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The association of plasma androgen levels with breast, ovarian and endometrial cancer risk factors among postmenopausal women

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Although androgens may play an etiologic role in breast, ovarian and endometrial cancers, little is known about factors that influence circulating androgen levels. We conducted a cross-sectional analysis among 646 postmenopausal women in the Nurses' Health Study to examine associations between adult risk factors for cancer, including the Rosner/Colditz breast cancer risk score, and plasma levels of testosterone, free testosterone, androstenedione, dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEAS). All analyses were adjusted for age, laboratory batch and other cancer risk factors. Free testosterone levels were 79% higher among women with a body mass index of ≥30 *vs.* <22 kg/m^2 (p-trend <0.01) and 25% higher among women with a waist circumference of >89 *vs.* ≤74 cm (p-trend = 0.02). Consuming >30 g of alcohol a day *vs.* none was associated with a 31% increase in DHEA and 59% increase in DHEAS levels (p-trend = 0.01 and <0.01, respectively). Smokers of ≥25 cigarettes per day had 35% higher androstenedione and 44% higher testosterone levels than never smokers (p-value, F-test = 0.03 and 0.01, respectively). No significant associations were observed for height or time since menopause with any androgen. Testosterone and free testosterone levels were ~30% lower among women with a hysterectomy *vs.* without (both p-values < 0.01). Overall breast cancer risk was not associated with any of the androgens. Thus, several risk factors, including body size, alcohol intake, smoking and hysterectomy, were related to androgen levels among postmenopausal women, while others, including height and time since menopause, were not. Future studies are needed to clarify further which lifestyle factors modulate androgen levels.

Sex steroid hormones play a key role in the development of breast, ovarian and endometrial cancers.[1–4] As associations with estrogens have been increasingly well-delineated, more attention has focused on androgens. Prospective studies have linked circulating androgen levels to the risk of postmenopausal breast cancer.[5–8] Excessive androgen levels also have been proposed as a causal mechanism in the pathogenesis of ovarian cancer, given the relatively high levels of circulating androgens compared with estrogens, presence of androgen receptors in normal ovarian epithelial cells, and animal data suggesting that testosterone may increase ovarian tumor growth.[9] Epidemiologic data have been conflicting but provide some support for an association between androgens and ovarian cancer risk.[10–13] Similarly, 2 prospective studies on endometrial cancer have produced discrepant results regarding associations with androgen levels.[14,15] Androgens have been hypothesized to increase endometrial cancer risk, likely through the aromatization of androgens into estrogens,[16] but alternatively might decrease risk by decreasing the proliferative effects of estrogens in the endometrium.[17,18]

Although androgens may be important in disease etiology, relatively little is known about nongenetic determinants of circulating levels among postmenopausal women. To assess whether factors associated with breast, ovarian and endometrial cancers might influence cancer risk by altering androgen levels, we examined associations between several adult risk factors for cancer and plasma levels of testosterone, free testosterone, androstenedione, dehydroepiandrosterone (DHEA)

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