

1 Comparison of resting and total energy expenditure in peritoneal dialysis  
 2 patients and body composition measured by dual energy X ray absorptiometry  
 3 (DXA)  
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43

44 Abstract

45 Background/Objective

46 Under basal resting conditions muscle metabolism is reduced, whereas  
47 metabolism increases with physical activity. We wished to determine whether  
48 there was an association between resting energy expenditure (REE) and total  
49 energy expenditure (TEE) in peritoneal dialysis (PD) patients and lean body mass  
50 (LBM).

51 Subjects/Methods

52 We determined REE and TEE by recently validated equations using doubly  
53 labelled isotopic water, and LBM by dual energy X-ray absorptiometry (DXA)  
54 scanning.

55 Results

56 We studied 87 patients, 50 male (57.4%), 25 diabetic (28.7%), mean age  
57  $60.3 \pm 17.6$  years, with a median PD treatment of 11.4 (4.7-29.5) months. The  
58 mean weight was  $70.1 \pm 17.7$  kg with a REE of  $1509 \pm 245$  kcal/day and TEE  
59  $1947 \pm 378$  kcal/day. REE was associated with body size; (weight  $r=0.78$ , BMI  
60  $r=0.72$ ), and body composition (LBM  $r=0.77$ , lean body mass index (LBMI)  $r=0.76$ ,  
61  $r=0.62$ ), all  $p < 0.001$ . For TEE, there was an association with weight  $r=0.58$ , BMI  
62  $r=0.49$ , and body composition (LBM  $r=0.64$ , LBMI ( $r=0.54$ ), all  $p < 0.001$ . We  
63 compared LBMI measured by DXA and that estimated by the Boer equation  
64 using anthropomorphic measurements, which overestimated and underestimated  
65 LBM for smaller patients and heavier patients respectively.

66 Conclusions

67 Muscle metabolism is reduced at rest, and increases with physical  
68 activity. Whereas previous reports based on REE did not show any association  
69 with LBM, we found an association between both REE and TEE, using a recently  
70 validated equation derived from dialysis patients, and LBM measured by DXA  
71 scanning. Estimation of muscle mass from anthropomorphic measurements  
72 systematically overestimated lean body mass for small patients and conversely  
73 underestimated for heavier patients.

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76

## 77 Introduction

78 More than 300,000 patients with chronic kidney disease stage 5 (CKD5d)  
79 are now treated by peritoneal dialysis (PD) worldwide. The current paradigm is  
80 to assess PD by measuring urea clearance. However prospective studies have  
81 failed to demonstrate that increasing urea clearance is associated with greater  
82 patient survival [1]. An alternative suggestion is that the amount of dialysis a PD  
83 patient requires would depend upon their metabolic activity, as urea is generated  
84 as a by-product of cellular nitrogen metabolism [2]. Metabolic activity comprises  
85 both resting metabolic rate and that secondary to physical activity. Many  
86 studies concentrated on measuring resting energy expenditure (REE) [3], but  
87 this excludes activity energy expenditure (AEE), and so under estimates total  
88 energy expenditure (TEE).

89 We recently validated an assessment of TEE, and REE in dialysis patients  
90 using a patient self-reported questionnaire and double isotopic labelled water  
91 [4]. To determine whether there was an association between body composition  
92 and energy expenditure we compared TEE and REE with body composition  
93 measured by dual energy X-ray absorptiometry (DXA) scanning.

94

#### 95 Patients and methods

96 Adult patients with chronic kidney disease under the care of the Royal  
97 Free Hospital treated by PD were recruited when attending for outpatient  
98 assessments of peritoneal dialysis adequacy. Corresponding spent dialysate  
99 effluent and serum samples were analysed by standard methods, and weekly  
100 dialysis dose calculated as  $Kt/V_{urea}$ . Nitrogen protein accumulate rate was  
101 estimated using the Bergström equation, and normalised for body weight (nPNA)  
102 g/kg.

103 DXA scanning was performed in a standardised manner, with all patients  
104 draining out peritoneal dialysate. Patients were then asked to empty the  
105 bladder, and scanning was then performed with patients wearing a paper gown  
106 (Hologic QDR 400, Malborough, USA) [5,6]. Lean body mass (LBM) and fat mass  
107 was measured by DEXA scanning, and lean body mass index (LBMI) calculated by  
108 LBM divided by height squared. In addition LBM was estimated using the Boer  
109 equation based on anthropomorphic measurements (Appendix)

110 Physical activity data was obtained through the validated Recent Physical  
111 Activity Questionnaire (RPAQ) [4]. The RPAQ collects information about

112 activities performed at home, work and leisure time and also the time spent on  
113 each activity in the preceding 4 weeks. The RPAQ has been validated against  
114 doubly labelled water technique in general population [4], and has been shown to  
115 be a reliable tool for estimation of energy expenditure in patients with chronic  
116 kidney disease [7]. Physical activity data was determined by each reported  
117 activity being assigned a Metabolic Equivalent of Task (MET) value according to  
118 the Compendium of Physical Activities [8]. The equations for calculating Resting  
119 Energy Expenditure (REE) and Total Energy Expenditure (TTE) are described in  
120 the Appendix, along with the Boer equation for estimating lean body mass from  
121 anthropomorphic measurements.

122 Patient comorbidity was determined using the Stoke-Davies co-morbidity  
123 grading, and normalised nitrogen protein equivalent appearance rate (nPNA)  
124 calculated from total 24 hour urea removal.

125 Ethical approval was granted by the UK National Research Ethics  
126 Committee - Essex and the study was registered in UK Clinical Research  
127 Network (CRN) Portfolio number 14018. All patients provided written informed  
128 consent in keeping with the declaration of Helsinki.

129

### 130 Statistical analysis

131 Statistical analysis was by paired analysis, students' t tests, or Wilcoxon  
132 pair analysis, with appropriate correction for multiple testing, Pearson or  
133 Spearman's correlation (GraphPad Prism version 6.0, San Diego, USA), and Bland  
134 Altman comparison (Analyse-It version 3.0, Leeds, UK). Data are presented as

135 mean  $\pm$  standard deviation, median (inter quartile range), or mean and 95%  
136 confidence limits (CL), or as a percentage.

137

### 138 Results

139 We studied 87 patients, 50 male (57.4%), 25 diabetic (28.7%), mean age  
140 60.3 $\pm$ 17.6 years, with a median duration of peritoneal dialysis 11.4 (4.7-29.5)  
141 months. The mean weight was 70.1 $\pm$ 17.7 kg with a median co-morbidity grade of 1  
142 (0-1). The mean REE was 1509 $\pm$ 245 kcal/day and TEE 1947 $\pm$ 378 kcal/day,

143 Male patients were heavier than females, but this was not significant due  
144 to the wide variation in weights, and body mass index (BMI) was similar (table 1).  
145 Whereas male PD patients had significantly greater lean body mass, both  
146 measured by DEXA and estimated by the Boer equation, female patients had  
147 greater body fat mass. Patient co-morbidity, serum albumin and CRP and dialysis  
148 adequacy, as assessed by weekly Kt/Vurea were similar between the sexes.  
149 Similarly assessment of dietary protein intake was similar. Male patients had  
150 higher haemoglobin, but after correcting for multiple statistical testing this  
151 difference was no longer significant. Male patients had a greater REE but not  
152 TEE (table 1).

153 On univariate analysis, REE was associated with body size; (weight  $r=0.78$ ,  
154 BMI  $r=0.72$ , both  $p<0.001$ ), and body composition (lean mass (DXA)  $r=0.77$ , lean  
155 body mass Boer  $r=0.81$ , lean body mass index (DXA)  $r=0.76$ , lean body mass index  
156 (Boer)  $r=0.62$ , fat mass  $r=0.56$ , all  $p<0.001$ ). Similarly for TEE, there was an  
157 association with body size; (weight  $r=0.58$ , BMI  $r=0.49$ , both  $p<0.001$ ), and body

158 composition (lean mass (DXA) (Figure 1), lean body mass Boer  $r=0.60$ , lean body  
159 mass index (DXA) ( $r=0.54$ ), lean body mass index (Boer)  $r=0.40$ , all  $p<0.001$  and  
160 fat mass  $r=0.35$ ,  $p=0.001$ ). There was no association between percentage body  
161 fat and either REE or TEE ( $r=0.07$  and  $r=-0.04$ ,  $p>0.05$ ) respectively. Separating  
162 the cohort by gender, then there was a positive correlation between fat mass  
163 and REE (males  $r=0.53$ , women  $r=0.73$ ,  $p<0.000$ ), and also between TEE and lean  
164 body mass index (Figure 1).

165         Although there was a significant correlation between lean body mass and  
166 lean body mass index between that measured by DXA, and that estimated by  
167 the Boer equation ( $r=0.8$ ,  $r=0.66$ ,  $p<0.001$  respectively), on Bland Altman  
168 comparison, the estimation by the Boer equation systematically over estimated  
169 lean body mass and index for smaller patients, and then under-estimated lean  
170 body mass and index for heavier patients (Figure 2).

171

## 172 Discussion

173         Traditionally the amount of dialysis delivered to patients with end stage  
174 kidney failure is based on urea clearance adjusted for total body water volume.  
175 However as uraemic toxins are generated by cellular metabolism, and in  
176 particular it has been suggested that the amount of dialysis required for  
177 patients should be based on metabolic rate [2]. Studies to-date have  
178 concentrated on resting metabolic rate [3], but this ignores physical activity,  
179 and as such under estimates TTE. We therefore set out to determine both REE

180 and TEE using equations based on patient self-reported physical activity  
181 questionnaire, which has been validated using doubly labelled isotopic water [4].

182         Muscle activity is reduced when at rest, and as such basal metabolic rate  
183 may not reflect muscle mass. Similarly as physical inactivity leads to loss of  
184 muscle we wished to determine whether there was an association between  
185 muscle mass and both REE and TEE. We found that there was a positive  
186 association for both REE and TEE and both muscle mass, and muscle mass index  
187 whether measured by DXA scanning, or estimated by the Boer equation. The  
188 correlations between REE and TEE were statistically greater for lean body  
189 mass, than for fat mass, BMI or weight, and there was no association with  
190 percentage body fat. Correlations with TEE and REE were stronger for lean  
191 body mass for men, and for fat mass with women, respectively. Previous studies  
192 which have concentrated on either measuring basal metabolic rate or maximal  
193 exercise capacity in peritoneal dialysis patients failed to demonstrate an  
194 association between REE and muscle mass [9,10]. As such these studies were  
195 unable to estimate TEE, whereas our equation estimating both REE and TEE  
196 demonstrates a strong association with lean body mass and index.

197         Although there was a strong association between lean body mass and lean  
198 body mass index measured by DEXA scanning and that estimated by the Boer  
199 equation using anthropomorphic measurements, the Boer equation systematically  
200 over-estimated lean body mass and index for smaller patients and then under-  
201 estimated lean body mass and index for heavier patients. As such, for this group  
202 of peritoneal dialysis patients then measurement of lean body mass with DEXA



203 scanning is to be preferred than estimating muscle mass by anthropomorphic  
204 based equations. Understanding the relationship between body composition and  
205 energy expenditure is important as patients with greater energy expenditure  
206 generate more waste products of metabolism , and as such require greater  
207 clearances by dialysis.

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215

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258 Figure 1: correlation between lean body mass index measured by dual electron X  
 259 ray absorption (DEXA) and total energy expenditure (TEE). (males  $r = 0.62$ ,  
 260  $p < 0.001$  and females  $r = 0.45$ ,  $p < 0.001$ ).  
 261  
 262  
 263

264 Figure 2: Bland Altman analysis of lean body mass index measured using dual  
 265 electron X-ray absorption (DEXA) and lean body mass calculated by the Boer  
 266 equation. Mean bias 1.5 kg/m<sup>2</sup> (95% confidence limits -2. to 5.4 kg/m<sup>2</sup>).  
 267 .  
 268  
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 270

## 271 Appendix

272  
 273 Resting Energy Expenditure (REE) was estimated from a newer novel predictive  
 274 equation which was derived and validated in a cohort of HD patients [4].  
 275

$$276 \text{ REE} = -2.497 * \text{Age}(\text{years}) * \text{Factor}_{\text{age}} + 0.011 * \text{Height}^{2.023}(\text{cm}) + 83.573 * \\ 277 \text{Weight}^{0.6291}(\text{kg}) + 68.171 * \text{Factor}_{\text{sex}}$$

278  
 279 where Factor age is 0 if age <65 and 1 if ≥65 and Factor sex is 0 if female and 1  
 280 if male  
 281

282 Physical activity data - Each reported activity was assigned a Metabolic  
 283 Equivalent of Task (MET) value as per the Compendium of Physical Activities [4].  
 284 Sleep time per day was assumed to be 8 hours and any unreported time during

285 the day was assumed as the time performing light activities at home. A Mean  
286 daily MET value was calculated.

287

288 Total Energy Expenditure (TEE) was estimated from the following equation.

289 
$$\text{TEE} = \text{REE} * \text{Mean Daily MET}$$

290 .

291

292 Boer equation

293

294 Lean body mass (male) =  $(0.407 \times \text{Weight kg}) + (0.267 \times \text{height cm}) - 19.2$

295

296

297 Lean body mass (female) =  $(0.252 \times \text{Weight kg}) + (0.473 \times \text{height cm}) - 48.3$

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