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Original article

Body composition in children with renal disease: use of dual energy X-ray absorptiometry

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Abstract. Dual energy X-ray absorptiometry (DEXA) is a non-invasive accurate method which estimates bone mineral content and density (BMD), as well as fat (FM) and lean (LM) body mass. This method was used in control children in order to establish normal values for BMD of lumbar spine and whole body composition {logistic curves, general equation $E = k+K/[1+\alpha\exp(-\beta A)]$}. In children with chronic renal failure (CRF), LM correlated with the urinary excretion of creatinine ($r = 0.97$, $P = 0.0001$) independently from glomerular filtration rate. However, the assessment of LM by DEXA must take into account the hydration level, since there is a positive correlation between fluid loss and reduction in LM in children on hemodialysis ($r = 0.98$, $P = 0.0001$). After renal transplantation, a significant loss of BMD (median −9.2%) was observed at 6 months which returned to 95% of pretransplant values by the end of the 1st year. Maximal changes in LM and FM occurred during the first 3 months (−7.8% and +7.2%, respectively) and may be due to steroids; these should be influenced by physical activity since FM correlated inversely with maximal oxygen consumption ($r = 0.69$, $P = 0.0001$). Recombinant growth hormone treatment could also increase LM and decrease FM, as shown in 9 patients. DEXA appears therefore to be a reliable method for evaluating therapeutic interventions affecting nutritional status in children with CRF.

Key words: Bone mineral density – Bone mineral content – Body composition – Chronic renal failure – Dual energy X-ray absorptiometry – Growth hormone – Hemodialysis

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Introduction

Dual energy X-ray absorptiometry (DEXA) is widely used in quantitative bone investigation to measure bone mineral density (BMD, in grams of hydroxyapatite per square centimeter of bone projected area) at the spine and hip level. The development of new software to measure the bone mineral content (BMC) of the entire skeleton as well as the fat mass (FM) and the lean soft-tissue mass (LM) is an important advance. The precision and accuracy of DEXA have been previously compared with other methods [1–4]. The present work aims to summarize our experience with the use of DEXA in controls and children with chronic renal failure (CRF).

Patients and methods

Patients. The study population included healthy controls, children with various levels of glomerular filtration rate (GFR), children on hemodialysis, renal transplant recipients, and children under recombinant human growth hormone (rhGH) therapy.

Methods. DEXA was performed with a Hologic QDR 1000 W system (Hologic, Waltham, Mass., USA) using a switching-pulse dual energy photon source (70/140 kV). In order to calculate the FM, the device was equipped with a special step phantom made of acrylic (fat equivalent) and aluminum, and calibrated to stearic acid (100% fat) and pure water. The whole body software V5.47 was used. The patients were scanned using a standard protocol: pencil beam, rectilinear x-y scanning from head to toes, line spacing 1.3 cm, point resolution 1.5 mm. The procedure took 15–20 min and the radiation dose was less than 2 mrem. The average coefficient of variation in adults and neonates ranged between 0.65% and 2.80% for BMC, 1.54% and 0.65% for FM, and 0.89% and 2.80% for LM, respectively. A highly significant positive linear correlation ($r^2 = 1.000$, $P = 0.0001$) between gravimetric body weight (BW) obtained conventionally and BW measured by DEXA was found in 205 patients with a BW ranging from 1 to 95 kg.

Renal investigations included inulin and creatinine clearances (Cr) and were performed in overnight fasting patients. Inulin (Inutest 25%, Laevosan-Gesellschaft, Vienna, Austria) was administered via a 3-h intravenous constant infusion, and urine samples were collected every 30 min. Inulin was measured in plasma and urine using previously reported methods [5].

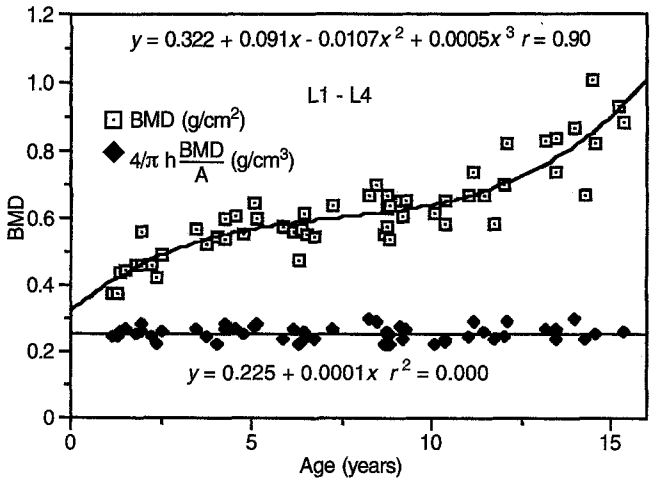

Fig. 1. Bone mineral density (*BMD*) (in g/cm²) plotted against age in 135 children showing a curvilinear positive correlation (r = 0.90). When corrected for vertebral volume (4/π.h.BMD/A, in g/cm³) the BMD had a constant value

Results

Measurement of BMD of the lumbar spine in normal children

The BMD (g/cm²) of the lumbar spine (L1–L4) was measured by DEXA in 135 healthy children aged 1–15 years: it increased with age from 0.45 ± 0.05 g/cm² at 1 year to 0.63 ± 0.07 g/cm² at 10 years and 0.89 ± 0.13 g/cm² at 15 years. The increase was steeper during puberty, reaching values over 0.80 g/cm² after puberty. BMD (g/cm²) was also closely correlated with height, BW, body surface, and bone age [6]. In order to take into account the influence of vertebral growth between each measurement, it was necessary to correct the measured BMD values (in g/cm²); a simple method was to approximate the lumbar spine to a cylinder of height h and diameter A/h (A and h being obtained from DEXA analysis). The bone density (d) (expressed in g/cm³) was then given by: d = 4/π.h.BMD/A. Using this approach, d had a constant value (0.255 ± 0.015 g/cm³), as shown in Fig. 1.

Normal values for whole body composition

BMC of the entire skeleton, LM and FM were measured in 72 normal controls (40 girls, aged 1–25 years). Their values were plotted against age and represented by logistic curves of general equation: $E = k+K/[1+\alpha\exp(-\beta A)]$ (Fig. 2).

Assessment of LM with DEXA in children with different levels of GFR

Sixty children (24 girls, aged 1–18 years) had concomitant GFR and DEXA investigations. Since there was no significant relationship between GFR and urinary excretion of Cr (UCr) – a reliable LM index [7] –, a close positive correlation was established between UCr and LM estimation from DEXA (r = 0.97, P = 0.0001) (Dubourg et al., in preparation).

Changes in body composition in children on hemodialysis

Sixteen children on dialysis (8 girls, aged 5–17 years) were examined before and after one hemodialysis session. They were on hemodiafiltration (BSM22, Monitral S, Hospal, France) using a AN69 membrane (Biospal, Hospal, France); the mean (±SD) duration of the session was 3.5 ± 0.5 h. DEXA was performed 1.2 ± 0.3 h before and repeated 1.2 ± 0.3 h after hemodialysis. A positive correlation was obtained between fluid loss during hemodialysis and reduction in LM (r = 0.983, P = 0.0001), whereas there was no significant change in both FM and BMC (Fig. 3).

BMD after renal transplantation

Longitudinal bone mineral changes after renal transplantation were studied in 14 children aged 8 ± 4 years with a well-functioning graft [8]. Triple immunosuppressive therapy (prednisone, azathioprine, cyclosporine A) was given to all patients. BMD measurements (g/cm²) of the first four lumbar vertebrae were performed before renal transplantation and 6, 12, and 24 months afterwards (M_0, M_6, M_{12}, and M_{24}, respectively). Significant decreases in BMD (g/cm²) and spine volume-corrected BMD (g/cm³) were observed at M_6 ($P < 0.05$), with a median loss of BMD (g/cm²) and spine volume-corrected BMD (g/cm³) of 9.2% and 15.6%, respectively. Between M_6 and M_{12}, BMD increased significantly up to 95% of pretransplantation values and reached 97.2% at M_{24}. Similarly, the spine volume-corrected BMD (g/cm³) reached 87.5% of the pretransplantation values both at M_{12} and M_{24}. The same features were noted when BMD was expressed as a standard deviation score. A negative correlation was found between the cumulative prednisone dose and BMD (g/cm²) at M_6, M_{12}, and M_{24}.

Assessment of body composition in children after renal transplantation

The evolution of LM and FM (as a percentage of total BW) in children has been followed after renal transplantation. Twenty children (7 girls, aged 10.3 ± 5.0 years at the time of transplantation) were enrolled into a prospective longitudinal study. DEXA was performed at M_0 and repeated at M_3, M_6, and M_{12} post transplant. Individual FM increased by a median of 7.2% ($P < 0.05$) in the first 3 months after transplantation, but did not change significantly in the periods M_0–M_6 and M_0–M_{12}. Similarly, LM diminished by a median of 7.8% in the period M_0–M_3 ($P < 0.05$); the decrease was not significant in the periods M_0–M_6 and M_0–M_{12}.

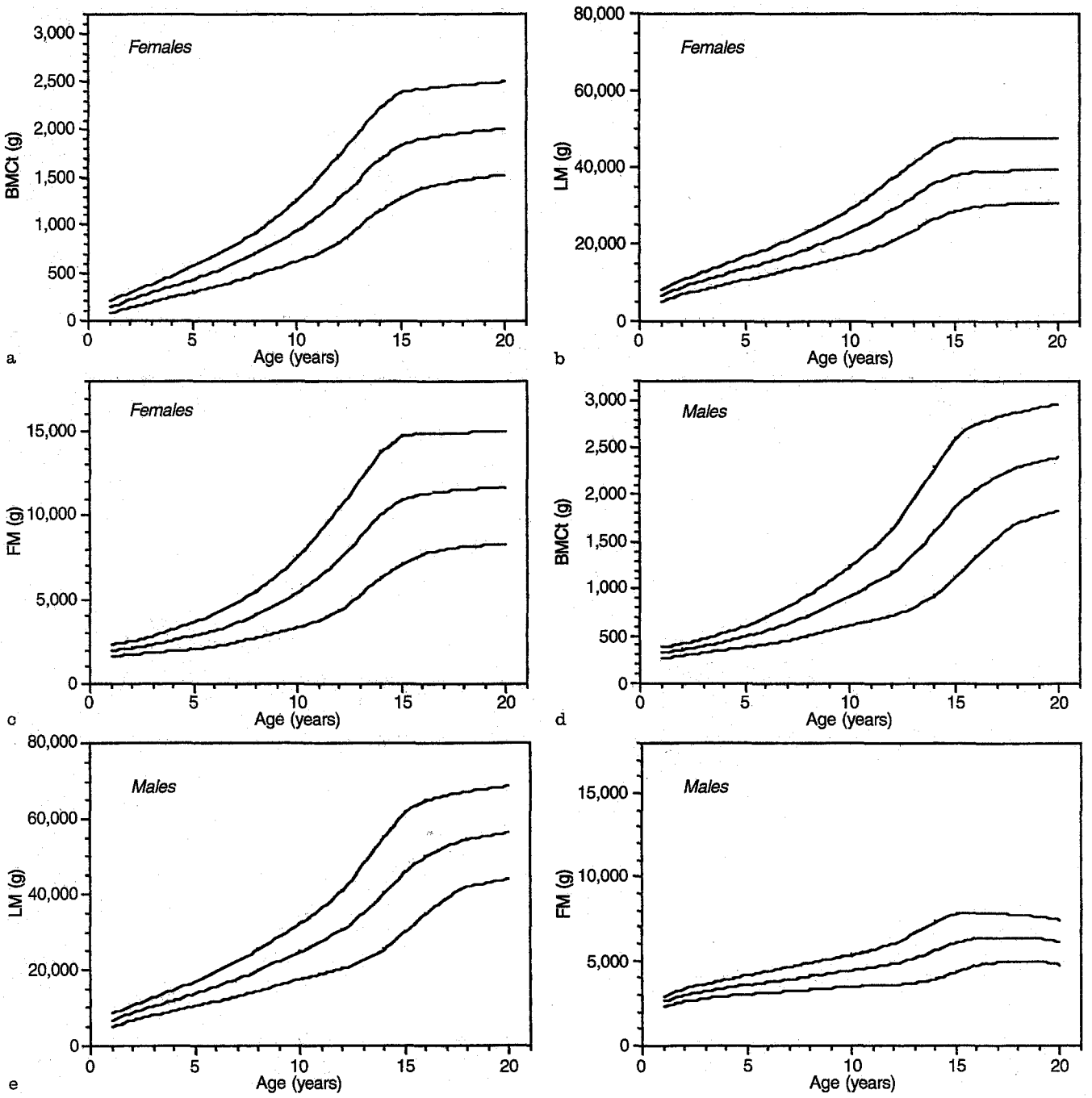

Fig. 2. Normal values for bone mineral content (BMC) of the entire skeleton (*BMCt*), lean (*LM*), and fat mass (*FM*) in 40 normal girls (**a, b, c**) and 32 normal boys (**d, e, f**) aged 1–25 years. Logistic curves (mean ± 1 SD) were obtained from a general equation: $E = k+K/[1+\alpha\exp(-\beta A)]$, where A = age (in years); $\alpha = 30$ in boys and 45 in girls for BMCt, LM, and FM; $\beta = 0.30$ in boys and 0.38 in girls for BMCt, LM, and FM; k for BMCt, LM, and FM in boys = 125, 4,500, and 2,810, respectively; k for BMCt, LM, and FM in girls = 75, 6,000, and 1,900, respectively; K for BMCt, LM, and FM in boys = 2,350, 55,000 and 3,975, respectively; K for BMCt, LM, and FM in girls = 2,000, 35,000 and 9,950, respectively

Body composition and physical performance after renal transplantation

Thirty-two renal transplant recipients (19 girls, aged 8.0–18.9 years) with GFR > 44 ml/min per 1.73 m^2 had concomitant DEXA and spiroergometry examinations at least 1 year post transplantation. FM (as a percentage of total BW) correlated inversely with maximum oxygen consumption (VO_{2max} in watts per kilogram BW) ($r = 0.69$, $P = 0.0001$) [9].

Table 1. Individual changes in lean and fat body mass in children on recombinant human growth hormone (rhGH) therapy[a, b]

Patient no.	Change in lean mass (SDS)	Change in fat mass (SDS)	Duration on rhGH (months)
Girls (age at start of rhGH, years)			
1 (13.2)	+0.05	+0.15	15
2 (14.9)	+0.70	–0.75	21
3 (8.8)	+0.35	–0.85	12
4 (12.3)	+0.40	–1.40	12
Boys (age at start of rhGH, years)			
5 (15.2)	+0.05	–0.60	12
6 (17.1)	+0.85	–0.70	20
7 (14.0)	+0.15	+0.30	6
8 (12.7)	+0.60	–4.35	6
9 (13.6)	+0.25	–0.90	18

[a] Results are standard deviation scores (SDS)
[b] SDS are obtained from normal values shown in Fig. 1

Changes in body composition in children under rhGH

Preliminary results of a longitudinal study were obtained from 9 children with CRF (conservative treatment 1, hemodialysis 1, renal transplantation 7) in a stable condition, who required rhGH (Genotonorm, Pharmacia) 1 U/kg BW per week using daily subcutaneous injection; transplant children were started on rhGH at least 2.2 years after transplantation. DEXA was performed at M_0, then M_6 and M_{12} on therapy. A significant increase in LM was shown: 3.6% at M_6 and 2.7% at M_{12} in girls, 4.4% at M_6 and 5.5% at M_{12} in boys ($P \leq 0.01$). Similarly FM decreased by 11.2% at M_6 and 10.7% at M_{12} in girls and 12.4% at M_6 and 16.2% at M_{12} in boys ($P \leq 0.004$); individual data are given in Table 1. There was no significant change in BMC nor BMD.

Discussion

DEXA separately measures the three main components of the body: FM, LM – i.e., muscle, inner organs, and body water – and BMC; it does not separate the LM into water and protein. The interpretation of changes in these parameters is quite difficult in growing children. The change in BMD with age seen when it is measured in grams per square centimeter is based on skeletal growth together with a change in vertebral geometry and does not indicate that the BMD per volume of bone (BMD/A) is changed. In addition, the deviation of measurements of BMD (g/cm^2) is much bigger in healthy [6] and in transplant [8] children, indicating that BMD (g/cm^2) might not be the optimal way of expressing the data and may lead to false conclusions (Fig. 1); change in spine volume-corrected BMD (g/cm^3) therefore seems to be a more relevant parameter.

DEXA has been shown to be accurate for body composition measurements in vitro and in humans from premature infants to obese subjects [1, 10, 11]: the measurement errors are equal to or smaller than those of traditional body composition methods (neutron activation analysis, total body potassium, under water weighing, bioelectrical impedance, dual photon absorptiometry, etc). Being noninvasive and simple to perform, DEXA is therefore useful for monitoring body composition and nutritional status of CRF children during the course of a therapeutic intervention. Although the child with CRF is submitted to varying conditions – e.g., progression of renal failure or change in hydration – which should alter the reliability of the method, the striking correlation we found between UCr and LM clearly indicated that DEXA is a reliable method for assessing body composition independently from GFR.

The assessment of body composition in children undergoing hemodialysis is hazardous and the accuracy of methods such as anthropometry or bioelectrical impedance analysis is probably poor, since they are based on equations [12–14]. The usefulness of DEXA in dialysis patients has been shown in adults, where there was a significant correlation (20 patients, $r = 0.676$, $P < 0.001$) between fluid loss and reduction in fat free mass (i.e., LM+BMC) [15]. We found a higher correlation in children using reduction in LM (Fig. 3). These findings imply that changes in LM are accurately estimated by DEXA and that nutritional as-

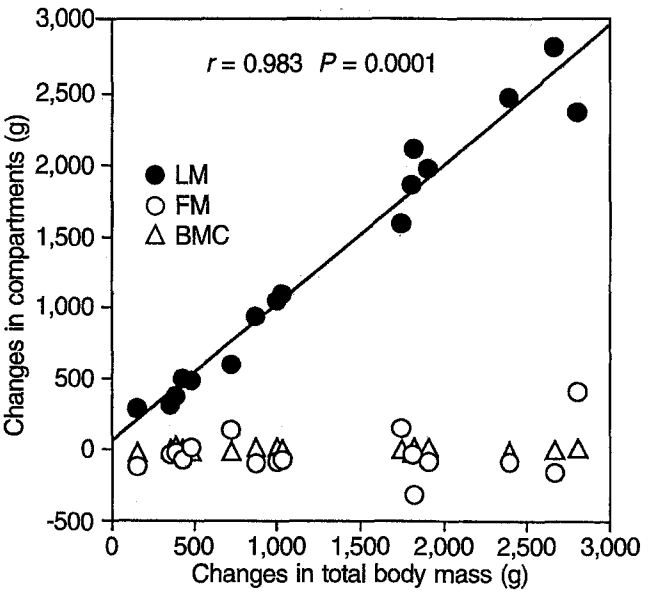

Fig. 3. Changes in body composition before and after hemodialysis. A strong correlation was obtained between change in total body mass (fluid loss) and change in lean body mass ($r = 0.983$, $P = 0.0001$). There was no significant change in both FM and BMC

sessment of CRF patients should be performed after dialysis. The same problem might be encountered in assessing nephrotic patients.

After renal transplantation, children experience a transient decrease of BMD (in g/cm^2 as well as in g/cm^3) despite normal graft function and growth improvement, probably due to the cumulative prednisone dose; it further normalizes by the end of the 1st year [8]. Weight gain following renal transplantation is a well-known phenomenon both in children [16] and adults [17]. We found that nadir changes in body composition after transplantation occurred during the first 3 months and consisted of a marked increase in FM, which parallels a decrease in LM, probably due to the effect of corticosteroids on appetite and metabolism. It appears that these early side effects could be counteracted by adequate diet and physical exercise, as shown in our study of 32 children whose FM correlated inversely with maximal physical load during spiroergometric examination. This also suggests that exercise training programs might be useful after renal transplantation, since obesity is related to increased mortality, graft dysfunction, and postoperative complications [18].

Our preliminary results suggest that DEXA should also be of interest in evaluating the nutritional effects of rhGH in children with CRF. They clearly identify the important role of GH in lipolysis and protein metabolism by showing a reduction in adipose tissue and an increase in LM [19]. Probably because of the small number of patients, we observed no significant change in BMC or BMD, whereas rhGH is known to increase BMD in children with GH deficiency [20].

In conclusion, DEXA is a reliable and non-invasive technique for the determination of body composition in children with renal disease. It is therefore the method of choice for evaluating therapeutic interventions affecting nutritional status and/or water balance, such as rhGH or erythropoietin, enteral or parenteral nutrition, assessment of dry weight in dialyzed patients, impact of physical activity, etc.

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