Decreased resting energy expenditure in non-dialysed chronic kidney disease patients

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Abstract

Background. Non-dialysed chronic kidney disease (CKD) patients may have altered resting energy expenditure (REE) because of the important metabolic functions of the kidneys. The aim of the present study was to evaluate whether REE in clinically stable, non-diabetic and non-dialysed CKD patients with no clinical signs of inflammation, was different from that of gender and age pair-matched healthy controls.

Subjects and methods. REE in 45 patients (20 male and 25 female; age 44.9±11.7 years; mean±SD) and 45 healthy individuals (20 male and 25 female; age 44.6±11.5 years) was measured by indirect calorimetry after a 12-h fast. In both groups, body composition was assessed by bioelectrical impedance. Glomerular filtration rate was assessed by creatinine clearance only in the CKD patients.

Results. The mean creatinine clearance and serum creatinine of the CKD patients were 29.1±14.6 ml/min/1.73 m² and 3.48±2.48 mg/dl, respectively. Body fat (BF) and lean body mass (LBM) were similar between the two groups (CKD patients: BF 28.6±11.3%, LBM 46.9±10.0 kg; and healthy individuals: BF 28.1±7.54%, LBM 49.5±10.5 kg). REE of CKD patients was significantly lower than that of healthy individuals (1325±206 vs 1448±258 kcal/day; P = 0.01, respectively) even after adjusting for LBM by multiple regression analysis. In fact, the presence of chronic renal insufficiency reduced REE by 103.2 kcal/day (P = 0.02; 95% confidence interval (−15.9; 190.5)).

Conclusion. REE of clinically stable non-dialysed, non-diabetic patients in stages 2–5 of CKD was lower than that of age and gender pair-matched healthy individuals. Although the cause of reduced REE was unclear, it may be related to decreased food intake and to metabolic disturbances inherent with deterioration of renal function. Further studies will be necessary to clarify this issue.

Keywords: chronic kidney failure; predialysis; resting metabolic rate

Introduction

In patients with diseases involving organs that have important metabolic functions, energy metabolism is frequently altered [1–3]. For example, the kidneys have important metabolic functions and perform a number of oxygen-dependent activities [4]. Oxygen consumption by the kidneys rises as a function of glomerular filtration rate [4]. In healthy individuals the kidneys account for ~7% of the resting energy expenditure (REE) [5]. Moreover, a previous study suggested that renal failure is associated with a hypometabolic and hypothermic state due to profound abnormalities in cell metabolism [6]. In fact, Kurnik et al. [7] have shown that patients with moderate loss of renal function have lower renal blood flow and lower renal oxygen consumption per kidney than healthy individuals. Therefore, it is possible that patients with chronic kidney disease (CKD) and decreasing glomerular filtration rate may have reduced REE. Alternatively, the progression of renal insufficiency is associated with certain metabolic disturbances, such as metabolic acidosis, insulin resistance, and inflammation, that increase protein catabolism [8,9] and could in turn raise REE. It has also been shown that CKD patients with poorly controlled diabetes mellitus and with severe hyperparathyroidism have increased REE [10,11].

Only a few studies have compared the REE of non-dialysed and haemodialysed CKD patients with that of healthy individuals. These studies reported either increased [12], decreased [13] or similar REE to that of healthy individuals [14,15]. The causes of these disparities may be secondary to differences in...
study protocols. For example, it is not clear whether the groups were matched for factors that may influence REE, such as gender and age or whether the measurements were adjusted lean body mass (LBM), which is the main determinant of REE.

The aim of the present study was to evaluate whether REE in clinically stable CKD patients is altered compared with that of gender and age-matched healthy control individuals.

Subjects and methods

Subjects

Forty-five non-dialysed CKD patients were recruited from the renal outpatient clinic of the Federal University of Sao Paulo—Oswaldo Ramos Foundation (Sao Paulo, SP, Brazil). The study included clinically stable patients older than 18 years who had normal thyroid function. Exclusion criteria included history of diabetes mellitus, pregnancy, treatment with corticosteroid or immunosuppressive drugs, or clinical signs of infection. The majority of the patients (94%, n = 42) were taking diuretics and anti-hypertensive medications and 40% of the patients (17/42) were taking β-blockers. A diet containing ∼30–35 kcal/kg/day of which 0.6–0.8 g/kg/day was protein was prescribed for 89% of the patients (n = 40). Forty-five healthy adult individuals, most of them related to the CKD patients and to the clinic employees, were also recruited to form a control group. Inclusion criteria for the control group were ages greater than 18 years and normal thyroid function. Exclusion criteria included illnesses, pregnancy, or clinical signs of infection. All control subjects underwent blood tests to ensure that they had normal renal function and that none were taking medication.

All subjects enrolled in the study were asked about their level of physical activity. In both groups, the majority of subjects were sedentary [31 patients (69%) in the CKD group and 29 subjects (64.4%) in the control group]. Walking two to five times/week for 15–50 min was the main physical activity of the remaining subjects of both groups. None of the subjects practiced heavy physical activities.

The Human Investigation Review Committee of the Federal University of Sao Paulo approved the study and informed consent was obtained from each subject.

Study design

We used a cross-sectional study design that compared 45 non-dialysed CKD patients with 45 healthy individuals. Subjects in the two groups were pair-matched for gender and age (matching limit for age was ±5 years). All CKD patients and healthy controls were initially interviewed to test for inclusion criteria and to obtain informed consent. On the same day, the CKD patients were instructed to fill out a 4 day food diary and to collect urine for a 24 h period. At 1–3 weeks later, the subjects underwent fasting blood tests, measurements of REE and body composition, as well as assessment of nutritional status.

Biochemical data

Blood samples were drawn after an overnight fast of 12 h. Serum creatinine, urea, bicarbonate, intact parathyroid hormone (PTH), C-reactive protein (CRP), albumin, glucose, insulin, leptin and thyroid stimulating hormone (TSH) were measured in all CKD patients. The healthy controls were measured for serum determinations of creatinine, glucose, insulin, leptin, CRP and TSH.

Serum creatinine, urea and glucose were determined using a standard autoanalyser. Bicarbonate was measured by an automated potentiometer (normal range: 23–27 mmol/l), TSH (normal range: 0.3–4.0 mU/l) and insulin by immuno-fluorometric assays and albumin by green bromocresol technique. Intact PTH (normal range: 10–65 pg/ml) and high-sensitivity CRP (inflammatory state: >0.5 mg/dl) were determined by immunochemiluminescence. Leptin was measured using an immunoenzymatic assay (ELISA) kit (Quantikine™, R&D Systems, Minneapolis, MN, USA).

Glomerular filtration rate was evaluated using standard creatinine clearance (24 h urine collection) corrected for body surface area (1.73 m²). Proteinuria and urinary urea were estimated from 24 h urine samples.

Homeostasis model assessment (HOMA)

Insulin resistance was estimated from HOMA scores, which were calculated using the equation: fasting serum insulin (µU/ml) × fasting plasma glucose (mmol/l)/22.5, as described by Matthews and coworkers [16]. According to this method high HOMA scores denote insulin resistance.

Resting energy expenditure

REE was measured by indirect calorimetry using an open circuit ventilated computerized metabolic system (Vmax series 29n, SensorMedics Corp; Yorba Linda, CA, USA). Initially, the flow sensor was calibrated with a syringe piston in order to allow measurements of high and low inspiratory and expiratory flows. Oxygen and carbon dioxide sensors were then calibrated before each REE measurement with the use of mixed reference gases of known compositions. All subjects had been instructed to maintain their regular medication, to refrain from any unusual physical activity (playing sports, lifting weight, jogging, walking, etc.) for 24 h prior to the test and to maintain their usual sleep schedule during the night before the REE measurement. They were admitted to the clinic at 08:00 after an overnight fast of 12 h. After resting for 30 min in a recumbent position, subjects breathed for 30 min through a clear plastic canopy placed over their heads in a quiet dimly lit thermoneutral room. They were instructed to avoid hyperventilation, fidgeting or falling asleep during the test. Oxygen consumption and carbon dioxide production were measured at 1 min intervals and the mean of the last 20 min was used to calculate the REE according to the Weir’s equation [17]. These measurements did not include urinary urea nitrogen. The respiratory quotient was calculated as the ratio of volume of carbon dioxide expired to the volume of oxygen consumed. Predicted basal metabolic rate was calculated according to the Harris and Benedict equation [18] and estimated total energy expenditure was calculated by multiplying measured REE by 1.50 (factor for low physical level) [19].

Body composition

Body composition was determined by bioelectrical impedance with a portable device (model BIA 101 Quantum,
Nutritional assessment

Anthropometric measurements included body weight, height, triceps skinfold thickness and midarm circumference and were performed in the morning by the same observer. In the CKD group, skinfold measurements of triceps, biceps, suprailiac and subscapular regions were performed in order to assess LBM and BF. Body density was calculated according to the formula of Durnin and Womersley [20], and percent BF was then derived from the Siri’s equation [21]. Skinfold thickness was measured using a Lange Caliper (Cambridge Instrument, Cambridge, MD, USA). The measurements were performed on the non-dominant arm. Midarm muscle circumference was calculated using the formula: arm circumference – 0.314 × triceps skinfold thickness. Percent standard of triceps skinfold thickness and mid-arm muscle circumference were obtained using the National Health and Nutrition Examination Survey (NHANES) percentile distribution tables adapted by Frisancho. Body mass index (BMI) was calculated as body weight divided by squared height, and desirable body weight was based on the data from the Metropolitan Life Insurance table adapted by Grant.

Energy and protein intakes were estimated from a 4 day food diary (3 week days and 1 weekend day). Food diaries were reviewed in detail with each patient using various models of foods and measuring tools to estimate portion sizes and to improve the accuracy of the registry. Energy and protein intakes were calculated using computer software developed by the Federal University of Sao Paulo, which contains the US Department of Agriculture (USDA) tables as the nutrient database. Protein equivalent of nitrogen contains the US Department of Agriculture (USDA) tables developed by the Federal University of Sao Paulo, which were introduced into the subject and resistance and reactance were measured. The software provided by the manufacturer calculated the total body water, LBM, and body fat (BF).

Statistical analysis

All data are expressed as mean± standard deviation (SD). For comparisons between CKD patients and the healthy individuals, two-tailed paired Student’s-t-tests and chi-square test were used, as appropriate. Continuous variables that did not present approximately normal distribution by the Kolmogorov-Smirnov test were log-transformed (natural base) and their values are presented in terms of geometric means and range. Pearson correlation coefficients were used to determine which variables presented linear correlation with REE. The use of ratios for adjusting REE for LBM may create errors and differences between the two groups may be found when there is no actual difference [23]. In order to compare REEs between the two groups that were independent of differences in LBM, REE was adjusted for LBM using multiple linear regression with robust estimation for the error structure due to the matching design of the study [24]. The significance level for REE comparisons between the CKD and control groups was fixed at 0.05 and the power was fixed at 0.80. Differences with P-values <0.05 were considered statistically significant. Statistical analyses were completed using the software Stata 7.0 (Stata Corp., College Station, TX, USA).

Results

The main characteristics of the CKD and control groups are presented in Table 1. Each group had 20 men and 25 women. The two groups were matched for age, and BMI did not differ between CKD patients and controls. The main causes of CKD were hypertensive nephrosclerosis in 15 patients (33%), chronic glomerulonephritis in 10 (22%), polycystic kidney disease in four (9%), indeterminate in 13 (29%) and other causes in three patients (7%). The majority of the CKD patients were in the stage 3 of CKD with a moderate loss of renal function, as judged by mean creatinine clearance along with the classification proposed by the K/DOQI guidelines—National Kidney Foundation. Detailed analysis revealed that 21 patients (48%) had metabolic acidosis ( serum bicarbonate <23 mmol/l) and 16 patients (36.6%) had secondary hyperparathyroidism (PTH >210 pg/ml). Compared with the control group, serum leptin was significantly lower in the CKD group.

Table 1. Main demographic and clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>CKD group</th>
<th>Control group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=45)</td>
<td>(n=45)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>20 (44.4%)</td>
<td>20 (44.4%)</td>
<td>NA</td>
</tr>
<tr>
<td>Age (years)</td>
<td>44.9±11.7</td>
<td>44.6±11.5</td>
<td>0.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.3±4.21</td>
<td>25.7±3.62</td>
<td>0.6</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>3.48±2.01</td>
<td>0.83±0.19</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Creatinine clearance (ml/min/1.73 m²)</td>
<td>29.1±14.6</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Range (ml/min/1.73 m²)</td>
<td>6–61</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Leptin (ng/ml)α</td>
<td>6.24 (0.22–135)</td>
<td>2.15 (0.20–11.0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Serum glucose (mg/dl)</td>
<td>88.1±9.61</td>
<td>84.4±10.6f</td>
<td>0.04</td>
</tr>
<tr>
<td>TSH (µIU/ml)</td>
<td>2.42±1.64</td>
<td>1.56±0.92</td>
<td>0.02</td>
</tr>
<tr>
<td>Serum urea (mg/dl)</td>
<td>96.1±47.8</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Serum bicarbonate (mmol/l)</td>
<td>230±4.25</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Intact PTH (pg/ml)</td>
<td>252.8±257.9</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>3.96±0.41</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Urinary protein excretion (g/24h)</td>
<td>1.33±1.73</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Values are means±SD; NA, not applicable.
αGeometric mean and range.
βP<0.01: male vs female.
εn = 30.
higher in CKD patients (Table 1), even after controlling for BF [CKD group: $2.15 \text{ng/ml} \,(0.20–11.0 \text{ng/ml})$ vs control group: $0.34 \text{ng/ml} \,(0.01–6.11 \text{ng/ml})$; geometric mean and range; $P < 0.01$]. This difference remained even when the groups were compared according to gender (Table 1). In addition, leptin concentrations were higher in female patients in both groups. HOMA scores and CRP were similar in the groups, but a more pronounced insulin resistance (HOMA score $>3.0$) was present in eight patients (17.7%) in the CKD group vs only two subjects (6.6%) of the control group (chi-square test not significant).

Moreover, CRP concentrations were indicative of an inflammatory state (CRP $>0.5 \text{mg/dl}$) in 13 patients (28.8%) of the CKD group but only in five subjects (11.1%) of the control group (chi-square test not significant). Although serum glucose and TSH were significantly higher in the CKD group, they were within the normal range in both groups.

The data showing anthropometric parameters and body composition are presented in Table 2. Standard midarm muscle circumference and triceps skinfold thickness were similar in the two groups and the mean values were not indicative of malnutrition.

### Table 2. Anthropometric parameters and body composition

<table>
<thead>
<tr>
<th></th>
<th>CKD group ($n = 45$)</th>
<th>Control group ($n = 45$)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard MAMC (%)</td>
<td>96.0 ± 11.3</td>
<td>94.9 ± 8.51</td>
<td>0.5</td>
</tr>
<tr>
<td>Standard TSF (%)</td>
<td>106.5 ± 50.9</td>
<td>108.1 ± 36.4</td>
<td>0.9</td>
</tr>
<tr>
<td>LBM (kg)</td>
<td>46.9 ± 10</td>
<td>49.5 ± 10.5</td>
<td>0.24</td>
</tr>
<tr>
<td>SKF</td>
<td>46.6 ± 10</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>LBM (%)</td>
<td>71.3 ± 11.3</td>
<td>71.8 ± 7.54</td>
<td>0.7</td>
</tr>
<tr>
<td>BF (%)</td>
<td>70.2 ± 8.3</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>BIA</td>
<td>28.6 ± 11.3</td>
<td>28.1 ± 7.54</td>
<td>0.7</td>
</tr>
<tr>
<td>SKF</td>
<td>29.8 ± 8.3</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Body water (l)</td>
<td>34.6 ± 7.15</td>
<td>36.8 ± 8.35</td>
<td>0.12</td>
</tr>
<tr>
<td>Body water (%)</td>
<td>52.9 ± 6.5</td>
<td>50.0 ± 6.19</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Values are means ± SD. MAMC, midarm muscle circumference; TSF, triceps skinfold thickness; BIA, bioelectrical impedance; SKF, skinfold thickness.

$n = 30$.

*NS, comparison between BIA and SKF in the CKD group.

Similarly, there were no differences in LBM, percentage of BF or body water. In addition, LBM and the percentage of BF assessed by bioelectrical impedance and by the sum of the four skinfold thicknesses were not different.

The estimated energy intake of the CKD patients was $1510 ± 419 \text{kcal/day}$ or $26.2 ± 6.56 \text{kcal/kg/day}$. Protein intake estimated by food diaries was significantly lower than protein intake estimated by non-normalized PNA ($45.4 ± 14.1$ vs $54.3 ± 10.6 \text{g/day}$, respectively; $P < 0.01$) and by normalized PNA (nPNA) ($0.78 ± 0.24$ vs $0.92 ± 0.17 \text{g/kg/day}$, respectively; $P < 0.01$).

The REE data are shown in Table 3. REE was significantly lower in the CKD group than in the control group ($-123 \text{kcal/day} \; (−8.5\%)$. When REE was analysed according to gender, the absolute REE remained significantly lower in female patients than in controls. The male patients showed a tendency towards decreased REE. REE adjusted for body surface area was also lower in CKD patients than in controls. When REE was adjusted for LBM, using multiple regression analysis, the REE of CKD patients was $103.2 \text{kcal/day}$ lower than that of healthy individuals (Table 4 and Figure 2), which corresponds to 7.1% of REE in the healthy individuals. In addition, Table 3 shows that only the CKD group had REE values that were significantly lower than their predicted basal metabolic rates and that the ratio between measured REE and estimated basal metabolic rate was significantly lower in patients than in healthy individuals. The respiratory quotient was significantly higher in the CKD patients.

There were no differences in REE between patients taking β-blockers ($n = 17$; REE: $1360 ± 192 \text{kcal/day}$ or $28.7 ± 5.2 \text{kcal/kg LBM/day}$) and those not taking this anti-hypertensive ($n = 28$; REE: $1304 ± 215 \text{kcal/day}$ or $28.9 ± 4.6 \text{kcal/kg LBM/day}$).

In the CKD group, REE was significantly correlated with LBM ($r = 0.61$, $P < 0.01$) and with PNA ($r = 0.57$, $P < 0.01$; Figure 1). A correlation of borderline significance was found between REE and creatinine clearance ($r = 0.27$, $P = 0.06$). There were no correlations between REE and serum creatinine and energy or protein intake. In the control group, REE significantly correlated with LBM ($r = 0.74$, $P < 0.01$) and with HOMA scores ($n = 30$, $r = 0.61$, $P < 0.01$). REE was not correlated with CRP or with serum leptin in either group.

In order to estimate total energy expenditure, the measured REE of each patient was multiplied by 1.50 (factor for low physical activity level). The obtained

### Table 3. Resting energy expenditure

<table>
<thead>
<tr>
<th></th>
<th>CKD group ($n = 45$)</th>
<th>Control group ($n = 45$)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>REE (kcal/day)</td>
<td>1325 ± 206</td>
<td>1448 ± 258</td>
<td>0.01</td>
</tr>
<tr>
<td>Male</td>
<td>1447 ± 221</td>
<td>1590 ± 240</td>
<td>0.07</td>
</tr>
<tr>
<td>Female</td>
<td>1228 ± 130</td>
<td>1327 ± 206</td>
<td>0.01</td>
</tr>
<tr>
<td>REE (kcal/min/1.73 m²)</td>
<td>0.92 ± 0.11</td>
<td>0.97 ± 11</td>
<td>0.04</td>
</tr>
<tr>
<td>Predicted BMR (kcal/day)</td>
<td>1445 ± 195</td>
<td>1489 ± 241</td>
<td>0.3</td>
</tr>
<tr>
<td>Ratio REE/BMR</td>
<td>0.91 ± 0.09</td>
<td>0.98 ± 0.12</td>
<td>0.01</td>
</tr>
<tr>
<td>Respiratory quotient</td>
<td>0.89 ± 0.06</td>
<td>0.82 ± 0.07</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Values are means ± SD. BMR, basal metabolic rate.

* $P ≤ 0.01$, REE vs predicted BMR.

### Table 4. Multiple linear regression

<table>
<thead>
<tr>
<th></th>
<th>Coefficient (kcal)</th>
<th>$P$</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD group</td>
<td>$-103.2$</td>
<td>0.02</td>
<td>($-15.9$; $-190.5$)</td>
</tr>
<tr>
<td>LBM (kg)</td>
<td>27.2</td>
<td>&lt;0.01</td>
<td>(25.8; 28.6)</td>
</tr>
</tbody>
</table>
mean total energy expenditure obtained was 1989 ± 310 kcal/day and the total energy expenditure normalized for body weight was 30.3 ± 4.50 kcal/kg/day.

Discussion

In the present study, a representative group of clinically stable non-diabetic CKD patients with varying degrees of renal impairment but with no clinical signs of inflammation had lower REE than that of gender and age pair-matched healthy individuals. Only a few studies have measured REE in non-dialysed CKD patients. In the study by Montee et al. [14], energy expenditure was measured in 10 non-dialysed chronically uraemic patients, 16 haemodialysis patients and in 12 healthy individuals, during resting, quiet sitting, controlled exercise, and at 4 h after ingestion of a test meal. The authors reported that energy expenditure adjusted for body surface area of non-dialysed and haemodialysis patients were not different from that of healthy individuals. Similar results were obtained by Schneeweiss et al. [15], who found that REE values adjusted for body surface area of non-dialysed and haemodialysis patients were similar to that of healthy controls, except in patients with acute renal failure and sepsis. However, these studies failed to match the patients by gender or age, and REE values were not adjusted for LBM. The disparity in findings between these and the present study may be a consequence of differences in study protocols. In fact, our results are in accordance with those of O'Sullivan et al. [13] who found that REE adjusted for LBM in 15 elderly patients with a modest degree of renal impairment was lower than that in 15 healthy subjects that were pair-matched for gender, age, weight and height.

Our finding that CKD patients but not controls had REE levels that were significantly lower than predicted basal metabolic rate further indicates that REE was lower in CKD patients. Passey et al. [25] also reported that REE of non-dialysed CKD patients was 8% lower than the predicted basal metabolic rate calculated by the Harris and Benedict equation. In contrast, Neyra et al. [26] observed a tendency toward a higher REE in non-dialysed CKD patients compared with predicted values also obtained by the Harris and Benedict equation.

The exact causes of reduced REE of CKD patients are unknown, but there are several mechanisms that may be involved. Because LBM is the main determinant of REE [27], reductions in this parameter, which is frequent in CKD patients [13], may lead to a lower REE. Nevertheless, in the current study, LBM was similar in CKD patients and in controls and the multiple regression analysis indicated that REE adjusted for LBM was still significantly lower in CKD patients than in healthy controls (Table 4 and Figure 2). An impaired energy metabolism of skeletal muscle caused by uraemic toxins is an abnormality often present in pre-dialysis uraemic patients and may lead to reduced energy consumption by muscle [28]. Moreover, a previous study suggested that acute and chronic renal failure is associated with a hypometabolic and hypothermic state that is due to profound abnormalities in cell metabolism [6]. Impaired glucose oxidation, a common metabolic derangement of uraemia, may also be of importance, since elevations in glucose oxidation and improvements in tissue insulin sensitivity achieved following dietetic manipulation were accompanied by increases in REE [29]. However, in the present study, both groups had similar indices of insulin resistance, as evaluated by the HOMA score. The use of β-blockers may also play a role since these drugs have been shown to decrease REE [30]. However, the patients using β-blockers in our study had similar REE as those not given these drugs. An adaptive response to decreased food intake may also explain the decreased REE. Although we failed to show a correlation between REE and energy or protein intake estimated by food diaries, REE was directly and significantly correlated with PNA (r = 0.57, P < 0.01). Given that PNA is a better tool for estimating protein consumption in CKD patients [31] and that these patients were clinically stable, this correlation suggests a link between REE and protein and/or energy intake (Figure 1). Thus, the association of low protein intake with low REE may reflect an adaptive response to a decreased protein intake and possibly to a decreased mass.
energy intake. Such an adaptive response has already been reported in obese patients placed on a low-energy diet [32]. Finally, a reduced REE may result from decreased energy expenditure by the failing kidneys, which in healthy individuals are responsible for ~7% of the REE [5]. If this is true, a direct correlation between the degree of renal impairment and REE would then be expected. In accordance with the data reported by O’Sullivan et al. [13], we also observed a borderline significant correlation between REE and creatinine clearance (r = 0.27, P = 0.06). However, this result does not clearly demonstrate an association between REE and glomerular filtration rate.

In contrast to the possibilities described above, increased protein catabolism during chronic renal insufficiency would predict a higher level of REE. It is well established that metabolic acidosis, inflammation, and insulin resistance increase protein catabolism by acceleration of protein breakdown and degradation of branched-chain amino acids [33]. Since these metabolic pathways are energy consuming processes [34], we speculate that these derangements could lead to increases in REE. The increased serum leptin levels in the CKD patients may also play a role by interfering with appetite and energy expenditure. Because some of our CKD patients presented with metabolic acidosis, elevated CRP, insulin resistance, hyperparathyroidism and hyperleptinaemia, it is of note that none of these biochemical markers were correlated with REE. It is possible that the severity of these metabolic disturbances was not sufficient to increase REE in these patients. In previous studies examining non-CKD patients, only the occurrence of acute inflammation led to an elevation in REE [33,34]. In addition, only poorly controlled CKD diabetic patients [10] and haemodialysis patients with severe hyperparathyroidism [11] had increased REE levels.

Our patients had a low physical activity level. However, the mean estimated daily energy expenditure normalized per body weight in our CKD patients was 30.3 ± 4.50 kcal/kg/day, which is close to the 30–35 kcal/kg/day previously recommended for these patients. Even though daily energy expenditure was estimated and not measured, our result suggests that the amount of energy intake usually recommended for CKD patients was adequate, even with the reduced REE found in the CKD patients.

The use of bioelectrical impedance to evaluate LBM in CKD patients may have limited the present study because of possible alterations in hydration status. Nevertheless, body water in CKD patients was similar to that of healthy individuals, and no differences were observed when LBM and BF assessed by bioelectrical impedance of CKD patients were compared with measurements of skinfold thickness. It is therefore unlikely that estimations of LBM by bioelectrical impedance were a major problem in the present study.

In conclusion, clinically stable non-diabetic patients in stages 2–5 of CKD presented with reductions in REE. The mechanisms responsible for the reduced REE are unclear, but may be related to several factors including decreased food intake and various metabolic disturbances related to decreased renal function. Further studies will be necessary to clarify this issue.

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