EFFECTS OF POSTMENOPAUSAL HORMONE THERAPY ON INCIDENT ATRIAL FIBRILLATION: THE WOMEN'S HEALTH INITIATIVE RANDOMIZED CONTROLLED TRIALS

ACC Moderated Poster Contributions
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Session Title: Arrhythmias: AF/SVT- Emerging Risk Factors for Atrial Fibrillation
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Background: Atrial fibrillation (AF) is less prevalent in women than in men, but is associated with a higher risk of stroke and death in women. The effects of postmenopausal hormone therapy on AF have not been well characterized.

Methods: The Women’s Health Initiative (WHI) randomized postmenopausal women aged 50-79 to either placebo or conjugated equine estrogens (CEE; 0.625 mg/d) plus medroxyprogesterone acetate (MPA; 2.5 mg/d) if they had a uterus (N=16,608) or to placebo or CEE only if they had a prior hysterectomy (N=10,739). WHI data were linked with Center for Medicare and Medicaid Services (CMS) Medicare data. Nearly 97% of Medicare-eligible WHI participants were successfully linked, allowing for a more complete ascertainment of AF than was previously possible in WHI. In both the estrogen plus progestin (E+P) and estrogen alone (E-alone) trials, incident cases of AF were identified by electrocardiograms and diagnosis codes from Medicare claims or hospitalization records. The hazards of developing AF were estimated using Cox proportional hazards regression models.

Results: After excluding 968 participants with AF at baseline, there were 611 incident AF cases over a mean 5.6 year follow-up among 16,128 E+P trial participants, and 683 cases over a mean 7.1 year follow-up among 10,251 E-alone participants. Incident AF did not differ between active CEE + MPA versus placebo (HR 1.07, 95% CI 0.91-1.25), whereas, CEE alone significantly increased incident AF (HR 1.17, 95% CI 1.00-1.36, p=0.045), particularly among women reporting diabetes at baseline (HR 1.73, 95% CI 1.13 to 2.61). When the two trials were combined, AF incidence was increased in active versus placebo groups (HR 1.12, CI 1.00 to 1.24, p=0.05), particularly among women reporting diabetes. Adjustment for incident stroke, coronary heart disease, and heart failure attenuated these findings.

Conclusion: Postmenopausal estrogen plus progestin therapy did not increase the risk of incident AF in women with a uterus, whereas estrogen only modestly increased the risk of developing AF in women with prior hysterectomy, particularly among known diabetics, possibly mediated by incident cardiovascular disease.