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High levels of fat and (*n*-6) fatty acids in cancellous bone in osteoarthritis

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Abstract

Background: Osteoarthritis (OA) is strongly linked with obesity and patients with osteoporosis (OP) have a low body mass index. Anecdotal evidence, clinical and laboratory, suggests that OA bone contains more fat. However, conversion of osteoblasts to adipocytes is reported in OP and this would suggest that the more porous OP cancellous bone would have a high fat content.

Objectives: To test the hypothesis that OA bone contains more fat than OP bone.

Methods: Cores of cancellous bone were obtained from femoral heads of patients undergoing surgery for either OA or OP. Lipids were extracted using chloroform-methanol, weighed and expressed as a fraction of core mass and volume. A fatty acid analysis was performed using gas chromatography.

Results: OA bone contained twice as much fat per unit volume of tissue as OP. Levels of *n*-6 fatty acids were elevated in OA, especially arachidonic acid (C20:4 *n*-6) which was almost double that found in OP.

Conclusions: These data support the hypothesis that lipids may play a significant role in the pathogenesis of OA and may provide part of the key to understanding why OA and OP lie at opposite ends of the spectrum of bone masses.

Background

Osteoarthritis (OA) and osteoporosis (OP) are the two most significant musculoskeletal causes of ill-health, and even death, in the increasingly elderly western population. Bone is badly affected in both diseases. In OP, a loss of bone results in fragility and increased risk of fracture. In OA, there is a proliferation of poorly mineralised bone [1]. In parallel with these changes in the bone, patients with OP generally have a below average body mass index whereas in primary generalised OA there is a recognised link with obesity and a suggested systemic aetiology [2,3] independent of weight-bearing.

Bone forming osteoblasts share a common mesenchymal stem cell precursor with adipocytes. Defective co-regulation and lipid metabolism suggests possible mechanisms for the bone pathologies observed in these diseases [3,4]. Osteoblasts can be stimulated *in vitro* towards an adipocytic phenotype by increasing various fatty acids in the culture environment [5]. In OP there are fewer osteogenic

cells and a greater number of adipocytes in the marrow [6]. Structurally, OP bone has few and narrow trabeculae with large spaces between them. In OA the trabeculae are thicker and so have less space between them. The greater porosity in OP combined with a change in tissue types suggests that one might expect to find a higher fat content in OP cancellous bone. However, anecdotal evidence suggests an increased amount of fat in OA bone: in the laboratory fat globules are often found floating in the cell culture medium, and during surgery fat is commonly expressed from the bone during resection of the tissue. To try to resolve this we have measured the fat content of the bone from the femoral heads of patients with either OP or OA.

Methods

Tissue was obtained from 5 femoral heads from patients undergoing total hip replacement for OA and 5 having a hemiarthroplasty for osteoporotic fracture of the femoral neck. A 9 mm diameter core of bone containing marrow was removed from the superior aspect of each femoral head as described previously [1,7]. Cores were broken up into fragments, frozen in liquid nitrogen and ground in a freezer mill (Model 6750, Glen Creston Ltd, Middlesex, England). Lipids were extracted from a known mass of tissue using chloroform-methanol extraction [8] and weighed.

The fatty acid composition of the extracted lipid was determined. First, the fatty acids were converted to their methyl esters (FAME) by transmethylation using 0.5 M sodium methoxide as described by Christie [9] with one modification; the sample lipid was dissolved in toluene instead of tetrahydrofuran. Samples and standards were analyzed by running for 40 minutes on a Varian 3800 Gas Chromatograph fitted with a J & W Scientific Column, DB-225.

Results

The mass of lipid per unit mass of tissue, was found to be 0.24 ± 0.04 g/g (mean ± sd, n = 5) in the OA group and 0.21 ± 0.05 g/g in the OP group. Bone mass was taken to be tissue mass minus lipid mass, and lipid/bone became 0.31 ± 0.07 g/g (OA) and 0.27 ± 0.07 g/g (OP). However, the proliferation of bone in OA and the loss in OP means that the apparent density of OA bone is considerably greater (0.71 g cm^{-3}) than OP bone (0.38 g cm^{-3}) [1] so the fractional volume available for the fat is considerably smaller; porosity 59% in OA, 80% in OP. Assuming that the bone defines the total tissue volume, this volume was found by dividing the mass of the bone by the apparent density. The amount of lipid per unit volume of tissue then became 0.22 ± 0.05 g cm^{-3} in OA and 0.10 ± 0.02 g cm^{-3} in OP (P = 0.002, t-test).

There were a number of differences in the fatty acid composition of the extracted lipids between OA and OP. Those that were significant (Student's t-test) are shown in Table 1. The saturated stearic acid (C18:0) was lower in OA than OP bone, but the omega-6 (n-6) fatty acids were higher by between 50–90%.

Discussion

Despite the greater marrow space available in OP bone, this study shows that the amount of fat in a given volume of OA cancellous bone tissue is approximately twice that found in the same volume of OP bone. There are also significant differences in the fat composition in terms of fractional amounts of specific fatty acids between the two diseases. It is notable that all the fatty acids significantly increased in OA are of the omega-6 (n-6) variety, which are the precursors to the most strongly pro-inflammatory eicosanoids. Of particular note is arachidonic acid, the precursor for prostaglandin E_2. Arachidonic acid is reported to be increased in cartilage, serum and synovial fluid of OA patients [10] and our study shows it to be almost double in OA bone compared with OP bone.

Table 1: Fatty acid composition of lipids extracted from bone and marrow which differed between osteoarthritic and osteoporotic patients, expressed as a percentage of total fatty acid mass (mean ± sd). Significance values were obtained using Student's t-test.

Fatty acid	OP Mass %	OA Mass %	*P*
C16:1 Palmitoleic	4.1 ± 1.1	7.0 ± 1.2	0.005
C18:0 Stearic	4.67 ± 0.30	3.26 ± 0.47	<0.001
C20:2n-6 Eicosadienoic	0.102 ± 0.023	0.151 ± 0.023	0.011
C20:4n-6 Arachidonic acid	0.245 ± 0.029	0.479 ± 0.067	<0.001
C20:3n-6 Dihomo gamma-linolenic acid	0.117 ± 0.028	0.166 ± 0.019	0.012
C22:4n-6 Docosatetraenoic	0.119 ± 0.017	0.178 ± 0.020	0.001

We have hypothesised that primary generalized osteoarthritis (OA) may be a systemic disorder affecting the whole musculoskeletal system and involving altered lipid metabolism [3]. The proliferation of bone and fat in OA points towards lipids playing a significant role in the pathogenesis of OA and the increased levels of (*n*-6) fatty acids suggest there may be an inflammatory component, albeit perhaps, requiring a broader interpretation of inflammation. It may also provide part of the key to understanding why OA and OP appear to lie at opposite ends of the spectrum of bone masses, though the mechanisms mediating this are still unclear.

Authors' Contributions

MSP participated in the 'High fat content of bone in osteoarthritis' and undertook all the laboratory work and performed statistical analysis. MSP drafted the manuscript and read and approved the final manuscript.

RMA proof read the manuscript and approved the final version.

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