Relationships of Trabecular Bone Structure with Quantitative Ultrasound Parameters: In Vitro Study on Human Proximal Femur Using Transmission and Backscatter Measurements

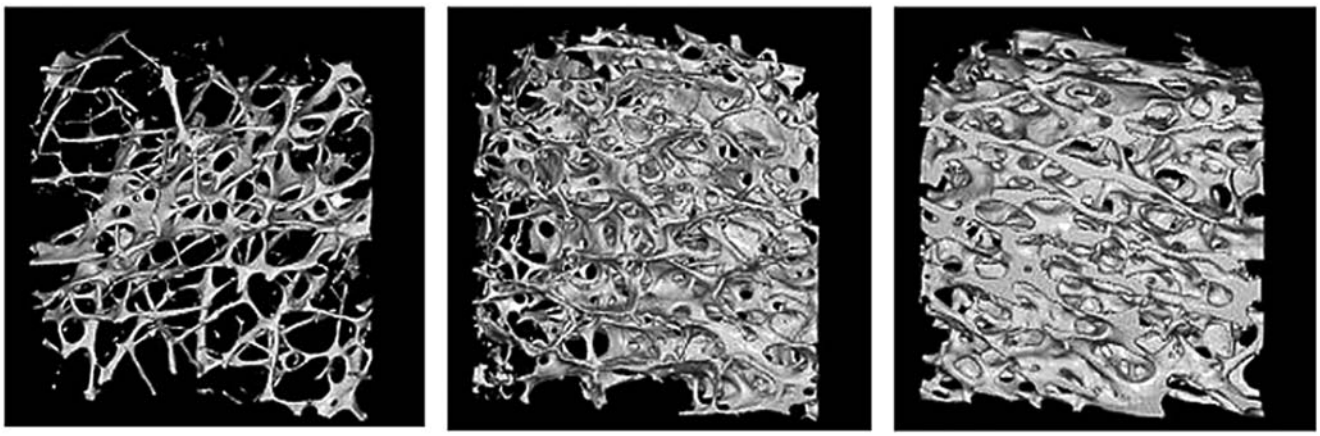
Trabeküler Kemik Yapısı ile Kantitatif Ultrason Parametrelerinin İlişkisi

Padilla F, Jenson F, Bousson V, Peyrin F, Laugier P

Bone 2008;42:1193-202

Summary

In 37 specimens of trabecular bones from upper parts of fresh human femurs., 8 mm diameter cylindrical cores were extracted. All QUS parameters correlated to BMD (R=0.83 for nBUA, R=0.81 for SOS and R=0.69 for BUB) and to microarchitectural parameters (R=-0.79 between nBUA and Tb.Sp, R=-0.81 between SOS and Tb.Sp, R=-0.65 between BUB and BS/BV) and microstructural parameters adds 10%, 19%, and 4% to the respective BMD alone contribution for the three variables BUA, SOS and BUB. Moreover, the RMSE was reduced by up to 50% for SOS, by up to 21% for nBUA and up to 11% when adding structural variables to BMD in explaining QUS results. The variability of SOS was completely explained by a multivariate model including BMD and independent structural parameters (R(2)=0.94). The predictions (in terms of R(2) or RMSE) of microarchitectural parameters was not enhanced when combining 2 or 3 QUS in multiple linear regressions compared to the prediction obtained with one QUS parameter alone. The best model was found for the prediction of Tb.Th from BUA (R(2)=0.58, RMSE=17 mum). Given the high values of RMSE, these linear models appear of limited clinical value, suggesting that appropriate models have to be derived in order to solve the inverse problem. In this regard, a very interesting multivariate model was found for nBUA and BUB with Tb.Th and Tb.N, in agreement with single scattering theories by random medium. However, the source of residual variability of nBUA and BUB (15% and 45%, respectively) remained unexplained.



BVITV: 4% BVITV: 9.20% BVITV: 19.35%

Figure 1. Examples of 3D reconstruction from synchrotron μ-CT experiments. Reproduced from Bone, 42:1193-202, Copyright (2008), with permission from Elsevier.

Effects of Once Versus Twice-Daily Parathyroid Hormone 1-34 Therapy in Children with Hypoparathyroidism

Hipoparatiroidili Çocuklarda Günde Bir veya İki Paratiroid Hormonu 1-34 Tedavisinin Etkileri

Winer KK, Sinaii N, Peterson D, Sainz B, Jr., Cutler GB, Jr.

J Clin Endocrinol Metab 2008; [Epub ahead of print]

Summary

Fourteen children aged 4-17 years with chronic hypoparathyroidism were studied in a randomized crossover trial, lasting 28 weeks using once-daily vs. twice-daily PTH1-34. Twice-daily PTH 1-34 increased serum calcium and magnesium levels more effectively than a once-daily dose. PTH 1-34 normalized mean 24 h urine Ca excretion on both treatments. This was achieved with half the PTH 1-34 dose during the twice-daily regimen compared to the once-daily regimen (twice-daily, 25±15 μg/d vs. once-daily, 58±28 μg/d, P<0.001). A twice-daily regimen produced significantly improved metabolic control compared to once-daily PTH 1-34.

Positive Effects of Exercise on Falls and Fracture Risk in Osteopenic Women

Osteopenik Kadınlarda Egzersizin Düşme ve Kırık Riski Üzerine Etkisi

Hourigan SR, Nitz JC, Brauer SG, O'Neill S, Wong J, Richardson CA

Osteoporos Int 2008;19:1077-86

Summary

98 community-dwelling osteopenic women aged 41-78 years were randomized into either a control (receiving no intervention), or exercise group (two one-hour exercise sessions per week for 20 weeks with a trained physiotherapist). 98 women (mean age 62.01 years, SD 8.9 years) enrolled. The mean number of classes attended for the 42 participants in the exercise group who completed the program was 28.2 of a possible 40 classes (71%). At the completion of the trial the intervention group showed better performances in balance (unilateral and bilateral stance sway measures, lateral reach, timed up and go and step test) ($p < 0.05$) with positive training effects reflecting improvements of between 10% to 71%. Similarly there were gains in strength of the hip muscles (abductors, adductors, and external rotators), quadriceps and trunk extensors with training effects between 9% and 23%. Specific workstation exercises can improve balance and strength in osteopenic women.

Delayed Pubertal Development by Hypothalamic Suppression Causes an Increase in Periosteal Modeling But a Reduction in Bone Strength in Growing Female Rats

Hipotalamik Baskılamaya Bağlı Gecikmiş Pubertal Gelişmenin Dişi Ratlarda Etkisi

Yingling VR, Taylor G

Bone 2008;42:1137-43

Summary

23-day-old female rats were injected with a GnRH-antagonist at 2 dosage levels (n=15/group). The low dose group (1.25 mg/kg/dose) received daily injections for 27 days (sacrifice 49 days). The high dose group received (5.0 mg/kg/dose) only 5 days per week over a 26 day period (sacrifice 48 days). Significant delays in pubertal development. Femoral lengths were shorter in the and serum IGF-1 were higher. Bone strength and stiffness were lower in the GnRH-a groups. Cortical bone area was decreased and total area was not different. There was a decrease in % Ct.Ar/T.Ar. Stress and Young's modulus were also decreased. Endocortical bone formation rates decreased and there was an increase in periosteal labeled surface. A dose response between bone strength and GnRH-antagonist dosage was found.

Determinants of Bone Turnover Markers in Healthy Premenopausal Women

Sağlıklı Premenopozal Kadınlarda Kemik Döngüsü Belirleyicileri

Adami S, Bianchi G, Brandi ML, Giannini S, Ortolani S, Dimunno O, Frediani B, Rossini M

Calcif Tissue Int 2008;82:341-7

Summary

Serum C-telopeptide of type I collagen (CTX), osteocalcin (OC), and N-terminal propeptide of type I procollagen (P1NP), serum calcium, creatinine, phosphate, magnesium, and follicle-stimulating hormone (FSH) were measured in 638 healthy premenopausal women aged 20-50 years. In 83 women on the contraceptive pill (CP), the levels of the three BTMs were 14-26% lower (P<0.005) than in non-CP users. In 18 women considered perimenopausal for serum FSH levels >30 IU/mL despite having regular menses, BTM levels were higher than in age-matched women. This group of subjects and the women on the CP were excluded from further analysis. The three BTMs decreased with advancing age and were negatively and independently correlated with body mass index (P<0.001) and serum phosphate. An increase in BTM concentrations can be observed in perimenopausal women, iBTMs decrease with advancing age, and this appears to be associated with changes in body weight and serum phosphate.

The Role of Nitric Oxide in the Mechanical Repression of RANKL in Bone Stromal Cells

Kemiğin Stromal Hücrelerinde RANKL Üzerinde Nitrik Oksideri Etkisi

Rahnert J, Fan X, Case N, Murphy TC, Grassi F, Sen B, Rubin J

Bone 2008;43:48-54

Summary

Mechanical loading and nitric oxide (NO) have positive influences on bone mass. NO is induced by strain via upregulation of eNOS mRNA and protein. Strain causes decreased RANKL. Primary stromal cells from wild-type (WT) and eNOS(-/-) mice showed strain inhibition of RANKL expression was prevented by NOS inhibitors (L-NAME and L-NMMA) in WT stromal cells. Stromal cells from eNOS(-/-) mice showed mechanical repression of RANKL expression ($p<0.05$). Mechanical strain still increased NO production in the absence of eNOS, and was abolished by SMTC, a specific nNOS inhibitor. nNOS mRNA and protein expression were increased by strain in eNOS(-/-) but not in WT cells, revealing that nNOS was mechanically sensitive. When NO synthesis was blocked with either SMTC or siRNA targeting nNOS in eNOS(-/-) cells however, strain still was able to suppress RANKL expression by 34%. Strain suppression of RANKL can occur through non-NO dependent pathways.

Hip and Other Osteoporotic Fractures Increase the Risk of Subsequent Fractures in Nursing Home Residents

Bakımevinde Yaşayanlarda Osteoporotik Kırıklar İlerki Kırık Riskini Artırır

Lyles KW, Schenck AP, Colon-Emeric CS

Osteoporos Int 2008;19:1225-33

Summary

Medicare enrollees aged 50 and older in a nursing home in North Carolina in 2000 (n=30,655) were identified and hospitalization claims in the preceding 4 years showed hip fracture (n=7257) or other fracture (n=663) cases. We followed participants from nursing home entry until the end of 2002 using Medicare hospital claims to determine which participants were hospitalized with a subsequent fracture (n=3381). Among residents with no recent fracture history, 6.8% had a hospital claim for a subsequent fracture, while 15.1% of those with a prior non-hip fracture and 23.9% of participants with a prior hip fracture sustained subsequent fractures. Persons with prior hip fractures are at three times higher risk (HR=2.99, 95% CI: 2.78, 3.21) and those hospitalized with other non-hip fractures are at 1.8 times higher risk of subsequent fractures (HR=1.84, 95% CI: 1.50, 2.25). Nursing home residents hospitalized with a prior osteoporotic fracture are at increased risk of a fracture.

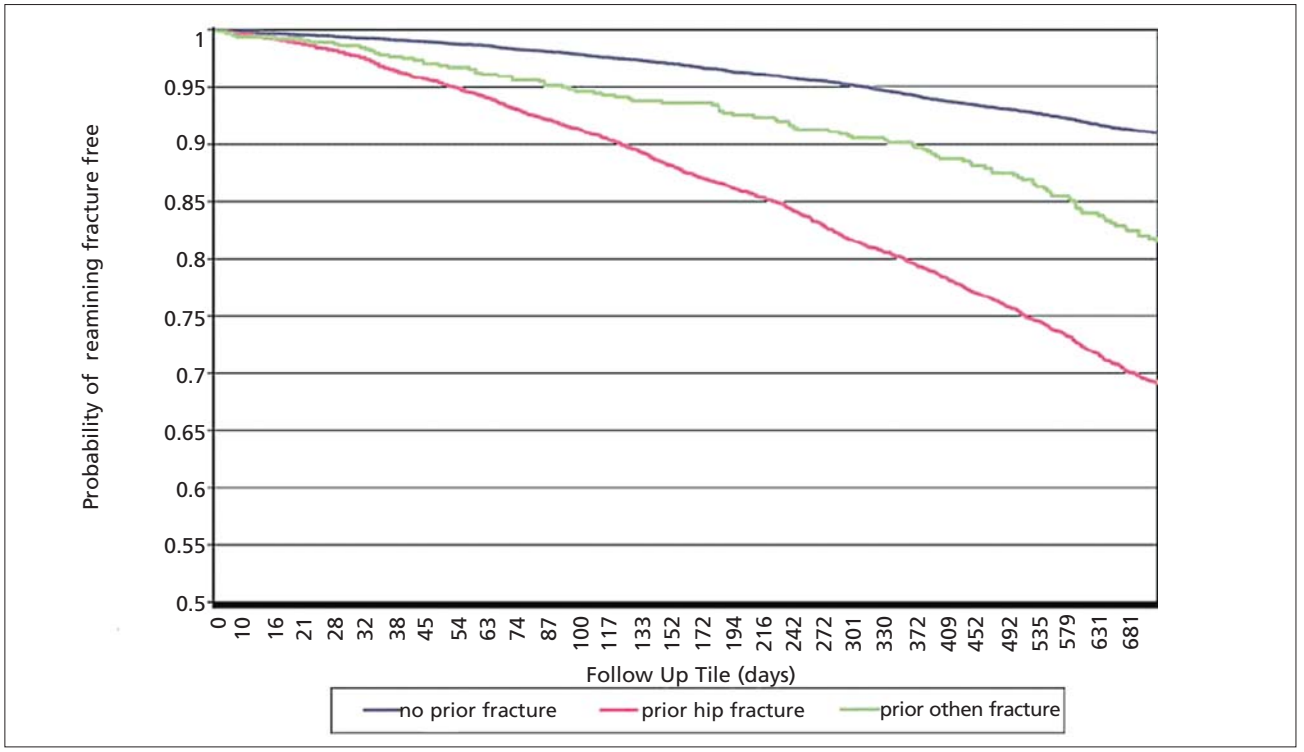


Figure 1. Estimate of time to fracture for North Carolina Medicare enrollees admitted to a nursing home in 2000, by prior fracture status. Reproduced from Osteoporos Int 2008;19:1225-33 with permission from Springer.

Bone Mineral Metabolism and its Relationship to Kidney Disease in a Residential Care Home Population: A Cross-Sectional Study

Kemik Mineral Metobolizması ve Böbrek Hastalığı ile İlişkisi

Carter JL, O'Riordan SE, Eaglestone GL, Delaney MP, Lamb EJ

Nephrol Dial Transplant 2008; [Epub ahead of print]

Summary

In 188 residents not receiving vitamin D/calcium [mean age 85 (range 68- 100) years, 75% female] and in 52 residents receiving vitamin D/calcium, in the former, median PTH increased with declining GFR (P<0.0001), particularly as GFR (mL/min/1.73 m(2)) fell below 45. PTH was suppressed by increasing 25-D, but not 1,25-D (P>0.05) concentration. Nearly all (92%) had 25-D deficiency or insufficiency and this was uninfluenced by kidney function (P>0.05). Concentration of 1,25- D declined with worsening renal function but 1,25-D deficiency was prevalent at all stages of kidney disease, including amongst residents receiving vitamin D/calcium supplementation. Vitamin D deficiency and secondary hyperparathyroidism are common irrespective of renal function. However, as GFR falls below 45, the prevalence of secondary hyperparathyroidism and 1,25-D deficiency increases.

Effect of Denosumab on Bone Density and Turnover in Postmenopausal Women with Low Bone Mass After Long-Term Continued, Discontinued, and Restarting of Therapy: A Randomized Blinded Phase 2 Clinical Trial

Postmenopozal Kadınlarda Denosumab'ın Kemik Yoğunluğu ve Döngüsü Üzerine Etkisi

Miller PD, Bolognese MA, Lewiecki EM, McClung MR, Ding B, Austin M, Liu Y, San Martin J, For The Amg 162 Bone Loss Study G

Bone 2008;43:222-9

Summary

In 188 residents not receiving vitamin D/calcium [Denosumab is a fully human monoclonal antibody inhibits RANKL, a mediator of osteoclast formation, function, and survival, decreases bone turnover and increases BMD. Postmenopausal women with a spine T-score of -1.8 to -4.0 or proximal femur T-score of -1.8 to -3.5 were randomized to denosumab every 3 months (Q3M; 6, 14, or 30 mg) or every 6 months (Q6M; 14, 60, 100, or 210 mg); placebo; or open-label oral alendronate weekly. After 24 months, patients receiving denosumab either continued at 60 mg Q6M for an additional 24 months, discontinued therapy, or discontinued for 12 months then re-initiated denosumab (60 mg Q6M) for 12 months. The placebo cohort was maintained. Alendronate-treated patients discontinued alendronate and were followed. Overall, 262/412 (64%) patients completed 48 months. Continuous treatment increased BMD at the lumbar spine (9.4% to 11.8%) and total hip (4.0% to 6.1%). BTM were consistently suppressed over 48 months. Discontinuation was associated with a BMD decrease of 6.6% at the spine and 5.3% at the total hip within the first 12 months of discontinuation. Retreatment increased spine BMD by 9.0% from original baseline. BTMs increased on discontinuation and decreased with retreatment. The effects on bone turnover were fully reversible with discontinuation and restored with subsequent retreatment.

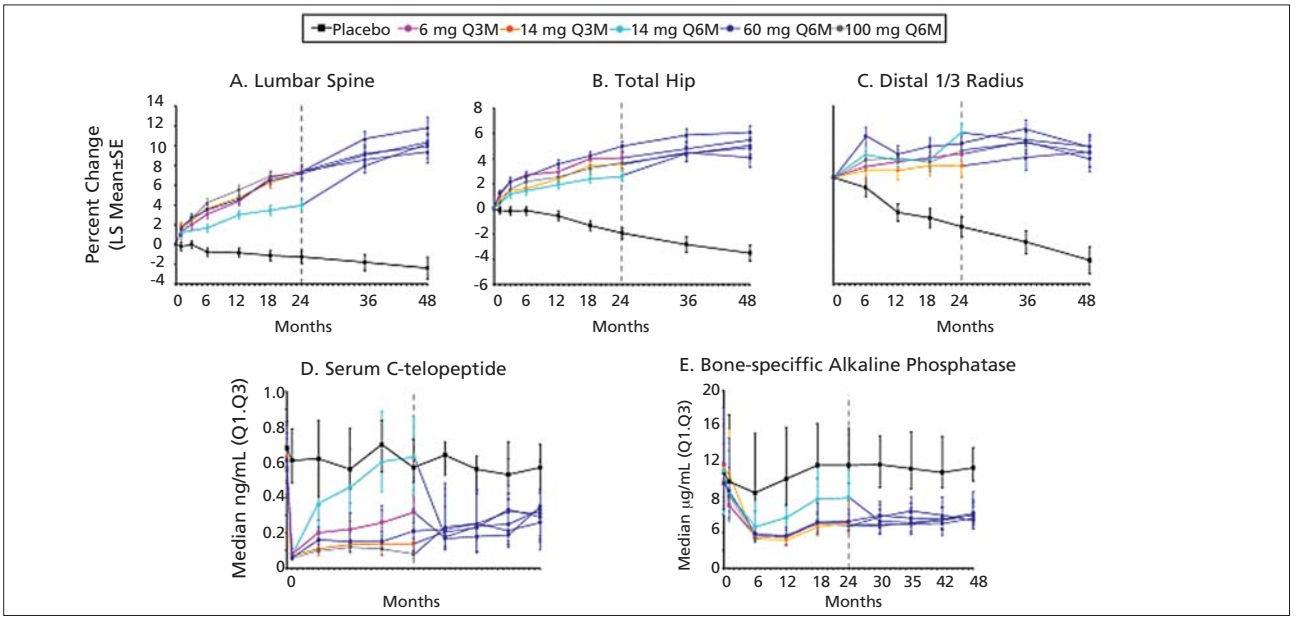


Figure 1. Percentage change in bone mineral density (BMD) and actual values of biochemical markers of bone turnover (BTM) in patients who continued denosumab treatment for 48 months: (A) lumbar spine; (B) total hip; (C) distal 1/3 radius; (D) serum C-telopeptide; (E) bone-specific alkaline phosphatase. BMD values are shown as percentage change from baseline (least square mean±standard error), while BTM levels are shown as absolute values (median with interquartile range) at the end of each dosing cycle. The dashed line at month 24 indicates the time at which patients were reallocated to the 60 mg Q6M dose. Reproduced from Bone, 43:222-229, Copyright (2008), with permission from Elsevier.

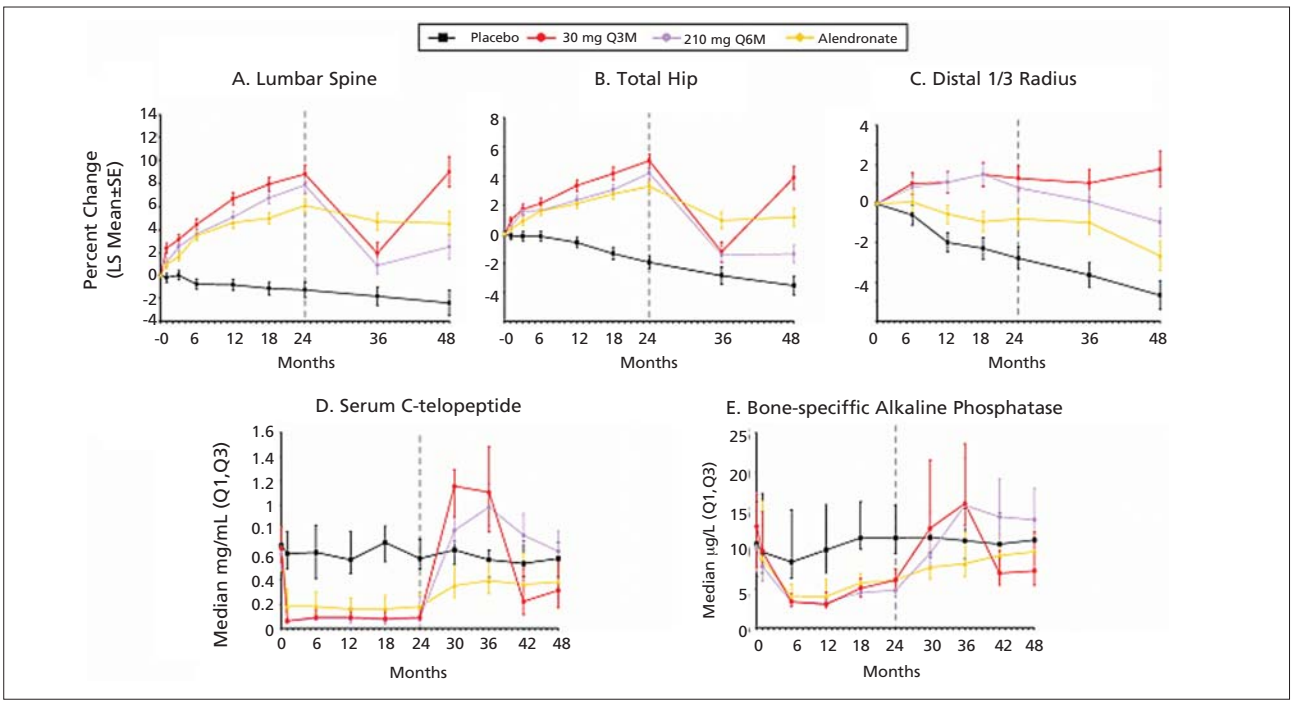


Figure 2. Percentage change in bone mineral density (BMD) and actual values of biochemical markers of bone turnover (BTM) in patients who discontinued denosumab treatment for the last 24 months (210 mg Q6M), were re-treated with denosumab 60 mg Q6M at month 36 (30 mg Q3M), or discontinued alendronate treatment: (A) lumbar spine; (B) total hip; (C) distal 1/3 radius; (D) serum C-telopeptide; (E) bone-specific alkaline phosphatase. BMD values are shown as percentage change from baseline (least square mean±standard error), while BTM levels are shown as absolute values (median with interquartile range) at the end of each dosing cycle. The dashed line at month 24 indicates the time at which dosing was reallocated. Reproduced from Bone, 43:222-229, Copyright (2008), with permission from Elsevier.

Randomized Controlled Trial of the Effects of Calcium with or Without Vitamin D on Bone Structure and Bone-Related Chemistry in Elderly Women with Vitamin D Insufficiency

D Vitamini Yetersizliği Olan Yaşlı Kadınlarda Kalsiyum ve D Vitaminin Etkisi (RKÇ)

Zhu K, Bruce D, Austin N, Devine A, Ebeling PR, Prince RL

J Bone Miner Res 2008;23:1343-8

Summary

302 elderly women (age, 77.2±4.6 yr) with serum 25(OH)D <60 nM participated in a 1-yr randomized, double-blind, placebo-controlled trial. All subjects received 1000 mg calcium citrate per day with either 1000 IU ergocalciferol (vitamin D(2)) or identical placebo (control). At baseline, calcium intake was 1100 mg/d, and 25(OH)D was 44.3±12.9 nM; this increased in the vitamin D group by 34% but not the control group after 1 year (59.8±13.8 versus 45.0±13.3 nM, p<0.001). Total hip and total body BMD increased, and procollagen type I intact N-terminal propeptide (PINP) decreased with no difference between the treatment groups (hip BMD change: vitamin D, +0.5%; control, +0.2%; total body BMD change: vitamin D,

+0.4%; control, +0.4%; PINP change: vitamin D, -3.9%; placebo, -2.8%). Although the fasting plasma and urine calcium increased in both groups equally, there was no detectable change in serum PTH. The increase in 25(OH)D had no extra effect on active fractional intestinal calcium absorption, which fell equally in both groups (vitamin D, -17.4%; control, -14.8%). In patients with a baseline calcium intake of 1100 mg/d and vitamin D insufficiency, vitamin D(2) 1000 IU for one year has no extra beneficial effect on bone structure, bone formation markers, or intestinal calcium absorption over an additional 1000 mg of calcium.

The Remodeling Transient and the Calcium Economy

Yeniden Yapılanma Döngüsü ve Kalsiyum

Aloia JF, Arunabh-Talwar S, Pollack S, Yeh JK

Osteoporos Int 2008;19:1001-9

Summary

Calcium and vitamin D in 208 postmenopausal African-American women where the remodeling transient was considered a priori in the study design. Both groups (calcium alone vs. Calcium +20 μg (800 IU) vitamin D(3)) were ensured a calcium intake in excess of 1200 mg/day. There were no differences between the two groups in changes in BMD over time. These BMD changes were therefore interpreted to reflect increased calcium intake in both groups but not any influence of vitamin D. A transient increase in BMD was observed during the first year of study, followed by a decline. The remodeling period was 9 months, which is similar to histomorphometric estimates. It is problematic to draw conclusions concerning interventions that influence the calcium economy without considering the remodeling transient in study design. Studies of agents that effect bone remodeling must be carried out for at least two remodeling cycles and appropriate techniques must be used in data analysis.

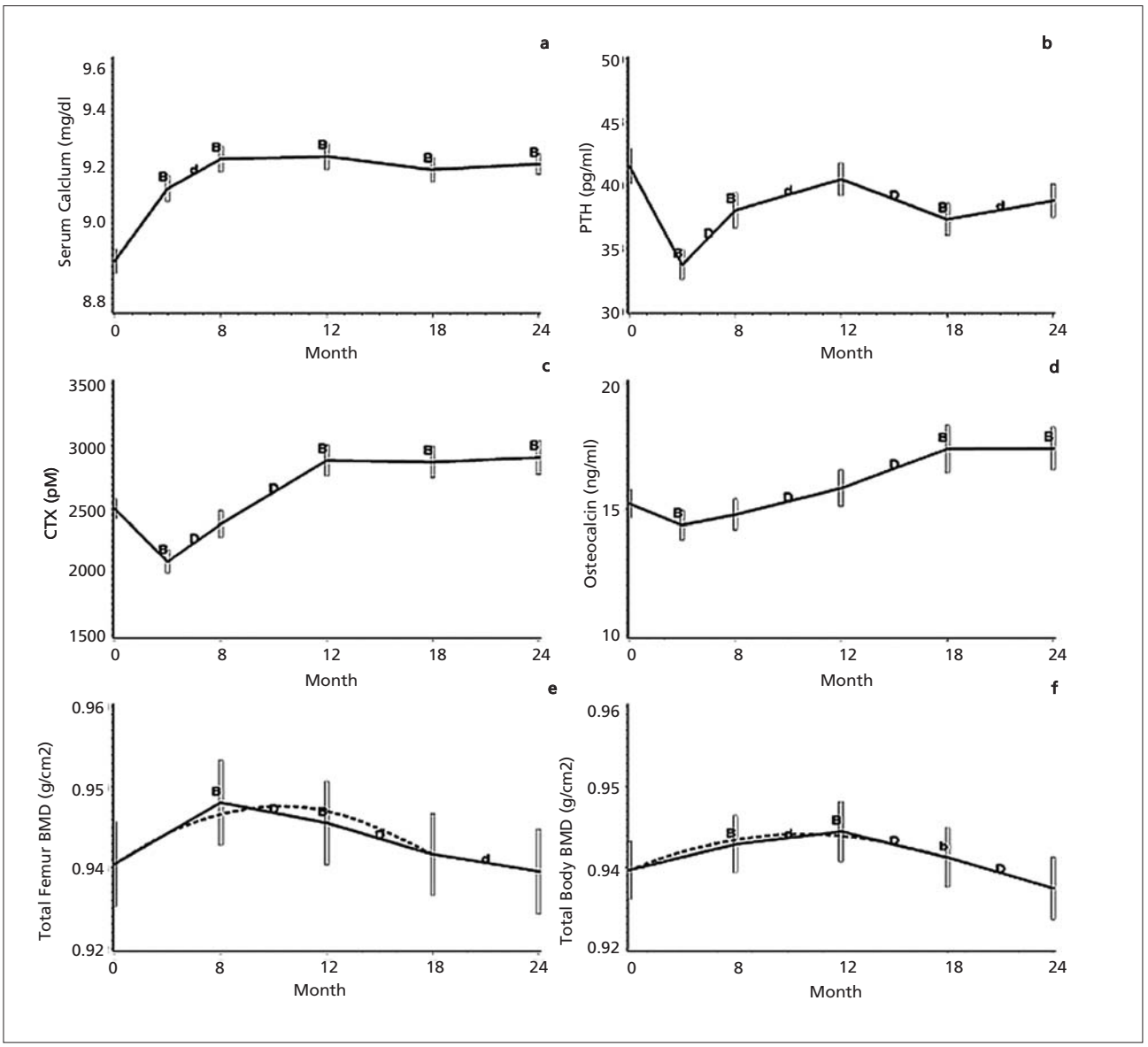


Figure 1. Concomitant changes with calcium supplementation: Absolute values (±2 SEM). Panel (1a): Serum calcium, Panel (1b): PTH, Panel (1c): CTX, Panel (1d): Osteocalcin, Panel (1e): Total femur BMD, Panel (1f): total body BMD, B: significantly different from baseline, p<0.002, b: significantly different from baseline, p<0.05, D: significantly different from preceding period, p<0.002, d: significantly different from preceding period, p<0.05, The dashed line in Panels 1e and 1f represent the quadratic model fitted to the data over 18 months. Reproduced from Osteoporos Int 2008;19:1001-9 with permission from Springer.

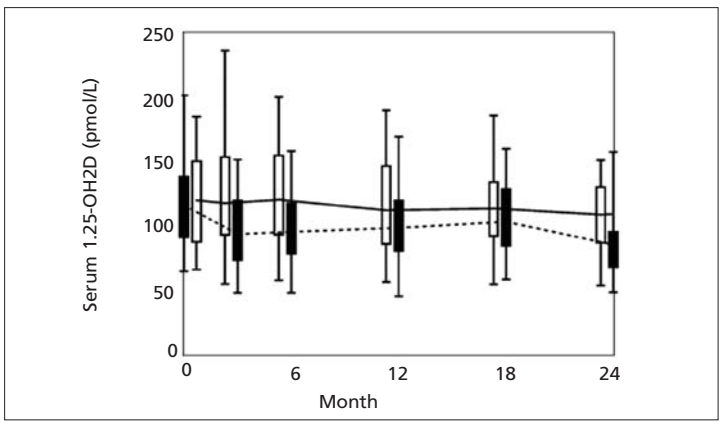


Figure 2. Initial and sustained changes in 1,25OHD2D in the calcium only group (dashed lines) are not experienced by the vitamin D + calcium group (solid line). p<0.01 group comparisons at each line point; p<0.01 for all comparisons with baseline for the calcium group but not for the vitamin D+calcium group. Reproduced from Osteoporos Int 2008;19:1001-9 with permission from Springer.

Effect of Soft Shell Hip Protectors on Pressure Distribution to the Hip During Sideways Falls

Yumuşak Kabuklu Kalça Koruyucuları ve Yana Doğru Düşmeler

Laing AC, Robinovitch SN

Osteoporos Int 2008;19:1067-75

Summary

15 women participated in "pelvis release experiments," which safely simulate the impact stage of a sideways fall. During the trials, we measured total impact force and mean pressure over the greater trochanter with the participant unpadded, and while wearing two commercially available soft shell protectors. Mean pressure over the greater trochanter was reduced by 76% by a 14-mm thick horseshoe-shaped protector and by 73% by a 16-mm thick continuous protector. Total force was reduced by 9% by the horseshoe and by 19% by the continuous protector.

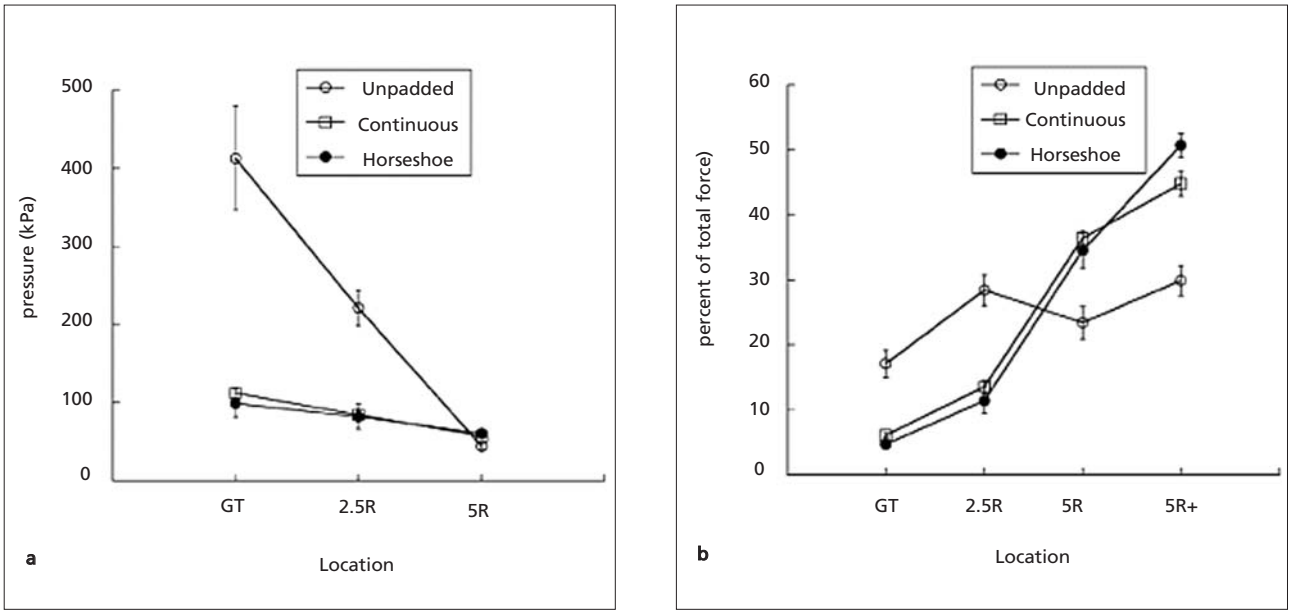


Figure 1. Effect of hip protectors on a the pressure and b the percentage of total force applied to various hip locations. Both hip protectors caused a dramatic reduction in pressure over the GT, and redistribution of force to a region at least 2.5 cm outside the GT. Error bars show standard errors. Reproduced from Osteoporos Int 2008;19:1067-75 with permission from Springer

Impact Exercise Increases BMC During Growth: An 8-Year Longitudinal Study

Büyüme Sırasında İmpaktlı Egzersiz Kemik Mineral İçeriğini Arttırır

Gunter K, Baxter-Jones AD, Mirwald RL, Almstedt H, Fuchs RK, Durski S, Snow C

J Bone Miner Res 2008;23:986-93

Summary

BMC of the hip over 8 yr in prepubertal children who participated in a 7-mo jumping intervention compared with controls who participated in a stretching program (N=57; jumpers=33, controls=24; 47% of the original participants). After 7 mo, those children that completed high-impact jumping exercises had 3.6% more BMC at the hip than control subjects ($p<0.05$) and 1.4% more BMC at the hip after nearly 8 yr ($p<0.05$).

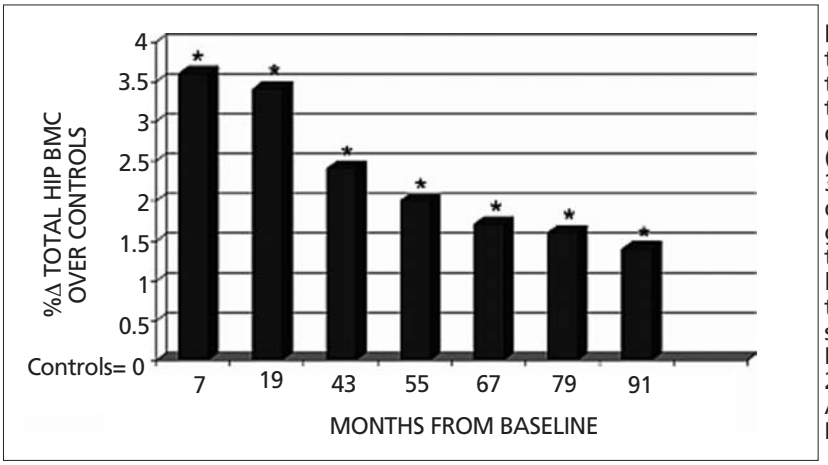


Figure 1. Jumping intervention effect on total hip BMC after 8 yr. Percent change in total hip BMC in jumpers above that of controls after 7 mo of exercise training, 1 yr of detraining (19 mo), and 4-8 yr of detraining (43-91 mo). The intervention participants had 3.6% greater bone mass than controls immediately after the intervention and 1.4% greater bone mass at the total hip than controls after 8 yr. *Results are adjusted for baseline age, ΔHt, ΔWt, maturity, and sports participation and are significant at each of the seven measurement intervals ($p<0.05$). Reproduced from J Bone Miner Res 2008;23:986-93 with permission of the American Society of Bone and Mineral Research.

Bone Metabolism in Adolescent Boys with Anorexia Nervosa

Anoreksiya Nervozalı Adolesan Erkeklerde Kemik Metabolizması

Misra M, Katzman DK, Cord J, Manning SJ, Mendes N, Herzog DB, Miller KK, Klibanski A

J Clin Endocrinol Metab 2008; [Epub ahead of print]

Summary

In 17 anorexia nervosa (AN) boys and 17 controls 12-19 years, boys with AN had lower BMD and corresponding Z-scores at the spine, hip, femoral neck, trochanter, intertrochanteric region, and whole body compared with controls. Height adjusted measures (lumbar BMAD and whole body BMC/height) were also lower. Bone formation and resorption markers were reduced. Testosterone and lean mass predicted BMD. IGF-1 was a predictor of turnover markers. AN boys have low BMD at multiple sites associated with decreased bone turnover markers at a time when bone mass accrual is critical for attainment of peak bone mass.

Mechanical Loading Enhances the Anabolic Effects of Intermittent Parathyroid Hormone (1-34) on Trabecular and Cortical Bone in Mice

Mekanik Yüklenme Aralıklı Paratiroid Hormonun Anabolik Etkisini Artırır

Sugiyama T, Saxon LK, Zaman G, Moustafa A, Sunters A, Price JS, Lanyon LE

Bone 2008;43:238-48

Summary

Female C57BL/6 mice from 13 to 19 weeks of age were given daily PTH (1-34) (20, 40 or 80 μg/kg/day). For three alternate days per week during the last two weeks of this treatment, the tibiae and ulnae on one side were subjected to a single period of dynamic axial loading (40 cycles at 10 Hz, 10-second, between each cycle). Two levels of peak load were used; one sufficient to engender an osteogenic response, and the other insufficient to do so. In the tibia, loading at a level sufficient by itself to stimulate osteogenesis produced an osteogenic response in the low-dose iPTH (1-34)-treated trabecular bone and in the proximal and middle cortical bone treated with all doses of iPTH (1-34). In the ulna, loading at a level that did not stimulate osteogenesis was osteogenic at the distal site with 80 μg/kg/day iPTH. At both levels of loading, there were synergistic effects in cortical bone volume of the proximal tibia and distal ulna between loading and high-dose iPTH from increases in endosteal and periosteal bone formation. No woven bone was induced by iPTH (1-34), whereas the combination of iPTH (1-34) and the "sufficient" level of loading stimulated woven bone formation on endosteal and periosteal surfaces of the proximal cortex in the tibiae.

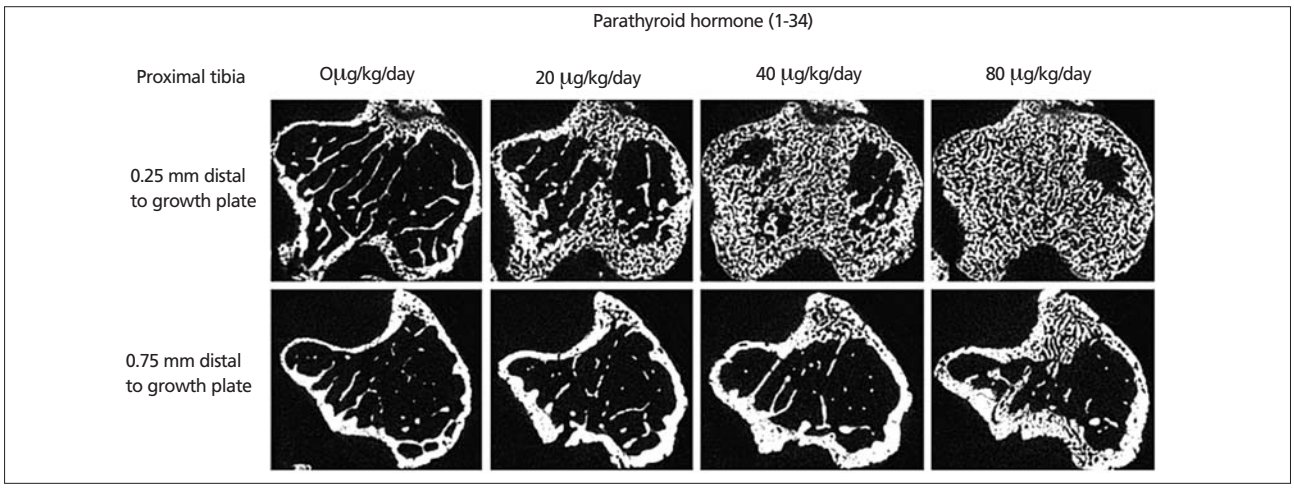


Figure 1. Representative transverse μCT images of the trabecular bone in 17 week old female C57BL/6 mice treated with 4-weeks of intermittent parathyroid hormone 1-34). Reproduced from Bone, 43:238-48, Copyright 2008), with permission from Elsevier.

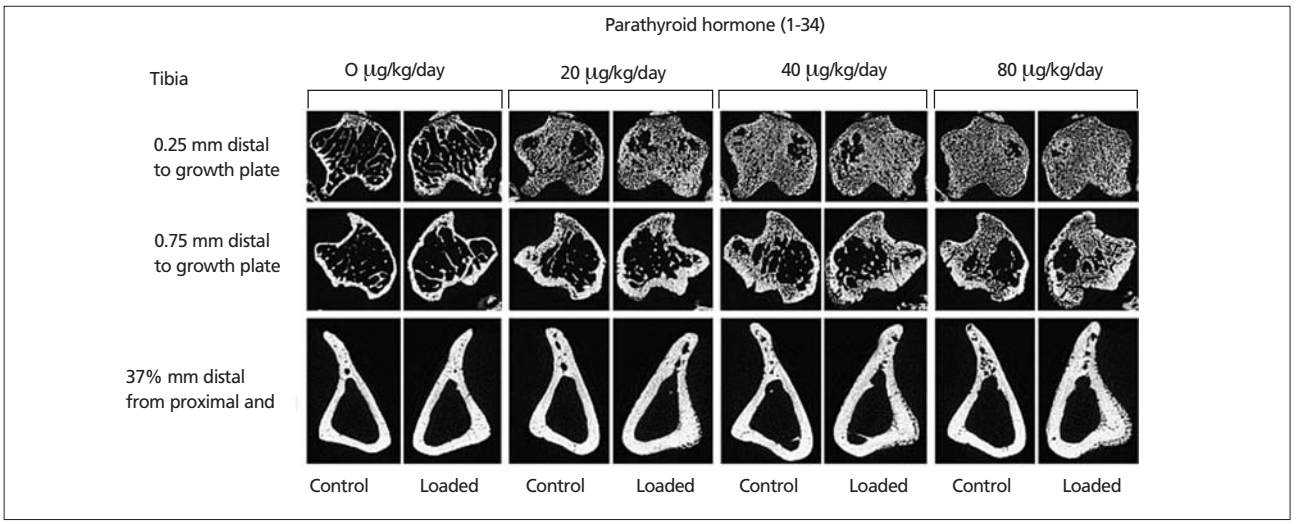


Figure 2. Representative transverse μCT images of the trabecular and cortical bone in 19 week old female C57BL/6 mice treated with 6-weeks of intermittent parathyroid hormone (1-34) and 2-weeks of mechanical loading. Level of peak load: sufficient to engender an osteogenic response. Reproduced from Bone, 43:238-48, Copyright (2008), with permission from Elsevier.