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Original article

Reproductive factors and ovarian cancer risk in African-American women

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ABSTRACT

Purpose: Reproductive characteristics, the most established ovarian cancer risk factors, differ markedly between African-American and white women. Studies in predominantly white populations suggest that associations between reproductive characteristics and ovarian cancer vary by timing of the events and menopause status. This analysis examined associations between number, duration, and timing of reproductive events and epithelial ovarian cancer among African-American women.
Methods: Data from a multicenter case-control study of ovarian cancer in African-American women (641 cases/752 controls) were used to examine associations with oral contraceptive (OC) use and pregnancy characteristics. Odds ratios (ORs) and 95% confidence intervals (CIs) associated with reproductive characteristics were calculated with logistic regression models.
Results: OC use (OR = 0.7, 95% CI 0.5–0.9), parity (OR = 0.5, 95% CI 0.3–0.6), and breastfeeding for >12 months (OR = 0.3, 95% CI 0.2–0.5) were inversely associated with ovarian cancer. More recent pregnancies and OC use had stronger associations with ovarian cancer than pregnancies or OC use that occurred earlier in life, especially among premenopausal women.
Conclusions: This study provides the first thorough documentation that pregnancy, breastfeeding, and OC use are inversely associated with ovarian cancer in African-American women, similar to what has been observed in white women. The associations with timing of the exposures suggest that these factors have both short- and long-term effects.

Introduction

Epithelial ovarian cancer has a median age of diagnosis of approximately 63 years [1]. Despite being a disease that is more frequently diagnosed among postmenopausal women, the factors that most influence ovarian cancer risk are reproductive characteristics such as pregnancy, oral contraceptive (OC) use, and breastfeeding that typically occur when a woman is in her 20s or 30s [2]. Analyses conducted within predominantly white populations suggest that the associations between reproductive characteristics and ovarian cancer depend on the timing of the exposure and may differ for ovarian cancer diagnosed before and after menopause [3–12]. Most notably, the inverse association with pregnancy seems to be stronger for premenopausal women, which

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may be due to the effect of time since last pregnancy [3,4,6,8,12]. More recent pregnancies have been associated with a greater reduction in ovarian cancer risk that appears to be independent of the total number of pregnancies. These findings suggest that reproductive risk factors may operate through multiple biological pathways that may have both short- and long-term effects on ovarian cancer risk.

African-American women differ markedly from white women in their incidence of ovarian cancer (9.8/100,000 and 12.8/100,000 in African-Americans and whites, respectively) [1] and in many of their reproductive characteristics. On average, African-American women experience more total pregnancies [13], an earlier age at first pregnancy [13], less breastfeeding [14], and less OC use [15]. There are only a few published reports describing the association between reproductive characteristics and ovarian cancer risk in African-American women, and all have had very modest sample sizes [16–19]. Although these studies have reported inverse associations with pregnancy and OC use similar to what has been reported in white women, none of them has presented results stratified by menopausal status, and all were limited in their ability to examine effects by duration, number, or timing of the reproductive events.

The purpose of this report is to describe associations between ovarian cancer and the reproductive characteristics of OC use, parity, and breastfeeding stratified by menopausal status, using data from a multicenter, case-control study of ovarian cancer in African-American women. We present overall associations with ovarian cancer risk and examine the effect of the number of pregnancies, the duration of exposure to OCs, and timing of the exposures.

Methods

The data used in these analyses are from the African American Cancer Epidemiology Study (AACES), a population-based, case-control study of ovarian cancer in African-American women in 11 geographic regions: North Carolina, South Carolina, Georgia, Alabama, Tennessee, Louisiana, Texas, New Jersey, Ohio, Chicago, and Detroit. Duke University is the lead institution for the study. Institutional review board approval was obtained from the Duke University School of Medicine and all participating institutions. The methods of the study have been previously reported [20] and are described here briefly.

Women with ovarian cancer were identified using rapid case ascertainment systems through state cancer registries, Surveillance, Epidemiology and End Results registries or individual hospital registries. Inclusion criteria were self-identified African-American/black race, aged 20–79 years, diagnosis of invasive, epithelial ovarian cancer, no prior history of ovarian cancer, and ability to complete an interview in English. Of 1546 eligible cases identified, physician consent was not obtained for 1% of the women, 17% died before they could be contacted, 16% could not be contacted, 23% refused to participate, and 42% were enrolled in the study. Controls were selected using random digit dialing, frequency matched to cases on age and geographic region. Eligibility criteria were similar to cases plus they must not have had bilateral oophorectomy or a prior history of ovarian cancer. Of 1450 eligible controls identified, 0.2% died, 24% could not be contacted for an interview, 24% refused to participate, and 52% were enrolled in the study. The current analyses are based on women enrolled from December 2010 through January 2016 and include 641 cases and 752 controls.

Data were collected via an interviewer-administered computer-assisted telephone interview. Survey information included demographic characteristics; reproductive, gynecologic, and medical history; hormone use; family history of cancer; and lifestyle characteristics such as smoking, alcohol consumption, and physical activity. For the pregnancy characteristics, women provided detailed information on each pregnancy including outcome, duration, date pregnancy ended, and breastfeeding information. A full-term pregnancy for the purposes of these analyses was defined as one lasting more than 6 months. OC information was based on a detailed lifetime contraceptive history of the type and timing of each method used.

Menopausal status was based on self-reported menstrual history. Women were categorized as postmenopausal if their menstrual periods had stopped naturally 12 or more months before diagnosis/interview or their periods stopped due to chemotherapy or radiation. Women who had started menopausal hormones before their periods stopped and had been taking them for at least 2 years or thought that they began menopause at least 4 years before diagnosis or interview were categorized as postmenopausal. Women who had a premenopausal hysterectomy without bilateral oophorectomy were considered postmenopausal if they were aged 50 years or older at diagnosis/interview or, if they were aged younger than 50 years, at least 4 years had passed since they thought they began menopause.

Demographic and other descriptive characteristics of cases and controls were compared using the chi-square test. Unconditional logistic regression analyses were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for parameters related to OC use and pregnancy history. Variables included as potential confounders included study site, age (continuous), family history of breast or ovarian cancer in a first degree relative (yes/no), age at menarche (continuous), tubal ligation (yes/no), and body mass index (in kg/m^2, continuous). Analyses that simultaneously examined the timing of exposure and duration of OC use or timing and number of pregnancies were restricted to ever users of OCs and parous women, respectively. To perform tests for trend, categories of the variables were coded as continuous variables. Tests for interaction were conducted by including in the model a product term for menopausal status and the individual reproductive exposure variable. All analyses were conducted using SAS version 9.3 software.

Results

Descriptive characteristics of cases and controls stratified by menopausal status are presented in Table 1. For most characteristics, the direction of the associations were similar for premenopausal and postmenopausal women, although the magnitude of the differences between cases and controls varied between premenopausal and postmenopausal cases for several characteristics including family history of cancer, and infertility, which had stronger associations in premenopausal women. A notable exception was that postmenopausal cases had higher body mass index than controls, which was not the case in premenopausal women.

Table 2 presents associations between patterns of OC use and ovarian cancer for all women and stratified by menopausal status. The point estimate for ever use of OCs was 0.7 (95% CI 0.5–0.9) for all women and was similar for premenopausal and postmenopausal women, with ORs of 0.6 (95% CI 0.4–1.2) and 0.7 (95% CI 0.5–0.9), respectively, although the association was statistically significant only among the postmenopausal women. Compared with premenopausal women, we observed among postmenopausal women that increasing duration of OC use was associated with greater reductions in ovarian cancer risk, test for trend $P = .005$. Differences in associations by menopausal status were observed in relation to the timing of OC use. Among premenopausal women, the data suggested that more recent use was associated with greater reduction