# Selección de Resúmenes de Menopausia

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## The mid-life transition and the risk of cardiovascular disease and cancer II: Strategies to maximize quality of life and limit dysfunction and disease.

Kase NG1, Friedman EG2, Brodman M2.

Chronic dysfunction, disabilities and complex diseases such as cardiovascular disease, Diabetes Mellitus Type 2, osteoporosis and certain cancers among other burdens emerge and accelerate in midlife women. Previously in Part l we have described clinical and laboratory research findings which more readily explain and clarify the underlying pathogenetic mechanisms driving these clinical burdens. Included were new findings on how in particular visceral obesity and the emergence and acceleration of various components of the Metabolic Syndrome - glucotoxicity, lipotoxicity and a chronic systemic inflammatory state abetted by loss of ovarian production of estradiol and the inevitable inroads of aging generate this spectrum of clinical problems. These research insights translate into opportunities for effective care strategies leading to prevention, amelioration, possible correction and enhanced quality of life. To achieve these goals, updated detailed diagnostic, management and therapeutic guidelines implemented by a reprogrammed, repurposed "menopause" office visit is described. A triage mechanism-when to refer other specialists for further care is emphasized. The formerly polarized views of Menopausal Hormone Therapy (MHT) have narrowed significantly leading to construction of a more confident, unified and wider clinical application. Accordingly, a MHT program providing maximum benefit and minimum risk, accompanied by an algorithm for enhanced shared decision-making is included.

**Bone. 2020 Jun 9:115475. doi: 10.1016/j.bone.2020.115475. [Epub ahead of print]**

## The impact of thiazide diuretics on bone mineral density and the trabecular bone score: The Rotterdam study.

van der Burgh AC1, Araghi SO2, Zillikens MC3, Koromani F4, Rivadeneira F2, van der Velde N5, et al.

The decreased risk of osteoporotic fractures in thiazide diuretics (TD) users is possibly not only caused by an increase in bone mineral density (BMD), but by an increase in other determinants of bone strength as well, such as the trabecular bone score (TBS). To test this hypothesis, we studied the association between TD use and both lumbar spine BMD (LS-BMD) and lumbar spine TBS (LS-TBS) cross-sectionally in 6096 participants from the Rotterdam Study, as well as the association between TD use and bone turnover estimated by serum osteocalcin levels. We found that past and current use of TD were associated with an increase of LS-BMD (β = 0.021 g/cm2 (95% CI: 0.006;0.036) and β = 0.016 g/cm2 (95% CI: 0.002;0.031), respectively). Use of ≥1 defined daily dose (DDD) (β = 0.028, 95% CI: 0.010;0.046; p for trend within DDD of use <0.001) and use of >365 days (β = 0.033, 95% CI: 0.014;0.052; p for trend within duration of use <0.001) were positively associated with LS-BMD. No significant association between TD use and LS-TBS was observed. Mean serum osteocalcin levels were significantly different between users and non-users of TD (20.2 ng/ml (SD 8.3) and 22.5 ng/ml (SD 17.0), respectively, p < 0.001). Furthermore, linear regression analysis showed that the use of TD was associated with a 3.2 ng/l (95% CI: -4.4.; -2.0) lower serum osteocalcin level compared to non-use of TD, when adjusted for Rotterdam Study cohort, age and sex. Our results may implicate that the decreased fracture risk in TD users is explained by increased bone mass rather than by improved bone microarchitecture. Alternatively, changes in bone microarchitecture might not be detected through TBS and more sophisticated techniques are possibly needed to study a potential effect of TD on bone microarchitecture.

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## Mechanical stress regulates bone regulatory gene expression independent of estrogen and vitamin D deficiency in rats.

Nepal AK1, van Essen HW1, van der Veen AJ2, van Wieringen WN3,4, Stavenuiter AW5, Cayami FK6,7, et al.

Mechanical stress determines bone mass and structure. It is not known whether mechanical loading affects expression of bone regulatory genes in a combined deficiency of estrogen and vitamin D. We studied the effect of mechanical

loading on the mRNA expression of bone regulatory genes during vitamin D and/or estrogen deficiency. We performed a single bout in vivo axial loading with 14 N peak load, 2 Hz frequency and 360 cycles in right ulnae of nineteen weeks old female control Wistar rats with or without ovariectomy (OVX), vitamin D deficiency and the combination of OVX and vitamin D deficiency(N=10/group). Total bone RNA was isolated 6 hours after loading, and mRNA expression was detected of Mepe, Fgf23, Dmp1, Phex, Sost, Col1a1, Cyp27b1, Vdr and Esr1. Serum levels of 25(OH)D, 1,25(OH)2 D and estradiol were also measured at this time point. The effect of loading, vitamin D and estrogen deficiency and their interaction on bone gene expression was tested using a mixed effect model analysis. Mechanical loading significantly increased the mRNA expression of Mepe, and Sost, whereas it decreased the mRNA expression of Fgf23 and Esr1. Mechanical loading showed a significant interaction with vitamin D deficiency with regard to mRNA expression of Vdr and Esr1. Mechanical loading affected gene expression of Mepe, Fgf23, Sost and Esr1 independently of vitamin D or estrogen, indicating that mechanical loading may affect bone turnover even during vitamin D deficiency and after menopause.

**Cancer. 2020 Jun 12. doi: 10.1002/cncr.33002. [Epub ahead of print]**

## Insulin resistance and breast cancer incidence and mortality in postmenopausal women in the Women's Health Initiative.

Pan K1, Chlebowski RT1, Mortimer JE2, Gunther MJ3, Rohan T4, Vitolins MZ5, Adams-Campbell LL6, et al.

BACKGROUND: Insulin resistance is associated with higher all-cause and cancer-specific mortality in postmenopausal women. However, to the authors' knowledge, information regarding insulin resistance and breast cancer mortality risk is limited. Therefore, the authors examined associations between insulin resistance and breast cancer incidence and mortality in a subsample of Women's Health Initiative participants. METHODS: A total of 22,837 postmenopausal women with fasting baseline glucose and insulin levels were followed for incident breast cancer and breast cancer mortality. Breast cancers were verified by medical record review and serial National Death Index linkage-enhanced mortality findings. Insulin resistance was estimated using the homeostatic model assessment of insulin resistance (HOMA-IR). Multivariable Cox proportional hazards models were used to compute hazard ratios (HRs) with 95% confidence intervals (95% CIs) for quartile comparisons. Outcomes included breast cancer incidence, deaths from breast cancer, and deaths after breast cancer (breast cancer followed by death from any cause). RESULTS: During a median of 19.8 years of follow-up of 1328 breast cancer cases, there were 512 deaths reported, 151 of which were from breast cancer. Breast cancer incidence was higher in women in the highest HOMA-IR quartile (HR, 1.34; 95% CI, 1.12-1.61 [P for trend = .003]). Although HOMA-IR was not found to be associated with risk of death from breast cancer (HR, 1.04; 95% CI, 0.60-1.79), women in the highest versus those in the lowest HOMA-IR quartile were at a higher risk of death after breast cancer (HR, 1.78; 95% CI, 1.32-2.39 [P for trend <.001]). CONCLUSIONS: Higher levels of insulin resistance in postmenopausal women are associated with higher breast cancer incidence and higher all-cause mortality after breast cancer.

**Ceska Gynekol. 2020 Winter;85(2):84-93.**

## Is the finding of endometrial hyperplasia or corporal polyp an mandatory indication for biopsy?

Vinklerová P, Felsinger M, Frydová S, Ovesná P, Hausnerová J, Weinberger V.

OBJECTIVE: The aim of our study was to analyze a group of patients referred for endometrial biopsy. To evaluate the ultrasound finding of hyperplasia/polyp, the symptomatology of patients related to the result of definitive histology, to determine the severity of individual variables in connection with the detection of precancerosis/cancer. Due to the complexity of information identify women who are suitable for conservative approach. METHODS: All patients over 50 years who underwent surgical endometrial biopsy at our department in the period of 2017-2018 (n = 754) were included. RESULTS: Perimenopause - the median of endometrial thickness in both benign and malignant histology was 8 mm (p = 0.448), the median of the largest polyp dimension was 18 mm. All patients with precancerosis/malignancy were symptomatic with irregular/excessive bleeding, no carcinoma was found in polyp. Postmenopause - the median of endometrial thickness in benign histology was 7 mm versus 16 mm in precancerosis/malignancy (p < 0.001), the median of the largest polyp dimension was the same in both histologies (13 mm, p = 0.274). The risk of malignancy was more than threefold in bleeding versus asymptomatic patients with both hyperplasia and polyp (OR 3.39, 3.79). In asymptomatic patients the risk of cancer was similar for selected cut-offs (5, 8 and 12 mm), statistically significant only for 12 mm (OR 3.54), while in symptomatic patients the risk was high for all cut-offs, however with wide confidence intervals, statistically significant for cut-offs of 8 mm (minimum 3.58) and 12 mm (minimum 4.94). CONCLUSION: We have shown that symptomatology is a strong risk factor for

the presence of precancerosis/malignancy in patients with endometrial hyperplasia or polyp. The thickness of the endometrium or polyp size in asymptomatic patients does not play a major role. Ultrasound alone does not have sufficient accuracy for detection or even screening of endometrial cancer. We recommend a conservative procedure, monitoring changes in the ultrasound scan and symptomatology of the patient over time.

**Int J Environ Res Public Health. 2020 Jun 4;17(11). pii: E3996. doi: 10.3390/ijerph17113996.**

## Visceral Fat Is a Negative Determinant of Bone Health in Obese Post-menopausal Women.

Sharma DK1, Anderson PH1, Morris HA1, Clifton PM1.

The protective effect of obesity on bone health has been challenged by studies that link visceral adiposity to poor bone microarchitecture in young obese men and women. In postmenopausal women, the role of visceral adipose tissue (VAT) on bone turnover markers (BTMs) has not been investigated. The aim was to investigate the impact of VAT on BTMs, total bone mineral density (BMD), vitamin D metabolites and parathyroid levels (1-84 PTH) levels in postmenopausal women. A total of 76 lean and overweight women (without osteoporosis) underwent VAT measurements by dual-energy X-ray absorptiometry (iDXA). Blood samples were analyzed for serum C-terminal telopeptide of type 1 collagen (CTX-1), osteocalcin, bone-specific alkaline phosphatase (bone ALP), 1-84 PTH and vitamin D (25 hydroxyvitamin D, 25(OH)D) levels. VAT volumes ranged from 91 to 3392 cm3 and body mass index (BMI) ranged from 18.3 to 53.9 kg/m2. Women in the highest VAT quartile had significantly lower CTX-1, 25(OH)D, osteocalcin and the highest BMD ($p < 0.05$, for all). While VAT positively associated with BMD, after controlling for BMI, VAT was a negative predictor of BMD ($\beta = 0.368$, $p < 0.05$). VAT was an independent negative predictor of CTX-1 ($\beta = -0.263$, $p < 0.05$) and osteocalcin levels ($\beta = -0.277$, $p < 0.05$). Among all measures of adiposity, VAT was the strongest independent determinant of BMD and BTMs. In clinical settings, VAT, and not BMI, may be a sensitive predictor of bone health in obese women.

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## Lipid Profile Status in Natural and Surgical Menopausal Women: A Comparative Study.

Paul J1, Khanam RA, Mirza TT, Saha MK, Halim MA, Basher MS, Asaduzzaman M.

This cross sectional, study was carried out in the department of Obstetrics and Gynaecology in Mymensingh Medical College Hospital (MMCH), Mymensingh, Bangladesh from October 2015 to September 2016. The objective of the study was to evaluate dyslipidaemia between natural and surgical menopausal women. Patients who attended the menopausal clinic of Mymensingh Medical College Hospital, Mymensingh were included in the study. For this purpose 91 patient were divided into study (n=46) and comparison (n=45) groups. Serum total cholesterol (TC), serum triglyceride (TG), Serum high density lipoprotein cholesterol (HDL-cholesterol) were estimated by colorometric method and serum low density lipoprotein cholesterol (LDL-cholesterol) was calculated by using Friedwald's formula. Age range of menopausal women was 45 to 60 years. The mean age with SD was in study group 50.26±2.57 years and control group 49.02±3.13 years. It was observed that women with surgical menopause had higher mean plasma level of total cholesterol with standard deviation 192.84±52.43mg/dl while that of mean and standard deviation of natural menopause 192.26±27.56mg/dl i.e. Mean difference was statistically insignificant ($p>0.05$). Mean plasma levels of Triglyceride (TG) with standard deviation (215.87±67.73mg/dl) higher in surgical menopause as compared with natural menopause (147.33±65.17mg/dl) which was statistically significant ($p<0.001$). There was significant rise of mean with standard deviation of HDL cholesterol in natural menopause was (44.42±8.14mg/dl) as compared to surgical menopause (34.61±8.55mg/dl) and the mean difference was statistically highly significant ($p<0.001$). Mean with standard deviation of plasma LDL cholesterol (122.02±49.16mg/dl) rise in surgical menopause as compared to physiological menopause (118.06±20.56mg/dl) and was statistically insignificant ($p>0.05$). Serum total cholesterol, serum triglyceride (TG) and serum low density lipoprotein (LDL) was found significant higher level in surgical menopause. And only serum high density lipoprotein (HDL) was found significantly higher level in physiological menopause. So, surgical menopausal women were marked dyslipidaemia.