SKELETAL STATUS IN RHEUMATOID ARTHRITIS:

A PRELIMINARY REPORT

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Mark N. Mueller and John M. Jurist
Departments of Radiology and Medicine
University of Wisconsin Medical Center
Madison, Wisconsin

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SYNOPSIS

Twenty-six women with ARA classic or definite rheumatoid arthritis age-matched with controls were evaluated for bone mineral content and rigidity. Significant bone loss occurred in arthritics treated with corticosteroids. Bone losses at diaphyseal and metaphyseal sites were of similar magnitude--suggesting no preferential loss of trabecular bone. A significant decrease in relative ulnar rigidity was observed in rheumatoids not receiving corticosteroids. An even larger decrease was noted in subjects receiving corticosteroids.

INTRODUCTION

Osteoporosis is commonly held to be associated with rheumatoid arthritis.¹⁻⁹ Radiographic descriptions of rheumatoid arthritis frequently cite juxta-articular and generalized bone loss as being characteristic of this disease.¹⁰⁻¹² The etiology of the bone loss is not understood, but is attributed to multiple factors such as local inflammation, immobilization, generalized catabolic processes secondary to the disease itself, poor nutrition and the nature and duration of therapy with corticosteroids or other anti-inflammatory agents. The specific role of each factor is poorly defined at present--partly because of the lack of sensitive quantitative techniques of evaluating changes in mass or structural properties of the skeleton.

For the past 10 years, the Bone Measurement Laboratory at the University of Wisconsin has been developing a technique for the precise determination in vivo of bone mineral content by monoenergetic photon absorptiometry.^{13,14} Recently, we extended our interest in the physical evaluation of skeletal status to include measurement of bone resonant frequency.^{15,16} This paper reports preliminary data on the mineral content and resonant frequency of bone in patients with rheumatoid arthritis.

METHODS

Subjects

All patients attending the University of Wisconsin Arthritis Clinic

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are evaluated for bone mineral and resonant frequency on a routine basis. Twenty-six women with classic or definite rheumatoid arthritis (hereinafter referred to as rheumatoids) by American Rheumatism Association criteria¹⁷ were sequentially selected from the Clinic and matched for age with equal numbers of female control subjects (controls) who were free of any identifiable arthritis or other diagnosis commonly associated with osteoporosis.

All study patients with rheumatoid arthritis had active systemic disease as evidenced by morning stiffness with a duration of more than one hour, persistently elevated erythrocyte sedimentation rates, aching pain with objective swelling in multiple peripheral joints. All patients in the study had bilateral wrist involvement. The degree of involvement of finger joints was variable. However, the degree of hand involvement and the number of patients with elbow involvement was similar in the steroid group and the nonsteroid group. The control subjects were selected from University of Wisconsin staff, visitors and local women's groups and were not University of Wisconsin Hospital or Clinic patients. None of the control patients had taken or were taking corticosteroids or any other medication which might be considered to influence bone metabolism.

Monoenergetic Photon Absorptiometry

Traditional roentgenographic or densitometric techniques are unsatisfactory for objective evaluation of bone mass because of large systematic errors and poor reproducibility. The monoenergetic photon absorptiometric technique was developed to eliminate the major sources of error associated with radiographic photodensitometry.

The photon absorptiometric technique measures attenuation of a photon beam (usually the 27.4 keV photon of ^{125}I) passing through the bone of interest (Fig. 1). The bone mineral mass (M_B) at any point in the path of the photon beam is proportional to $\ln(I_0^*/I)$ when the total "tissue" thickness is constant both above and at the sides of the bone. The measured quantities are the intensity of the beam through the soft tissue adjacent to the bone (I_0^*) and through a point of the bone (I). The proportionality constant relating M_B and $\ln(I_0^*/I)$ may be determined empirically or may be obtained from tabulated absorption coefficients since a single, well-defined photon energy is used. The photon absorptiometric technique has been described in detail elsewhere.^{18,19} The precision of photon absorptiometry is 1-2%.

Measurement of Vibratory Properties

The measurement of relative bone rigidity is of interest because of the reported correlations between bone strength, mineral content, geometry, and elastic moduli as measured in vitro.^{20,21} Thus, if reliable in vivo estimation of rigidity can be made, it will ultimately be possible to predict the bone strength of patients with disorders affecting the skeleton.

The speed of sound in a material is related to both elasticity and density.^{22,23} Hence, measurement of the speed of sound propagation in bone affords a possible way of estimating the elasticity and therefore

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strength of this material. We are studying measurement in vivo of the speed of sound in the ulna, tibia and pelvis. Our most effective approach has been to determine resonant frequency of a long bone such as the ulna from a recording of the response of the bone to mechanical vibration as a function of frequency (Fig. 2).

The resonance of the ulna (or any other long bone) may be described by $F_a L = KC$, where F_a and L are the measured ulnar resonant frequency and length, C is the speed of sound in the ulna, and K is a proportionality constant dependent on the mode of vibration, boundary conditions and geometrical factors. Since $Y = \rho C^2$, where Y is Young's elastic modulus of bone and ρ is its density Y is proportional to $(F_a L)^2$. Thus, the measured value of $F_a L$ may be used as an indication of relative bone rigidity or elasticity. On repeated resonant frequency determinations, a coefficient of variation of 2-4% is obtained.²⁴

Measurements

The bone mineral content (BM) and width (W) of the left radial diaphysis was measured at a distance of 30% of the ulnar length proximal to the ulnar head in 26 women with ARA classic or definite rheumatoid arthritis. Measurement at this site provides an index of compact bone mass. In addition, BM and W were measured near the distal end of the left radius in these women (at a site 2 cm. proximal to the ulnar head) in order to obtain an index of the mass of trabecular bone. These two measurement sites are termed diaphyseal and metaphyseal sites, respectively.

The product of ulnar resonant frequency and length ($F_a L$) was measured on both left and right ulnae of 23 women with classic or definite rheumatoid arthritis. The left and right $F_a L$ values of each woman were averaged.

Statistical Analysis:

The student's T-test for paired variates was used to test differences between rheumatoid and control subjects for significance.

RESULTS

A summary of our findings is presented in Figures 3-5. Bone mineral/width ratios (BM/W) for rheumatoid subjects without prior corticosteroid treatment are not significantly different from those of their age and sex-matched controls. Resonant frequency measurements ($F_a L$) were approximately 20% less than those of control subjects.

Corticosteroid-treated rheumatoid women demonstrate significant differences in mineral content at both diaphyseal and metaphyseal sites of the radius relative to their controls. Resonant frequency differences between the steroid-treated rheumatoids and their controls are more marked than for the rheumatoids not treated with steroids.

The mean metaphyseal-diaphyseal ratio of BM/W in control subjects is 0.71. The corresponding ratios for nonsteroid and steroid-treated rheumatoids are not significantly different.

DISCUSSION

Although any conclusions to be drawn from this preliminary study are necessarily limited by the small number of subjects involved, some generalizations may be made. In noncorticosteroid-treated subjects, no apparent difference in bone mineral content was observed at the metaphyseal or diaphyseal site. With larger numbers of patients, significant differences may become apparent, particularly when the variable of disease duration and severity are considered. Although no comparative analysis of x-rays on this group of patients was made in this preliminary study, it is of interest that no selective bone loss was observed at diaphyseal sites using the sensitive absorptiometric technique.

The differences between control subjects and corticosteroid-treated rheumatoids at both sites of the radius are significant. Whether these differences are a result of corticosteroid administration or are related to a possible selective process in women for whom cortisone is prescribed is not clear. Further studies to resolve this question by matching rheumatoids on cortisone with those not on cortisone for disease duration and severity are in progress.

The apparent loss of skeletal mass in corticosteroid-treated rheumatoids is of similar magnitude at the diaphyseal and metaphyseal sites of the radius. This finding does not support the hypothesis that a preferential loss of bone occurs at the metaphyseal site, as would be implied from radiographic descriptions of "juxta articular" osteoporosis.

The F_{aL} determination provides an index of the relative rigidity of bone. Rigidity of any long object is a function of mass, the spatial distribution of material about the long axis of the object and the mechanical quality or elasticity of the material. A decrease in bone mass would therefore produce a consequent decrease in F_{aL} . However, in our observations, a relatively small percentage change in bone mineral (or bone mass) apparently leads to a large change in F_{aL} . This suggests that the structural or mechanical quality of the long bone as well as its mass may be altered by corticosteroid therapy.

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Legends

1. Schematic diagram illustrating the basic principles used in measuring bone mineral mass with a monoenergetic photon source. The bone mineral mass per unit area in the beam path is given by the equation.
2. Method of measuring ulnar resonant frequency. Resonant frequency is determined from a recording of the acceleration response as a function of driving frequency.
3. Diaphyseal BM/W for rheumatoids and their age-matched controls. The difference (Δ) between the mean BM/W of the rheumatoid and control groups is expressed as a percentage of the mean control value for the N pairs of subjects.
4. Metaphyseal BM/W for rheumatoids and their age-matched controls.
5. Ulnar F_{aL} for rheumatoids and their age-matched controls.

$$M_B = \frac{\rho_B \ln(I_0^*/I)}{(\mu_B \rho_B - \mu_S \rho_S)}$$

= BONE MINERAL MASS
PER UNIT AREA IN
RADIATION BEAM PATH
(GM/CM²)

μ = MASS ABSORPTION
COEFFICIENT (CM²/GM)

ρ = MICROSCOPIC
DENSITY (GM/CM³)

Figure I. Schematic diagram illustrating the basic principles used in measuring bone mineral mass with a mono-energetic photon source. The bone mineral mass per unit area in the beam path is given by the equation.

Figure 2. Method of measuring ulnar resonant frequency. Resonant frequency is determined from a recording of the acceleration response as a function of driving frequency.

Figure 3. Diaphyseal BM/W for rheumatoids and their age-matched controls. The difference (Δ) between the mean BM/W of the rheumatoid and control groups is expressed as a percentage of the mean control value for the N pairs of subjects.

Figure 4. Metaphyseal BM/W for rheumatoids and their age-matched controls.

Figure 5. Ulnar FaL for rheumatoids and their age-matched controls.