Oral Abstracts

2C (Clinical) - Fracture risk, bone mass, nutrient intake

O15

Histomorphometric analysis of fracture healing cascade in acute osteoporotic vertebral body fractures

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Background: Little is known about the fracture healing process of acute vertebral fractures.

Aim: We present a descriptive histomorphometric analysis of fracture healing cascade in acute osteoporotic vertebral body fractures.

Subjects and Methods: Transpedicular bone biopsy was performed in patients undergoing percutaneous vertebroplasty. Undecalcified biopsy specimens were prepared from cores of cancellous bone taken from vertebral bodies with MRI evidence of bone marrow oedema. These were analysed by light microscopy using

grid analysis and defined using bone histomorphometry criteria. Normative data obtained from 5 age-matched volunteers without evidence of metabolic bone disease was used for comparison.

Results: Adequate biopsy specimens were obtained in 72 patients (15 men and 57 women), mean age 75.6 years. All biopsies confirmed severe osteoporosis with reduced cancellous bone volume (mean of 13.5%; P<0.001 compared to controls). The timing of biopsies varied from 1 to 24 weeks (median of 6 weeks) after the fracture occurrence. While 4 stages of fracture healing were identified, an overlap of the various stages was evident. No evidence of intramembranous ossification was noted. There were 17 (24%) patients with Stage I, 16 (22%) with Stage II, 22 (30%) with Stage III and 17 (24%) with Stage IV fracture callus. The time interval since fracture occurrence correlated significantly with most parameters of fracture callus and was the most important predictor of the stage of the fracture callus (R=0.32; P<0.001).

Conclusion: Histomorphometric changes of orderly microfracture repair and bone remodelling occurs in osteoporotic vertebral bodies after acute fracture.

O16

Thiazide diuretics and fracture risk: a posthoc analysis from the ANBP2 trial

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Aims: Observational evidence suggests that thiazide diuretics protect against hip and possibly other fractures. However, there have been no randomised controlled trials (RCTs) with fracture outcomes.

We aimed to determine whether thiazide diuretics protect against fracture in a post hoc analysis of a RCT of diuretic vs. ACE inhibitor for the treatment of hypertension (ANBP2).

Methods: ANBP2 was undertaken in 6083 hypertensive Australian general practice patients aged 65-84 years, followed for a median of 4.1 years. Patients were randomised to initially receive either a diuretic (hydrochlorothiazide recommended first-line) or ACE inhibitor. Fractures were ascertained by review of GPs' records.

Relative risks (RR) were calculated using log-binomial Generalized Estimating Equations and time to first fracture was analysed using Cox's proportional hazards regression with robust variance estimation.

Results: In the diuretic group, 251 subjects had a fracture (8.3%), compared to 236 (7.8%) in the ACE group. There was no evidence of a protective effect of thiazide diuretics. The age- and sex-adjusted RR for fracture in the diuretic compared to ACE groups was: 1.06 (95% CI 0.90-1.25) for all fractures and 1.16 (95% CI 0.72-1.86), 1.02 (95% CI 0.66-1.57) and 1.15 (95% CI 0.82-1.62) for hip, vertebral and upper limb fractures respectively.

Conclusion: This large trial excludes a 20% reduction in the risk of all fractures with thiazide diuretics. It suggests that there is no protective effect for upper limb, hip or symptomatic vertebral fracture and does not support the use of thiazide diuretics for preventing osteoporotic fracture in older subjects with hypertension.

O17

Anteroposterior and mediolateral bone deposition rates at the tibial shaft differ in pubertal girls

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Introduction: Long bone shaft is not a perfect cylinder with a single diameter and single cortical thickness. Its shape is a result of interaction of genetic and environmental factors. Mechanical loading is believed to be one of these factors. Exploring bone deposition in different directions in a bone transverse plane during growth may provide important information concerning the adaptation of bone to its mechanical usage.

Subjects and Methods: 258 10-13-year-old health girls were included in the study at baseline. Peripheral quantitative computed tomography (Stratec XCT-2000) was used to scan the left tibial shaft at baseline, 12-

month and 24-month follow-up. Image processing and calculation of bone polar distribution were done using Geanie 2.1 (Bonalyse Oy, Jyväskylä, Finland). Bone polar distribution is a measure of bone mass at different direction in the bone transverse plane. The change in the bone polar distribution over two-years was calculated using student's t-test.

Results: More of the bone in a given cross section was deposited at the anterior and posterior sites (18.6± 6.8mg and 10.2±5.9mg, respectively) than at the lateral and medial sites (4.1±3.4mg and 4.3±2.4mg, respectively) during 2-year's pubertal growth ($p<0.001$) (Fig.). The ratio of bone mass in the anteroposterior direction to that in the mediolateral direction (BM_{AP}/BM_{ML}) was higher at 24-month follow-up than at baseline (2.7±0.4 vs 2.3±0.5, $p<0.001$).

Conclusion: The shape of tibial shaft changes during puberty, in part, to accommodate local loading circumstances. The assumption of circular shapes in cross sections of tubular bones is an over simplification.

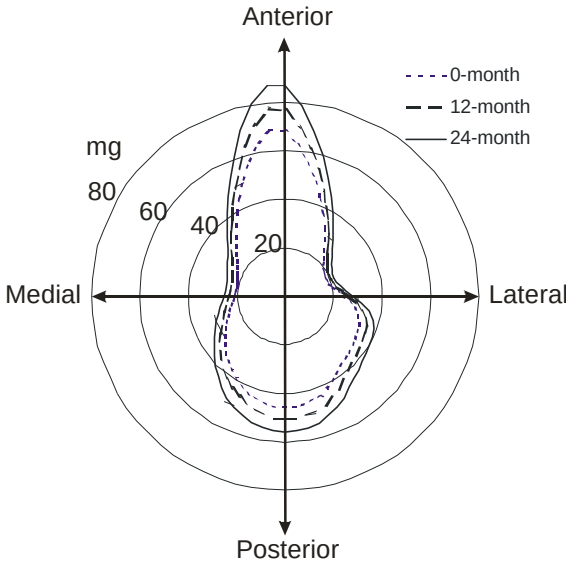

Fig. Bone mass polar distribution of the tibial shaft.

O18

Absolute fracture risk after a low trauma fracture is similar in men and women: a 15 year follow-up study from the Dubbo Osteoporosis Epidemiology Study

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There are few long-term data on risk of subsequent fracture following low-trauma fracture. The aim was to examine subsequent fracture risk in men and women (60+) over 15 years.

All clinical low-trauma fractures from 2245 women and 1760 men were recorded (1989–2005). Subsequent fracture rates were compared with population initial fracture rates according to sex, age (60-69, 70-79 and 80+), type and time since fracture.

There were 880 and 329 incident (women and men) and 253 and 71 subsequent (women and men) fractures. Relative risk of subsequent fracture increased 1.6-2.4 fold for women and 2.8-4.3 fold for men, with resultant absolute risks comparable between the sexes. Thus, 60-69 year old women or men had subsequent fracture risks of 36 and 37/1000 p-yrs; (CI 26-48 and 23-59), respectively, comparable with the initial fracture risk of 27/1000 p-yrs (CI 24-30) for a 70-79 year old woman and 32/1000 p-yrs (CI 27-39) for an 80+ year old man. Absolute fracture risk was elevated for 7-12 years by which time 40-60% had re-fractured. All fracture types, apart from rib (men) and ankle (women), resulted in increased subsequent risk with highest relative risks following hip and vertebral fractures in younger men.

After an initial fracture, absolute risk of subsequent fracture was similar between the sexes and at least as great as the initial fracture risk of a woman 10 years older. This increased risk occurred for virtually all clinical fractures. These data stress the high re-fracture risk after clinical osteoporotic fractures, particularly in men.

O19

Vertebral fractures increase spinal loads *in vivo*

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Examination of physiologic loading of vertebral bodies in vivo may help to explain mechanisms underlying fracture and recurrent fracture. The aim of this study was to model physiologic load parameters in individuals with and without osteoporotic vertebral fractures, to investigate any differences in spinal loading profiles between the groups. Gravitational flexion moments and compression and shear forces due to gravity and trunk muscle force were calculated from T2-L5 in 12 participants with fractures 32 without fractures Gravitational loading estimates were solved using static analysis for each vertebral level, while muscle forces were calculated using a detailed trunk muscle model driven by mathematical optimisation. Non-linear regression was used to describe normalised load profiles over vertebral levels and allow comparisons between groups. Load parameters were also compared between groups at the level of fracture and the vertebral level inferior. The fracture group demonstrated greater flexion moments across vertebral levels (9-82%, $p=0.03$). Significantly greater compression force ($p<0.0001$) and shear force ($p=0.002$) profiles (1-17% and 13-162% respectively) were observed in the fracture group. The fracture group had significantly greater flexion moments ($p=0.001$) and shear forces ($p<0.001$) at the level of fracture and greater flexion moments ($p=0.002$) and compression force ($p=0.007$) at the level below the fracture, compared to the equivalent level in the non-fracture group. The differences observed in multilevel spinal loading between the groups may partly explain the reasons for increased risk of subsequent vertebral fractures. These results may provide valuable insight into interventions to improve posture and/or restore normal vertebral morphology.

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O20

The relationship of nutrient intake to bone density in females: a twin study

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To assess the relationship between dietary intake and bone mineral density (BMD) in females between 41 – 65 years, we assessed 265 twins (including 78 monozygotic and 187 dizygotic individuals) who had completed a 4-day food record, and who underwent dual energy Xray absorptiometry measurement of lumbar spine (LSBMD) and total hip BMD (THBMD) and total body bone mineral content (TBBMC) (n=242). The mean age was 48.2 (6.0)(SD) years, body mass index (BMI) 25.8(4.4) g/m², energy 7.8 (1.6) MJ, % energy protein 17.9 (3.1), calcium 812.7(294.0) mg. Cross-sectionally (adjusting for clustering in twins), and after adjustment for age and BMI, there was a positive association between dietary energy, protein, fat, monounsaturated fat, alcohol(log), zinc, iron, folate, thiamin, riboflavin, niacin, potassium, calcium, magnesium, phosphorus and serves of dairy, and combined servings of meat and dairy with LSBMD. After adjustment for energy, only protein, alcohol (log), niacin and riboflavin remained associated. A similar range of nutrients was positively associated with THBMD. After adjustment for energy, % energy protein, protein (10g/d with 30g TBBMC), niacin, riboflavin, calcium (100mg/d with 20g TBBMC), magnesium (10mg/d with 5.5g TBBMC), phosphorus and dairy (1 serve with 47g TBBMC) remained significantly associated with TBBMC. The within twin pair co-twin analysis confirmed these associations for % energy protein, calcium, phosphorus and serves of dairy for TBBC. Although multiple nutrients were associated with bone, there were some consistent findings. A diet containing a relatively high intake of protein and calcium (probably from dairy products) was associated with increased BMD and TBBMC.

O21

SSRI use and bone mineral density in women with a history of depression: Geelong Osteoporosis Study (GOS)

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Selective serotonin reuptake inhibitors (SSRIs) are a first line treatment for depression. SSRIs have been reported to regulate serotonin (5-HT) receptors and the transporter 5-HTT on osteoclasts and osteoblasts. Previous studies reporting reduced bone mineral density (BMD) among SSRI users may have been confounded by the effects of depression, which has been associated with reduced BMD in some studies.

Among women enrolled in the GOS, a history of depression was ascertained by clinical interview (SCID-I/NP). BMD was measured at the PA-spine, hip, total body and forearm using dual energy absorptiometry (Lunar DPX-L) and medication use was self-reported.

Among 177 women with a lifetime history of depression, current users of bisphosphonates, glucocorticoids, hormone therapy and other anti-depressants were excluded (n=49). Of the remaining 128 (median age 51.5yr, range 30-74), 26 (20.3%) reported current SSRI use. SSRI users were shorter than non-users (1.59±0.06 vs 1.62±0.06 m, p=0.01), however there were no differences in age, weight or smoking history. Using ANCOVA and controlling for age, weight, height and smoking history, BMD among SSRI users was 5.7% lower at the femoral neck (0.977±0.015 vs 0.922±0.025 g/cm^2, p=0.03), 6.1% lower at the trochanter (0.813±0.010 vs 0.763±0.021 g/cm^2, p=0.04) and 4.4% lower at the mid-forearm (0.745±0.009 vs 0.712±0.015 g/cm^2, p=0.03) than non-users. No differences in BMD were detected at other sites.

Among women with a lifetime history of depression, SSRI use is associated with reduced BMD. Although the mechanism remains unclear, these observations are consistent with a role for the serotonergic system in regulating bone metabolism.

O22

Lean body mass: more important than calcium intake on bone mineral accretion in peripubertal boy and girl elite athletes: a 3-year longitudinal study

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Aim: In a 3-year longitudinal study of physically active boys and girls, we evaluated the influence of Total Body Lean Tissue Mass (LTM) and dietary Calcium Intake (CI), on Total Body Bone Mineral Content (TBMC) and Total Body Bone Area (TBA) accretion.

Method: 50 children had TLM, TBMC and TBA measured by dual energy X-ray absorptiometry (DXA) (LUNAR Prodigy) at a mean age of 9.69±0.56 years and 3 years later at 13.5±0.62 years. Boy Controls (BCn= 7), Boy elite (>4 hours training/week at state level) Tennis players (BTn=10) and Boy elite Swimmers (BS n=12). Girl Controls (GCn= 15) and Girl elite Tennis players (GTn= 6). Controls and athlete were matched for age, height (137.29±5.14cm) and weight (32.70±4.08kg), at baseline and all were pre-pubertal. At second follow-up puberty ranged from Tanner stage 3 to 4. CI was assessed on 3 occasions by a 3-day food record and a validated 12-month FFQ (149 items). All subjects were grouped in a single cohort for analysis. Correlations between CI at baseline (0) and final (F)TBMC, TBA, LTM and change with time (Δ) in TBMC, TBA, LTM were tested by bivariate correlation. Following correcting for height, similar correlations were performed with LTM.

Results: Average CI (1095±194 mg/day) did not differ significantly between controls and athletes. A weak correlation (p=0.05) was seen between average CI and TBA0, TBAF, TBMCF, LTM0, LTMF, and ΔLTM in controls and athletes. It correlated with ΔTBMC only in controls. LTM at baseline and final assessment positively correlated (p=0.01) with TBMC and TBA at baseline and final assessment respectively. ΔLTM positively correlated (p=0.01) with ΔTBMC for all groups but only with ΔTBA in swimmers and tennis players.

Conclusion: LTM was a strong determinant of TBMC and TBA before and during the pubertal years. CI had a less significant role in bone development, but appeared to influence LTM. In young adolescents who are not exercising at elite level CI may play a more important role in bone mineral accrual.