Sex-Specific Developmental Changes

Büyüme Sırasında Cinsiyete Özgü Farklılıklar

Hogler W, Blimkie CJ, Cowell CT, Inglis D, Rauch F, Kemp AF, Wiebe P, Duncan CS, Farpour-Lambert N, Woodhead HJ

Bone 2008;42:982-9

Summary

In 145 healthy subjects (6-25 years, 94 females). MRI and DXA were used to determine femur length, bone mineral content, cortical bone mineral density, bone diameter; cortical thickness; total, cortical and medullary areas; cross-sectional and polar moments of area; bone strength index and muscle area at the proximal one-third site of the femur. Results were dimensionally scaled by raising two-, three- and four-dimensional variables to the power of 1/2, 1/3 and 1/4, respectively. In prepubertal children, unscaled results expressed as percentages of adult values were lowest for variables with the highest dimensions (e.g., moments of area < bone mineral content < cross-sectional areas < femur length). However, when dimensionally scaled, results in children represented similar percentages of the respective average adult values. Before puberty, there was no sex difference in adjusted bone or muscle variables. After puberty, males had greater total and cortical bone area, bone diameter, moments of area, bone strength index and muscle area than women, both in absolute terms as well as adjusted for femur length and weight. The largest sex difference was found for muscle area. When compared relative to muscle size, young adult women attained greater total and cortical bone area than men. Postpubertal females have narrower femora, less bone strength and muscle size than males. However, when muscle size is taken into account, females have a larger femoral bone cross-section and more cortical bone.

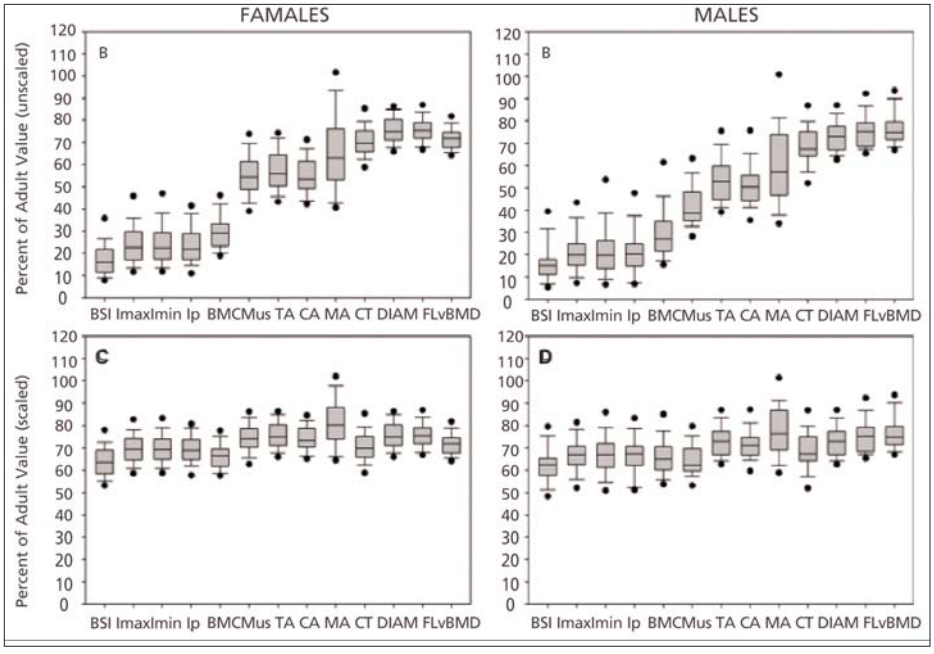

Figure 1. Results in prepubertal children expressed as percentages of the average result in young adults of the same sex. Panels A and B represent unscaled results, panels C and D show dimensionally scaled results. Shown are boxplots which indicate the median, interquartile range and 10th and 90th centiles. Dots represent the 5th and 95th centiles. Abbreviations of variables (with decreasing geometrical dimensions from left to right): BSI, Bone strength index; Imax, maximum moment of area; Imin, minimum moment of area; Ip, polar moment of area; BMC, bone mineral content; Mus, total muscle area; TA, total bone area; CA, cortical bone area; MA, marrow area; CT, cortical thickness; DIAM, external bone diameter; FL, femur length; and vBMD, cortical bone mineral density. Reproduced from Bone, 42:982-9, Copyright (2008), with permission from Elsevier.

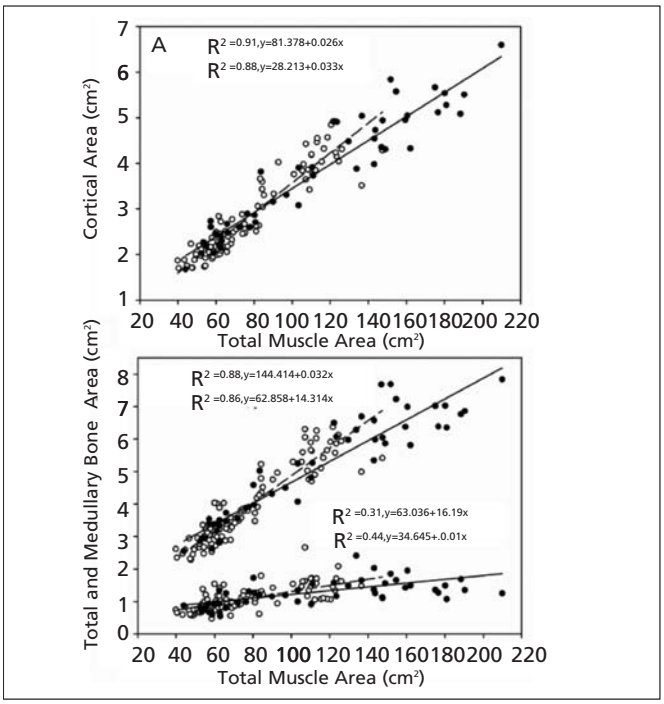

Figure 2. Cortical area (A), as well as total and medullary area (B) in relation to muscle area in females (open circles, dotted regression lines) and males (filled circles, straight regression lines). Intercepts and slopes of the regression lines for total and cortical area were greater in females than males relative to muscle area ($p<0.05$). 95% CI of Intercepts (IC) and slopes: Cortical area vs. muscle area: Females IC 7.971-48.454, slope 0.030-0.035; males IC 51.505-111.251, slope 0.024-0.029 ($p<0.001$). Total area vs. muscle area: Females IC 34.429-91.287, slope 0.039-0.046; males IC 102.08-186.748, slope 0.029-0.036 ($p<0.001$). Marrow area vs. muscle area: Females IC 16.283-53.008, slope 0.007-0.012; males IC 32.536-93.535, slope 0.003-0.008 (p=n.s.). Reproduced from Bone, 42:982-9, Copyright (2008), with permission from Elsevier.

Fracture Risk With Different Oral Corticosteroids

Değişik Oral Kortikosteroidlerle İlişkili Kırık Riski

Vestergaard P, Rejnmark L, Mosekilde L

Calcif Tissue Int 2008;82:249-57

Summary

Cases were all subjects with any fracture (n=124,655). For each case, three controls (n=373,962) matched on age and gender were randomly drawn from the population. Oral prednisolone/prednisone was associated with a dose-dependent increase in fracture risk starting from 6.7 mg/day. Oral budesonide was not associated with an increase in fracture risk, but the doses in were low (<3 mg/day). Oral hydrocortisone was not associated with risk of fractures. Oral methylprednisolone was only used intermittently and was not associated with an increase in overall fracture risk at the low doses used. After termination of oral prednisolone/prednisone, it took more than 1 year for fracture risk to return to background.

Glucocorticoid Excess Affects Cortical Bone Geometry in Premenopausal, But Not Postmenopausal, Women

Glukokortikoid Fazlalığı Sadece Premenopozal Kadınlarda Kortikal Kemik Geometrisini Etkiler

Kaji H, Yamauchi M, Chihara K, Sugimoto T

Calcif Tissue Int 2008;82:182-90

Summary

Ninety-six women receiving oral GC and 10 women with Cushing syndrome (CS) were compared to controls using peripheral quantitative computed tomography. Total area, periosteal circumference, and polar strength strain index (SSIp) were lower in patients compared with control subjects in premenopausal women. Moreover, cortical area and thickness as well as periosteal circumference and SSIp were lower in patients with CS compared to controls in premenopausal women. Total area, cortical area, cortical thickness, periosteal circumference, as well as SSIp were lower in GC-treated patients with vertebral fractures compared to those without vertebral fractures in premenopausal women. In conclusion, endogenous or exogenous GC excess affects bone geometry of forearms of premenopausal, but not postmenopausal

Impact of Glucose-Dependent Insulinotropic Peptide on Age-Induced Bone Loss

Glukoza Bağlı İnsulinotropik Peptidin Yaşa Bağlı Kemik Kaybına Etkisi

Ding KH, Shi XM, Zhong Q, Kang B, Xie D, Bollag WB, Bollag RJ, Hill W, Washington W, Mi QS, Insogna K, Chutkan N, Hamrick M, Isales CM

J Bone Miner Res 2008;23:536-43

Summary

Glucose-dependent insulinotropic peptide (GIP) is an enteric hormone whose receptors are present in osteoblasts, and GIP is known to stimulate osteoblastic activity in vitro. In vivo, GIP-overexpressing C57BL/6 transgenic (GIP Tg (+)) mice have increased bone mass compared with controls. Bone histomorphometric data suggest that GIP increases osteoblast number, possibly by preventing osteoblastic apoptosis. Changes in BMD, biomechanics, biomarkers of bone turnover, and bone histology were assessed in C57BL/6 GIP Tg(+) versus Tg(-) (littermate) mice between the ages of 1 and 24 mo of age. In addition, age-related changes in GIP receptor (GIPR) expression and GIP effects on differentiation of BMSCs were also assessed as potential causal factors in aging-induced bone loss. Bone mass and strength in GIP Tg(+) mice did not drop in a similar age-dependent fashion as in controls. GIP Tg (+) mice had increased osteoblastic activity compared with wild-type control mice. BMSCs express GIPR, that the expression decreases in an age-dependent manner, and that stimulation of BMSCs with GIP led to increased osteoblastic differentiation. Elevated GIP levels prevent age-related loss of bone mass and bone strength and suggest that age-related decreases in GIP receptor expression in BMSCs may play a role in this bone loss. Elevations in GIP may be an effective countermeasure to age-induced bone loss.

FRAX™ and the Assessment of Fracture Probability in Men and Women From the UK

FRAX™ ve İngiliz Kadın ve Erkeklerde Kırık Olasılığının Değerlendirilmesi

Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E

Osteoporos Int 2008;19:385-97

Summary

To apply an assessment tool for fracture prediction with clinical risk factors (CRFs) (BMI, a prior fracture, a parental history of hip fracture, use of oral glucocorticoids, rheumatoid arthritis and other causes of osteoporosis, current smoking, and alcohol intake ≥3 units daily) with and without BMD. Four models were constructed comprising the 10-year probability of hip fracture, with and without femoral neck BMD, and the 10-year probability of a major osteoporotic fracture, with and without BMD. In the absence of BMD, hip fracture probability in women with a fixed BMI (25 kg/m²) ranged from 0.2% at the age of 50 years for women without CRFs to 22% at the age of 80 years with a parental history of hip fracture (approximately 100-fold range). In men, the probabilities were lower, as was the range (0.1-11% in the examples above). For a major osteoporotic fracture the probabilities ranged from 3.5-31% in women, and from 2.8-15% in men in the example above.

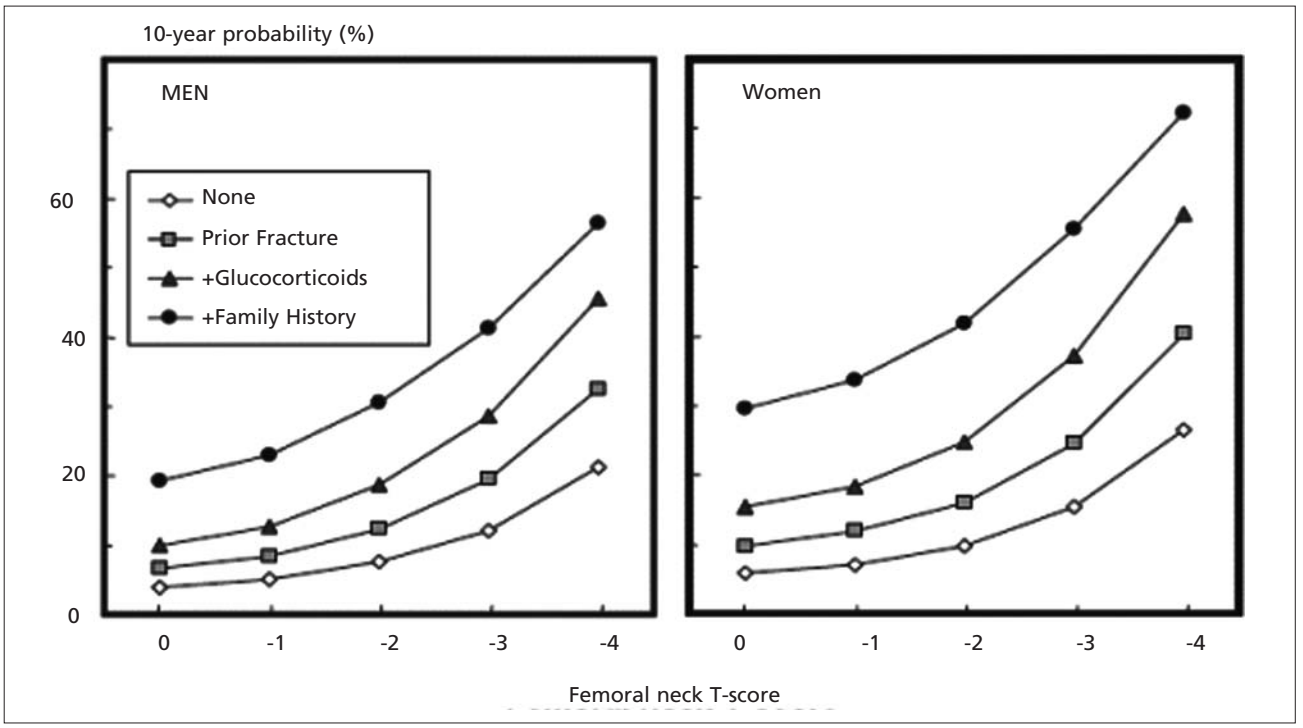

Figure 1. 10-year probability of a major osteoporotic fracture in men and women aged 65 years according to T-score and clinical risk factors. Body mass index is set at 25 kg/m². Reproduced from Osteoporos Int 2008;19:385-97 with permission from Springer.

Development and Application of a Japanese Model of the WHO Fracture Risk Assessment Tool (FRAX™)

DSÖ'nün Kırık Riski Değerlendirme Yöntemi (FRAX ™)'nin Japon Modelinin Geliştirilmesi ve Uygulanması

Fujiwara S, Nakamura T, Orimo H, Hosoi T, Gorai I, Oden A, Johansson H, Kanis JA
Osteoporos Int 2008;19:429-35

Summary

To evaluate a Japanese version of FRAX, fracture probabilities were computed from published data on the fracture and death hazards in Japan. Probabilities took account of age, sex, the presence of clinical risk factors and femoral neck BMD. The 10-year probabilities of a major osteoporosis related fracture that corresponded to current intervention thresholds ranged from approximately 5% at the age of 50 years to more than 20% at the age of 80 years. The use of femoral neck BMD predicts fracture as well as or better than BMD tests at the lumbar spine.

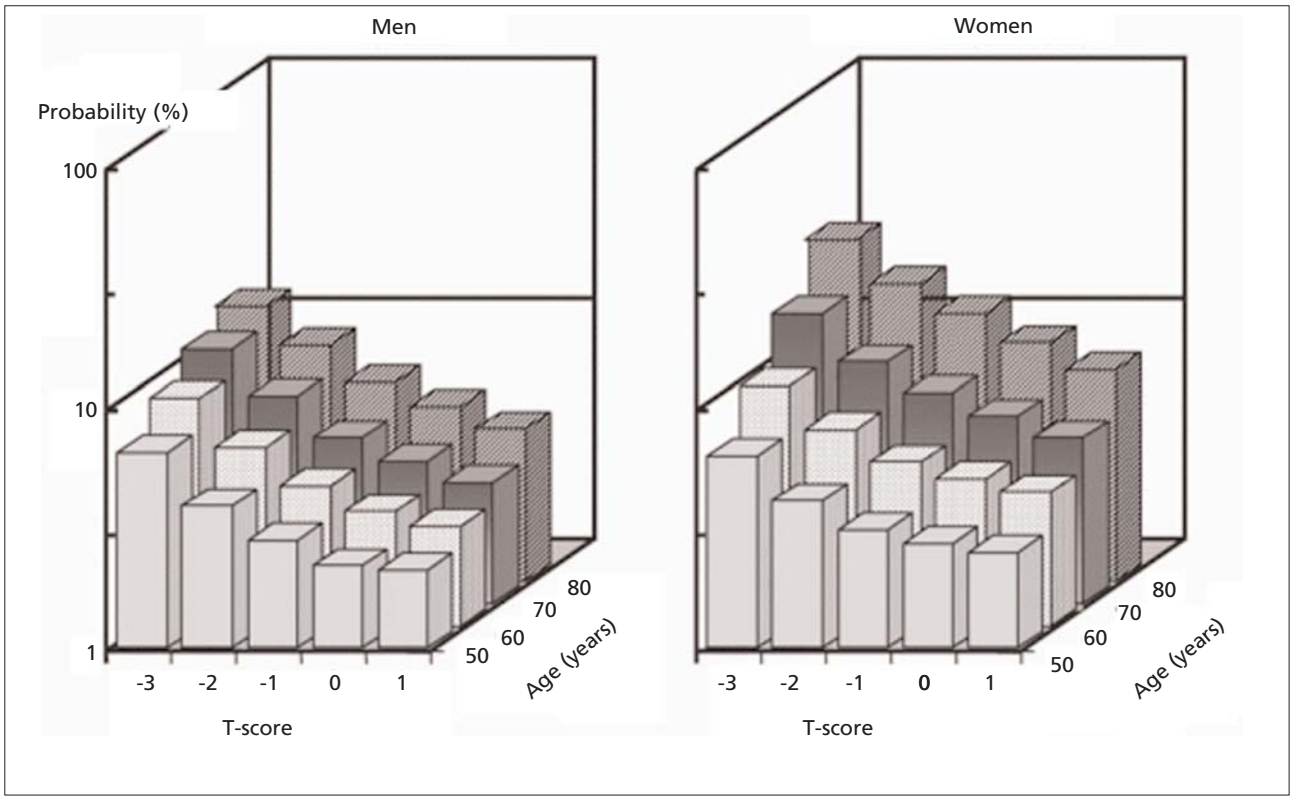

Figure1. Ten-year probability (%) of osteoporotic fracture (hip, clinical spine, humerus, forearm) in Japanese men and women without clinical risk factors according to age and T-score for BMD at the femoral neck. Reproduced from Osteoporosis Int 2008;19:429-35 with permission from Springer.

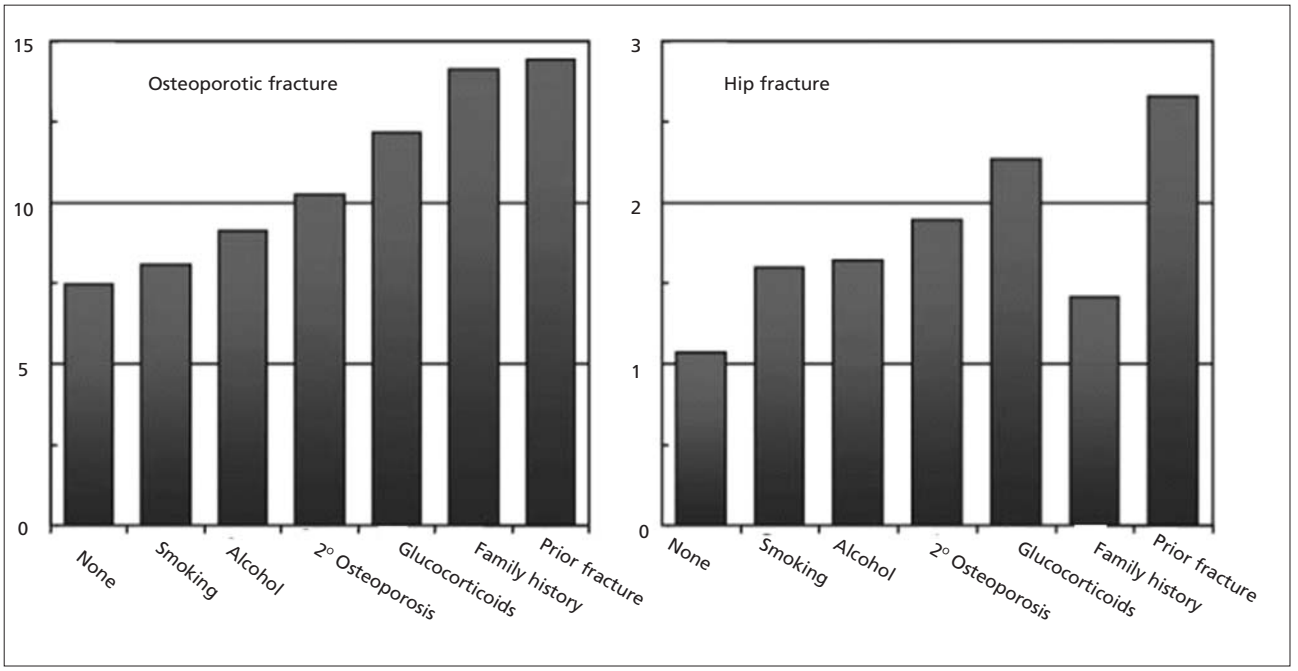

Figure 2. Ten-year probability for osteoporotic (hip, clinical spine, humerus, forearm) and hip fracture (%) according to the presence of a clinical risk factor, in women at the age of 65 years and with a BMI of 23.4 kg/m^2. Reproduced from Osteoporosis Int 2008;19:429-35 with permission from Springer.

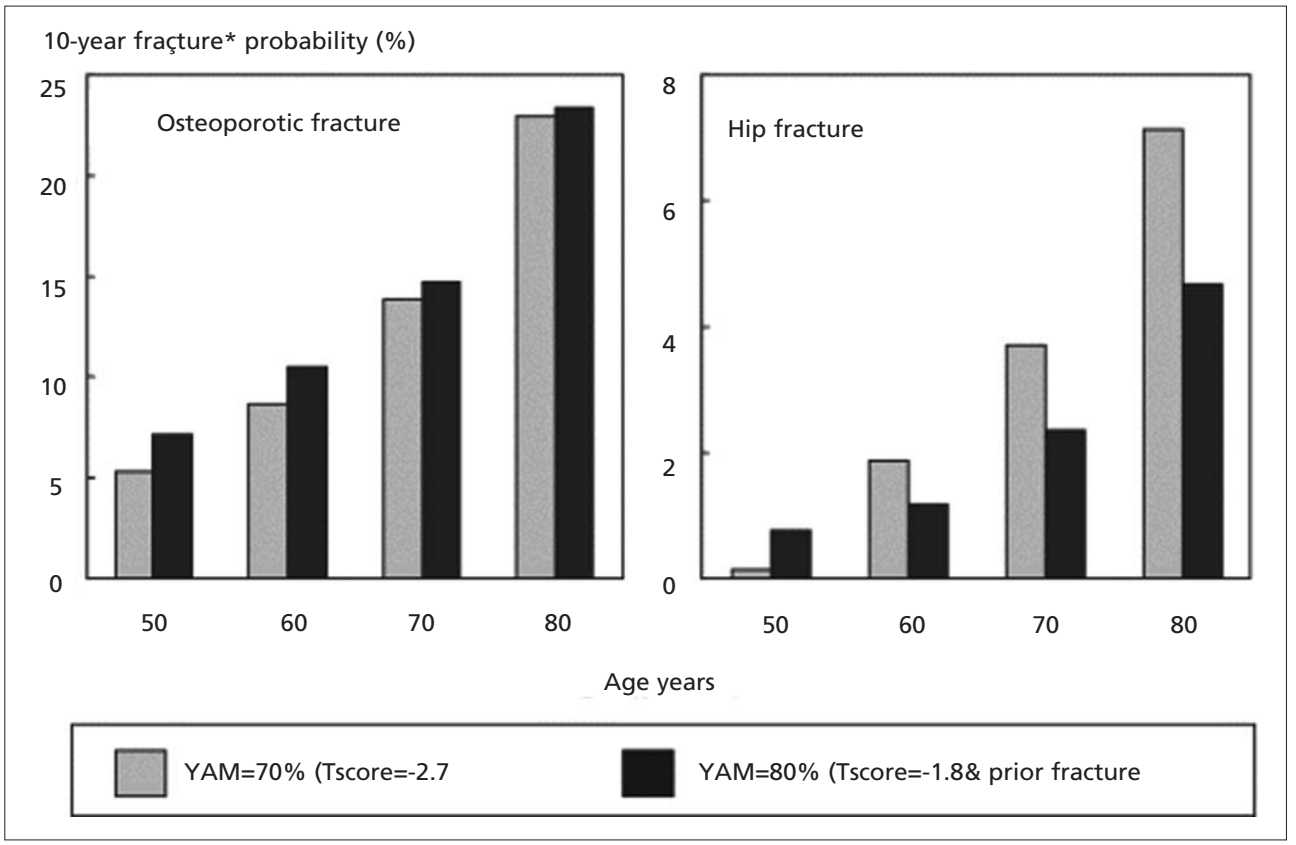

Figure 3. Ten-year probability of osteoporotic (hip, clinical spine, humerus, forearm) and hip fracture based on women at the threshold for the diagnosis of osteoporosis using the criteria of the Japanese Bone Mineral Metabolism Association. Reproduced from Osteoporosis Int 2008;19:429-35 with permission from Springer.

Bazedoxifene in Postmenopausal Women

Postmenopozal Kadınlarda Bazedoksifen

Siris ES, Simon JA, Barton IP, McClung MR, Grauer A

Osteoporos Int 2008;19:681-6

Summary

Postmenopausal women with osteopenia and no prevalent vertebral fractures were identified from BMD Multinational, BMD North America, VERT Multinational and VERT North America). 620 women with osteopenia were included, receiving either placebo (n=309) or risedronate 5 mg (n=311). Risedronate reduced the risk of fragility fractures by 73% over 3 years versus placebo (p=0.023); cumulative fragility fracture incidence was 6.9% in placebo-treated vs. 2.2% in risedronate-treated patients.

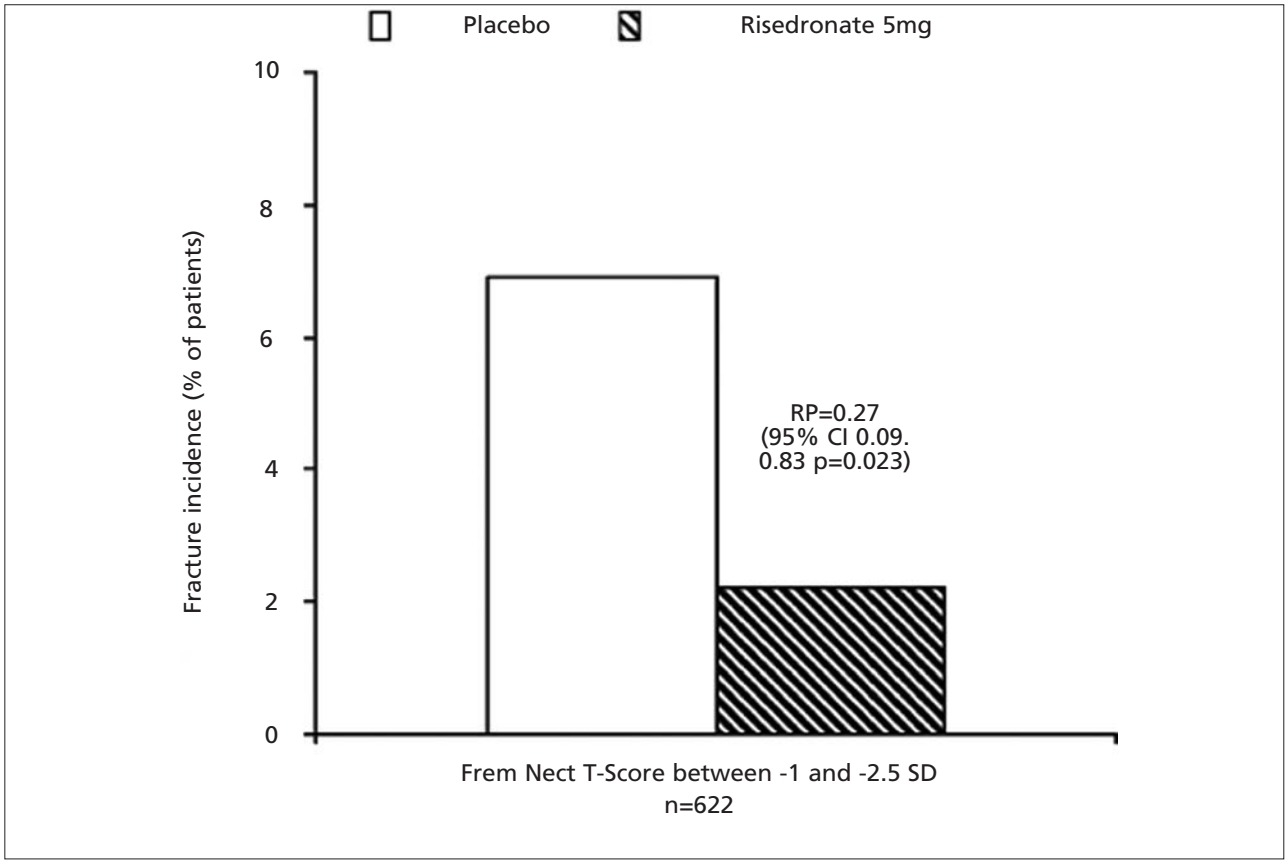

Figure 1. Reduction of fragility fracture risk in patients with femoral neck T-score between -1 and -2.5 SD and no prevalent vertebral fractures. Reproduced from Osteoporosis Int 2008;19:681-6 with permission from Springer.

Raloxifene After PTH Therapy

PTH Tedavisini İzleyen Raloksifen

Cosman F, Nieves JW, Zion M, Barbuto N, Lindsay R

Osteoporos Int 2008;19:529-35

Summary

Forty-two postmenopausal women with osteoporosis on raloxifene were randomized to raloxifene or 1-34 PTH daily for 12 months and continuing raloxifene. Women were then followed for 12 months on raloxifene alone. Biochemical indices increased rapidly during PTH with peak increments of 125-584% for the three markers. After one year of PTH, mean BMD increases were 9.6% for spine, 2.7% for total hip, 3.6% for trochanter (all p<0.005) and 1.2% in femoral neck (NS), while BMD declined 4.3% in the radius (p=0.003). After PTH withdrawal, on continued raloxifene, BMD declined (0.7-2.9% losses; NS) at all sites, except the femoral neck, where BMD increased modestly (p=0.04). At 24 months, spine and femoral neck BMD remained higher than baseline, while radius BMD remained lower (all p<0.04). Gains in BMD of the spine and hip, but not the radius, are seen with one year of PTH in patients on raloxifene. After PTH is discontinued, raloxifene partially maintains PTH-induced BMD gains in the spine and hip.

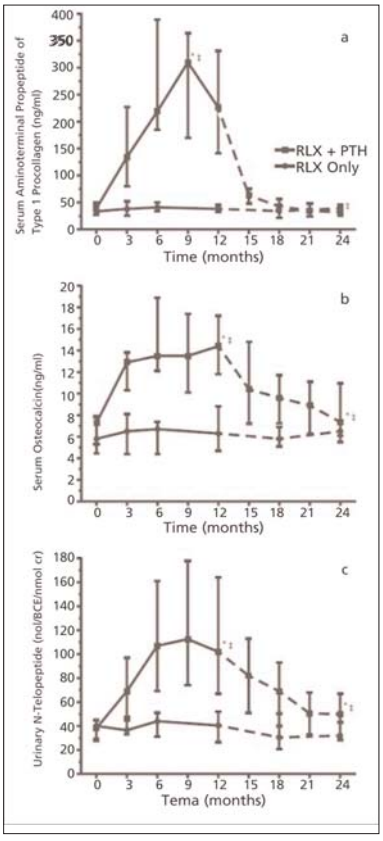

Figure 1. Bone turnover biochemistry in subjects randomized to 1-34PTH treatmentwith ongoing raloxifene compared to raloxifene alone for 1 year (solid lines) followed by continued raloxifene in all subjects for an additional year (dotted lines). Data are presented as medians with interquartile ranges.Within group changes (*p<0.05 at 12 and 24 months vs. baseline, by paired t-tests) and between group differences over 12 months and over 24 months (‡p<0.05 by repeated measures ANOVA). a. Serum aminoterminal propeptide of type I procollagen (ng/ml), b. Serum osteocalcin (ng/ml), c. Urinary N-telopeptide (nmol BCE/nmol cr). Reproduced from Osteoporosis Int 2008;19:529-35 with permission from Springer.

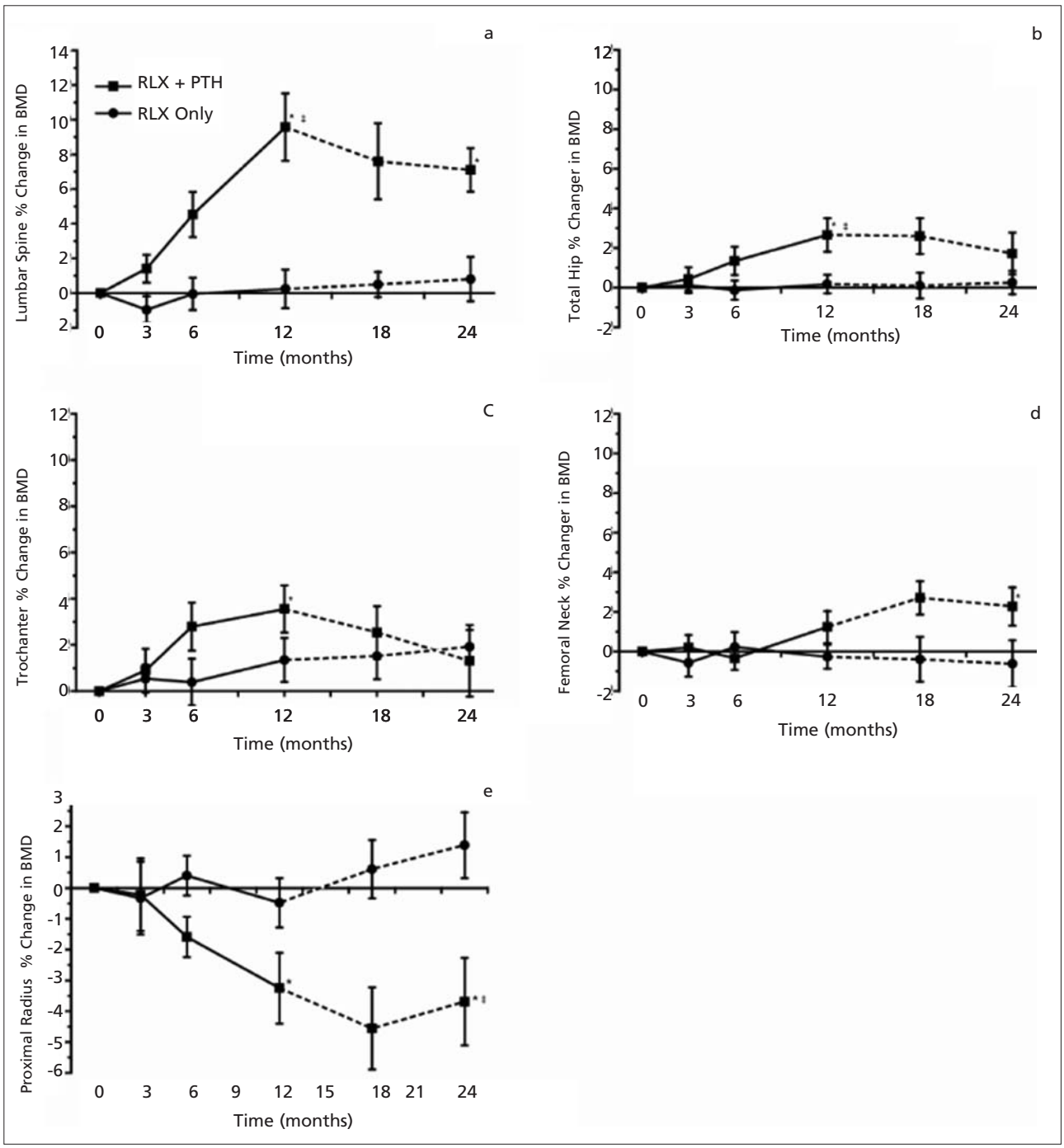

Figure 2. Percent change in bone density in subjects randomized to 1-34PTH treatment with ongoing raloxifene compared to raloxifene alone for 1 year (solid lines), followed by continued raloxifene in all subjects for an additional year (dotted lines). Data are presented as means with standard errors. Within group changes (*p<0.05 at 12 and 24 months vs. baseline, by paired t-tests) and between group differences over 12 months and over 24 months (‡p<0.05 by repeated measures ANOVA). a. Lumbar spine, b. Total hip, c. Trochanter, d. Femoral neck, e. Proximal radius. Reproduced from Osteoporosis Int 2008;19:529-35 with permission from Springer.

Effects of Risedronate on Fracture Risk in Postmenopausal Women With Osteopenia

Risedronatın Postmenopozal Osteopenide Kırık Riski Üzerine Etkinliği

Miller PD, Chines AA, Christiansen C, Hoeck HC, Kendler DL, Lewiecki EM, Woodson G, Levine AB, Constantine G, Delmas PD

J Bone Miner Res 2008;23:525-35

Summary

Bazedoxifene is a selective estrogen receptor modulator that increased BMD and bone strength in experimental models, without stimulating breast or uterus. This 24-mo, randomized, double-blind study in postmenopausal women with a BMD T-score at the lumbar spine or femoral neck between -1.0 and -2.5 or clinical risk factors for osteoporosis assigned to bazedoxifene 10, 20, or 40 mg/d, placebo, or raloxifene 60 mg/d. All received calcium. The intent-to-treat population included 1434 women (mean age, 58 yr; mean time from last menstrual period, 11 yr). All doses of bazedoxifene and raloxifene prevented bone loss. Mean differences in percent change in spine BMD from baseline to 24 mo relative to placebo were 1.08±0.28%, 1.41±0.28%, 1.49±0.28%, and 1.49±0.28% for 10, 20, and 40 mg bazedoxifene and 60 mg raloxifene, respectively ($p<0.001$). Comparable BMD responses were observed at other body sites. Significant and comparable decreases in serum osteocalcin and C-telopeptide levels from baseline and relative to placebo with active treatment were observed as early as 3 mo and were sustained ($p<0.001$). Adverse events, serious adverse events, and discontinuations caused by adverse events were similar between groups. The most common adverse events included headache, infection, arthralgia, pain, hot flush, and back pain. Bazedoxifene prevented bone loss and reduced turnover as well as raloxifene and was well tolerated.

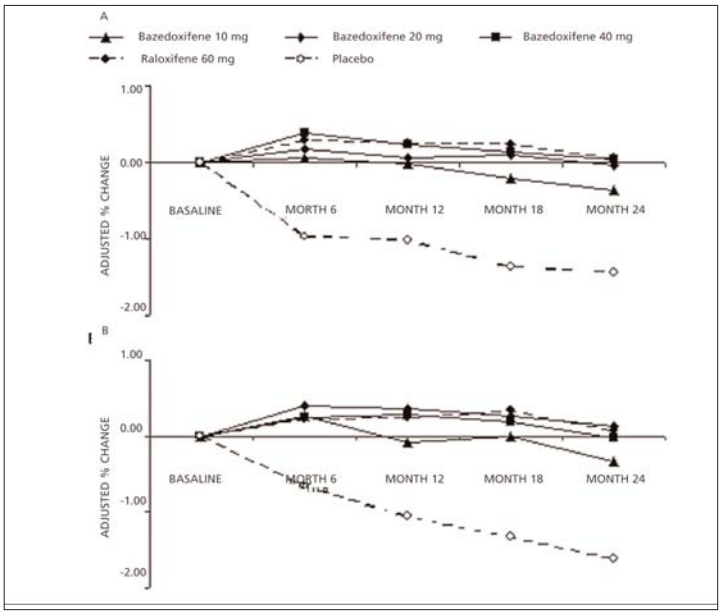

Figure 1. (A) Median percent change from baseline in BMD of the lumbar spine (corrected L1-L4; $p<0.001$) vs. placebo for all bazedoxifene (BZA) groups at each time point. (B) Median percent change from baseline in total hip BMD ($p<0.001$) vs. placebo for all bazedoxifene (BZA) groups at each time point. Reproduced from J Bone Miner Res 2008;23:525-35 with permission of the American Society of Bone and Mineral Research.

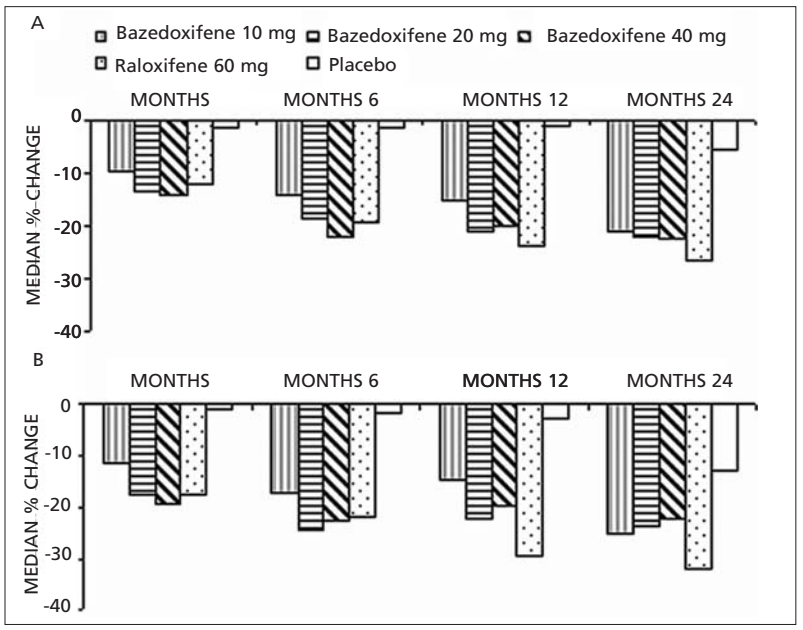

Figure 2. 113b (A) Median percent change from baseline in osteocalcin levels ($p<0.001$), all bazedoxifene and raloxifene treatment groups vs. baseline at all time points; placebo vs. baseline at 24 mo; and all bazedoxifene treatment groups vs. placebo at all time points. (B) Median percent change from baseline in CTX levels ($p<0.001$), all bazedoxifene and raloxifene treatment groups vs. baseline at all time points; placebo vs. baseline at 24 mo; and all bazedoxifene treatment groups vs. placebo at all time points. Nonparametric ANCOVA. Reproduced from J Bone Miner Res 2008;23:525-35 with permission of the American Society of Bone and Mineral Research.

Calcium, Vitamin D and Bone Mass

Kalsiyum ve D Vitamininin Kemik Kütlesi Üzerine Etkisi

Nieves JW, Barrett-Connor E, Siris ES, Zion M, Barlas S, Chen YT

Osteoporos Int 2008;19:673-9

Summary

In 76,507 postmenopausal Caucasian women, vitamin D intake was calculated from milk, fish, supplements and sunlight exposure. BMD was measured at the forearm, finger or heel. Approximately 3 years later, 36,209 participants returned a questionnaire about new fractures. Higher lifetime calcium intake was associated with reduced odds of osteoporosis (peripheral BMD T-score≤-2.5; OR=0.80; 95% CI 0.72, 0.88), as was a higher current calcium (OR=0.75; (0.68, 0.82)) or vitamin D intake (OR=0.73; 95% CI 0.0.66, 0.81). Women reported 2,205 new osteoporosis-related fractures. The 3-year risk of any fracture combined or separately was not associated with intake of calcium or vitamin D.

Osteoporosis Drugs for Nonvertebral Fractures

Osteoporoz İlaçları ve Nonvertebral Kırıklar

Cadarette SM, Katz JN, Brookhart MA, Sturmer T, Stedman MR, Solomon DH

Ann Intern Med 2008;148:637-46

Summary

This is a seriously flawed document for obvious reasons. Enrollees in 2 statewide pharmaceutical benefit programs identified 43,135 new recipients of bisphosphonates, nasal calcitonin, and raloxifene who began treatment from 2000 to 2005. 1051 nonvertebral fractures were observed within 12 months. No differences in fracture risk were found between risedronate or raloxifene relative to alendronate. Among those with a fracture history, raloxifene users had more nonvertebral fractures (HR, 1.78 [CI, 1.20-2.63]) than alendronate users. Calcitonin users had more nonvertebral fractures than alendronate users (HR, 1.40, [CI, 1.20-1.63]). What inferences can be made about the drug, about the type of recipient about the reasons a doctor might choose one drug over another.

Strontium Ranelate Prevents Quality of Life Impairment

Stronsiyum Ranelat Yaşam Kalitesinin Bozulmasını Önler

Marquis P, Roux C, de la Loge C, Diaz-Curiel M, Cormier C, Isaia G, Badurski J, Wark J, Meunier PJ

Osteoporos Int 2008;19:503-10

Summary

The SOTI study used the SF-36(R) questionnaire and disease-specific QUALIOST(R) module, and demonstrated that treatment improved quality of life. QoL was assessed 6 monthly over 3 years using the QUALIOST(R) and SF-36(R) questionnaires in 1,240 women were included (strontium ranelate: n=618 and placebo: n=622). The QUALIOST(R) total score decreased in the strontium ranelate group, indicating preserved QoL compared with a deterioration in the placebo group (P=0.016). Strontium ranelate patients had reduced QUALIOST(R) emotional and physical dimension scores (P=0.019 and 0.032, respectively, vs. placebo). There was a trend towards better SF-36(R) scores in the strontium ranelate group, although there were no between-group differences. More strontium ranelate patients (+31%) were free from back pain over 3 years vs. placebo (P=0.005), with an effect from the first year of treatment (P=0.023).

Loss of Treatment Benefit due to Low Compliance with Bisphosphonate Therapy

Bifosfonatlara Düşük Uyuma Bağlı Tedavi Yararlanımında Kayıp

Penning-van Beest FJ, Erkens JA, Olson M, Herings RM

Osteoporos Int 2008;19:511-7

Summary

New female users of alendronate or risedronate between 1999-2004, aged ≥45 years were identified and were followed until first hospitalisation for an osteoporotic fracture, death, or end of study period. Compliance with bisphosphonates was measured over 90-day intervals using Medication Possession Ratio (MPR). In 8822 new female bisphosphonate users (22,484 person-years of follow-up), 176 fractures occurred (excluding the first six months). Noncompliant bisphosphonate use was associated with a 45% increased fracture risk compared to compliant use (MPR≥80%). Fracture risk increased with poorer compliance (p-value <0.05 for trend). A MPR <20% was associated with an 80% increased fracture risk compared to a MPR≥90%.

Adherence to Biphosphonates and Hip Fracture Risk

Bifosfonatlara Uyum ve Kalça Kırığı Riski

Rabenda V, Mertens R, Fabri V, Vanoverloop J, Sumkay F, Vannecke C, Deswaef A, Verpooten GA, Reginster JY

Osteoporos Int 2008;19:811-8

Summary

Compliance at 12 months was quantified using the medication possession ratio (MPR). Persistence was calculated as the number of days from the initial prescription to a gap of more than 5 weeks after completion of the previous refill. A logistic regression model was used to estimate the impact of compliance on the risk of hip fracture. The impact of persistence on hip fracture risk was analysed using the Cox proportional hazards model. The mean MPR at 12 months was higher among patients receiving weekly (n=15.021) compared to daily alendronate (n=14,136) (daily=58.6%; weekly=70.5%; p<0.001). At 12 months, the rate of persistence was 39.45%. For each decrease of the MPR by 1%, the risk of hip fractures increased by 0.4% (OR: 0.996:0.994-0.998). The relative risk reduction for hip fractures was 60% (HR: 0.404: 0.357-0.457) for persistent compared to nonpersistent patients. These results confirm that adherence to current therapeutic regimens remains suboptimal.

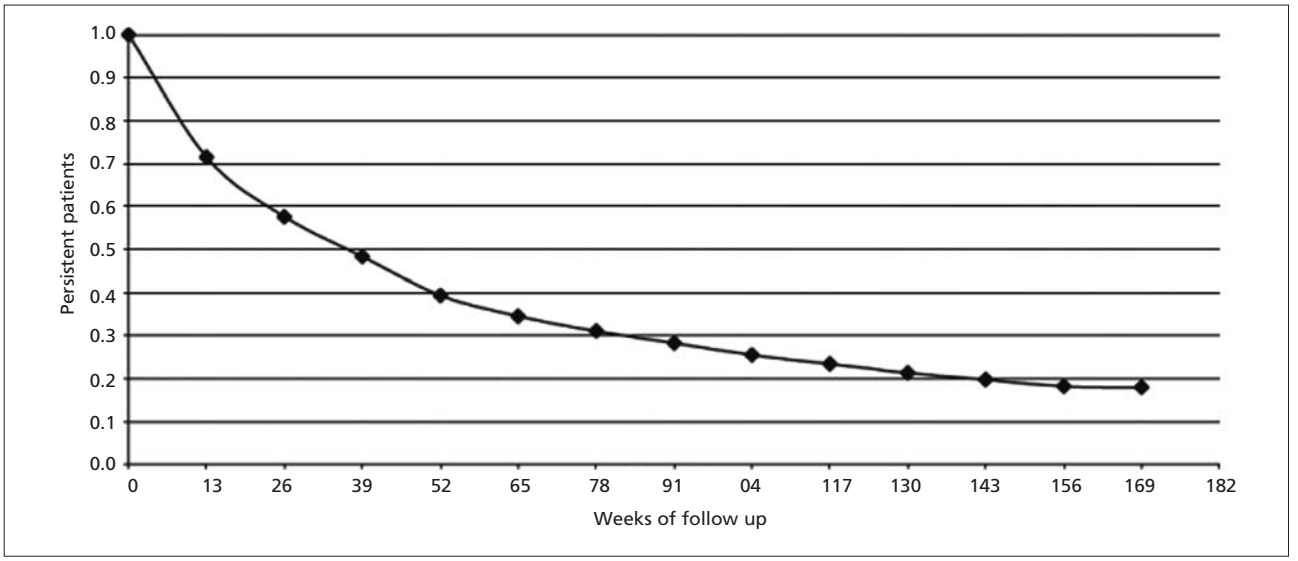

Figure-1. Persistence in the total population treated by alendronate (daily group, weekly group and switch group). Reproduced from Osteoporos Int 2008;19:811-8 with permission from Springer.

Alendronate and Atrial Fibrillation

Alendronat ve Atrial Fibrilasyon

Heckbert SR, Li G, Cummings SR, Smith NL, Psaty BM

Arch Intern Med 2008;168:826-31

Summary

The HORIZON (Health Outcomes and Reduced Incidence With Zoledronic Acid Once Yearly) trial reported a higher risk of serious atrial fibrillation (AF) in zoledronic acid recipients. In this study ever use of alendronate in a clinical practice setting identified 719 women with AF and 966 controls without AF. More AF case patients had ever used alendronate (6.5% [n=47] vs. 4.1% [n=40]; P=0.03), so ever use of alendronate was associated with a higher risk of incident AF (odds ratio, 1.86; 95%CI 1.09-3.15). The authors estimated that 3% of incident AF in this population might be explained by alendronate use.