



## Selección de Resúmenes de Menopausia

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### Hypertension in Women Across the Lifespan

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Purpose of review: We will highlight the biological processes across a women's lifespan from young adulthood through menopause and beyond that impact blood pressure and summarize women's representation in hypertension clinical trials. Recent findings: Throughout their lifetime, women potentially undergo several unique sex-specific changes that may impact their risk of developing hypertension. Blood pressure diagnostic criteria for pregnant women remains 140/90 mmHg and has not been updated for concordance with the 2017 ACC/AHA guideline due to a lack of data. Although on a population level, women develop hypertension at later ages than men, new data shows women's BP starts to increase as early as the third decade. Understanding how age and sex both contribute to hypertension in elderly women is crucial to identify optimal blood pressure and treatment targets. Effective screening, monitoring, and treatment of hypertension throughout a women's lifespan are necessary to reduce CVD risk. We highlight several gaps in the literature pertaining to understanding sex-specific hypertension mechanisms.

**JB JS Open Access. 2021 Jun 14;6(2):e20.00142.doi: 10.2106/JBJS.OA.20.00142. eCollection Apr-Jun 2021.**

### Rates of Osteoporosis Management and Secondary Preventative Treatment After Primary Fragility Fractures

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Fragility fractures are often sentinel events in documenting new cases of osteoporosis. Numerous analyses have demonstrated low rates of adequate osteoporosis evaluation and treatment following primary fragility fractures. The purpose of this study was to quantify the incidence of primary fragility fractures in America and the rates of osteoporosis screening and management before and after fracture. Methods: A retrospective review of the PearlDiver database was conducted using the International Classification of Diseases, Ninth Revision (ICD-9) and ICD, Tenth Revision (ICD-10) and Current Procedural Terminology codes. Patients who were 60 to 80 years of age and had primary fragility fractures of the hip, wrist, spine, pelvis, humerus, and other unspecified locations were included. The rates of dual x-ray absorptiometry (DXA) screening and osteoporosis pharmacotherapy were assessed for 2 years before and 2 years after the primary fracture. Results: In this study, 48,668 patients with a primary fragility fracture were identified. Within this cohort, 25.8% (12,573 of 48,668) had received osteoporosis screening or treatment in the prior 2 years. In the 36,095 patients with no management before the fracture, 19% (6,799 patients) were diagnosed with osteoporosis and 18.4% (6,653 patients) received a DXA scan and/or filed claims for pharmacotherapy in the following 2 years. Patients with an osteoporosis diagnosis were more likely to receive both types of management (odds ratio [OR], 11.55 [95% confidence (CI), 10.31 to 12.95]), and male patients were less likely to receive both types of management (OR, 0.23 [95% CI, 0.17 to 0.27]). Secondary fragility fractures within the next 2 years were diagnosed in 8.4% (3,038 of 36,095) of patients at a mean of 221 days following the primary fracture. Conclusions: The rates of appropriate osteoporosis evaluation, diagnosis, and management following primary fragility fractures remain unacceptably low. Less than one-third of patients with primary fragility fractures had been evaluated or treated for osteoporosis in the 2 years prior to fracture. Furthermore, among patients without pre-fracture management, <20% received osteoporosis screening or treatment within the next 2 years.

**J Osteoporos. 2021 May 26;2021:5526359.doi: 10.1155/2021/5526359. eCollection 2021.**

### Ascending Aortic Calcification as a Potential Predictor for Low Bone Mineral Density: A Pilot Study

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Background: Identifying the factors related to low bone mineral density (BMD) can have significant implications for preventing hip fractures. The correlation between ascending aortic calcification and BMD has never been reported. Therefore, the purpose of the current study is to confirm the hypothesis that ascending aortic calcification can be used

as a predictive factor for low BMD and to find a radiographic sign to show it. Method: Plain film and computed tomography (CT) images of the thorax were obtained from 91 patients with hip fractures. Using the images, the calcification line of the ascending aorta adjacent to the aortic arch was evaluated. A prominent calcification line confirmed by both plain film and CT was classified as +2. A line which was ambiguous on plain film but confirmed by CT was classified as +1. Cases with no calcification were categorized as 0 (control). We compared the classified score with the BMD and calculated the kappa coefficient to measure intraobserver reliabilities for this radiographic finding. Results: Twenty-eight patients showed a +2 line, twenty-four patients showed a +1 line, and thirty-nine patients showed 0 lines. The median BMD of each group was 0.37 for the +2 line, 0.45 for the +1 line, and 0.51 for the 0 line. The BMD for the +2 group was significantly lower than the others. The kappa coefficient was approximately 0.6 ( $p < 0.01$ ). Conclusion: The imaging finding of calcification of the ascending aorta might be considered as a potential surrogate marker of low BMD. In such subjects, BMD might be ordered for the confirmation of diagnosis of osteoporosis.

**Maturitas 2021 Jul;149:26-33.doi: 10.1016/j.maturitas.2021.05.004. Epub 2021 May 24.**

### **Are vitamin D deficiency and VDR gene polymorphisms associated with high blood pressure as defined by the ACC/AHA 2017 criteria in postmenopausal women?**

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Objectives: To assess the vitamin D levels, prevalence of vitamin D deficiency and genotypes of Fok-I, Bsm-I, Apa-I and Taq-I polymorphisms in the VDR gene and to determine whether vitamin D deficiency and VDR gene variants are associated with blood pressure levels and systemic arterial hypertension as defined by the 2017 ACC/AHA criteria. Study design: A cross-sectional study of biobanked blood samples from 339 postmenopausal women. Main outcome measures: Blood pressure strata were defined according to the 2017 ACC/AHA cutoffs. Circulating 25(OH)D levels were considered deficient if  $<20$  ng/mL. Results: Mean serum total 25(OH)D levels were  $22.99 \pm 8.54$  ng/mL, and 40.1% of participants were deficient in vitamin D. Overall, 7.7% had elevated blood pressure, 36.6% had stage 1 and 37.8% had stage 2 hypertension. Mean total ( $p = 0.014$ ) and free 25(OH)D levels ( $p = 0.029$ ) were lower in women with stage 2 hypertension than in those with normal blood pressure. A higher prevalence rate of stage 2 hypertension was associated with age (PR 1.058; 95%CI 1.033-1.083;  $p < 0.001$ ), BMI (PR 1.046; 95%CI 1.025-1.068;  $p < 0.001$ ), vitamin D deficiency (PR 1.333; 95%CI 1.016-1.749;  $p = 0.038$ ) and Taq-I polymorphism (PR 1.764; 95%CI 1.030-3.019;  $p = 0.039$ ). Women with vitamin D deficiency and the AA+AG genotype of Taq-I polymorphism were 33% and 76% more likely to have stage 2 hypertension, respectively, but these associations lost significance when adjusted for age and BMI. Conclusion: The results suggest that vitamin D deficiency and Taq-I polymorphism are associated with stage 2 hypertension, depending on age and BMI, in postmenopausal women.

**J Frailty Sarcopenia Falls. 2021 Jun 1;6(2):86-91.doi: 10.22540/JFSF-06-086. eCollection 2021 Jun.**

### **Change in BMI affects the risk of falling in postmenopausal osteopenic and osteoporotic women**

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Objectives: To investigate the impact of the body mass index (BMI) change on risk of falling in postmenopausal women with osteopenia or osteoporosis. Also, we aimed to evaluate and associate the individuals' functionality, mobility and balance with the risk of falling. Methods: This one-year prospective observational study assessed 498 postmenopausal Greek women over the 50th year of age suffering from either osteoporosis or osteopenia. Parameters such as the height, weight and BMI were documented. Furthermore, the subjects were asked whether they experienced a fall the preceding year. Balance was evaluated using the Berg Balance Scale, the Timed-Up-And-Go test, and the 30 Seconds Sit-to-Stand test. Hand-grip strength was assessed with the Jamar Hydraulic Hand Dynamometer. Results: The observed one-year BMI change was associated with falls in postmenopausal osteopenic and osteoporotic women over the age of 70. Additionally, there were statistically significant changes in the BBS, TUG, 30CST and the hand-grip strength on both hands at the one-year follow-up but there were not associated with an increased fall risk. Conclusion: The one-year change in BMI was associated with the risk of falling in postmenopausal osteopenic and osteoporotic women over the 70th year of age. Whereas, the one-year change in balance, mobility and grip strength were not linked to an increased risk of falling.

**Eur J Clin Nutr. 2021 Jun 15.doi: 10.1038/s41430-021-00957-8. Online ahead of print.**

## **Dietary calcium intake and change in bone mineral density in older adults: a systematic review of longitudinal cohort studies**

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Many older adults do not achieve recommended intakes of calcium and there is some concern over the potential impact of this on bone health. The objective of this review was to examine evidence from cohort studies on the relationship between calcium intake and change in bone mineral density (BMD) in older adults, something not undertaken in the last two decades. Data sources included Ovid Medline, Embase, and PubMed and references from retrieved reviews and articles. The final search was performed in February 2021. We included cohort studies of calcium intake in participants aged >50 years with change in BMD over  $\geq 1$  year as an outcome. We identified 23 studies of women and 7 of men. Most studies found no association between calcium intake and change in BMD in women (71%) or men (71%). Among women, five studies reported high rates (>30% of participants) of hormone treatment or osteoporosis therapy (HT/OT) use; 80% of these studies reported a positive association between calcium intake and change in BMD, compared with 10% of studies in which HT/OT use was low. No study in women in which the mean age was >60 years reported a positive association between calcium intake and change in BMD. We conclude that calcium intake across the ranges consumed in these studies (mean intake in all but one study >500 mg/day) is not an important determinant of bone loss, particularly among women >60 years. The positive findings in studies with high rates of HT/OT use are likely to arise from confounding as a result of co-administration of calcium supplements with these medications.

**J Prim Care Community Health. Jan-Dec 2021;12:21501327211025170.doi: 10.1177/21501327211025170.**

## **Perceived Loneliness and Severe Sleep Disorders in Adult Women during the Covid-19 Quarantine: A Cross-Sectional Study in Colombia**

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Background: Quarantine is a measure to control COVID-19 spread, resulting in an increased perception of loneliness. In turn, sleep disorders (SD) may be more frequently reported in uncertain circumstances. Objectives: To identify the association between loneliness and severe SD, in women quarantined due to the COVID-19 pandemic. Methods: A cross-sectional study carried out in women, between 40 and 79 years and living in Colombia. The women were invited through social network to complete 5 digital instruments: de Jong Gierveld Loneliness Scale, Menopause Rating Scale, Fear of COVID-19 Five-item Version, Coronavirus Anxiety Scale, and Francis Religion Scale. Bivariate analysis and adjusted logistic regression between loneliness and SD were performed. Results: 1133 women participated, half of them under 50 years old. 43.1% had emotional loneliness, 39.9% social loneliness and 43.3% general loneliness. SD were identified in 6 out of 10 women, those with mild SD presented an OR of 1.84, 1.85, and 1.64, for emotional, social and general loneliness, respectively. Loneliness was associated twice with moderate SD, and more than twice with severe SD. Very severe SD reached OR:5.81 for emotional loneliness, OR:4.38 social loneliness and OR:4.02 general loneliness. In the presence of religiosity, fear and anxiety due to COVID-19, statistical significance was retained for associations, except intense SD with general loneliness. Conclusions: SD were significantly associated with loneliness in our study population. It is important to assess sleep quality and perception of loneliness in middle-aged women, especially during periods of quarantine due to a pandemic to avoid health implications.

**J Bone Metab. 2021 May;28(2):101-113.doi: 10.11005/jbm.2021.28.2.101. Epub 2021 May 31.**

## **Application of the Trabecular Bone Score in Clinical Practice**

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The trabecular bone score (TBS) was introduced as an indirect index of trabecular microarchitecture, complementary to bone mineral density (BMD), and is derived using the same dual energy X-ray absorptiometry images. Recently, it has been approved for clinical use in Korea. Therefore, we conducted a comprehensive review to optimize the use of TBS in clinical practice. The TBS is an independent predictor of osteoporotic fractures in postmenopausal women and men aged >50 years. The TBS is potentially useful in monitoring the skeletal effects of anabolic agents but not of antiresorptive agents. In postmenopausal women with type 2 diabetes mellitus, the TBS assesses osteoporotic fracture risk not captured by BMD. However, high body mass index and soft tissue thickness can cause underestimation of the TBS; however, this limitation has been improved in recent versions of the TBS software. However, a high precision error and low reproducibility limit the use of TBS. This review may provide information on the application of the TBS in clinical practice based on reliable evidence.

**J Breast Cancer. 2021 May 14.doi: 10.4048/jbc.2021.24.e28. Online ahead of print.**

## **A Nationwide Study on the Incidence of Breast Cancer in Korean Women with Osteoporosis Receiving Raloxifene Treatment**

Jihyoun Lee, Ji Sung Lee, Jong Eun Lee, Zisun Kim, Sun Wook Han, Sung Mo Hur, Young Jin Choi, Sungmin Park

**Purpose:** Raloxifene is a selective estrogen receptor modulator (SERM), and raloxifene treatment for osteoporosis is reimbursable under the Korean National Health Insurance. Evidence suggests that SERMs use reduces the risk of breast cancer in Asian population. Herein, we retrospectively investigated the protective effect of raloxifene on breast cancer rates in Korean population. **Methods:** Using the Health Insurance Review and Assessment Service database, we selected women with osteoporosis aged 50 years and above. Patients treated for at least 2 years with raloxifene were assigned to the user group, whereas the remaining patients were assigned to the non-user group. The effect on breast cancer risk was assessed using the Cox proportional-hazards model with a time-dependent covariate to adjust for immortal time bias. **Results:** A total of 322,870 women who were registered between 2010 and 2011 were included. The user group comprised 0.7% (n = 2,307) of the total population. The mean age was  $65.7 \pm 8.0$  years and  $67.2 \pm 8.6$  years in the user and non-user groups, respectively ( $p < 0.001$ ). There was no difference in the previous use of estrogen replacement between the 2 groups ( $p = 0.087$ ). The incidence of breast cancer per 1,000 person-years was 0.49 (n = 8) and 0.68 (n = 1,714) in the user and non-user groups, respectively (hazard ratio [HR], 0.63, 95% confidence interval [CI], 0.32-1.27). HR decreased with increase in the treatment duration, but this change was not statistically significant (HR, 1.00, 95% CI, 0.32-3.11 in 2-3 years; HR, 0.63, 95% CI, 0.20-1.94 in 3-4 years; and HR, 0.41, 95% CI, 0.10-1.65 in 4-5 years). **Conclusion:** Long-term treatment with raloxifene in women with osteoporosis was not significantly associated with a reduction in breast cancer rates. However, further investigation is required for a conclusive proof.

**Br J Cancer. 2021 Jun 14. doi: 10.1038/s41416-021-01459-x. Online ahead of print.**

## **Mammographic microcalcifications and risk of breast cancer**

Shadi Azam, Mikael Eriksson, Arvid Sjölande, Marike Gabrielson, Roxanna Hellgren Kamila Czene, Per Hall.

**Background:** Mammographic microcalcifications are considered early signs of breast cancer (BC). We examined the association between microcalcification clusters and the risk of overall and subtype-specific BC. Furthermore, we studied how mammographic density (MD) influences the association between microcalcification clusters and BC risk. **Methods:** We used a prospective cohort (n = 53,273) of Swedish women with comprehensive information on BC risk factors and mammograms. The total number of microcalcification clusters and MD were measured using a computer-aided detection system and the STRATUS method, respectively. Cox regressions and logistic regressions were used to analyse the data. **Results:** Overall, 676 women were diagnosed with BC. Women with  $\geq 3$  microcalcification clusters had a hazard ratio [HR] of 2.17 (95% confidence interval [CI] = 1.57-3.01) compared to women with no clusters. The estimated risk was more pronounced in premenopausal women (HR = 2.93; 95% CI = 1.67-5.16). For postmenopausal women, microcalcification clusters and MD had a similar influence on BC risk. No interaction was observed between microcalcification clusters and MD. Microcalcification clusters were significantly associated with in situ breast cancer (odds ratio: 2.03; 95% CI = 1.13-3.63). **Conclusions:** Microcalcification clusters are an independent risk factor for BC, with a higher estimated risk in premenopausal women. In postmenopausal women, microcalcification clusters have a similar association with BC as baseline MD.