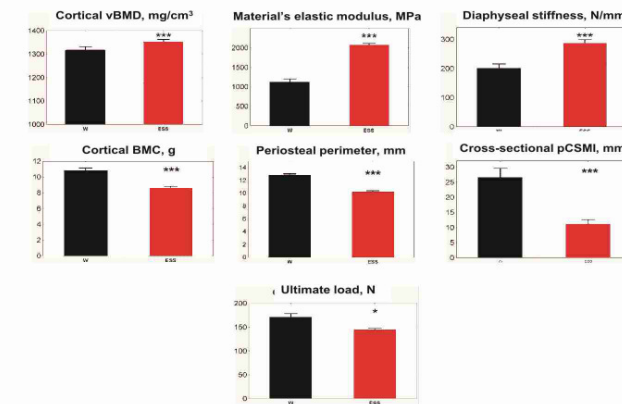
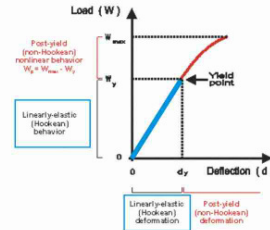
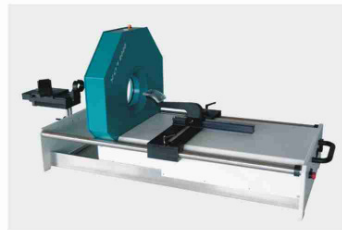


# CORRELATION BETWEEN CORTICAL BONE STRUCTURE AND BIOMECHANICS AND METABOLIC INDICATORS IN SPONTANEOUSLY DIABETIC, eSS RATS. A pQCT study.

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## GENERAL BACKGROUND AND AIM OF THE STUDY

The biomechanical impact of the diabetic condition on the skeleton is not completely described nor understood. Animal models offer different instances of study.

This paper investigates the skeletal condition in spontaneously diabetic, eSS rats (IIM, Natl Univ of Rosario) with an inherited type-II diabetic condition, studied before the development of renal alterations.

The aim of the study was to describe the skeletal structure and biomechanics of these animals (analyzed by mid-diaphyseal pQCT scans and 3-point bending tests) as related to some biochemical indicators of their carbohydrate, oxidative and phosphocalcic metabolism.

## MATERIALS AND METHODS

With that purpose, the femur diaphyses and blood and urine samples of 9 adult male eSS rats weighing 400-450g and 10 unaffected, age-paired "e" strain controls were studied.

Variables determined by pQCT included indicators of bone "mass" (total, cortical and trabecular BMC, cortical area), bone material's "quality" (cortical vBMD, known to vary linearly with bone material's stiffness), diaphyseal design (CSMI's, proportional to the perforization of the cortical design with respect to selected reference axes for deformation under loads), and strength (Bone Strength Index -BSI-, Strength-Stress Index -SSI's-, all proportional to the product:  $cortical\ vBMD * CSMI's$ ).

Variables assessed by mechanical tests included diaphyseal stiffness (load/deformation ratio during the elastic period), yield load (indicative of bone resilience, or resistance to the first crack), post-yield load (indicative of bone resistance to crack generation and progression - bone toughness -), and maximal load (indicative of the bone ultimate or "fracture" strength).

The elastic modulus E of cortical bone (indicative of the mechanical "quality" - intrinsic stiffness - of bone material) was calculated indirectly from mechanical and tomographic data.

Metabolic data included serum urea, creatinine, glucose, fructosamine, triglycerides, T-bars, antioxidant activity, Ca, P, and PTH, and urine Ca and P.

Bone mechanical and tomographic data were correlated with metabolic data in order to test their eventual pathogenetic interrelationships.

## RESULTS

Body weight was similar between groups. The eSS rats showed

a. excessive cortical tissue vBMD and stiffness (vCId, E) and diaphyseal stiffness, with low resilience and toughness (figure 1),

b. impaired bone mass-geometry indicators (BMC, periosteal perimeter, CSMI's) with respect to body weight (figure 1), and

c. low diaphyseal strength (fracture load), with respect to controls (ANOVA, always  $p < 0.001$ , figure 1). The Bone Strength Index, BSI =  $CSMI * vCId$ , which disregards mineralization-unrelated microstructural factors, underestimated the actual bone strength. eSS rats were also hypercalciuric, and serum PTH varied directly with blood glucose, fructosamine and P (figure 2) and inversely with plasma Ca (not shown).

Despite their generally low values in eSS, bone mass and geometry indicators improved as a function of blood PTH, glucose and fructosamine (not Ca or P) (figure 3).

Bone "material" or strength indicators did not vary with metabolic indicators in eSS but they did when analyzed together with controls (Figures 4 & 5).

## INTERPRETATION

Results suggest that skeletal alterations in eSS rats might result from

1. delayed bone growth with respect to body growth;
2. bone matrix hypermineralization and altered microstructural properties, associated to altered glycosylation indicators;
3. excessive stiffness of bone tissue and bones with impaired resilience and toughness (associated to 2);
4. inadequate bone geometry, perhaps because the reduced bone strain by customary usage reduced bone mechanostat stimulation (associated to 3), and
5. bone weakness (associated to 3-4).

Enhanced PTH activity, secondary either or both to hypercalciuria or to the diabetic condition, would have been anabolic on bone formation but not enough to compensate for the primary delay of bone growth.

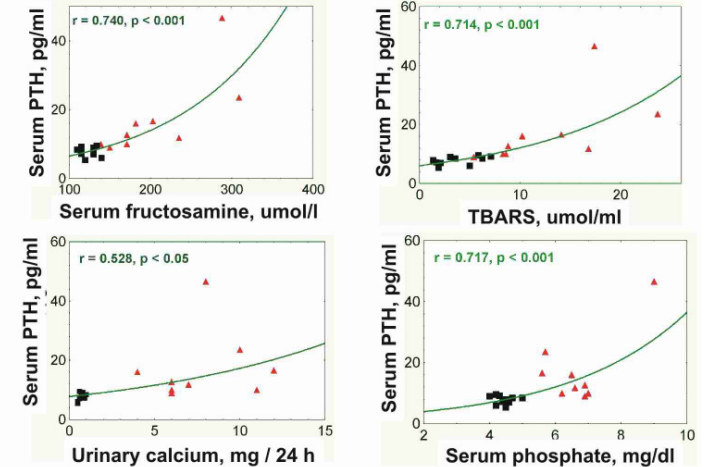


Figure 2

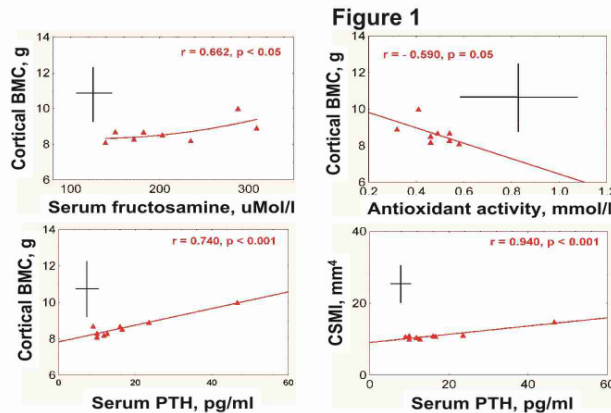


Figure 3

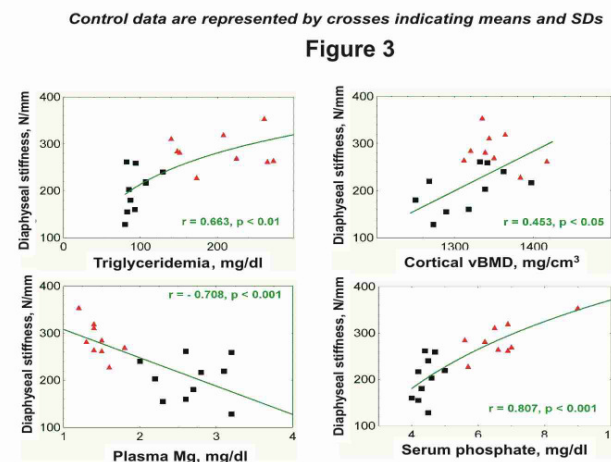


Figure 4

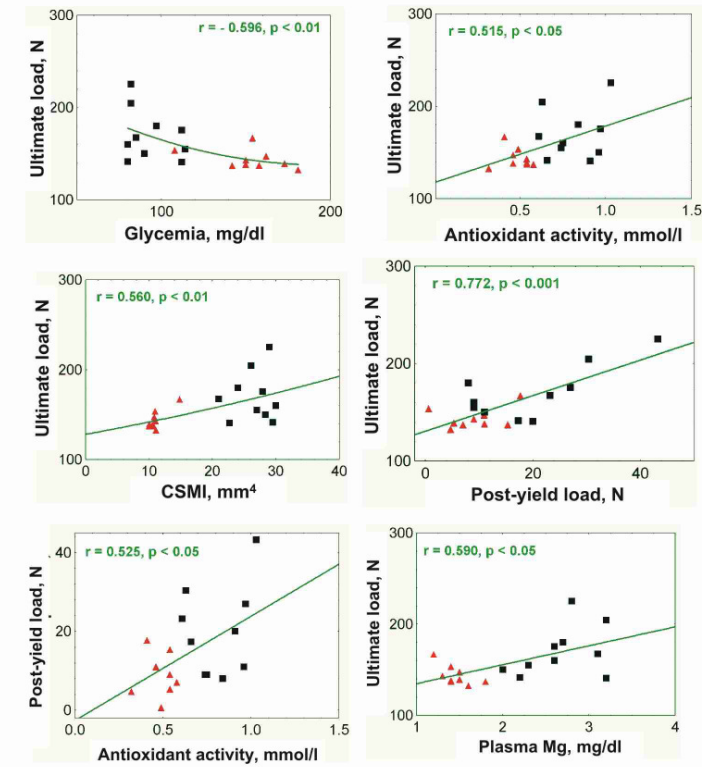


Figure 5