performed alternately for each hand and the best performance was used for analysis and expressed in kg (Reijnierse et al., 2017). Outpatients were asked to maintain standing balance with eyes open in three different positions (side-by-side, semi-tandem and tandem) and were classified as able or unable to maintain standing balance for 10 s. A timed four-meter walk test at usual pace was performed (Pasma et al., 2014). The timing started when the first whole foot touched the floor after the starting line and stopped when the first whole foot touched the floor after the 4-meter line. Outpatients were instructed to walk through approximately 5 m to prevent slowing down before reaching the end of the course. The fastest time of the two performances was used to compute the gait speed (m/s). The Chair Stand Test (CST) included a timed five rises from a chair to an upright position as fast as possible without the use of arms. The timing started when the instruction "start" was given and stopped when the buttocks touched the seat on the last repetition. The Short Physical Performance Battery (SPPB) score was computed based on the performance of the aforementioned subtests i.e. balance tests, four-meter walk and CST. Higher SPPB score indicates a higher degree of lower extremity functioning (Guralnik et al., 1994). Outpatients also completed the Timed Up and Go test (TUG) in which they were asked to rise from a chair, walk for three meters, turn around a cone, then walk back to the chair and sit down at their normal pace. The timing started when the instruction "start" was given and stopped when the outpatients sat down with a straight back. Shorter time to complete the TUG test indicates greater physical mobility (Podsiadlo & Richardson, 1991). Outpatients who were not able to perform the CST and TUG test or used their hands to get up were given a time score of 100 s to be able to include them in the analysis (de Bruine et al., 2019).

The Mini-Mental State Examination (MMSE) was used to assess the global cognitive function (Folstein, Folstein, & McHugh, 1975), with a lower score indicating poorer cognitive functioning. The 15-item Geriatric Depression Scale (GDS-15) was used to detect depressive symptoms (Yesavage & Sheikh, 1986). Higher scores indicate more depressive symptoms. Resting systolic and diastolic blood pressure (mmHg) and heart rate (bpm) were measured in supine position after a resting period of at least 5 min with a digital blood pressure monitor.

2.4. Resting metabolic rate

RMR was measured using indirect calorimetry using a canopy hood (Amsterdam: QUARK RMR, COSMED, Rome, Italy; Melbourne: Fitmate GS, COSMED, Rome, Italy) in a quiet environment and supine position. Patients were instructed to limit movement and talking and to avoid sleeping. The QUARK RMR contains both oxygen (VO_2) and carbon dioxide (VCO_2) sensors and therefore directly measured the actual respiratory quotient (RQ). The Fitmate GS system does not contain a carbon dioxide sensor so it calculates the RMR by estimating carbon dioxide production from a fixed RQ of 0.85 based on the abbreviated Weir equation (Weir, 1949): [3.9 x oxygen consumption (VO_2) + 1.1 × (RQ x VO_2)] × 1.44. Both the QUARK RMR and Fitmate GS have been shown to be reliable in RMR measurement, compared with a previously

validated DELTATRAC II™ (Blond et al., 2011), COSMED QUARK CPET (Vandarakis, Salacinski, & Broeder, 2013) and COSMED QUARK RMR (Yeung et al. 2019, unpublished results).

Before each measurement, calibration was performed according to the manufacturer's guidelines. After that, the canopy hood was placed over the patients' head. Due to application in clinical practice, most outpatients were not fully post-absorptive before RMR measurement. The time of the last meal before the RMR measurement was recorded. RMR was measured for 30 min in Amsterdam and for 20 − 30 min in Melbourne depending whether the steady state was reached. Steady state was reached when the coefficient of variation (CV) in VO_2 was less than 10 %. The first 5 min of data were discarded to allow adaptation to the testing procedures, and data of the remaining minutes were averaged and used in the analysis. RMR was expressed as an absolute value in kcal/day.

2.5. Statistical analysis

Continuous variables with a normal distribution were presented as mean and standard deviation (SD) or if skewed as median and interquartile range (IQR). Categorical variables were presented as number (n) and percentage (%).

RMR was standardized by country and sex-specific z-score due to the use of different equipment and sex difference in the RMR (Henry, 2005; McMurray, Soares, Caspersen, & McCurdy, 2014). Linear regression analyses were performed to examine the associations between clinical determinants within domains of the CGA (independent variables) with standardized RMR (dependent variable). The analysis was adjusted for age and sex (model 1). Data were presented as effect estimates (β) and standard error (SE). When determinants within a domain were significantly associated with standardized RMR, these determinants were further standardized into sex-specific z-score to allow comparison of effect estimates. Significant differences between determinants within a domain were tested using Z-values calculated with the formula $((\beta_1 - \beta_2)/\sqrt{(SE_1^2 + SE_2^2)})$ and p-values were derived from the standard normal distribution table.

As body weight had the highest standardized effect estimate, the association between determinants within domains of the CGA and standardized RMR was further adjusted for body weight (model 2) to test if the association found in model 1 was confounded by body weight. Sensitivity analyses of the linear regression were performed excluding the 10 outpatients without a measurement of body composition (reasons: with pacemaker or electrode implant (n = 7), unable to stand for a few minutes for the measurement (n = 2), full pressure stockings and need machine to fit (n = 1)).

Statistical analyses were performed using the Statistical Package for the Social Sciences version 25.0 (SPSS Inc, Chicago, IL, USA). To address for multiple testings, a Bonferroni correction was applied using a corrected significance level of $p < 0.0015$ (0.05/33 variables). Results were visualized using GraphPad Prism version 5.

3. Results

Table 1 presents the characteristics of outpatients. A flowchart of patient inclusion is shown in Supplementary Fig. S1. A total of 84 outpatients (54 females) were included in this study. The median age was 78.3 years [IQR: 73.0 − 85.3]. The median number of chronic diseases was 6 [IQR: 5 − 8]. Metabolic demanding diseases and polypharmacy was present in 37 and 66 out of 84 outpatients respectively. Mean BMI was 27.2 ± 5.0 kg/m^2.

Table 2 shows the associations between clinical determinants and RMR in geriatric outpatients. In model 1, diseases, physical function, cognition, psychological wellbeing and blood pressure were not associated with RMR in geriatric outpatients. Determinants within the nutritional domain (except relative SMM and MNA score) were significantly associated with RMR ($p < 0.0015$).

Fig. 1 compares the association between standardized sex-specific clinical determinants within the nutritional domain with RMR. Absolute measures had higher effect estimate (β) than relative measures. Within the absolute measures, body weight showed the strongest association with RMR ($\beta = 0.58$, $p < 0.001$), while the effect estimate (β) of body weight was not statistically significantly different from the effect estimates (β) of other absolute measures (i.e. BMI, SMM, FFM and FM in kg).

After further adjustment for body weight (model 2), the significant associations between determinants within the nutritional domain with RMR lost significance. No significant associations between other clinical determinants with RMR were found in model 2.

In outpatients with an available measurement of body composition (n = 74), the associations between clinical determinants and RMR were similar to the results in the total population (n = 84) (data not shown).

4. Discussion

In a clinically relevant population of geriatric outpatients, clinical determinants within the nutritional domain were associated with RMR, with body weight showing the strongest association with RMR. These significant associations were dependent on body weight. The findings indicate that clinicians should take body weight into account when estimating RMR in geriatric care.

In contrast to our hypothesis, diseases were not positively associated with RMR in geriatric outpatients. A limited number of studies examined the associations between chronic diseases with RMR in older adults but the results are controversial (Fabbri et al., 2015; Nagel, Jungert, Spinneker, & Neuhauser-Berthold, 2017; Schrack, Knuth, Simonsick, & Ferrucci, 2014). Aforementioned studies consisted of community-dwelling older adults (Fabbri et al., 2015; Nagel et al., 2017; Schrack et al., 2014) with larger heterogeneity and a wider range of age, physical activity level and health status than our cohort of geriatric outpatients. There may be a ceiling effect for the association between the number of chronic diseases and RMR. The increase in RMR due to the increased number of diseases may have been masked to some extent by a simultaneous decrease in FFM and physical activity level resulting in a decrease in RMR (Nagel et al., 2017). Furthermore, more diseases were covered in this study as the number of diseases were assessed by physicians without the use of a predefined list, while previous studies included sampling predefined diseases (Fabbri et al., 2015; Nagel et al., 2017; Schrack et al., 2014) and using a self-report questionnaire (Nagel et al., 2017). In contrast to previous studies (Arshad et al., 2007; Binymin et al., 2011; Obisesan et al., 1996), no association between the severity of diseases and RMR was found in the present study. This may be due to the focus on the severity of one particular (and also metabolic demanding) disease in the previous studies, while the current study examined the overall severity in organ systems. Cancer (Nguyen et al., 2016), COPD (Ramires et al., 2012; Sergi et al., 2006), CKD (Ikizler et al., 2002; Utaka et al., 2005), rheumatoid arthritis (Arshad et al., 2007; Binymin et al., 2011), Parkinson's disease (Kistner et al., 2014) and heart failure (Poehlman et al., 1994) were chosen to examine in this study as they are known to be metabolic demanding. Our study failed to show an association between the type of diseases and RMR, which may be due to the low prevalence of these diseases in our population of older adults attending a geriatric outpatient clinic for mobility problems. Another possible explanation is that geriatric outpatients with these diseases were in the stage of disease remission or during periods of reduced disease activity at the time of assessment and therefore the effect on RMR was not observed.

Within the nutritional domain, both absolute and relative measures were associated with RMR. Body weight showed the strongest association with RMR, while body weight was not statistically significantly different from the other absolute measures (i.e. BMI, SMM, FFM, FM) in the associations with RMR. This finding is expected because total body weight represents the sum of body composition (i.e. SMM, FFM and FM)

Table 1
Descriptive characteristics[a] of geriatric outpatients, stratified by location (n = 84).

Characteristics	N	Total	SHAPE	
			Melbourne (n = 58)	Amsterdam (n = 26)
Age, years, median [IQR]	84	78.3 [73.0 – 85.3]	77.2 [71.7 – 83.5]	81.1 [75.9 – 86.6]
Sex, female, n (%)	84	54 (64.3)	39 (67.2)	15 (57.7)
Independent living, n (%)	84	79 (95.2)	55 (94.8)	25 (96.2)
Diseases				
Nr. of diseases, median [IQR]	84	6 [5 – 8]	7 [4 – 8]	6 [5 – 8]
CIRS score	84	9.6 ± 3.5	9.4 ± 3.8	10.2 ± 2.8
CIRS severity index	84	1.7 ± 0.3	1.7 ± 0.3	1.8 ± 0.3
Hypertension, n (%)	84	43 (51.2)	31 (53.4)	12 (46.2)
Osteoarthritis, n (%)	84	44 (52.4)	36 (62.1)	8 (30.8)
Osteoporosis, n (%)	84	28 (33.3)	17 (29.3)	11 (42.3)
Cataracts, n (%)	84	31 (36.9)	24 (41.4)	7 (26.9)
Depression, n (%)	84	31 (36.9)	26 (44.8)	5 (19.2)
Diabetes, n (%)	84	16 (19.0)	14 (24.1)	2 (7.7)
Cancer, n (%)	84	12 (14.3)	8 (13.8)	4 (15.4)
COPD, n (%)	84	11 (13.1)	8 (13.8)	3 (11.5)
Chronic kidney disease, n (%)	84	12 (14.3)	8 (13.8)	4 (15.4)
Rheumatoid arthritis, n (%)	84	3 (3.6)	2 (3.4)	1 (3.8)
Parkinson's disease, n (%)	84	5 (6.0)	2 (3.4)	3 (11.5)
Heart failure, n (%)	84	7 (8.9)	4 (6.9)	3 (14.3)
Metabolic demanding disease[b], n (%)	84	37 (44.0)	23 (39.7)	14 (53.8)
Polypharmacy[c], n (%)	84	66 (78.6)	47 (81.0)	19 (73.1)
Nutrition				
Body weight, kg	84	72.0 ± 15.0	72.6 ± 15.5	70.6 ± 14.2
BMI, kg/m^2	83	27.2 ± 5.0	27.9 ± 5.0	25.6 ± 4.6
SMM, kg, median [IQR]	74	23.2 [20.0 – 29.4]	22.7 [19.9 – 28.0]	23.9 [20.4 – 31.2]
FFM, kg, median [IQR]	74	43.8 [37.9 – 54.3]	43.4 [37.6 – 53.6]	44.4 [38.0 – 58.0]
FM, kg	74	25.8 ± 10.3	27.3 ± 10.5	23.2 ± 9.6
SMM, %	74	34.6 ± 5.2	33.6 ± 4.6	36.3 ± 5.8
FFM, %	74	64.9 ± 9.8	63.4 ± 9.1	67.7 ± 10.5
FM, %	74	35.1 ± 9.8	36.6 ± 9.1	32.4 ± 10.5
MNA, score, median [IQR]	74	25.0 [22.5 – 30.0]	25.0 [22.5 – 28.0]	25.0 [21.0 – 27.0]
Physical function				
Handgrip strength, kg	73	21.2 ± 9.4	23.2 ± 8.4	17.5 ± 10.1
Balance, side by side[d], n (%)	79	71 (89.9)	48 (88.9)	23 (92.0)
Balance, semi-tandem[d], n (%)	76	62 (81.6)	41 (80.4)	21 (84.0)
Balance, tandem[d], n (%)	76	42 (55.3)	29 (56.9)	13 (52.0)
Gait speed, m/s	79	0.83 ± 0.28	0.83 ± 0.26	0.82 ± 0.31
CST, second, median [IQR]	81	20.0 [14.1 – 33.3]	21.1 [15.9 – 35.0]	15.5 [12.8 – 27.7]
SPPB, score, median [IQR]	75	8 [5 – 10]	8 [5 – 10]	9 [6 – 10]
TUG, second, median [IQR]	74	14.0 [10.7 – 19.6]	13.3 [10.6 – 18.2]	16.2 [12.8 – 21.8]
Cognition				
MMSE, score, median [IQR]	84	28 [26 – 30]	29 [26 – 30]	28 [26 – 29]
Psychological wellbeing				
GDS, score, median [IQR]	67	3 [2 – 6]	4 [2 – 6]	3 [2 – 6]
Blood pressure				
Systolic, mmHg	84	139 ± 21	138 ± 20	143 ± 24
Diastolic, mmHg	84	78 ± 10	77 ± 8	81 ± 12
Heart rate, bpm	83	68 ± 13	69 ± 13	68 ± 12
Resting metabolic rate				
Last meal, hours, median [IQR]	81	1.6 [1.0 – 3.0]	2.2 [1.3 – 3.5]	0.7 [0.5 – 1.3]
Respiratory quotient	84	Not applicable	0.85 (fixed)	0.78 ± 0.07
VO_2, ml/min, median [IQR]	84	193 [172 – 244]	179 [168 – 206]	253 [195 – 275]
RMR, kcal/day, median [IQR]	84	1342 [1199 – 1690]	1251 [1178 – 1432]	1740 [1361 – 1851]

BMI, body mass index; CIRS, Cumulative Illness Rating Scale; COPD, chronic obstructive pulmonary disease; CST, chair-stand test; FFM, fat-free mass; FM, fat mass; GDS, Geriatric Depression Scale; IQR, interquartile range; MMSE, Mini-Mental State Examination; MNA, Mini-Nutritional Assessment; Nr., number; RMR, resting metabolic rate; SMM, skeletal muscle; SPPB, Short Physical Performance Battery; TUG, Timed Up & Go; VO_2, oxygen consumption.

[a] Variables are presented as mean ± standard deviation, unless otherwise specified.

[b] Metabolic demanding diseases included: cancer, COPD, chronic kidney disease, rheumatoid arthritis, Parkinson's disease, heart failure.

[c] ≥5 medications.

[d] Able to maintain for 10 s.

Table 2
Association between clinical determinants and standardized Resting Metabolic Rate in geriatric outpatients.

Clinical determinants	Z RMR (Model 1: age and sex)			Z RMR (Model 2: As 1 + body weight)		
	β	SE	p	β	SE	p
Diseases						
Nr. of diseases	−0.05	0.04	0.194	−0.07	0.03	0.028
CIRS total score	−0.03	0.03	0.349	−0.04	0.03	0.096
CIRS severity index	−0.05	0.32	0.887	0.14	0.26	0.592
Cancer	−0.22	0.24	0.369	−0.12	0.19	0.540
COPD	−0.30	0.31	0.339	−0.07	0.25	0.798
Chronic kidney disease	−0.20	0.31	0.533	−0.31	0.25	0.221
Rheumatoid arthritis	0.20	0.56	0.718	0.37	0.45	0.416
Parkinson's disease	−0.10	0.44	0.815	0.29	0.35	0.417
Heart failure	0.26	0.41	0.529	−0.09	0.33	0.792
Metabolic demanding disease	−0.25	0.22	0.262	−0.12	0.18	0.490
Polypharmacy	−0.10	0.25	0.690	−0.27	0.20	0.180
Nutrition						
Body weight, kg	0.04	0.01	< 0.001*	–	–	–
BMI, kg/m^2	0.09	0.02	< 0.001*	−0.04	0.04	0.284
SMM, kg	0.15	0.03	< 0.001*	0.04	0.04	0.250
FFM, kg	0.08	0.02	< 0.001*	0.02	0.02	0.249
FM, kg	0.05	0.01	< 0.001*	−0.02	0.02	0.334
SMM, %	−0.07	0.02	0.004	0.03	0.03	0.312
FFM, %	−0.04	0.01	0.001*	0.01	0.01	0.328
FM, %	0.04	0.01	0.001*	−0.01	0.01	0.328
MNA, score	0.09	0.03	0.004	0.06	0.02	0.011
Physical function						
Handgrip strength, kg	0.01	0.01	0.699	−0.01	0.01	0.580
Balance, side-by-side	0.41	0.36	0.258	0.55	0.28	0.059
Balance, semi-tandem	0.12	0.29	0.678	0.29	0.23	0.215
Balance, tandem	0.27	0.23	0.230	0.28	0.18	0.123
Gait speed, m/s	−0.27	0.41	0.507	0.19	0.33	0.568
CST, second	−0.00	0.00	0.486	−0.00	0.00	0.749
SPPB, score	0.05	0.04	0.280	0.08	0.03	0.021
TUG, second	−0.01	0.01	0.476	−0.01	0.01	0.185
Cognition						
MMSE, score	0.06	0.04	0.128	0.04	0.03	0.149
Psychological wellbeing						
GDS, score	−0.04	0.03	0.244	−0.05	0.03	0.068
Blood pressure						
Systolic, mmHg	0.00	0.01	0.488	−0.00	0.00	0.811
Diastolic, mmHg	0.01	0.01	0.358	0.02	0.01	0.813
Heart rate, bpm	−0.01	0.01	0.456	−0.00	0.01	0.582

β, beta; BMI, body mass index; CIRS, Cumulative Illness Rating Scale; COPD, chronic obstructive pulmonary disease; CST, chair-stand test; FFM, fat-free mass; FM, fat mass; GDS, Geriatric Depression Scale; MMSE, Mini-Mental State Examination; MNA, Mini-Nutritional Assessment; Nr., number; p, p- value; SE, standard error; SMM, skeletal muscle mass; SPPB, Short Physical Performance Battery; TUG, Timed Up & Go; Z RMR, country and sex specific z-score of resting metabolic rate.

* Indicates statistically significant p values after Bonferroni correction ($p < 0.0015$).

and similarly RMR reflects the summated heat production rate of FFM and FM (Heymsfield et al., 2018). While FFM is a metabolically active component, adipose tissue which contains approximately 80 % of FM (Shen et al., 2003) has a small heat production rate at rest.

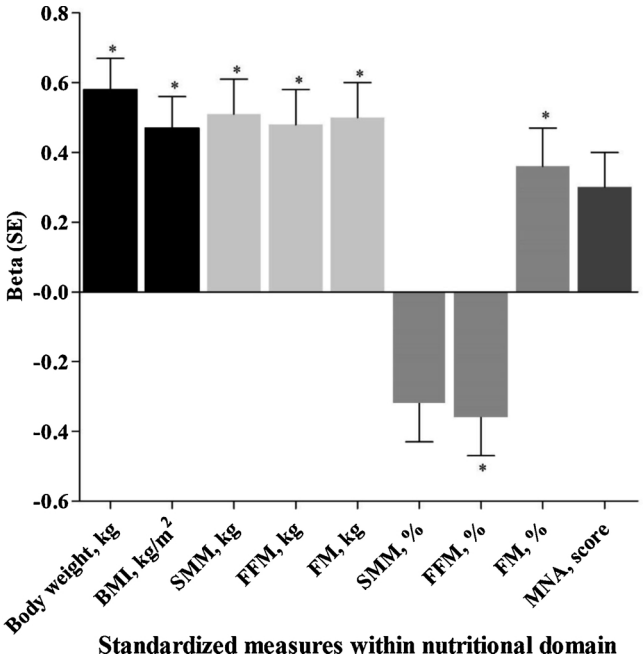

Fig. 1. Associations between standardized measures within the nutritional domain and standardized Resting Metabolic Rate in geriatric outpatients.
All p values were assessed with linear regression analyses adjusting for age and sex. Measures within nutritional domain were standardized into sex specific z-scores and data was presented as beta (SE). *$p < 0.0015$ BMI, body mass index; FFM, fat-free mass; FM, fat mass; MNA, Mini-Nutritional Assessment; SE, standard error; SMM, skeletal muscle mass.

Additionally, it has been suggested that greater adipose tissue may impose mechanical loads on the musculoskeletal system and metabolic loads on metabolic system organs, which will then result in a greater level of resting heat production (Heymsfield et al., 2018). Our result may explain why FFM-based predictive equations did not always improve prediction accuracy of RMR compared to weight-based predictive equations among hospitalised older patients (Neelemaat, van Bokhorst-de van der Schueren, Thijs, Seidell, & Weijs, 2012) and community-dwelling older adults (Karlsson et al., 2017).

4.1. Clinical implications

To provide optimal nutritional care to patients, accurate estimation of their energy requirements is essential. Energy requirements are often estimated using predictive equations in clinical practice. However, most of these equations are based on data that underrepresents older adults (Reeves & Capra, 2003). Our findings suggested that adding information on the number, severity and type of diseases is unlikely to enhance the RMR estimation, neither the information of physical function, cognition, psychological wellbeing and blood pressure. Our findings indicate that although measuring body composition is valuable for assessing nutritional status (Cederholm et al., 2015) and diagnosing sarcopenia (Cruz-Jentoft et al., 2019), it is mainly body weight as a clinical determinant of RMR in geriatric outpatients. This study strengthens the need to include body weight as part of the predictive equations for RMR estimation. In clinical practice, if the objective measurement of RMR is not feasible, clinicians should choose a predictive equation which takes body weight into account, such as World Health Organization (FAO/WHO/UNU, 1985) and Owen (Owen et al., 1986, 1987).

4.2. Strength and limitations

To the best of our knowledge, this is the first study examining a range of clinical determinants and their associations with objectively

measured RMR in geriatric outpatients, which is a unique and clinically relevant population. Diagnosed diseases were ascertained by physicians rather than via a self-reported questionnaire. The severity of diseases was not limited to one single disease but the overall severity in an individual. One of the limitations of this study is the cross-sectional design, therefore causality of the association cannot be drawn. In addition, there was a limited number of patients with completed RMR measurements related to the additional time required for a full nutritional assessment, which is not part of current routine care for those who had normal nutritional status. Furthermore, even when edema was only prevalent in a very small proportion of outpatients, muscle mass could have been overestimated in outpatients with edema. Although DEXA and computed tomography may be more accurate in body composition measurement, BIA can be easily operated in clinical settings.

5. Conclusions

In a relevant group of geriatric outpatients, body weight is the strongest clinical determinant of RMR and should be taken into account when estimating RMR in geriatric care. Other determinants within domains of the CGA are unlikely to contribute to enhancing RMR estimation.

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Author contributions

SSYY, EMR, MCT, CGMM and ABM designed the research; SSYY and EMR conducted the research; SSYY, EMR, MCT, CGMM and ABM analysed and interpreted the data; SSYY drafted the manuscript; EMR, MCT, CGMM and ABM critically revised the manuscript for important intellectual content; ABM had the primary responsibility for final content. All authors read and approved the final manuscript.

Declaration of Competing Interest

The authors have no conflicts.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.archger.2020.104066.

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