

## Body composition changes in haemodialysis patients with secondary hyperparathyroidism after parathyroidectomy measured by conventional and vector bioimpedance analysis

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Considering the negative effects of secondary hyperparathyroidism (SHPT) in patients with chronic renal failure (CRF), the objective of the present study was to evaluate body composition changes using conventional and vector bioimpedance analysis in patients before and after parathyroidectomy (PTX). Twelve adult patients, mean age 43.4 (SD 12.7) years, were evaluated prior to and 6 months after PTX. Diets were assessed with 3 d dietary records, and mean energy, protein, calcium and phosphorus intake were estimated from these inventories. Weight, height, BMI and bioelectrical impedance were measured; and biochemical markers of nutritional status (albumin and total protein) and bone metabolism (calcium, phosphorus and intact parathyroid hormone) were determined. No significant differences were observed in mean energy, protein and phosphorus after surgery. There was a significant increase in calcium intake after PTX (382.3 (SD 209.6) mg to 656.6 (SD 313.8) mg;  $P < 0.05$ ). Mean weight, BMI, conventional bioelectrical impedance measurements, total body fat, lean body mass and total body water were unaffected by surgery. However, the phase angle and reactance significantly increased after PTX (5.0° (SD 1.4) to 5.6° (SD 1.3); 44.1 (SD 15.6) Ω to 57.1 (SD 14.4) Ω, respectively). The high levels of intact parathyroid hormone before surgery had a negative effect on total body fat ( $r = -0.69$ ,  $P < 0.05$ ). After PTX, the mean albumin significantly increased (3.9 (SD 0.4) g/dl to 4.2 (SD 0.6) g/dl;  $P < 0.05$ ). PTX for SHPT is associated with certain changes in laboratory values, dietary intake and body composition. The latter is best seen with bioimpedance vector analysis.

### Body composition: Secondary hyperparathyroidism: Bioimpedance vector analysis

Most patients with stage 5 chronic kidney disease develop secondary hyperparathyroidism (SHPT; Francisco, 2004). SHPT is an adaptive response to chronic kidney disease and is associated with disruptions in the homeostatic control of serum phosphorus, calcium and vitamin D. SHPT remains a significant cause of morbidity in patients with chronic renal failure (CRF), with roughly 50% of patients receiving dialysis developing this form of renal osteodystrophy (Salem, 1997; Amann *et al.* 1999).

There are multiple clinical manifestations of SHPT including muscle dysfunction, negative cardiac inotropic effects, leucocyte and T-cell dysfunction, increased vascular calcification, elevated rates of fracture, calciphylaxis, osteoarticular pain, pruritus, abnormal taste, loss of appetite and weight loss (Khajehdehi *et al.* 1999; Cozzolino *et al.* 2005).

Malnutrition is a significant factor influencing morbidity and mortality in patients with chronic kidney disease, with roughly 40% of CRF patients on maintenance haemodialysis (Bergström & Lindholm, 1993; Qureshi *et al.* 2002) showing

elements of malnutrition. Many factors contribute to the malnutrition associated with chronic kidney disease and chronic maintenance dialysis therapy, including decreased energy and protein intake, chronic inflammation, physical inactivity, concurrent acute or chronic conditions or illnesses, and the catabolic stimulus of dialysis itself (Kaysen, 2001, 2004; Kaysen *et al.* 2001). Furthermore, the persistently high levels of parathyroid hormone may contribute to malnutrition directly: high parathyroid hormone levels promote derangements in protein and energy metabolism, leading to a weight loss, weakness and muscle atrophy (Bacynski *et al.* 1985; Miroslaw *et al.* 1988).

The treatment of SHPT includes multiple dietary and pharmaceutical interventions including administration of calcium salts, vitamin D metabolites, calcimimetics, phosphate-binding agents and dietary phosphorus restriction. Surgical interventions such as percutaneous intra-parathyroid glandular ethanol or calcitriol injections, and parathyroidectomy (PTX), are available. The latter is the treatment of choice in patients

with severe SHPT, and is the main option when other clinical approaches have failed (Jofré *et al.* 2003).

Nutritional status optimization is essential to the care of dialysis patients. The need for prospective evaluation of body composition is a key element in achieving this goal. Assessment of total body water, lean body mass, fat mass and body cell mass over time is of clinical importance in order to define 'dry weight' accurately and to identify individuals at risk of malnutrition (Dumler & Kilates, 2000). Several investigators have used bioelectrical impedance in order to evaluate body composition (Chertow *et al.* 1995; Foster & Lukasky, 1996; Oldham, 1996). Bioelectrical impedance analysis (BIA) is a non-invasive, simple and reproducible technique to evaluate changes in body composition. The BIA parameters resistance ( $R$ ), reactance ( $Xc$ ) and phase angle closely correlate with intracellular and extracellular water content, body cell mass, fat free mass and fat mass content (Cooper *et al.* 2000; Kusher & Roxe, 2002).

To predict masses and volumes in these various compartments, conventional BIA uses simple or multiple regression equations derived from the study of subjects with normal soft tissue water content (73%). Because these algorithms can produce biased estimates of body compartments in patients with CHD, bioimpedance vector analysis (BIVA) has been developed (Piccoli & Pastori, 2002). BIVA assumes a bivariate distribution of impedance measurements standardized by height ( $H$ ) and expressed in units of  $\Omega/m$ . Values are reported as  $R/H$  and  $Xc/H$  plotted on a diagram called the RXc-graph (Piccoli *et al.* 1994).

Here, we used BIVA to monitor the changes in body composition of patients with CRF undergoing PTX for SPHT.

## Materials and methods

### Subjects

The study was carried out in the Renal Osteodystrophy Outpatient Clinic at São Paulo University. From March 2002 to April 2004, twelve haemodialysis (seven male, five female) patients with SHPT were evaluated. Nutritional and biochemical data were measured before PTX and 6 months after surgery. Patients who had recent infections, were being treated for latent tuberculosis, had gastrointestinal diseases, chronic alcoholism, malignant diseases, coronary artery disease or chronic obstructive pulmonary disease; or used mineralocorticoids and anabolic agents were excluded. Patients who received kidney transplants were also excluded.

Dialysis was performed three times, 4 h weekly. Dialysis protocols were adjusted to the  $Kt/V$ , the dialysate calcium was 2.5 mEq/l before PTX and 3.5 mEq/l after PTX. Phosphate binders (calcium carbonate or sevelamer) and calcitriol were used by all patients according to the clinical status before the PTX. After PTX the calcium carbonate was used as a supplement (after the meals). No patients received calcimimetics at the onset of the study.

### Nutritional assessment

Dietary records (3 d) were recorded in order to estimate mean energy, protein, calcium and phosphorus intake. Patients completed detailed dietary records before and after surgery.

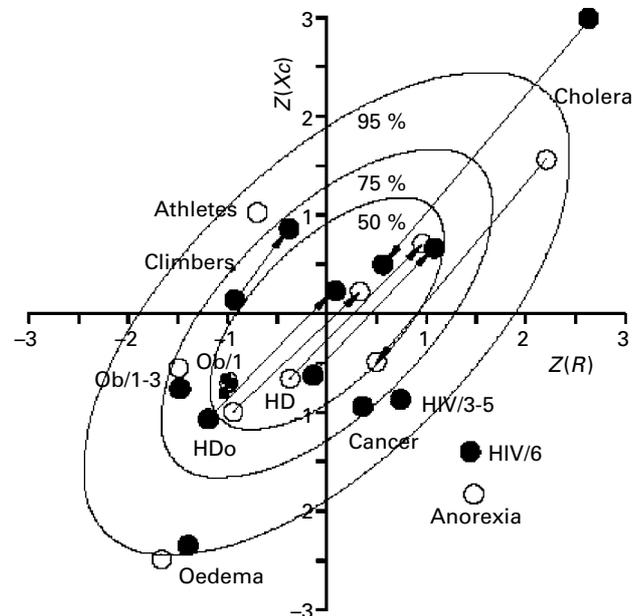
Nutwin (São Paulo, SP, Brazil) house software was used to calculate mean nutrient intake. Weight, height, BMI and bioelectrical impedance were measured at the same time, between two haemodialysis sessions. BIA was performed using a bioelectrical impedance analyser (model BIA-101Q; RJL Systems Inc., Detroit, MI, USA). All evaluation was conducted on the patients' right side using the four surface standard electrode (tetrapolar) technique on the hand and foot (Lukaski *et al.* 1985).  $R$  and  $Xc$  were directly measured in ohms ( $\Omega$ ) at 50 kHz and 800  $\mu$ A. The phase angle (in degrees) was calculated using the following equation:

$$\text{Phase angle} = (\text{resistance/capacitance}) \times (180/\pi)$$

RXc-graphs (Fig. 1) were generated with BIVA 2002 (Piccoli & Pastori, 2002), using a Caucasian undergoing chronic haemodialysis as the reference population (Piccoli, 1998).

### Biochemical assessment

Blood samples were drawn from the patients before and after PTX. Serum intact parathyroid hormone (iPTH; normal range 8–76 pg/ml) was measured by using an RIA (ELISA PTH; Cis-Bio International, Gif-sur-Yvette, France). Serum total calcium (normal range 8.5–10.5 mg/dl) and serum phosphorus (normal range 2.3–4.6 mg/dl) were determined with an automated analyser (Auto Analyzer Covas-Integra; Roche,



**Fig. 1.** The reference RXc-graph with 95%, 75% and 50% tolerance ellipses. Both dimensionless Z scores, i.e. resistance score  $Z(R)$  and reactance score  $Z(Xc)$ , are the difference of individual  $R$  and  $Xc$  values from the mean divided by the standard deviation of the reference population. ●, male; ○, female; →, repeated score vectors from climbers before and after high altitude dehydration, haemodialysis (HD) patients, either lean or obese (HD0) before and after fluid removal with a dialysis session, and dehydrated patients with cholera before and after fluid infusion. Single score vectors are from athletes, obese subjects of class I to III (Ob/1–3) or class I (Ob/1) [NHANES III population]. Patients with chronic renal failure (CRF) in conservative treatment, nephrotic syndrome (oedema), lung cancer, AIDS in stage WR 3–5 (HIV/3–5) or WR6 (HIV/6), and anorexia nervosa.

**Table 1.** Demographic characteristics, dietary intake and biochemical parameters of haemodialysis patients with secondary hyperparathyroidism\*

|                             | Pre-parathyroidectomy<br>(n 12) |             | Post-parathyroidectomy<br>(n 12) |            | P      |
|-----------------------------|---------------------------------|-------------|----------------------------------|------------|--------|
|                             | Mean                            | SD          | Mean                             | SD         |        |
| Age (years)                 | 43.4                            | 12.7        | 43.4                             | 12.7       | –      |
| Time in dialysis (years)    | 10.6                            | 2.8         | 10.6                             | 2.8        | –      |
| Height (cm)                 | 160.0                           | 10.0        | 160.0                            | 10.0       | –      |
| Dry weight (kg)             | 57.6                            | 17.2        | 57.8                             | 18.1       | 0.850  |
| BMI (kg/m <sup>2</sup> )    | 21.9                            | 5.1         | 21.9                             | 5.5        | 0.884  |
| Dietary intakes             |                                 |             |                                  |            |        |
| Energy [kJ (kcal)/kg per d] | 129.3 (30.9)                    | 55.6 (13.3) | 146.4 (35.1)                     | 39.8 (9.5) | 0.184  |
| Protein (g/kg per d)        | 1.2                             | 0.5         | 1.3                              | 0.6        | 0.644  |
| Ca (mg/d)                   | 382.2                           | 209.6       | 656.6                            | 313.8      | 0.008  |
| P (mg/kg per d)             | 13.6                            | 6.0         | 17.4                             | 6.8        | 0.117  |
| Biochemical parameters      |                                 |             |                                  |            |        |
| Total Ca (mg/dl)            | 9.3                             | 1.2         | 8.5                              | 1.1        | 0.091  |
| Inorganic P (mg/ml)         | 6.7                             | 1.8         | 4.5                              | 1.5        | <0.001 |
| iPTH (pg/ml)                | 1221.6                          | 685.1       | 153.1                            | 189.2      | 0.001  |
| Albumin (g/dl)              | 3.9                             | 0.4         | 4.2                              | 0.6        | 0.047  |
| Total protein (g/dl)        | 7.0                             | 0.9         | 7.6                              | 0.5        | 0.023  |

iPTH, intact parathyroid hormone.

\* For details of procedures, see p. 354.

Mannheim, Germany). Serum albumin (normal range 3.5–5.0 g/dl) and serum total protein (normal range 6.0–8.0 g/dl) were measured by using a nephelometric biochemical assay. The analyses were performed at the Central Laboratory in the Hospital das Clinicas at São Paulo University.

#### Statistical analysis

All results were expressed as means and standard deviations. The variables distribution was analysed by Kolmogorov–Smirnov test. Since all the variables had normal distributions, the Student's paired *t*-test was performed for comparison of a single mean, and Pearson's correlation was performed for comparison of overall correlation. Hotelling's  $T^2$  test for paired data was performed for testing the size of change in vector position.  $P < 0.05$  was considered significant. All calculations were performed using SPSS for Windows, version 11.0 (SPSS Inc., Chicago, IL, USA).

#### Results

The demographic characteristics, dietary intakes and biochemical parameters of the twelve subjects are reported in Table 1. All patients were adults and had received dialysis for over 10 years. No significant changes were observed in the dry weight and BMI after PTX. Using the 1995 BMI classification of the WHO, all the patients were well nourished. No statistically significant differences were found in mean energy, protein and phosphorus intake after surgery; however, there was a significant increase in calcium intake after PTX. As expected, the serum phosphorus and the iPTH decreased significantly after PTX. Interestingly, the mean albumin and the total protein significantly increased after PTX.

There were no statistically significant changes in fat body mass, lean body mass, total body water, intracellular or extracellular water after PTX (9.9 (SD 8.1) to 11.6 (SD 8.5) kg, 47.2

(SD 12.8) to 45.5 (SD 14.9) kg, 33.7 (SD 8.9) to 32.2 (SD 9.8) litres, 18.5 (SD 6.5) to 18.9 (SD 6.7) litres, 15.3 (SD 3.5) to 17.2 (SD 10.1) litres, respectively).

There were significant increases in reactance and phase angle (Table 2). Resistance also increased; however, the difference did not reach statistical significance. Unlike conventional measurements, BIVA demonstrates a decrease in total body water, as shown in the RXc-graph (Fig 2) where the vector lengthening of most vectors is apparent in the direction of the major axis of tolerance ellipses, indicating dehydration. The size of change in vector position was significant ( $T^2$  9.7,  $P < 0.05$ ).

A negative correlation between fat body mass and iPTH was observed before the surgery (Fig 3). However, this correlation was not significant after PTX. No significant correlations were observed between nutrient intakes, lean body mass and serum phosphorus, calcium and iPTH before and after PTX (data not shown).

#### Discussion

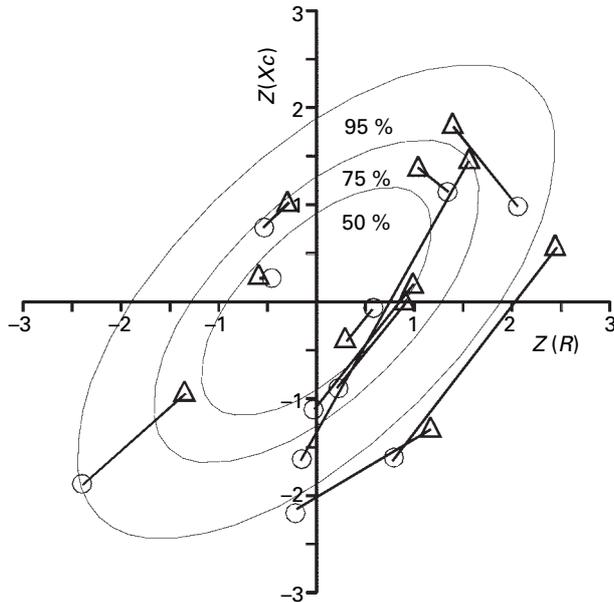
Inadequate dietary intake is a frequent and important cause of malnutrition in haemodialysis patients. Although it has been

**Table 2.** Bioimpedance vector analysis parameters and phase angle of haemodialysis patients with secondary hyperparathyroidism\*

|                          | Pre-parathyroidectomy |      | Post-parathyroidectomy |       | P     |
|--------------------------|-----------------------|------|------------------------|-------|-------|
|                          | Mean                  | SD   | Mean                   | SD    |       |
| Resistance ( $\Omega$ )  | 539.9                 | 76.3 | 612.1                  | 117.2 | 0.059 |
| Reactance ( $\Omega$ )   | 44.1                  | 15.6 | 57.1                   | 14.4  | 0.020 |
| Phase angle ( $^\circ$ ) | 5.0                   | 1.4  | 5.6                    | 1.3   | 0.030 |
| Z(R/H)                   | –0.3                  | 1.5  | 0.8                    | 1.6   | 0.049 |
| Z(Xc/H)                  | –2.8                  | 1.5  | –1.9                   | 1.6   | 0.096 |

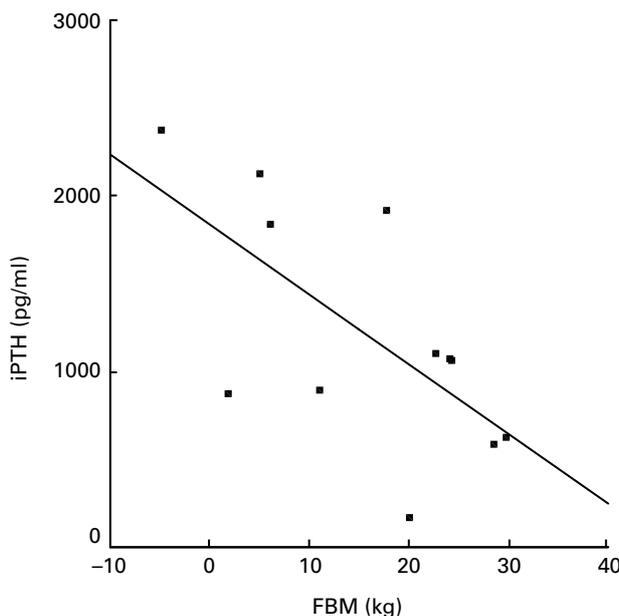
Z(R/H), Z-score of resistance/height; Z(Xc/H), Z-score of reactance/height.

\* For details of procedures, see p. 354.



**Fig. 2.** RXc-graph with 95%, 75% and 50% tolerance ellipses of haemodialysis patients with secondary hyperparathyroidism. For details of procedures, see p. 353.  $\Delta$ , Pre-parathyroidectomy;  $\circ$ , post-parathyroidectomy.

hypothesized that inadequate dietary intake might be secondary to uraemia, anorexia, underlying illness, psychosocial conditions, loss of dentures, depression, ageing or chronic inflammation, definitive data on the aetiology of inadequate dietary intake in haemodialysis patients are still lacking. Bossola *et al.* (2005) investigated dietary intake in thirty-seven patients maintained on regular haemodialysis, and observed that 70.2% had energy and protein intakes lower than recommended, 18.9% had adequate energy intake but



**Fig. 3.** Scattergram of intact parathyroid hormone (iPTH; pg/ml) versus fat body mass (FBM; kg) of haemodialysis patients with secondary hyperparathyroidism before parathyroidectomy. For details of procedures, see p. 354.

inadequate protein intake, 2.7% had adequate protein intake but inadequate energy intake, and only 8.1% had both adequate energy and adequate protein intake. They also observed that anorexia was present in 53% of patients with low protein and energy intakes.

The patients studied here had adequate energy, protein and phosphorus intake, while calcium intake was above the recommendations for CRF patients with SHPT (National Kidney Foundation, 2003). The significant increase in calcium intake after PTX may be due to increases in consumption of dairy products, as recommended by nutritionists. The long-term consequences of these changes require further study.

We observed a negative correlation between iPTH and fat body mass before the PTX. Others have found a similar correlation in CRF patients in haemodialysis with moderate and severe SHPT (Peters *et al.* in press).

Since high parathyroid hormone levels may have deleterious effects on the nutritional status of patients with SHPT, prospective study of patients undergoing PTX is warranted.

We used conventional BIA and BIVA to evaluate body composition changes in CRF patients with SHPT. The reactance and the phase angle significantly increased after PTX, while the conventional BIA parameters did not change. The present findings corroborate a 12-month study showing that there were no significant changes in the conventional BIA parameters (fat mass and lean body mass) while the phase angle decreases significantly (Johansen *et al.* 2003).

Reactance has been postulated to be an indicator of lean body mass. However, reactance reflects the functional capacity of total body protein stores, and may be a better marker of overall nutritional status than lean body mass (Ikizler *et al.* 1999). Indeed, we found that albumin and total protein increased significantly after PTX. Similarly, a positive correlation between reactance and nutritional markers like serum prealbumin and albumin has been observed in peritoneal dialysis patients (Mushnick *et al.* 2003). Chertow *et al.* (1997a) also reported direct correlations of prealbumin with phase angle and reactance in haemodialysis patients.

Dumler (2003), evaluating 142 patients on chronic dialysis for 12 consecutive months, concluded that overhydration is a contributor to hypoalbuminaemia in these patients. In the present study, the patients presented significant increase in albumin serum and dehydration status after PTX; indicating that the lower albumin levels observed before PTX could be explained in part by a possible overhydration status.

A decline in phase angle indicates a change in body composition, specifically the loss of body cell mass that may occur even in the absence of a change in weight or lean body mass. A likely explanation for such a finding in a dialysis population is that there is an increase in extracellular fluid that is proportional to a decrease in body cell mass. In other words, dry weight may not have been totally adjusted in response to changes in body composition, due to the improvement in clinical status following PTX.

Furthermore, Chertow *et al.* (1997b) reported a direct association between survival and phase angle in dialysis patients. Since the survival predictor was not evaluated in our study, the improvement in phase angle after PTX could indicate an increase in body cell mass and nutritional status, hence a better state of overall health.

In summary, we found that PTX has positive effects on the nutritional status of CRF, and demonstrated that BIVA identifies subtle changes in body composition following PTX that is not seen using conventional BIA. Further study is needed to determine if these changes affect survival of haemodialysis patients.

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