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Original article

# Impact of metabolic syndrome on resting energy expenditure in patients with chronic kidney disease

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SUMMARY

*Background & aims:* Resting energy expenditure (REE) changes in patients with chronic kidney disease (CKD) may contribute to mortality increase. The obesity and inflammation is associated with high REE and when not compensated by adequate intake, may determine an unfavorable clinical outcome in this population. We aimed to evaluate the influence of metabolic syndrome (MetS) on REE in CKD patients.
*Methods:* One hundred eighty-three patients were stratified according to glomerular filtration rate (GFR) and divided in groups: without CKD (GFR > 60 ml/min/1.73 $m^2$) and CKD (GFR < 60 ml/min/1.73 $m^2$) and according to the presence or absence of MetS. REE was measured by indirect calorimetry; body composition was assessed by bioelectrical impedance analysis and blood and urine were collected for biochemical tests.
*Results:* REE was lower in the group with CKD compared with those without CKD (1293 ± 364 vs 1430 ± 370 kcal/d, P = 0.01). The group with CKD without MetS showed decrease in REE compared to the groups without CKD, regardless the presence of Mets, and those with CKD and MetS (1173 ± 315 vs 1392 ± 324 vs 1460 ± 410 vs 1424 ± 376 kcal/d, P < 0.05, respectively). Multivariate analysis showed an independent association of CKD in determining REE when adjusted for lean body mass. The inclusion of MetS as an independent variable in the same analysis model neutralized the impact of CKD on the REE (P = 0.19). Patients without MetS, REE correlated with estimated GFR and the protein equivalent (r = 0.33, P < 0.01, r = 0.21, P = 0.04, respectively), whereas in MetS patients, these correlations were not observed.
*Conclusion:* The presence of CKD is independently associated with reduced REE. The observed decrease in REE is reversed in patients with MetS independent of renal function.


## 1. Introduction

Patients with chronic kidney disease (CKD) are prone to nutritional disorders, including protein-energy malnutrition and overweight/obesity [1]. The prevalence of obesity is dramatically increasing worldwide, and there may constitute 20–60% of patients with CKD [2,3]. Visceral obesity, core metabolic syndrome (MetS), is conceived as the pathophysiological basis of the epidemic incidence of cardiovascular events and renal dysfunction [4]. Chen et al. studied the risk of developing kidney disease in a cohort of NHANES III, where 7800 participants with normal renal function were followed for a period of 21 years. The presence of MetS resulted in a 2.6-fold risk for developing CKD [5].

Regardless of the cause of metabolic disorders, both malnutrition and overweight deserve proper treatment to maintain and/or restore nutritional status. Accordingly, the estimated resting energy expenditure (REE) should be properly adjusted to the lean body mass of these patients. In fact, Avesani et al. demonstrated a reduction of 123 kcal/day in the REE group of CKD patients when

*List of abbreviations:* REE, resting energy expenditure; CKD, chronic kidney disease; MetS, metabolic syndrome; GFR, glomerular filtration rate; eGFR, estimated glomerular filtration rate; DM, diabetes mellitus; PCR, C-reative protein; IC, indirect calorimetry; BMR, basal metabolic rate; BIA, bioelectrical impedance analyzer; TSF, triceps skinfold thickness; MAMC, mid-arm muscle circumference; CMI, corporal mass index; PNA, protein equivalent of nitrogen appearance.

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compared to a group of healthy subjects, and this reduction persisted after adjustment for lean body mass [6]. Subsequent studies have confirmed these findings, specifically analyzing subpopulations of older adults with CKD (O'Sullivan et al.) and subjects with non-dialysis renal dysfunction (Avesani et al.) [6,7]. In addition, evidence suggests a direct relationship of inflammation with energy expenditure in individuals presenting renal dysfunction. In this context, Utaka et al. demonstrated in a subpopulation of non-dialysis CKD patients that energy expenditure was higher in patients with inflammation and that REE was reduced after treatment for the inflammatory condition [8]. In patients undergoing renal replacement therapy, Ikizler et al. demonstrated an increased energy expenditure that was higher during hemodialysis [9].

The connection of visceral obesity with outcome and chronic inflammatory state determines significant changes in energy expenditure. On the other hand, the treatment of MetS with weight loss through both diet [10] and bariatric surgery [11] is been associated with a reduction in REE, indicating this condition as a potential marker of clinical outcome.

Hypermetabolism may be associated with increased mortality in general population and in CKD patients. In fact, Wang et al. demonstrated in a population of CKD that increased REE was associated with inflammation and higher mortality rate [12].

Thus, our study aimed to evaluate the influence of metabolic syndrome on REE in patients stratified according to glomerular filtration rate.

## 2. Subjects and methods

### 2.1. Subjects

This study included 200 patients in the Cardiovascular and Metabolism Hypertension Center at the Federal University of São Paulo - UNIFESP (São Paulo, SP, Brazil). They excluded patients taking anticoagulants or other medications that could influence the REE, dialysis patients or family hyperlipidemia, pregnancy, presence of acute inflammatory diseases, patients with degenerative tumors less than 5 years and presence of rheumatic disease activity. Hypertensive patients undergoing ambulatory routine biochemical and nutritional assessment were included. MetS was defined according to the criteria of the International Diabetes Federation - IDF (mandatory inclusion of central obesity, plus the presence of at least 2 other criteria, such as insulin resistance or diabetes mellitus (DM), hypertension, dyslipidemia, or microalbuminuria) [13], with age over 18 years.

Of the participants, 17 patients were excluded clinical signs and/or laboratory data that were indicative of infection, such as urinary infection, diagnosed by positive urine culture ($n = 7$); two were on anticoagulants, three had pneumonia and five influenza, who were diagnosed by clinical symptoms.

This study was approved by the Ethics and Research Committee of the Federal University of São Paulo.

### 2.2. Study design

It is a cross-descriptive study, participants were stratified according to glomerular filtration rate (GFR) using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) [14] equation and initially divided into 2 groups: group with no clinical CKD (GFR> 60 ml/min/1.73 $m^2$) and with CKD (GFR <60 ml/min/1.73 $m^2$). Subsequently, participants in the study ($n = 183$) were divided into 4 groups according to the presence of CKD/MetS. The outpatient routine consisted in the following: one week before the consultation, a blood sample and 24-h urine were obtained for laboratory tests, and on the day of office visit, REE, body composition and nutritional status were assessed during fasting.

### 2.3. Biochemical data

Blood samples were collected at the Center for Hypertension and Metabolism Cardiovascular UNIFESP after an overnight fast of 12 h. All patients were tested for serum creatinine, urea, C-reactive protein (CRP), albumin, triglycerides, total cholesterol and fractions, glucose, and glycated hemoglobin (the last only in diabetics).

Serum concentrations of glucose, total cholesterol, triglycerides, creatinine and urea were determined by an automated enzymatic method. The measurement of HDL-cholesterol and LDL-cholesterol was performed using commercial kits according to the manufacturer (Roche Diagnostics, Indianapolis, Ind., USA). High-sensitivity CRP was measured by immunofluorescence (inflammatory state: > 0.5 mg/dl) and albumin by the bromocresol green technique. Urinary urea was estimated in 24-h urine samples.

### 2.4. Resting energy expenditure

REE was measured by indirect calorimetry (IC) open circuit system (MetaCheck version 2.05, Korr ™ Techonologies Medical Inc). To implement the procedure, patients were accommodated in a quiet environment, with dim lighting and comfortable temperature to prevent changes caused by cold, heat or anxiety. They were admitted to the outpatient clinic at 7 am after fasting overnight for at least 8 h and were instructed to maintain habitual use of medications and to refrain from any sports activities such as jogging, hiking, etc. for 24 h before testing. IC was connected 20 min early to warm up and stabilize. During this calibration, the calorimeter measures the following parameters of the ambient air: concentration of oxygen ($O_2$), temperature, relative humidity and barometric pressure, resulting in increased accuracy of the test, since the values are automatically corrected to STPD (Standard Temperature and Pressure Dry) and therefore estimates REE in kcal/day from the measured $O_2$ consumption ($VO_2$). All patients were instructed to fast for 12 h and rest for at least 30 min, and thereafter, face-oxygen was introduced, where the individual remained breathing normally for 10 min. This mask remained connected directly to the unit to measure the amount of $O_2$ expired. Finally, at the end of the examination, the patient data for REE and other parameters were expressed in the IC monitor. Prediction of basal metabolic rate (BMR) was calculated according to the Harris & Benedict formula [15].

### 2.5. Body composition

Body composition was determined using a bioelectrical impedance analyzer (Quantum 101 Q - RJL Systems). The measurements were performed in the morning, with 12-h fast on the same day as nutritional consultation. To implement the examination, the patients lay supine on a gurney with non-conductive surface, with legs slightly apart and hands and arms away from the trunk. Four electrodes were positioned in the BIA predetermined anatomical points (ankle and hand on the same side) and measurements were taken of the bioelectrical parameters such as resistance and reactance. Once connected, the device emitted an electrical signal of a fixed frequency and low intensity.

The software (Vcorp) provided by the manufacturer allowed the calculation of the following variables: total body water and lean body mass and body fat both in kg/L and percentage.

### 2.6. Nutritional assessment

The following anthropometric parameters found in nutritional assessment: body weight, height, arm circumference, triceps skinfold thickness (TSF) and abdominal circumference. These measurements were obtained by the same examiner in the morning and on the same