1. Full Title: Variations in Blood Pressure Response to Postural Change Among Women by Menopausal Status and Hormonal Replacement Therapy Use
   b. Abbreviated Title: BP Ractivity in Women

2. Writing Group
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3. Timeline:
   Summer and Fall, 1996

4. Rationale:
   Lower rates of CHD among premenopausal women than among men and the cardioprotective effects of estrogen replacement therapy among postmenopausal women have been repeatedly noted in the epidemiologic literature (1,2). It has been hypothesized that one of the mechanisms by which estrogen favorably influences cardiovascular disease risk is through moderating the cardiovascular response to stress. There is some evidence to suggest that the physiologic processes underlying cardiovascular reactivity are influenced by estrogens (3). Several studies have also examined the association between menopausal/hormonal status and cardiovascular reactivity. One study found that postmenopausal women had significantly higher SBP and DPBP responses to mental stressors (serial subtraction, public speaking) than did premenopausal women, with differences persisting after controlling for age (4). A second study found a significant difference in SBP, but not DBP; however the greater response among postmenopausal women was limited to public speaking and not other stressors introduced in the study (5). Another group of investigators found that postmenopausal women had a significantly greater increase in both SBP and DBP in response to various stressors (public speaking, mental arithmetic, stroop color word, cold pressor) than did premenopausal women. This study was replicated several months later after treating half of the postmenopausal women with estradiol (via a dermal patch). Blood pressure reactivity was still significantly greater among the untreated, postmenopausal women than among the premenopausal women. However, among those postmenopausal women treated with the estradiol patch, the blood pressure responses to the various stressors were attenuated, no longer significantly differing from those of premenopausal women (6).
This suggests that estrogen protects against higher blood pressure reactivity in postmenopausal women.

Orthostasis (changing from the supine to standing position) is a physical stressor used as a measure of cardiovascular reactivity. An interesting characteristic of orthostasis is that it elicits a wide range of blood pressure responses. For example, in the ARIC cohort, mean change (Δ) in SBP was close to zero and mean Δ DBP was approximately +3 mmHg. However, the overall distribution was wide (range = +/- 60 mmHg) and approximately normally distributed (7). This is unique, as other measures of blood pressure reactivity are skewed in the direction of increase in blood pressure.

The ARIC study provides an opportunity to add to the existing literature on variations in blood pressure reactivity by menopausal status and HRT use. Only a few studies have been published to date and these were based on very small samples (n' of < 40). Our proposed study would provide data from a large, population-based cohort and include African-American women. Also, our measure of cardiovascular reactivity, the blood pressure response to orthostasis, will allow us to examine associations among those with a decrease as well as those with an increase in blood pressure in response to orthostatic stress, which no studies to our knowledge have investigated.

5. Main Hypothesis/Study Questions:

The main study question is:

Are there variations in blood pressure response to postural change by menopausal status/HRT use (premenopausal, postmenopausal - HRT use, postmenopausal - no HRT use)? Based on the existing literature, it is hypothesized that the blood pressure response to postural change will be greatest among postmenopausal women who do not use HRT and least among premenopausal women.

Additional Study questions include:

1. Does menopausal status/HRT use impact differently at opposite ends of the blood pressure reactivity distribution (i.e., hypo- versus hyper-reactivity)?
2. Are patterns of association attenuated after controlling for age, sitting blood pressure, and other potential covariates?
3. Do associations vary by ethnicity?
4. Do patterns of response vary by blood pressure index (SBP, DBP)?

6. Data:

The closed Visit 1 dataset will be used for all analyses. Participants will be limited to those with known menopausal and HRT status. There will be three "exposure" categories: premenopausal and HRT use, postmenopausal with current HRT use, and postmenopausal with no current HRT use. Perimenopausal women and women with unknown menopausal status will be excluded from analyses.

Δ SBP and Δ DBP will be classified both continuously and categorically. For analyses of postural change as a continuous variable, a univariate procedure will be used to display the distribution among the three menopausal/HRT status graphically, as well as to generate means, medians, and ranges. Analysis of covariance will also be used to generate age- and sitting blood pressure-adjusted means in each of the menopausal/HRT groups and to statistically test the difference between groups. Analyses will be done overall and then separately for African American and European American women (in the literature, cardiovascular reactivity in response to stressors vary by ethnicity).

Next, women will be divided into three categories based on deciles of postural change in blood pressure. This system was chosen to be consistent with earlier work done in ARIC. Those in the three lowest deciles (i.e., those with the greatest decreases in blood pressure upon standing) will be classified as "hypo-reactors,"
while those in the three highest deciles (i.e., those with the greatest increases in blood pressure upon standing) will be classified as "hyper-reactors"; those in the middle four deciles will be classified as the "no change" group. Age- and sitting blood pressure-adjusted proportions of women in each of the three postural change groups will be generated by menopausal/HRT status. Analyses will be done overall and then separately for African-American and European-American women.

References:


