

MENOPAUSAL AGE, ENDOTHELIAL FUNCTION AND CARDIOVASCULAR RISK

S. Mulvagh¹, T. Behrenbeck¹, B. Lahr¹, T. Zais¹, V.M. Miller¹

¹Mayo Clinic, Rochester, MN, USA

Objective: Cardiovascular disease progresses on a continuum throughout life and increases in women at menopause. Therefore, timing of interventions, such as for hormonal therapy, may be critical in order to slow disease progression. Peripheral flow-mediated reactive hyperemia (PRH) is accepted as a marker of endothelial dysfunction and an indicator of early disease processes. This study tested the hypothesis that endothelial dysfunction would increase with time past menopause.

Design and Method: A subset of asymptomatic women enrolled in KEEPS (Kronos Early Estrogen Prevention Study, a clinical trial of hormone therapy on cardiovascular disease in early (<3 year) menopause, were evaluated prior to randomization to treatment for conventional risk factors as well as CIMT by ultrasound, CAC by electron beam computed tomography, and PRH by ENDOPAT[®]

Results: One hundred and three women participated. All were Caucasian and none were diabetic. Four women were current smokers, 26 past smokers and 73 never smokers. Fourteen women had positive CAC scores (range 0.5-133) and two women had CIMT lesions >40%. There was no difference in conventional risk factor profiles between women with positive CAC and CIMT scores compared to those without. Total cholesterol and LDL were positively correlated with time past menopause; these values did not correlate with PHR. PHR did not correlate with time past menopause. However, PHR was inconclusive or abnormal in 40% of the entire cohort and in 45% of women within 12 months of menopause. These women could not be distinguished using conventional risk factors (see Table).

Conclusions: 1) Fifteen percent of women in this fairly low risk group exhibited quantifiable vascular lesions. 2) In a subset of women without lesions and in whom standard assessment algorithms did not detect risk, endothelial dysfunction was present within the first 12 months of menopause. PRH may provide an additional reference point to assess early disease processes in some menopausal women and possibly identify those for whom hormonal therapy may be beneficial.



| Menopausal age (months) | Chronological age (years) | PRH Score (n) | BMI (Kg/m ²) | Total cholesterol (mg/dL) | LDL (mg/dL) | Systolic blood pressure (mmHg) |
|-------------------------|---------------------------|--------------------------|--------------------------|---------------------------|-------------|--------------------------------|
| | | <u>Abnormal</u> < 2.1 | | | | |
| 6-12 | 52.4±2.5 | 1.8±0.2 (n=22) | 28.2± 5.2 | 210.4±30.1 | 137.0±27.4 | 122.9±13.4 |
| 13-24 | 53.1±1.8 | 1.7±0.3 (n=12) | 26.0±3.6 | 223.3±38.6 | 138.8±30.6 | 121.5±13.7 |
| 25-36 | 53.7±2.1 | 1.8±0.2 (n=7) | 30.6±1.9 | 244.6±38.5 | 160.3±38.8 | 125.8±14.2 |
| | | <u>Normal</u> >2.1 | | | | |
| 6-12 | 52.2±2.4 | 2.7±0.3 (n=27) | 26.0± 3.9 | 215.6±35.3 | 120.3±30.6 | 118.9±13.1 |
| 13-24 | 53.5±2.2 | 2.9±0.7 (n=24) | 27.6±4.1 | 218.7±27.1 | 139.0±27.1 | 127.4±13.8 |
| 25-36 | 53.9±2.2 | 2.8±0.3 (n=11) | 26.6±4.6 | 225.3±27.3 | 141.3±24.6 | 120.8±16.7 |