# Selección de Resúmenes de Menopausia

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## Association of menopausal hormone therapy with risk of cardiovascular disease in Korean women

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Objective: To evaluate the association between various regimens and combinations of menopausal hormone therapy (MHT) and the risk of cardiovascular disease (CVD) in clinical practice. Design: This was a population-based cohort study. Methods: This population-based cohort study used data from the Health Insurance Review and Assessment Service. The data of women who reported entering menopause at ≥40 years of age with no history of CVD in the national health examination between 2011 and 2014 were extracted. A total of 134 298 pairs were included in the MHT and non-MHT groups after 1:1 propensity score matching. The participants were followed until December, 31, 2020. Results: During a median follow-up of 7.9 (IQR 6.9-8.9) years, the incidences of CVD were 146 per 100 000 person/year and 179 per 100 000 person/year for the non-MHT and MHT groups, respectively. After adjusting for covariates, MHT use was associated with an increased CVD risk (hazard ratio [HR], 1.22 [1.14-1.31]) compared with the non-MHT group; the risk was based on an increased risk of stroke and coronary artery revascularization. Tibolone (HR, 1.38, [1.27-1.50]) was associated with increased CVD, but estrogen alone or combined estrogen/progestogen was not. There was no difference in CVD risk, regardless of the type of estrogen agent used. For combined estrogen/progestogen therapy, dydrogesterone was associated with reduced CVD risk. Conclusions: There was an increased risk of CVD in MHT users. By regimen, tibolone use was associated with increased risk of CVD, whereas estrogen either alone or in combination with progestogen was not. There was no difference according to the type of estrogen. The type of progestogen seems to modify the results, since dydrogesterone was associated with reduced CVD risk.

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## Are balance and lower extremity muscle strength correlated with fracture risk independent of bone mineral density in postmenopausal women?: A cross-sectional study

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**Background:** Postmenopausal women are at increased risk of fractures due to reduced bone mineral density (BMD) and impaired physical function. While fracture risk assessment tools like FRAX include clinical factors and BMD, they exclude functional measures such as balance and muscle strength, which are critical for fall prevention. This study aimed to evaluate the correlation between two functional tests- the 30-Second Sit to Stand Test (30STS) and the One Leg Stance Test (OLST)- and fracture risk, independent of BMD in postmenopausal women aged 50. **Methods:** This cross-sectional study included 156 postmenopausal women aged 50-70. Fracture risk was assessed using FRAX. Postural balance was evaluated using the OLST, while lower extremity muscle strength was measured with the 30STS. Both tests were analyzed for correlations with 10-year risks of major osteoporotic fractures (MOF), hip fractures, femoral neck BMD, and T-score at the lumbar spine and femoral neck. Participants were grouped based on OLST (<10 s) and 30STS (<15 repetitions) cut-offs, and fracture risks were compared. **Results:** OLST and 30STS scores were significantly negatively correlated with 10-year hip fracture risk ($r = -0.347$, $p < 0.001$ and $r = -0.197$, $p = 0.014$, respectively). A significant negative correlation was also observed between OLST scores and 10-year MOF risk ($r = -0.245$, $p = 0.002$). Participants with OLST <10 s had significantly higher 10-year hip and MOF risks, while those with 30STS <15 had significantly higher 10-year hip fracture risk only. No correlation was found with femoral neck BMD. **Conclusion:** LST and 30STS are associated with fracture risk independent of BMD in postmenopausal women aged 50-70. These practical tests may help identify individuals at higher fracture risk and support early interventions.

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## Preservation of Vascular Endothelial Function in Late-Onset Postmenopausal Women

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Background: Postmenopausal women (PMW) who complete menopause at a late age (55+ years) have lower cardiovascular disease risk than PMW who complete menopause at a normal age (45-54 years). However, the influence of late-onset menopause on vascular endothelial dysfunction is unknown. Moreover, the mechanisms by which a later age at menopause may modulate endothelial function remain to be determined. Methods: We measured endothelial function (brachial artery flow-mediated dilation [FMDBA]) in age-matched late- and normal-onset PMW and a young premenopausal reference group. We determined mitochondrial reactive oxygen species (mitoROS)-related suppression of endothelial function (change in FMDBA with an acute dose of the mitochondria-targeted antioxidant MitoQ; ΔFMDBA, MTQ) in PMW. The effects of serum from late- and normal-onset PMW and premenopausal women on mitoROS bioactivity in human aortic endothelial cells in culture were assessed. Metabolomics analyses in combination with serum metabolite level normalization and human aortic endothelial cell serum exposure experiments were performed to identify the circulating factors contributing to the serum effects on endothelial cell mitoROS bioactivity. Results: FMDBA in PMW was lower than in premenopausal women. However, FMDBA was >50% higher in late- versus normal-onset PMW and positively related to age at menopause. ΔFMDBA, MTQ was >50% lower in late- versus normal-onset PMW. Serum from normal-onset PMW but not late-onset PMW induced higher mitoROS bioactivity in human aortic endothelial cells compared with serum from premenopausal women. mitoROS bioactivity was negatively related to FMDBA and age at menopause. Seventeen metabolites significantly differed between late- and normal-onset PMW; 15 were lipid specific; 8 were triglyceride derived. TG(16:0) was most strongly correlated with mitoROS bioactivity. Normalization of TG(16:0) concentrations in serum from premenopausal women and late-onset PMW to match serum levels in normal-onset PMW abrogated differences in mitoROS bioactivity in serum-treated human aortic endothelial cells. Conclusions: Late-onset menopause is associated with preservation of endothelial function, which is mediated by lower mitoROS-associated oxidative stress. A more favorable profile of circulating lipid metabolites, specifically triglyceride-derived metabolites, contributes to lower endothelial cell mitoROS in late-onset PMW. These findings provide new insight into the possible mechanisms of reduced cardiovascular disease risk in late-onset menopause.

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## Impact of Early Menopause and Hormonal Therapy Replacement on Aortic Stenosis Progression

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Background: Early menopause has been associated with several cardiovascular diseases. Its impact on the progression of aortic stenosis (AS) remains unknown. We conducted an analysis to examine the impact of early menopause without hormonal replacement therapy (HRT) on the progression of AS in postmenopausal women with AS. Methods: This sub-analysis included 33 female patients with at least mild AS (mean age 65±10) prospectively enrolled in the PROGRESSA study (NCT01679431). Anatomical assessment of AS was performed by multidetector computed tomography, while hemodynamic assessment of AS was performed by Doppler-echocardiography. Results: Over a median follow-up of 2[1-4] years, early menopausal women without HRT showed faster progression of aortic valve calcification (AVC) (100[58-130] vs. 23[2-71] AU/year, p=0.03, mean pressure gradient (MG) 2.37[0.82-3.61] vs. 0.33[0.01-1.78] mmHg/year, p=0.04, and aortic valve area indexed to body surface area (AVAi) (-0.12[-0.23;0.002] vs. -0.004[-0.07;0.08] cm2/m2/year, p=0.07). In multivariate analysis adjusted for several clinical, echocardiographic and anatomic factors, early menopause without HRT remained independently associated with faster AVC progression (p=0.003). Women who received HRT showed a slower progression of AVC compared with those who never received HRT (62[2-100] vs. (20[10-42] AU/year, p=0.13). Multivariate analysis also showed that AVC progressed less rapidly in women who received HRT (p=0.04). Conclusion: In this study of post-menopausal women with AS, early menopause without HRT was associated with faster progression of AS, both anatomically and hemodynamically. However, the use of HRT was associated with slower progression of AS.