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Usefulness of bone uptake ratio of bone scintigraphy in hemodialysis patients

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Objective: It is important to estimate the bone metabolism in patients with renal osteodystrophy. The methods of estimation must be noninvasive, accurate, and able to measure repeatedly. ***Methods:*** The regions of interest on bone scintigraphy were drawn over the radius in 22 hemodialysis patients (10 males, 12 females). The bone/soft tissue ratio (B/ST ratio) was calculated for all patients. The bone soft tissue ratio of both skull (S) and radius (R) was obtained from the resultant count ratios. We investigated the correlation between intact parathyroid hormone (PTH), alkaline phosphatase (ALP) and the uptake ratios S and R. ***Results:*** Intact PTH had a significantly linear correlation with R ($r = 0.745$, $p < 0.0001$) and S ($r = 0.702$, $p = 0.0001$). ALP also had a significantly linear correlation with R ($r = 0.537$, $p = 0.009$) and S ($r = 0.772$, $p < 0.0001$). ***Conclusion:*** The measurement of the bone soft tissue ratio of radius on bone scintigraphy was crucial for estimating renal osteodystrophy.

Key words: bone scintigraphy, bone/soft tissue ratio (B/ST ratio), radius, skull

INTRODUCTION

IN THE MAINTENANCE of hemodialysis patients, renal osteodystrophy (ROD) is a major complication. Adequate assessment and management are necessary to prevent the progression of bone diseases in hemodialysis patients. Bone biopsy is the gold standard in the assessment of metabolic bone diseases, but it is invasive and is not tolerated by many patients. Therefore, non-invasive methods that enable us to take measurements repeatedly are required. X-ray films of the skull and lumbar vertebrae have been used to evaluate the bone mineral density of hemodialysis patients, and computed tomography (CT) and dual-X ray absorptiometry (DXA) have been used as methods of measuring bone mineral density. In the diagnostic imaging of secondary hyperparathyroidism, the skull is well known to have a salt and pepper appearance on X-ray film, and the lumbar vertebrae are known to have a rugger and jersey spine appearance.[1] It is reported that the bone mineral density of the radius is reduced on the DXA.[2,3] Unfortunately, bone X-ray film and DXA have been reported to appear the chronic morphological change of bone[4,5] and bone X-ray and DXA do not always reflect the bone metabolism at this time.

Bone scintigraphy has been considered to demonstrate functional changes on the bone before any anatomic pathology is apparent, and is used to investigate bone disease associated with chronic renal failure.[17] Bone scintigraphy is regarded as a highly sensitive and non-invasive method for the detection and assessment of the severity of ROD. Increased pyrophosphate uptake occurs in areas of the skeleton where the collagen metabolism is abnormal[6] and bone turnover is increased.[7]

Furthermore, we have researched the relationship between bone metabolic markers and bone scintigraphy in hemodialysis patients.[18] The aim of this study was to investigate the relationship between the bone/soft tissue ratio (B/ST ratio) of both the radius and skull and intact parathyroid hormone (PTH) or alkaline phosphatase (ALP), and to clarify the usefulness of bone scintigraphy in estimating bone disease in hemodialysis patients using a semi-quantitative method.

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MATERIALS AND METHODS

Study population

We evaluated 22 chronic hemodialysis patients. There were 10 males and 12 females with an age range from 22 to 67 years and a mean age of 45.3 years. The etiology of renal failure was chronic glomerulonephritis. The patients had been on hemodialysis for 63.41 ± 78.90 months and were dialyzed three times per week. No other medical problems such as liver disease, diabetes mellitus, or malabsorption were known to exist. Vitamin D_3 analogue and calcium supplements were gradually withdrawn a month prior to the study. None of the patients took steroids, estrogen, aluminum-containing phosphate binders, coumarins, anticonvulsants or medications known to interact with the calcium, vitamin D_3 or osteocalcin levels. All patients performed normal outdoor activities and were on an unrestricted diet with the exception of potassium and fluids. The middle-aged female patients who had diffuse uptake of cranium were excluded in the present study. Informed consent for participation in the present study was obtained from each patient or guardian as part of the protocol approved by the Institutional Clinical Subpanel on Human Studies at our university.

Bone scintigraphy

Tc-99m hydroxy-methylene disphosphonate (Tc-99m HMDP) (555 MBq, Nihon Medi-Physics Co. Ltd., Nishinomiya, Japan) was injected intravenously. In all patients, bone scintigraphy was obtained about 3 h after intravenous injection. Whole body images were recorded with a gamma camera (E.CAM, Toshiba and RC2600I Hitachi, scan speed 15 cm/min, matrix 256 × 1024). The whole body field was used to digitally record anterior and posterior views (256 × 1024) on a detected computer system (Toshiba 5500A/PI, Tokyo, Japan). Energy discrimination was provided by a 10% window centered on the 140 keV of Tc-99m.

Quantification of bone scintigraphy

Skeletal uptakes of Tc-99m HMDP were analyzed on a data processing system using the method reported by Fogelman et al.[8,9] In the posterior views of a whole-body scintigraphy, regions of interest (ROIs) were set over selected bony regions (Fig. 1). The B/ST ratio was measured by drawing ROIs around the skull (S), radius (R), and the middle parts of the soft tissue of the thigh. The means of these ROIs were calculated in all patients.

Laboratory data

Immunoreactive intact PTH was measured in all patients using the Allegro intact PTH kit (Nichols Institute Diagnostics, San Juan Capistrano, CA, USA). The serum calcium [cresolphthalein complexone (OCPC), Iyatron Co., Tokyo, Japan] and phosphorus (Enzyme assay, Kyowa Co., Tokyo, Japan) concentrations were also measured.

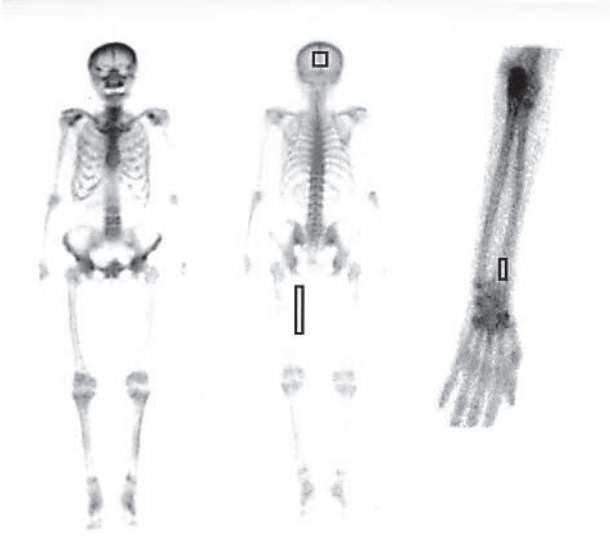

Fig. 1 Regions of interest (ROIs) were drown over skull, radius and soft tissue of medial thigh to calculate bone to soft tissue ratio (B/ST ratio) on the bone scintigraphy.

Intact PTH concentrations ranged from 59 to 1100 pg/m*l* (mean 463.13 ± 322.99 pg/m*l*; normal range, 10–65 pg/m*l*). Plasma concentrations of ALP were determined by standard methods. Serum calcium (Ca) and phosphorus (P) ranged from 6.8 to 11.3 mg/m*l* (mean 9.24 ± 1.26 mg/m*l*; normal range, 8.5–10.5 mg/m*l*), and 2.53 to 14.00 mg/m*l* (mean 6.11 ± 2.33 mg/m*l*; normal range 2.5–4.5 mg/m*l*). Plasma concentrations of ALP ranged from 97 to 863 U/*l* (mean 308.86 ± 209.02 U/*l*; normal range 115–359 U/*l*).

Statistical analysis

All quantitative data were expressed as the mean ± standard deviation. Correlations between the assays were assessed by linear regression analysis (Statview; Abacus Concepts Inc., Berkeley, CA). A probability level of less than 0.05 was considered significant.

RESULTS

Intact PTH had a significantly linear correlation with the B/ST ratio of skull (S) ($r = 0.702$, $p = 0.0001$) and the radius (R) ($r = 0.745$, $p < 0.0001$) (Fig. 2A, B). ALP had a significantly linear correlation with S ($r = 0.772$, $p < 0.0001$) and R ($r = 0.537$, $p = 0.009$) (Fig. 3A, B). The relationships of linear correlation between S and Ca or P were not significant (Ca $r = 0.189$, $p = 0.403$, P $r = 0.181$, $p = 0.4256$). Also, relationships of linear correlation between R and Ca, P were not significant (Ca $r = 0.191$, $p = 0.399$, P $r = 0.306$, $p = 0.162$).

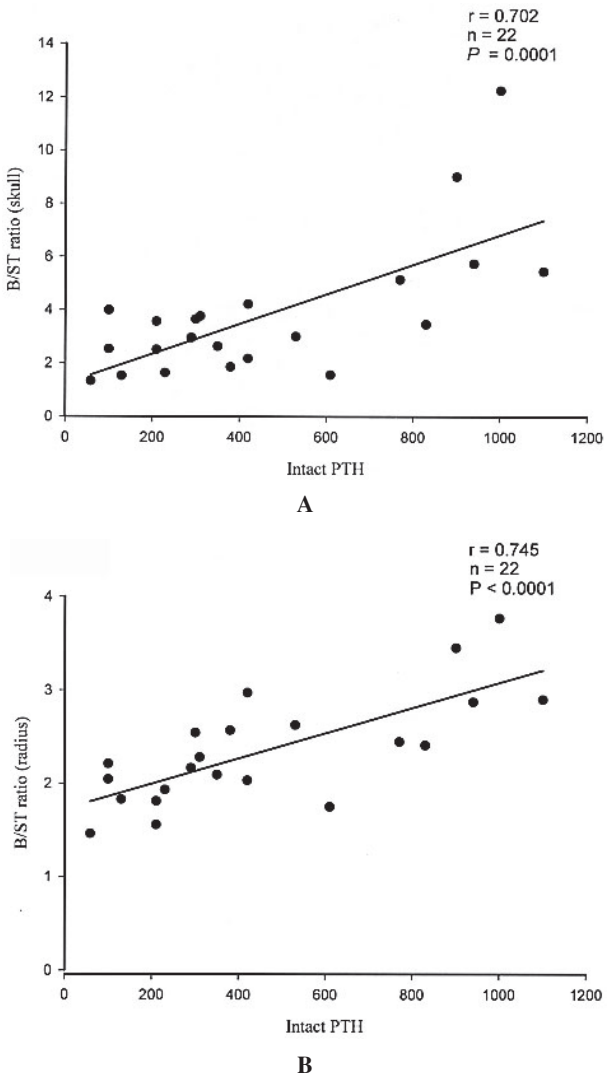

Fig. 2 Correlation between intact parathyroid hormone (intact PTH) and bone to soft tissue ratio (B/ST ratio) of skull ($r = 0.702$, $p = 0.0001$) (A), and of skull ($r = 0.745$, $p < 0.0001$) (B).

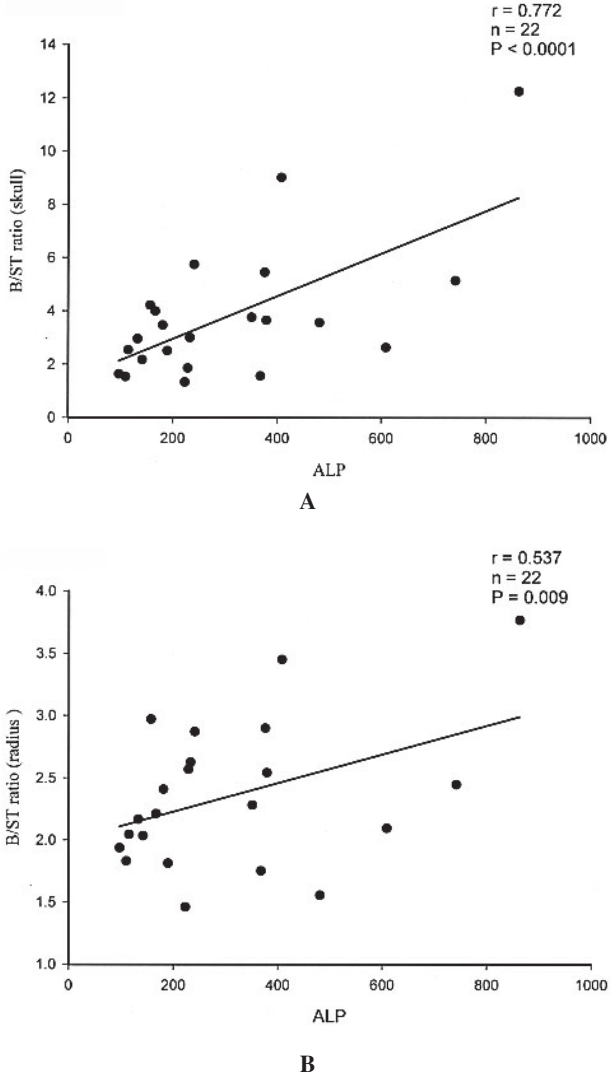

Fig. 3 Correlation between alkaline phosphatase (ALP) and bone to soft tissue ratio (B/ST ratio) of skull ($r = 0.772$, $p < 0.0001$) (A), and of radius ($r = 0.537$, $p = 0.009$) (B).

DISCUSSION

In hyperparathyroidism, increased bone resorption, associated with increased bone formation, has been observed. Using semi-quantitative scoring systems that incorporate some of the metabolic features listed, 83%–93% of patients were found to have mild, moderate or severe abnormalities on bone scintigrams.[10,11] The percentage of patients showing radiological abnormalities related to hyperparathyroidism was low (33%–46%), suggesting that bone scintigraphy may be useful in the detection of renal bone disease.[11,12] The scintigraphic features of metabolic bone disease that formed the basis of the Fogelman score were recognized: increased activity in the axial skeleton, increased activity in the long bone, increased in periarticular areas (wrist), prominent calvarium and mandible, beading of the costochondral junctions, increased activity in the sternum: "tie sternum," and a faint or absent kidney image.[1,13] The increased uptake of diphosphonates in osteomalacia is more difficult to explain. Thus, bone scintigraphy has been used to investigate ROD. Bone scintigraphy has been reported to reflect the coupling of bone formation and bone resorption,[5] and when the value of intact PTH is increased bone resorption exceeds bone formation. In this case, bone scintigraphy reflects the bone destruction. The reason that the B/ST ratio of the skull or radius correlated with intact PTH or ALP is that the ratio of cortical bone in the skull or distal radius was much higher than that of trabecular bone.[14] The ROIs were located around the selected areas, namely the skull and distal radius, because the bone mineral density of the radius has been reported to decrease,[2,3] and we took notice of the difference in the ratio of cortical bone to trabecular bone between the cranium and radius. Ninety-five percent

of the skull and radius have been reported to be made up of cortical bone.[14] As PTH affects cortical bone rather than trabecular bone,[15,16] the turnover of both the cranium and distal radius is considered to be accelerated along with the increase of intact PTH. As the estimations of bone mineral density measured by bone X-ray, DXA or CT are the result of chronic morphological change,[4,5] they do not always reflect the bone metabolism. As the B/ST ratio of bone scintigraphy was correlated with intact PTH and ALP, it may reflect the bone metabolism at this time; we have considered that the B/ST ratio of the skull and radius may be useful in evaluating the bone metabolism of hemodialysis patients. We thought that the B/ST ratio of the skull and radius, unlike in lumbar vertebrae and femoral bones, was scarcely affected by the bone remodeling due to loading and gravity.

To our knowledge, it has not been reported that the B/ST ratio of the skull and distal radius may be able to help in evaluating the bone metabolism of chronic hemodialysis patients. Bone scintigraphy enables us to evaluate the systemic bone in one examination, and it is possible to evaluate the bone formation at each bony lesion using the B/ST ratio. Provided that the B/ST ratio of both the skull and radius change dramatically after treatment with vitamin D pulse therapy or parathyroidectomy, we believe that they will be proven to function to evaluate the therapeutic effect of ROD. We should investigate the changes of both the B/ST ratio and other bone metabolic markers, and the usefulness of the B/ST ratio of both the skull and radius.

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