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5C (Clinical) - Clinical osteoporosis

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O59

Pamidronate or zoledronate reduce bone loss after allogeneic stem cell transplantation

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Rapid and early bone loss occurs after allogeneic stem cell transplantation (alloSCT), particularly from the proximal femur. We evaluated the effects of high-dose pamidronate therapy on bone mineral density (BMD) after alloSCT

in a randomised, multicentre open-label 12 month prospective study of intravenous pamidronate (90 mg/month) beginning just prior to conditioning versus no pamidronate. All 116 patients also received calcitriol (0.25 µg/day) and calcium (1000 mg/day), which were both continued for a further 12 months. The primary study outcome compared changes in BMD, measured by dual-energy x-ray absorptiometry (DXA), at 12 months post-alloSCT at the femoral neck, lumbar spine and total hip between the treatment arms. We also examined the influence of glucocorticoid and cyclosporine therapy on these changes. Compared with the no

pamidronate group, pamidronate reduced bone loss at the spine, femoral neck and total hip by 5.6%, 7.7% and 4.9% (all p≤0.003), respectively, at 12 months. However, BMD of the femoral neck and total hip was still 2.8% and 3.5% lower than baseline, respectively, (p<0.05) in the pamidronate group. At 24 months, only differences at the total hip remained significant between the two groups in favour of the pamidronate group. Benefits of pamidronate therapy on BMD were restricted to patients receiving an average daily prednisolone dose >10 mg and prolonged cyclosporin therapy within the first six months of alloSCT. In a subsequent uncontrolled, prospective study of 12 consecutive patients receiving zoledronic acid (ZA), within the first year post-alloSCT, BMD was measured at the spine and proximal femur pre-transplant, pre-ZA and post-ZA. The median annualised percentage change in femoral neck (FN) BMD pre-ZA was –13.2% (range –40% - +1.0%). Post-ZA, FN-BMD increased by a median of +1.4% (range –22.2% - +33.6%). Only one patient continued to lose bone from the FN post-ZA infusion. Thus, ZA reduced bone loss in the majority patients after alloSCT. In conclusion, pamidronate markedly reduced bone loss after alloBMT, but did not completely prevent it at the proximal femur and total hip.   Benefits on BMD were greatest in patients on higher doses of immunosuppressive therapy, but most were lost 12 months after stopping pamidronate. Preliminary data suggest ZA may be more effective at preventing bone loss after alloBMT and now require confirmation in a larger prospective, randomised dose-finding study.

O60

Perfusion indices in hip osteoporosis

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Purpose: To prospectively use magnetic resonance (MR) imaging to measure hip perfusion in female subjects of varying bone density.

Materials and methods: Following institutional study approval, dual x-ray absorpiometry and dynamic contrast-enhanced MR imaging of right hip was performed on 81 female subjects (age, 73 years; range, 67-84 years) using a whole-body 1.5T MR scanner. Signal intensity-time curves around the hip were obtained. Perfusion parameters (enhancement percentage and enhancement slope) of the proximal femur (head, neck and shaft), acetabulum and hip muscles were compared for different bone density groups (normal, osteopenia, and osteoporosis). Kruskal-Wallis test was used to compare perfusion indices for the three bone density groups.

Results: Of 81 subjects, 26 had normal bone density, 39 were osteopenic, and 16 were osteoporotic. Enhancement percentage was significantly lower in the femoral neck (p = 0.0193), shaft (p = 0.0016) and acetabulum (p = 0.0002) with reducing bone density, a trend not observed in the femoral head (p = 0.1461) or muscle (p = 0.655). Enhancement slope was also significantly lower in the femoral neck (p = 0.0209), shaft (p = 0.0079) and acetabulum (p = 0.0014) in subjects with reducing bone density, a trend not observed in the femoral head (p = 0.1027) or muscle (p = 0.5832).

Conclusion: Females demonstrate decreased marrow perfusion in the hip with decreasing bone density. Reduction in perfusion appears to occur only within the bone and does not occur in extraosseous tissues with the same arterial supply.

O61

Does calcium-vitamin D$_3$ fortified milk enhance the effects of exercise on aBMD in older men: an 18-month randomised controlled trial

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 We asked whether calcium-vitamin D$_3$ fortified milk enhanced the osteogenic effect of weight-bearing exercise at loaded sites in 180 men aged 61.0 ± 7.4 yrs (mean ± SD). In this 18 month study, men were randomised to either: 1) Ex+Ca-Vit D (n=45), 2) Ex (n=46), 3) Cal-Vit D (n=45) or 4) a control group (n=44). Exercise consisted of high intensity (60 - 85% 1RM) progressive resistance training and moderate impact

exercise 3 days/wk. Men assigned to fortified milk consumed 400 ml/d of low fat milk providing an additional 1000 mg/d calcium and 800 IU/d vitamin D_3. Mean (±SD) baseline dietary Ca and vitamin D intakes were 1002 ± 397 mg/d and 42 ± 80 IU/d. GEE analysis revealed a group-by-time interaction for FN BMD (p<0.001) and a trend for L_1-L_4 BMD (p<0.1). At the FN, exercise resulted in a 1.7% greater gain relative to non-exercise (1.2% vs -0.5% respectively, p<0.001). At the LS, BMD increased relative to baseline in the Ex+Ca-Vit D, Ex and Ca-Vit D groups (0.9 to 1.2%, all p<0.05) compared to controls (-0.08%). No exercise or calcium effects were observed at the total hip or TB; nor were there additive benefits of Ca-Vit D on the skeletal response to exercise. Exercise also had beneficial effects on LM (0.6 kg, p<0.01), FM (-1.1 kg, p<0.001) and muscle strength (41%, p<0.001) compared to no-exercise (p<0.05 to <0.001). In summary, exercise was effective for increasing BMD but additional calcium-vitamin D_3 did not enhance the osteogenic response.

O62

The relationship between age and measures of balance, strength and gait - analysis using non-linear modelling

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Background: Age-related decline in balance, gait and lower-extremity muscle strength measures may lead to increased risk of falls and fractures. Previous research has reported an age-related decline in these measures, but methodological and analytical problems limit interpretation. This study was undertaken to determine the association between these physical measures and age (as this may not always be linear).

Methods: Healthy community-dwelling women (n=212) aged 21-82 years were evaluated for strength [Nicholas Manual Muscle Tester (MMT)], gait [Clinical Stride Analyzer (CSA)] and static and dynamic balance [Chattecx Balance System (CBS) and the Step Test (ST)]. An additive model was developed for each outcome variable to estimate the functional relationship with age, as a continuous variable using the program R.

Results: Performance was maintained until the age of 45-55 years (varying depending on specific tasks), after which a decline in performance was seen with increasing age in all measures of balance, strength and gait. Varying and significantly non-linear relationships with age as a continuous variable were demonstrated for the majority of the strength measures (figure 1), stride velocity on the CSA and tests with side-to-side perturbations on the CBS.

Conclusions: Balance, lower-extremity muscle strength and gait declined with age. Non-parametric smoothing methods suggested the presence of non-linear associations between age and most of these variables in women, which may be explained at least partly by hormonal changes related to menopause. These findings may have implications for the optimal timing of exercise and other interventions to reduce risk of falls and fractures.
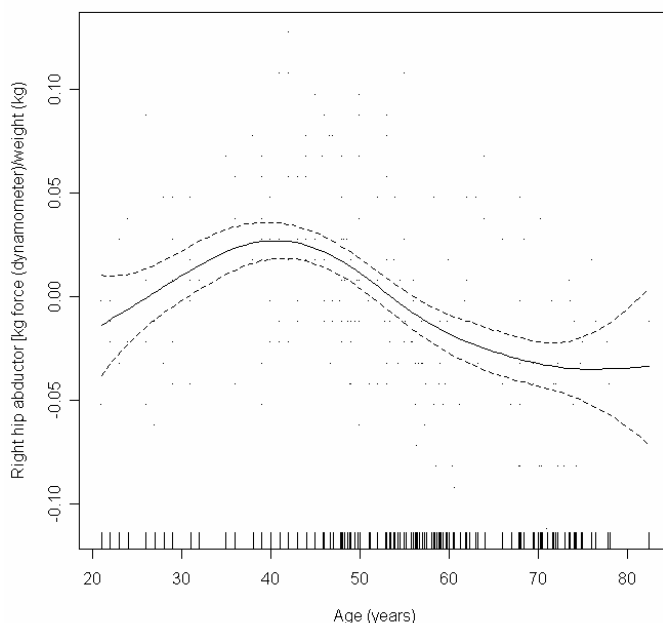

Figure 1: Additive model fit of age on right hip abductor strength adjusted for weight (kg). Smooth term is highly significant (p <0.001) and age explains 24.6% of the deviance.

O63

Beneficial effects of regular Tai Chi exercise on musculoskeletal system

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Objectives: To evaluate the potential benefits of regular Tai Chi Chun (TCC) exercise on bone mineral density (BMD), neuronmuscular function, and reduction of fractures in postmenopausal women in cross-sectional, case control, and prospective studies.

Methods: 1) Cross-sectional study, 99 healthy postmenopausal women with a mean age of 55.9±3.1 years and within 10 years of menopause were recruited; including 48 subjects who had been regularly practicing TCC exercise for more than 3 hours/week and 51 age and gender matched sedentary controls (CON). BMD was measured in the lumbar spine and proximal femur of non-dominant leg using Dual-energy X-ray Absorptiometry (DXA). Neuromuscular function was evaluated, including magnitude of trunk bend-and-reach, quadriceps muscle strength and single stance time of the non-dominant leg. 2) Case control study: postmenopausal women of same age range, including 17 self-selected regular TCC with over 4 years of regular exercise, and 17 age- and gender-matched nonexercising CON. BMD in the lumbar spine and proximal femur was measured at baseline and at follow-up 12 months using DXA, and in the distal tibia using multislice peripheral quantitative computed tomography (pQCT). 3) Prospective study: 132 healthy postmenopausal women within 10 years of menopause onset with a mean age of 54.0±3.5 years were recruited into the study and randomized into TCC (n=67) and group (CON) (n=65) for BMD measurement at the lumbar spine and proximal femur using DXA, and distal tibia using pQCT, respectively. Supervised TCC exercise was performed by TCC group for 45 min/day, 5 day/week for 12 months while control subjects retained a sedentary life style. All BMD measurements were repeated after 12 months. Fracture rate was also documented.

Results: 1) Cross-sectional study: The TCC group showed overall higher BMD at all measurement sites, with significant difference found at spine (7.09%), greater trochanter (7.17%) and Ward's triangle (7.14%) of the proximal femur. Functional tests revealed an average 43.3% significant greater quadriceps strength, 67.8% significant longer single stance time in the TCC group as compared with CON group, and a greater magnitude in trunk bend-and-reach in the TCC group. Bivariate linear correlation analysis showed that quadriceps muscle strength was significantly correlated with single stance time (r=0.40). 2) Case-control study: baseline results showed that the TCC group had significantly higher BMD (10.1%−14.8%) than the CON group in the lumbar spine, proximal femur, and the ultradistal tibia. Although both DXA and pQCT measurements revealed decelerated rates of bone loss in the TCC group, only the more sensitive pQCT showed significantly reduced rate of bone loss in trabecular and cortical BMD of the distal tibia. 3) Prospective study: a significant 2.6- to 3.6-fold retardation of bone loss was found in both trabecular and cortical compartments of the distal tibia in TCC group as compared with the controls measured by pQCT. A total of 4 fracture cases were documented during follow-up, including 3 subjects in the control group and 1 in the TCC group.

Conclusions: Our studies reveal that higher BMD, slower rate of bone loss and better neuromuscular functions, and lower fracture rate are demonstrated in postmenopausal women who participating in regular TCC exercises.

O64

The effects of a novel physical activity regime on parameters of hip fracture risk in postmenopausal caucasian women

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Aims: To test the effects of a novel 11-month exercise intervention on hip fracture risk factors in healthy Caucasian women aged 55 to 75.

Methods: Forty-five volunteers were randomly assigned to one of three groups. All groups attended one line dance class per week. Two groups additionally performed progressively loaded squats five times a week. One group additionally performed foot stomps twice daily. Hip fracture risk (HFR), broadband ultrasound

attenuation (BUA), proximal femoral and lumbar spine bone mineral density (PF & LS BMD), lower limb functional strength (LLFS), single leg stance (SLS), timed up and go (TUG), and forward and lateral step velocity were measured. Anthropometric and behavioural data were collected.

Results: There were no changes in HFR, BUA, PF or LS BMD, however, strong compliance effects were noted for BUA ($r = 0.769$, $\alpha = 0.008$) and PF BMD ($r = 0.56$, $\alpha = 0.05$) in participants who stomped. LLFS increased in all participants, especially in those performing all three activities ($\alpha = 0.0003$).   SLS times increased, and TUG times decreased in all participants with no difference between groups.   Forward step velocity did not change, but lateral step velocity increased at follow up for all subjects ($p = 0.048$, $\alpha = 0.05$), with no differences between groups.

Conclusions: Our novel intervention was appealing to independent living, postmenopausal women. It has the potential to stimulate adaptive changes in the proximal femur that slow the rate of bone loss, and to improve lower limb strength and balance, thus reducing hip fracture risk.

O65

Prevalent fracture in adolescents: association with different measures of bone mass

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Aims: It remains to be determined which measure of bone mass is the best measure of fracture risk in children. Our aim was to determine whether there is an association between different measures of bone mass and prevalent fracture in adolescents and to describe the associations between the various bone mass measures.

Methods: 415 adolescents [150 girls and 265 boys] mean age 16.3 years were examined. Calcaneal bone ultrasound attenuation [BUA], speed of sound [SOS], and heel stiffness were performed by Sahara densitometer. Distal radial ultrasound SOS was performed by Sunlight machine. Dual X-ray Absorptiometry [DXA] measures were performed at hip, spine, radius and total body. Metacarpal index was measured from hand X-ray. A questionnaire provided details of previous fractures.

Results: A total of 160 adolescents (39%) reported a previous fracture. Significantly lower heel BUA, SOS and heel stiffness was observed in participants with a history of upper limb fracture (all P<0.05). DXA had borderline associations with upper limb fracture (spine and radius, p=0.08). Radial ultrasound and metacarpal index did not discriminate participants with a history of fracture from those without. No significant difference was found when lower limb fracture or fracture at other sites were considered. Weak to modest correlation coefficients were observed between bone mass measures after controlling for height, weight, and age.

Conclusions: Calcaneal Quantitative Ultrasound was the best discriminator between adolescents with a history of upper limb fracture and those without, suggesting that QUS may be a better measure of upper limb fracture risk than DXA or metacarpal index. The modest correlation coefficients between the various bone mass measures suggest that they assess different aspects of bone.

O66

Bone markers can differentiate osteogenesis imperfecta from other types of osteoporosis in adults

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In adults with osteoporosis of unusual severity or early presentation, osteogenesis imperfecta (OI) is often a diagnostic possibility, but the radiographic and physical signs are not specific. OI results from mutations in the genes encoding the α1 or α2 chains of type I collagen, and laboratory tests are generally unhelpful, apart from skin biopsy for study of type I collagen, which is invasive and expensive.   Previous studies have suggested that the bone formation marker Procollagen-1N-Propeptide (P1NP) is low in OI, whereas osteocalcin is increased. We measured these markers and the ratio between them in 85 adults: 21 with type I OI, 26 with other types

of osteoporosis (OOP) and 38 controls. There was no difference in age (mean 38 years), or sex distribution between the groups.

	Controls	**Type I OI**	**Other osteoporosis**
Lumbar spine BMD – z score*	0.5 (1.3)	-2.3 (1.1)	-3.1 (0.6)
P1NP (ug/l)	39 (19-83)	24 (3-122)	39 (5-1972)
Osteocalcin (ug/l)	23 (9-40)	35 (8-142)	21 (6-178)
P1NP/osteocalcin ratio	1.7 (1.1-2.9)	0.6 (0.3-1.3)	2.0 (0.7-19)

(median values and range; *mean and SD)

The median value for P1NP was lower in the OI patients than in the other groups ($p<0.004$, Mann Whitney test), but there was considerable overlap. The P1NP/osteocalcin ratio was significantly lower in the OI patients than in both other groups ($p<0.0001$). 81% of OOP patients had ratios greater than the highest value in OI patients, and 71% of OI patients had ratios less than the lowest value in OOP patients. Measuring the ratio of plasma bone formation markers could help diagnose late-presenting OI.