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MASTER

COMPARISON OF TOTAL-BODY CALCIUM WITH RADIOGRAPHIC AND PHOTON ABSORPTIOMETRY MEASUREMENTS OF APPENDICULAR BONE MINERAL CONTENT

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ABSTRACT

Two groups of investigators utilized three techniques for evaluating bone mineral mass. In one institution, total body calcium (TBCa) by total body neutron activation analysis, and bone mineral content of the radius (BMC_r), by photon absorptiometry (Norland-Cameron Bone Mineral Analysis), were measured concomitantly. In the other institution, the mean bone mineral content of the three inner phalanges of the left hand (BMC_h) was measured by radiographic absorptiometry. These techniques were applied to two groups of subjects: 16 patients with primary osteoporosis and 14 healthy marathon runners.

In the athletic population, TBCa was significantly correlated with BMC_h ($P < 0.03$) and with BMC_r ($P < 0.01$). There was a highly significant correlation between TBCa and BMC_h ($P < 0.001$) and with BMC_r ($P < 0.001$) in the osteoporotic patients. These two parameters of appendicular BMC were also significantly correlated with each other ($P < 0.002$) in this population.

The higher correlation found in osteoporotic patients may be related to the diffuse nature of this condition and to differences in the distribution of skeletal mass in the marathon runners.

KEY-WORDS

Total Body Calcium

Bone Mineral Content

Radiograhic Absorptiometry

Osteoporosis

Athletes

INTRODUCTION

The evaluation of the degree of osteopenia has clinical and physiological relevance. In recent years, different techniques for the quantification of skeletal mineralization have been introduced. Several, relatively simple methods, study the periphery of the skeleton radiographically. In these studies of localized areas of appendicular bone there is always the question of the validity of extrapolation to the whole body calcium levels (Nordin, 1964; McLean, Urist, 1968). The technique of in vivo total body neutron activation analysis (TBNAA) has provided a practical method to compare the total body calcium (TBCa) with the appendicular measurements. In this way, the value of localized measurements in evaluating the mineralization of the skeleton could be measured.

Chesnut, Manzke, et al., (1973) reported in 14 osteoporotic patients a high correlation coefficient of 0.94, $p < 0.001$, between TBCa, measured by TBNAA, and the measurements of bone mineral content of the distal radius (BMC_r) measured by the photon absorptiometric technique. The same correlation measured at different sites of the arm produced values of the correlation coefficient ranging from 0.93 to 0.83. In the full paper, these authors also reported weak or nonsignificant correlation between TBCa and some radiographic morphometry of similar appendicular sites. The average correlation coefficient for TBCa versus cortical area in the different sites was 0.70, $p < 0.01$, (Manzke, Chesnut, et al., 1975).

We reported a significant correlation ($r = 0.83$, $p < 0.001$) between TBCa by TBNAA and BMC of the radius by photon absorptiometry in osteoporotic patients. The correlation was even higher in a group of normal subjects, $r = 0.97$, $p < 0.001$ (Cohn, Ellis, et al., 1973 and 1974). A more recent study of 36 osteoporotic females and 23 normal females reported correlation coefficients of 0.83 and 0.81, respectively (Cohn, Zanzi, et al., 1976). In an expanded group of 45 osteoporotic females a significant correlation of r = 0.70 has been published (Aloia, Vaswani, et al., 1977), and in an expanded group of 24 normal males and females a correlation coefficient of 0.94 was also reported (Cohn, Ellis, et al., 1975).

In a heterogenous group of 71 patients and normal subjects a correlation with r = 0.86, $p < 0.01$, was found between partial body calcium measurements by in vivo neutron activation analysis and x-ray densitometry of the proximal radius. However, a wide scatter about the regression line was observed in the whole group and for each subgroup of normal subjects or of patients with metabolic bone diseases (Harrison, McNeill, et al., 1974).

This study was designed to determine the relationship of total skeletal mass (TBCa) as measured by TBNAA with the appendicular measurements of bone mineral content (BMC) of the radius, as measured by photon absorptiometric technique, and of the phalanges, by radiographic absorptiometry. We also compared these two appendicular measurements with each other. We performed these evaluations in a group of osteoporotic patients and in a contrast population of normal marathon runners.

METHODS

Subjects: Fourteen healthy white male marathon runners were studied consecutively without bias. They were part of a group of marathon runners who completed an annual Earth Day Marathon and who were recruited to participate in a study of bone mass of athletes. Selection of the initial group was made on the basis of age (4th to 6th decade), willingness to participate in the study, and the length of time they had been running. Preference for inclusion in the study was given to those marathon runners who had been active for longer periods of time. These subjects were determined to be healthy by absence of a history of any disorders which would affect (or any chronic illness), a normal physical examination, and normal values of routine laboratory examinations. One additional subject initially studied was excluded because his measured values were far out of range; this exclusion was validated by appropriate statistical analysis. This population was analyzed and compared with a group of fourteen females and two male white patients with primary osteoporosis, ranging in age from 50 to 75. All of these patients were diagnosed on the basis of clinical, radiological, and blood chemical findings. Spinal radiolucency and one or more vertebral partial compression fractures were present in all these patients. Patients were consecutively allocated from a larger population beginning their participation in a therapeutic trial. All patients were ambulatory.

Total Body Calcium: The details of measurement of total body calcium (TBCa) by TBNAA has been described elsewhere (Cohn, Shukla, et al., 1972). The radiation dose to the subject per activation was 0.28 rem. Calibration with an anthropomorphic phantom indicated an accuracy of ± 4% and a precision of ± 1% (SD) for the measurement of Ca. Thus changes in TBCa of 2% or greater can be measured at the 95% confidence level (2 SD). The TBCa was normalized for body size, sex, and age by means of the Ca ratio ($TBCa/TBCa_p$) where TBCa represent the measured total body calcium and the $TBCa_p$ represented the total body calcium predicted from empirically derived formulae, (Cohn, Zanzi, et al., 1976). In marathon runners with an unusually high total body potassium ratio (Ellis, Shukla, et al., 1974), a correction of the Ca ratio by the potassium value was performed.

Photon Absorptiometry: The bone mineral content of the radius (BMC_r) and the width of the radius (BW) were measured with a Norland Instrument Absorptiometer. The accuracy of this technique is stated to be ± 5% (Cameron, Mazess, et al., 1968). The precision of this technique is ± 2.5% (Cohn, Ellis, et al., 1974). Measurements were made at a point one-third the distance from the distal end of the nondominant/radius (8 cm site). The BMC_r may be normalized for body size, sex, and age by the BMC_r ratio (BMC_r/BMC_r predicted) where BMC_r represents the observed bone mass of radius and BMC_r predicted represents the predicted local bone mass (Cohn, Zanzi, et al., 1976).

Radiographic Absorptiometry: The bone mineral content of the hand (BMC_h) was measured by scans of three phalanges in two lightly exposed left hand radiographs (Colbert, 1970). The second radiograph, taken at a different kilovoltage, was used to double check the findings. An aluminum alloy reference wedge was placed along side the index finger when the x-ray was taken at Brookhaven National Laboratory (BNL). From a scan of the image of this standard a computer calculated the linear absorption coefficient of the alloy and the background optical density due to fog and scatter. When calculating the BMC_h from scans of the bone image, the computer used three parameters to nullify the effects of between-film differences in kilovoltage, exposure and film processing. The image grey levels (pixels) were used to calculate estimates of BMC_h and mineral concentration. A modified Joyce-Loebl Mark IIIC scanner under computer control shone a narrow beam of light through the film image of the bone, traversing the image scan-by-scan. A photocell converted the light, modulated by the image, to an electrical signal which was digitized and transmitted to the computer. The images of middle phalanges II, III and IV were scanned in parallel sections spaced one millimeter apart. The computer calculated the average BMC_h of the three bones (Colbert, Bachtell, et al., 1975). The results were expressed in arbitrary units (AU), representing mineral weight, as a product of the mineral "density" and bone area. The precision of this technique is $\pm$ 2.0% (c.v.) (Colbert, Bachtell, 1978).

Pairs of radiographs taken of the subjects of this study were mailed to the Greene Memorial Hospital,Radiological Research Laboratory (RRL) and BMC_h findings were rendered to the investigators at BNL by mail. No information on the skeletal status of the subjects were divulged to RRL at any time during the study.

RESULTS

The measured total body calcium (TBCa), bone mineral content of the phalanges (hands, BMC_h), bone mineral content of the radius (BMC_r), calcium ratio, BMC_r ratio, and the ratio between BMC_r and width of the radius (BMC_r/BW) are presented in Table I. The number, sex and median of age for the osteoporotic patients and normal marathon runners are included. All the parameters measured a significant difference, at $P < 0.001$ by a nondependent t test, among the two populations studied with the exception of the values of the BMC_r ratio. The lack of separation for this parameter may have been due to the high total body potassium in some of the marathon runners affecting the algorithm used for calculating the BMC_r ratio.

The TBCa versus the BMC_h and the TBCa versus the BMC_r were compared for each of the two groups (Table II). There was highly significant and comparable correlations between these parameters in the osteoporotic patients ($r = 0.88$ and 0.84 with standard error of the estimates of 15 and 17%, respectively). The same data for 14 normal marathon runners are also included in Table II. The correlations between TBCa and BMC_h and between TBCa and BMC_r were significant in this group ($r = 0.57$ and 0.66) but not so high as in the osteoporotic patients. The SEE was smaller in the correlation between TBCa and BMC_h (7.4%) than when comparing TBCa and BMC_r (11.4%). When using BMC_r/BW instead of BMC_r in these groups, the correlations decreased in the osteoporotic patients ($r = 0.54$, $P < 0.03$, SEE 17.8%) and somewhat improved in the athletes ($r = 0.79$, $P < 0.001$, SEE 6.4%).

Table III shows the comparison between the values of BMC_r or BMC_r/BW with the corresponding values of BMC_h in the two groups of individuals. In the osteoporotic patients, there was a highly significant correlation between the BMC_r and BMC_h ($r = 0.73$), yet the SEE was large (22.3%). There was no correlation between BMC_r/BW and BMC_h. The reverse was found in the normal athletes; there was no correlation between BMC_r and BMC_h ($r = 0.51$ with a $P < 0.06$) and a modest correlation between the BMC_r corrected by the bone width (BW) compared with BMC_h ($r = 0.56$, $p < 0.04$, SEE of 7.5%). When the Ca ratio was compared with BMC_h, BMC_r or with BMC_r/BW, no significant correlation were found in the two groups of subjects.

Figures 1 and 2 show scattergrams and regression lines for TBCa versus BMC_h and BMC_r respectively, corresponding to the osteoporotic patients and the marathon runners. Overlap of values was noticeable among the two osteoporotic male patients and the normal marathon runners. The overlap was clearly greater with the values of BMC_r or BMC_h than when considering the TBCa values. Figure 3 shows the overlap between one of the male osteoporotic patients and most of the normal athletes when comparing the BMC_r and BMC_h measurements with each other. No clear difference was observed when comparing the overlap for each of these two parameters.

DISCUSSION

We found strong correlations between total body calcium (TBCa) and appendicular BMC of the radius ($r = 0.84$) and of the phalanges in ($r = 0.88$) in osteoporotic patients and modest correlations in normal marathon runners (0.66 and 0.57). This study represents the first validation of the BMC_r with respect to TBCa. It also confirms previous studies of the relationships between TBCa and BMC_r. A greater overlap of normal athletes and male osteoporotic patients was also observed when trying to separate the two groups by appendicular measurements than when using TBCa. This consideration, in addition to the somewhat large error in predicting one of the compared values, makes the appendicular measurements of BMC of limited value for predicting the TBCa of individual subjects. This conclusion is in agreement with previous studies for BMC_r in ostoeporotic patients by Cohn, Ellis, et al., (1974) ($r = 0.83$), and by Manzke, Chesnut, et al. (1975), ($r = 0.84$ for the "8 cm" site).

The opposite effects of correcting BMC_r by BW in lowering the correlation of TBCa versus BMC_r in osteoporotic patients and slightly improving the correlation in our younger athletes may be related to the reported lack of change of the width of the radius with age despite evidence of cortical thickening (Smith, Johnston, et al., 1972). The contrast between the lack of correlation of BMC_r/BW versus BMC_h in our osteoporotic patients and the weak correlation of these parameters in the marathon runners (with no significant correlation between the direct reading of BMC_r and BMC_h) would suggest differences in the significance of these two measurements of the appendicular BMC.

Although the limited number of probands in our study and the small magnitude of the differences incline us to guarded conclusions, the results suggest that BMC_r (8 cm site) was slightly better correlated with TBCa in the marathon runners and the BMC_h was slightly better correlated in the osteoporotic patients. A factor in the difference might be the inclusion of the area of phalanges in the calculation of BMC_h.

The normalization of TBCa represents an improvement in the separation of osteoporotic and normal populations. However, even this use of the Ca ratio does not give a complete separation of individual osteoporotic patients and normal subjects (Cohn, Zanzi, et al., 1976). The level of correlations attained between TBCa and the appendicular BMC measurements would be adequate for these BMC_r and BMC_h values to be used for serial evaluations of bone mass, particularly cortical bone, or in epidemiological surveys of the bone mass of populations. We had previously reported that changes in BMC_r following therapy for osteoporosis did not reflect changes in TBCa (Aloia, Ellis, et al., 1975; Cohn, Zanzi, et al., 1976).

An interesting point in this study is the lower correlation between TBCa and appendicular BMC measurements in normal marathon runners as compared with the values measured in osteoporotic patients. The correlation obtained in these athletes was lower than the values we found in normal subjects, $r = 0.97$ and $r = 0.94$ in two previous studies (Cohn, Ellis, et al., 1974; Cohn, Ellis, et al., 1975). Several studies have compared the appendicular bone mass of athletes and nonathletes and have yielded conflicting conclusions (Nilsson, Westlin, 1971; Kumlin, Wiikeri, et al., 1971; Dalen, Olsson, 1974). It may be possible that the chronic exercise of these marathon runners modify the usual uniformity of the skeletal bone mass, probably increasing mainly the trabecular bone mass in the loaded extremities or axial segments of the skeleton. Therefore, these subjects may have developed a less uniform distribution of bone mass than normal subjects and even osteoporotic subjects. If this hypothesis is true it may explain the surprising difference in correlations between total skeletal mass and BMC measured in the upper extremities in these marathon runners.

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Table I: Description of subjects and values

	Sex F/M	Age Median (y)	TBCa (kg)	BMC_h (A.U.)	BMC_r (g/cm)	Ca Ratio	BMC_r Ratio	BMC_r/BW (g/cm^2
Osteoporosis	14/2	68	0.651	168.61	0.735	0.915	0.997	0.576
(Mean ±S.E.)			(0.037	(13.31)	(0.054)	(0.083)	(0.166)	(0.028)
Marathon Runners	0/14	42	1.177	289.6	1.284	1.074	1.020	0.848
(Mean ±S.E)			(0.031)	(6.70)	(0.047)	(0.028)	(0.036)	(0.023)

TBCa = total body calcium.

BMC_h = bone mineral content of hand.

BMC_r = bone mineral content of radius.

BW = bone width.

A.U. = arbitrary units.

S.E. = standard error.

Table II. Relationship of total-body calcium (TBCa) to appendicular bone mineral content, of the phalanges (BMC_h) and of the radius (BMC_r), in osteoporotic patients and normal marathon runners.

	n	x	y	r	p<	SEE	SEE% $(\bar{y})$
Osteoporosis	16	TBCa	BMC_h	0.884	0.001	25.8	15.3
			BMC_r	0.836	0.001	0.12	16.6
Athletes	14	TBCa	BMC_h	0.570	0.03	21.5	7.4
			BMC_r	0.658	0.01	0.15	11.4

n = number of subjects. SEE = standard error of the estimates, percent calculated over mean of ordinate.

Table III. Relationship of bone mineral content of the radius (BMC_r) to bone mineral content of the phalanges (BMC_h) in osteoporotic patients and normal marathon runners.

	N	X	Y	R	P<	SEE% ($\overline{Y}$)
OSTEOPOROSIS	16	BMC_R	BMC_H	0.731	0.001	22.3
		BMC_R/BW	BMC_H	0.336	N.S.	
ATHLETES	14	BMC_R	BMC_H	0.509	N.S. (0.06)	7.8
		BMC_R/BW	BMC_H	0.558	0.038	7.5

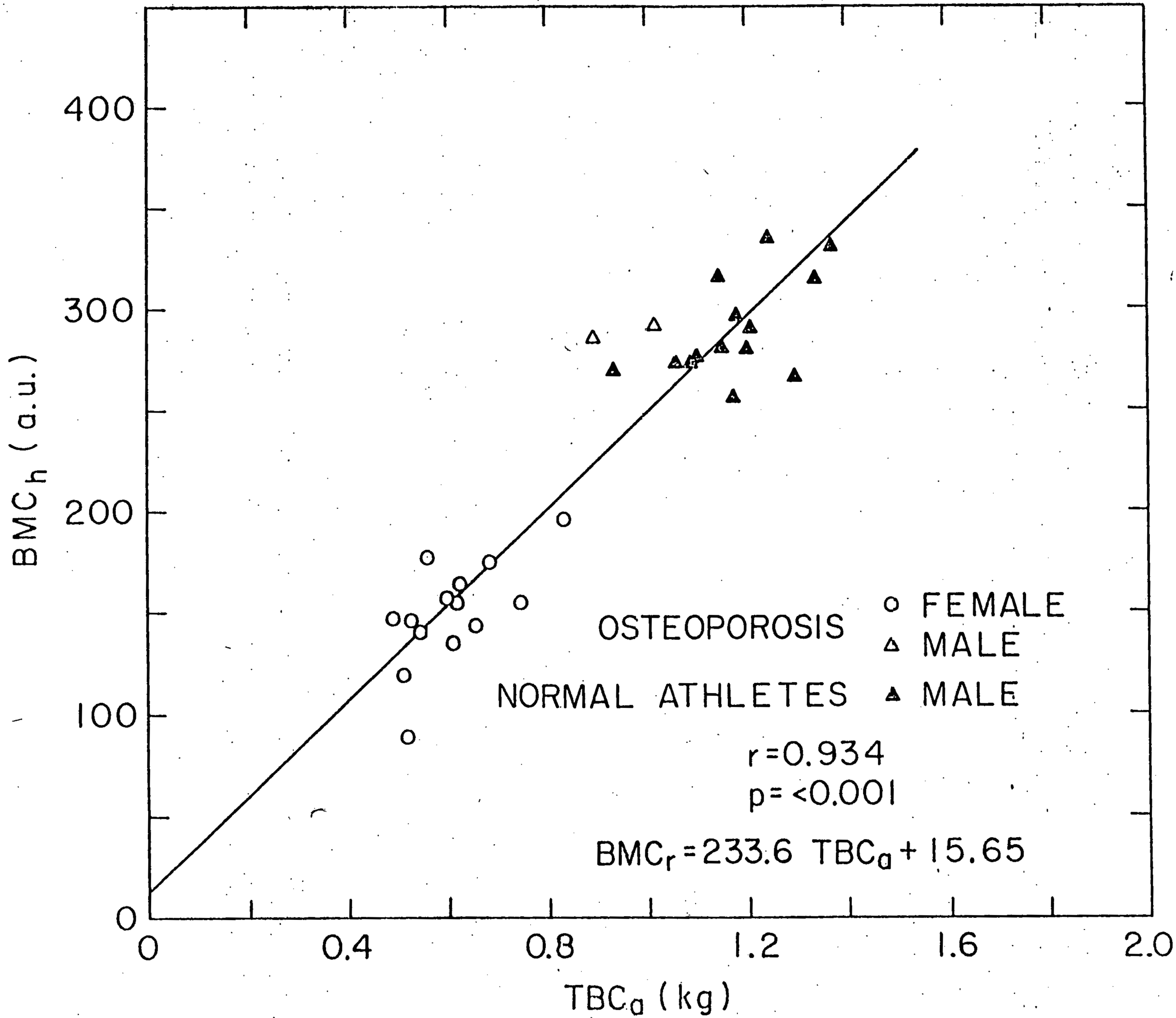

Fig. 1. Total-body calcium (TBCa) is plotted against bone mineral content of the phalanges (BMC_h) in osteoporotic patients and in normal marathon runners.

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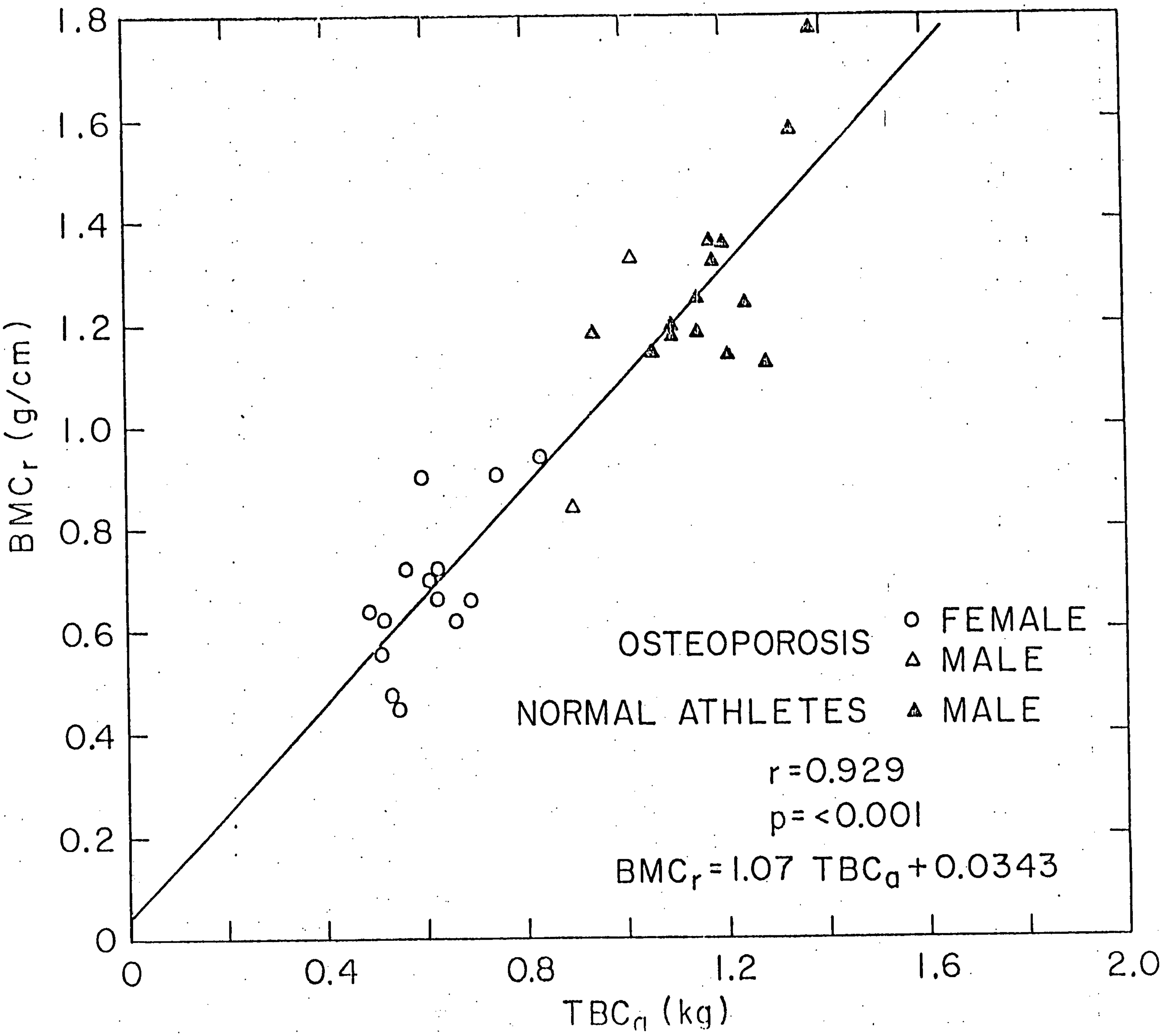

Fig. 2. Total-body calcium (TBCa) is plotted against bone mineral content of the radius (BMC_r) in osteoporotic patients and in normal marathon runners.

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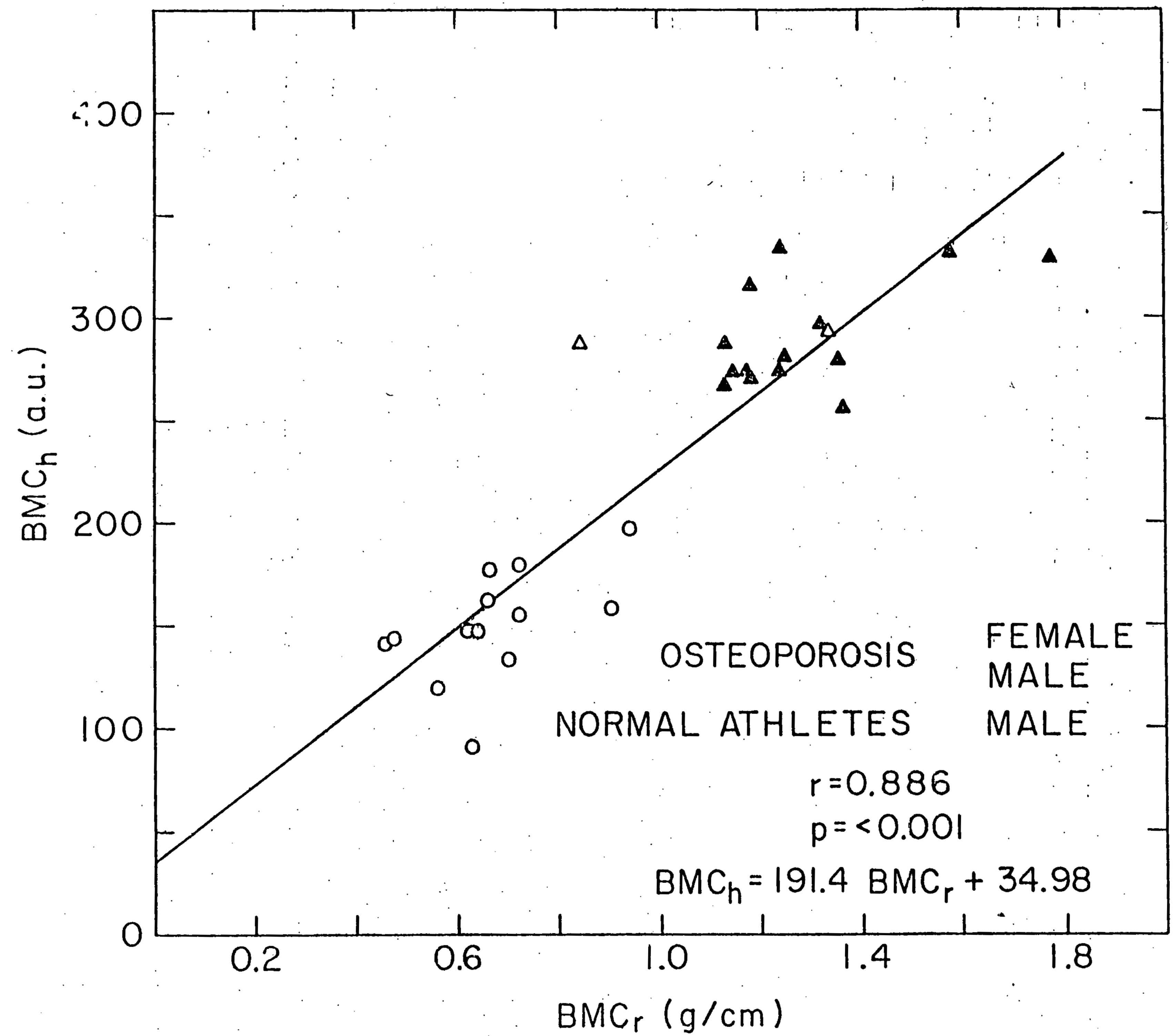

Fig. 3. Bone mineral content of the radius (BMC_r) is plotted against bone mineral content of the phalanges (BMC_h) in osteoporotic patients and in normal marathon runners.

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