Reproductive Aging: Window on general aging

Marcelle I. Cedars, M.D.
UCSF San Francisco, United States

Objectives

- assess the association between ovarian aging on long-term health
- identify women at increased risk for long-term health risk
- identify potential mechanisms underlying this relationship

Women have a 10-year lag in the onset of cardiovascular disease (CVD) compared with men. This lag has been attributed to the protective effect of endogenous estrogen. Supporting this hypothesis, early menopause is associated with increased CVD risk. But, a women’s entire reproductive history (e.g. menarcheal age, menstrual cycles, infertility, pregnancy, menopause) may pose unique risk. Women are unique in the universal loss of reproductive function at an age long before other vital systems fail. If accelerated ovarian aging is associated with long-term CVD risk, this knowledge would allow a unique opportunity to identify young at-risk women. Estimates of follicular reserve can now be assessed in women of all ages with antral follicle count (AFC), number of follicles visible by transvaginal ultrasound and anti-mullerian hormone (AMH), a biochemical marker of ovarian reserve. Disruptions in ovarian function among reproductive-age women have been related to greater CVD risk; however, studies included anovulation, lower estradiol and menstrual cycle irregularity, not assessments of ovarian reserve in estrogenized, normally cycling, women. Cycling women with elevated FSH have been shown to have unfavorable lipid levels. Cross-sectional studies indicate markers of ovarian age are associated with cardio-metabolic risk. In addition, studies of atherosclerotic plaque formation in monkeys showed a negative correlation with AMH levels and women with lower AMH appear to have increased risk for pregnancy complications such as pre-eclampsia, another risk factor for CVD.

Common underlying mechanisms of risk, such as telomere length, oxidative stress and mitochondrial DNA function, are only now being explored. This area may not only increase understanding of potential mechanisms of general aging, but also suggest new treatment strategies.