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Risk factors for estrogen receptor positive ductal carcinoma in situ of the breast in African American women

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ABSTRACT

Background: Compared to U.S. white women, African American women are more likely to die from ductal carcinoma in situ (DCIS). Elucidation of risk factors for DCIS in African American women may provide opportunities for risk reduction.

Methods: We used data from three epidemiologic studies in the African American Breast Cancer Epidemiology and Risk Consortium to study risk factors for estrogen receptor (ER) positive DCIS (488 cases; 13,830 controls). Results were compared to associations observed for ER+ invasive breast cancer (n = 2,099).

Results: First degree family history of breast cancer was associated with increased risk of ER+ DCIS [odds ratio (OR): 1.69, 95% confidence interval (CI): 1.31, 2.17]. Oral contraceptive use within the past 10 years (vs. never) was also associated with increased risk (OR: 1.43, 95%CI: 1.03, 1.97), as was late age at first birth (≥25 years vs. <20 years) (OR: 1.26, 95%CI: 0.96, 1.67). Risk was reduced in women with older age at menarche (≥15 years vs. <11 years) (OR: 0.62, 95%CI: 0.42, 0.93) and higher body mass index (BMI) in early adulthood (≥25 vs. <20 kg/m^2 at age 18 or 21) (OR: 0.75, 95%CI: 0.55, 1.01). There was a positive association of recent BMI with risk in postmenopausal women only. In general, associations of risk factors for ER+ DCIS were similar in magnitude and direction to those for invasive ER+ breast cancer.

Conclusions: Our findings suggest that most risk factors for invasive ER+ breast cancer are also associated with increased risk of ER+ DCIS among African American women.

1. Introduction

Ductal carcinoma in situ (DCIS) comprises more than 20% of all new breast cancer diagnoses, with about 62,930 new cases expected to be diagnosed in the U.S. in 2019 [1]. The clinical significance of a DCIS diagnosis, however, remains uncertain. Women who have had DCIS have an increased risk of both ipsilateral and contralateral invasive recurrence [2–4], and a recent meta-analysis further showed that African American (AA) women treated for DCIS had a significantly higher risk of invasive recurrence than white women [5]. Some DCIS cases are thought to be precursors of invasive breast cancer [6–9], given estimates that up to 50% of low-grade in situ breast cancers will ultimately progress to invasive cancer if left untreated [10–13]. Yet, most women in Western countries undergo treatment for DCIS and removal of these so-called precursor lesions has not resulted in decreased overall invasive breast cancer rates [14,15]. For these reasons, it has been suggested that invasive breast cancer may sometimes arise independently from DCIS [16–18].

Among women who are treated with mastectomy or breast conserving surgery (with or without radiation), mortality from DCIS is very low (approximately 2–5%) [4,19,20]. However, based on data from the U.S. Surveillance, Epidemiology, and End Results (SEER) Program, Narod et al. reported that AA women diagnosed with DCIS were more than twice as likely to die from breast cancer as U.S. white women with DCIS (7.0% vs. 3.0%) and most women who died had not experienced an invasive recurrence prior to death

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[4]; the risk ratio was unchanged with adjustment for surgery and/or radiation, suggesting that survival differences by race cannot be attributed to differences in treatment. A possible alternative explanation for these findings is that some DCIS tumors are inherently aggressive. It is well established that, relative to white women, AA women have a disproportionately high incidence of aggressive invasive breast cancer subtypes [21–23], and higher mortality from breast cancer [24]. Racial differences in the natural history of breast tumors could account for observed differences in survival after DCIS diagnosis between AA and white women. In support of this hypothesis, simulation models suggest that invasive breast tumors in AA women grow faster and metastasize earlier than those in white women [25].

Evaluation of risk factors for DCIS can inform our understanding of breast carcinogenesis. Previous studies, mostly in women of European ancestry, have shown that in situ and invasive breast cancer share some risk factors, including family history and reproductive factors such as younger age at menarche, higher parity, and older age at first birth [26–31]. However, only limited data are available from AA women. The objective of this analysis was to assess the relation of reproductive, anthropometric, and other factors to risk of ER+ DCIS in AA women.

2. Methods

2.1. Study population

We pooled data from three epidemiological studies participating in the African American Breast Cancer Epidemiology and Risk (AMBER) Consortium [32] – the Black Women's Health Study (BWHS) [33], the Carolina Breast Cancer Study (CBCS) [34], and the Women's Circle of Health Study (WCHS) [35]. Briefly, the prospective BWHS began in 1995 when 59,000 AA women ages 21–69 years (median age, 38 years) in the U.S. were enrolled. On biennial mailed and online questionnaires, participants provided information on demographic, anthropometric, reproductive, and lifestyle factors as well as incident cancer and other diseases. For the purposes of AMBER, a nested case-control study was established, which included incident breast cancer cases and up to four controls per case, frequency-matched to cases on five-year age category and most recent questionnaire completed prior to case diagnosis. CBCS and WCHS are case-control studies. Case ascertainment is described below. Control subjects in CBCS were identified from Division of Motor Vehicle lists (age <65 years) and Health Care Financing Administration lists (age ≥ 65 years). Control subjects in WCHS were identified through random digit dialing of residential telephone and cell phone numbers and through churches and community organizations [36]. For this analysis, data from the CBCS include AA breast cancer cases and controls aged 20–74 recruited in North Carolina between 1996 and 2001; data from WCHS include AA breast cancer cases and controls aged 20–75 years recruited in New York and New Jersey (2002–2013). Research protocols for each study were approved by the Institutional Review Board at the respective institutions.

2.2. Case ascertainment

Incident cases of invasive breast cancer in the BWHS were ascertained through self-report on biennial follow-up questionnaires (95% of cases) or identified through death records or linkage to 24 cancer registries in states covering 95% of participants (5% of cases) and confirmed by review of medical records, pathology reports, and cancer registry records. Data on tumor characteristics were also abstracted. In CBCS, breast cancer cases were identified by rapid case ascertainment through the North Carolina Central Cancer Registry. In WCHS, cases were identified through New York hospitals with large enrollments of AA women and by rapid case ascertainment conducted by the New Jersey State Cancer Registry. Pathology data from hospital records or cancer registries were used to classify cancers according to ER status for both case-control studies.

We restricted analyses to ER+ tumors because there were too few cases of ER- DCIS for meaningful analysis (n = 81). In total, this analysis includes 488 confirmed ER+ DCIS cases (86% of tumors with known ER status, n = 569) (median age at diagnosis, 54 years) and 13,830 controls (Table 1). We also compared results to associations observed for invasive ER+ breast cancer (n = 2,009; median age at diagnosis, 54 years). The majority of invasive ER+ tumors (82%) were of ductal histology.

2.3. Risk factor assessment

CBCS and WCHS both employed in-home interviews to collect risk factor information, including family history of breast cancer, anthropometric data, reproductive factors, and lifestyle factors. BWHS participants self-reported all exposure information via questionnaires. Self-reports of weight and adult height were significantly correlated with technician measurements in validation studies (correlation coefficients ≥0.97 and ≥ 0.92 for weight and height, respectively) [37–39]. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. For CBCS and WCHS, recent BMI was based on weight and height recalled one year before diagnosis or interview; for BWHS, BMI and all other time-varying exposures are based on information from the most recent questionnaire completed before the diagnosis date (or index date for controls). Early adult weight was reported for age 18 in the BWHS and CBCS and for age 20 for WCHS. Questionnaire and interview data from each study were harmonized by the AMBER Biostatistics and Data Management core [32].

2.4. Statistical analyses

Multivariable logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for risk of ER+ DCIS associated with family history of breast cancer, reproductive factors, and lifestyle factors, adjusted for matching factors (age, study, geographic region, and questionnaire time period), menopausal status, and use of postmenopausal hormones. Models for BMI were stratified by menopausal status. Analyses were repeated for invasive ER+ breast cancer. Data on mode of detection was not available in AMBER; therefore, in sensitivity analyses, we restricted analyses to women eligible for routine screening based on age (ages 40–74), because most DCIS are detected by mammography, whereas invasive breast cancers may be

Table 1
Cases and controls by contributing study and age.

Study	ER+ DCIS	ER+ Invasive	Controls
BWHS	250 (51.2%)	1016 (48.4%)	11,771 (85.1%)
CBCS	52 (10.7%)	353 (16.8%)	788 (5.7%)
WCHS	186 (38.1%)	730 (34.8%)	1271 (9.2%)
Age			
<40	25 (5.1%)	177 (8.4%)	1579 (11.4%)
40–49	132 (27.0%)	575 (27.4%)	4271 (30.9%)
50–59	160 (32.8%)	646 (30.8%)	4359 (31.5%)
60–69	117 (24.0%)	507 (24.2%)	2623 (19.0%)
≥70	54 (11.1%)	194 (9.2%)	998 (7.2%)
Total	488	2099	13,830

symptomatic [40,41]. We also stratified analyses by age (<50 vs. ≥50 years). All analyses were performed using SAS 9.4 (Cary, North Carolina).

3. Results

First-degree family history of breast cancer, earlier age at menarche, recent use of oral contraceptives (OCs), lower BMI at age 18 or 20, later age at first birth and postmenopausal obesity were risk factors for ER+ DCIS (Table 2). Specifically, a positive family history of breast cancer was associated with increased risk of ER+ DCIS (OR: 1.69; 95% CI: 1.31, 2.17). Age at menarche of ≥15 years was associated with reduced risk compared to age at menarche of ≤11 years (OR: 0.62; 95% CI: 0.42, 0.93). Women who used OCs within the last 10 years had approximately 40% increased risk of ER+ DCIS compared to those who never used OCs or used OCs for less than 1 year (OR: 1.43; 95% CI: 1.03, 1.97). The OR for duration of OC use ≥10 years vs. never use was 1.21 (95% CI: 0.91, 1.59). BMI at age 18 or 20 of ≥25 vs. <20 kg/m^2 was associated with 25% reduced risk of ER+ DCIS (OR: 0.75; 95% CI: 0.55, 1.01). The OR for ≥3 births vs. 1 birth was 0.86 (95% CI: 0.65, 1.15). Among parous women, age at first birth ≥25 vs. <20 years was associated with increased risk of ER+ DCIS (OR: 1.26; 95% CI: 0.96, 1.69). These associations were generally consistent in direction and magnitude for invasive cancer. Breastfeeding and years since last birth were not associated with either ER+ DCIS or invasive breast cancer (Table 2).

Among premenopausal women, there was no association for waist-to-hip ratio or recent BMI. Postmenopausal women with recent BMI ≥35 kg/m^2 were at increased risk of ER+ DCIS compared to women with BMI <25 kg/m^2 (OR: 1.64; 95% CI: 1.06, 2.53); a weaker association was observed for ER + invasive breast cancer (OR: 1.22; 95% CI: 0.97, 1.54) (Table 2). Among postmenopausal women who reported never using estrogen plus progestin, obesity was more strongly associated with ER+ DCIS (corresponding OR: 2.10; 95% CI: 1.14, 3.88) compared to invasive breast cancer (OR: 1.32; 95% CI: 0.97, 1.79). Current alcohol consumption was positively associated with risk of ER+ DCIS (OR for 1–6 drinks/week vs. 0-<1 drink/week: 1.37; 95% CI: 1.07, 1.86; OR for current ≥ 7 drinks/week vs. 0-<1 drink/week: 1.23; 95% CI: 0.82, 1.86) but not with invasive breast cancer (corresponding ORs: 0.94; 95% CI: 0.82, 1.39 and 1.12; 95% CI: 0.90, 1.39) (Table 2).

Results were similar in analyses restricted to women eligible for mammography screening based on age (i.e., ages 40–74) (data not shown). In age-stratified analyses, some risk factors, including family history of breast cancer, recent and long-term OC use, and older age at first birth, were more strongly associated with ER+ DCIS arising in women <50 years of age than those 50 or older; an exception was younger age at menarche, which was more strongly associated with DCIS among older women (Table 3).

4. Discussion

In general, associations of risk factors for ER+ DCIS were similar in magnitude and direction to those for ER+ invasive breast cancer in AA women. These risk factors included family history of breast cancer, earlier age at menarche, recent use of OCs, low BMI in early adulthood, lower parity, later age at first birth, and postmenopausal obesity.

Several findings from this study are consistent with previous literature in mostly white populations. Family history of breast cancer in a first-degree relative has been consistently associated with both invasive breast cancer and DCIS [6,18,26,27,29,31,41–47]; our results are in line with these findings. In contrast to an established association with invasive cancer, most prior studies of DCIS have not shown associations with age at menarche [6,18,26,29–31,41–44,48,49], including previous analyses of AA and white women within the CBCS (n = 108) [41,48]. Five published studies reported earlier age at menarche to be a risk factor for both in situ and invasive breast cancer [31,42,46,47,50]; the current results in AA women are in accord with these reports. We also found that use of OCs within the previous 10 years was associated with increased risk of ER+ DCIS. In a study based on 1,417 DCIS cases, Nichols et al. reported a small increase in risk associated with ever use of OCs (OR: 1.15; 95% CI: 1.01, 1.31), but no clear trends in time since last use [47]. Other studies generally considered ever vs. never use of OCs, and most reported no significant associations [26,30,41,44,48]. In contrast, Trentham-Dietz et al. noted a suggestive positive association for ever vs. never use of OCs with in situ breast cancer (n = 301) (OR: 1.24; 95% CI: 0.91, 1.68), which was somewhat stronger for women who used OCs for at least 5 years (OR: 1.33; 95% CI: 0.90, 1.95) [26].

Body composition measures were also examined for both DCIS and invasive cancer. Low BMI in adolescence and early adulthood is a well-established risk factor for invasive breast cancer [51–55], while postmenopausal obesity is consistently associated with increased risk of ER+ invasive breast cancer [55–59]. The results of the current analysis also support strong associations for DCIS, consistent with prior studies that reported positive associations of recent BMI with in situ breast cancer in postmenopausal women [31,42]. However, results from other studies of postmenopausal women were null [6,26,27,29,46,50,60]. With the exception of an analysis within the Million Women Study, which included 3,715 DCIS cases [29], sample sizes for these studies were generally <450, which could explain inconsistencies in findings from different studies. Four studies of younger and/or premenopausal women reported inverse associations of BMI with in situ breast cancer [42,43,50,61] as did two studies that included both pre- and postmenopausal women [41,45]; however, consistent with results of the present analysis in the AMBER Consortium, others did not report clear associations [6,27,30,46]. We also found that BMI at ages 18 or 20 was inversely associated with risk of ER+ DCIS; this finding is consistent with results from a pooled analysis of 545,740 premenopausal women from 15 prospective cohort studies which reported a strong inverse association of BMI in early adulthood (ages 18–24) with in situ breast cancer (hazard ratio per 5 kg/m^2: 0.71; 95% CI: 0.64, 0.80) [61]. Measures of central adiposity, such as waist circumference and waist-to-hip ratio have been rarely evaluated in studies of DCIS; our null finding in the BWHS is consistent with results from the Women's Health Initiative [60] and the CBCS [41].

Consistent with prior studies of both DCIS [6,26–31,42–44,47–50,62,63] and invasive breast cancer [28,64–68], later age at first birth was associated with a small increased risk of ER+ DCIS in the present study of AA women. Prior studies of DCIS have consistently reported inverse associations with number of full-term births [26,28,29,41–49,62,63]. We and others [26,28,30,41,48,49] found no apparent association of breastfeeding with risk of ER + DCIS. Finally, while the majority of studies report no association of alcohol consumption with risk of DCIS [29–31,43,44], our results concur with several reports of a positive association [26,41,46]. The lack of association with invasive breast cancer here and in a previous analysis in the CBCS [41], however, suggests that moderate alcohol consumption could be related to other factors, perhaps including screening mammography [69], rather than to the underlying disease process. In a prior analysis in AMBER, which included the BWHS, CBCS, WCHS, and the Multiethnic Cohort Study, heavy alcohol consumption (≥14 drinks/week) [70] was associated with an increased risk of invasive breast cancer, similar to studies in women of European ancestry [55].

Table 2
Breast cancer risk factors in relation to ER+ ductal carcinoma in situ (DCIS) of the breast and ER+ invasive breast cancer.

	controls	DCIS (n = 488)				Invasive (n = 2099)			
		cases	OR	95% CI		cases	OR	95% CI	
Family history of breast cancer									
No	12,508	403	1.00			1752	1.00		
Yes	1322	85	1.69	1.31	2.17	347	1.65	1.44	1.90
Age at menarche (yrs)									
<11	2954	66	1.00			241	1.00		
11-12	3234	193	0.74	0.55	0.99	906	0.95	0.81	1.12
13-14	3731	179	0.78	0.58	1.06	720	0.85	0.71	1.00
≥15	3855	47	0.62	0.42	0.93	225	0.79	0.64	0.98
Recency of oral contraceptive use									
Never or <1yr ago	6091	212	1.00			978	1.00		
≥10 yrs ago	5254	198	1.08	0.88	1.34	811	1.04	0.93	1.17
<10 yrs ago	2466	74	1.43	1.03	1.97	310	1.30	1.10	1.54
Duration of oral contraceptive use									
Never or <1 yr	6091	212	1.00			967	1.00		
1–4 yrs	3295	102	1.02	0.79	1.32	443	1.03	0.90	1.18
5–9 yrs	2365	90	1.25	0.96	1.64	345	1.11	0.96	1.29
≥10 yrs	2069	82	1.21	0.91	1.59	339	1.17	1.01	1.36
Parity									
Nulliparous	2954	93	1.05	0.74	1.49	410	1.07	0.89	1.28
1 birth	3234	119	1.00			491	1.00		
2 births	3731	133	0.91	0.70	1.19	552	0.91	0.79	1.04
≥3 births	3855	142	0.86	0.65	1.15	645	0.84	0.72	0.98
Age at first birth (yrs) [a]									
<20	3540	138	1.00			616	1.00		
20-24	3607	105	0.85	0.65	1.11	497	0.92	0.80	1.05
≥25	3517	150	1.26	0.96	1.69	558	1.10	0.95	1.28
Years since last birth[a,b]									
≥10	9276	359	1.00			1488	1.00		
<10	1256	33	1.05	0.66	1.69	177	0.92	0.73	1.15
Lactation [a]									
Never	6035	217	1.00			924	1.00		
Ever	4662	174	1.00	0.80	1.24	752	1.04	0.92	1.16
BMI at age 18 or 20 (kg/m^2)									
<20	5621	193	1.00			811	1.00		
20–24.9	5954	211	0.89	0.73	1.10	926	0.94	0.84	1.04
≥25	1957	65	0.75	0.55	1.01	290	0.76	0.65	0.89
Waist-to-hip ratio									
<0.75	3027	66	1.00			310	1.00		
0.75-0.84	5003	163	1.03	0.77	1.39	734	1.05	0.90	1.21
≥0.85	4420	227	1.17	0.87	1.58	910	1.10	0.94	1.28
Recent BMI (kg/m^2)[c]									
Premenopausal									
<25	1586	47	1.00			210	1.00		
25–29.9	1742	49	0.89	0.58	1.38	236	0.99	0.79	1.23
30–34.9	1231	44	1.09	0.68	1.75	295	1.07	0.83	1.36
≥35	1215	32	0.70	0.40	1.24	138	0.86	0.65	1.14
Postmenopausal									
<25	1332	39	1.00			183	1.00		
25–29.9	2328	80	1.06	0.71	1.59	359	1.06	0.87	1.30
30–34.9	1724	62	1.06	0.69	1.63	314	1.20	0.97	1.49
≥35	1437	78	1.64	1.06	2.53	299	1.22	0.97	1.54
Alcohol consumption (drinks)									
Never or <1/week	6571	235	1.00			1119	1.00		
1–6/week	3502	124	1.37	1.07	1.73	401	0.94	0.82	1.07
≥7/week	683	29	1.23	0.82	1.86	126	1.12	0.90	1.39
Past	3057	100	1.00	0.78	1.29	448	1.02	0.89	1.16

ER, estrogen receptor; OR, odds ratio; CI, confidence interval; BMI, body mass index ORs are adjusted for menopausal status; estrogen plus progestin use; age at menarche; recency of oral contraceptive use; family history of breast cancer; parity; age at first birth; lactation; BMI at age 18; current waist-to-hip ratio; age (5-year categories); study; geographic region; and time period.

[a] Among parous women only.

[b] Adjusted for all variables listed above, except age at first birth.

[c] Adjusted for all variables listed above, except waist-to-hip ratio and menopausal status.

Whether DCIS and invasive breast cancer represent distinct entities or two different stages of the same disease has been controversial. Previous observations of shared risk factors [26], including genetic factors [29], suggest these diagnoses have similar etiology. However, risk factor associations have not always been consistent for the two diseases. Brinton et al. [6] proposed that certain early risk factors (e.g., reproductive factors) might be more related to tumor initiation while others that operate later in life (e.g., central adiposity) might have a stronger influence on tumor promotion. Our findings of increased risk of ER+ DCIS associated with a number of earlier life reproductive factors in this study (e.g., age at menarche and age at first birth) support the hypothesis that these factors may be more related to tumor initiation; however, we did not find strong evidence in support of later life risk factors

Table 3
Breast cancer risk factors in relation to ER+ ductal carcinoma in situ (DCIS) of the breast, by age.

	Age <50 years (n = 157)				Age ≥50 years (n = 331)			
	cases	OR	95% CI		cases	OR	95% CI	
Family history of breast cancer								
No	133	1.00			270	1.00		
Yes	24	1.80	1.13	2.88	61	1.66	1.23	2.23
Age at menarche (yrs)								
<11	17	1.00			49	1.00		
11-12	65	1.06	0.61	1.86	128	0.63	0.44	0.90
13-14	60	1.10	0.62	1.95	119	0.66	0.46	0.94
≥15	14	0.95	0.45	2.01	33	0.53	0.33	0.84
Recency of oral contraceptive use								
Never or <1yr ago	46	1.00			166	1.00		
≥10 yrs ago	49	1.08	0.88	1.34	149	1.10	0.86	1.41
<10 yrs ago	62	1.54	1.01	2.37	12	1.14	0.60	2.15
Duration of oral contraceptive use								
Never or <1 yr	46	1.00			166	1.00		
1–4 yrs	35	1.04	0.66	1.66	67	1.02	0.75	1.39
5–9 yrs	32	1.25	0.77	2.02	58	1.34	0.97	1.87
≥10 yrs	43	1.63	1.34	2.56	39	1.00	0.69	1.46
Parity								
Nulliparous	44	1.62	0.86	3.03	49	0.85	0.55	1.32
1 birth	41	1.00			78	1.00		
2 births	44	1.19	0.75	1.90	89	0.85	0.61	1.17
≥3 births	28	0.94	0.54	1.66	114	0.83	0.59	1.17
Age at first birth (yrs) [a]								
<20	29	1.00			109	1.00		
20-24	22	0.90	0.50	1.61	83	0.85	0.62	1.15
≥25	62	1.87	1.08	3.22	88	1.09	0.78	1.51
Years since last birth[a,b]								
≥10 yrs	82	1.00			227	1.00		
<10 yrs	30	0.96	0.58	1.58	3	–	–	–
Lactation [a]								
Never	60	1.00			157	1.00		
Ever	50	0.71	0.47	1.10	124	1.09	0.84	1.41
BMI at age 18 or 20 (kg/m^2)								
<20	60	1.00			133	1.00		
20–24.9	65	0.83	0.57	1.19	146	0.93	0.72	1.19
≥25	29	0.82	0.51	1.33	36	0.71	0.48	1.05
Waist-to-hip ratio								
<0.75	26	1.00			40	1.00		
0.75–0.84	60	1.00	0.62	1.63	103	1.07	0.73	1.57
≥0.85	61	0.93	0.56	1.54	166	1.30	0.89	1.90
Recent BMI (kg/m^2) [c]								
<25	44	1.00			53	1.00		
25–29.9	46	0.91	0.59	1.43	100	0.97	0.68	1.38
30–34.9	34	0.93	0.57	1.54	83	1.03	0.71	1.49
≥35	31	0.75	0.42	1.32	89	1.33	0.90	1.96
Alcohol consumption (drinks)								
Never or <1/week	76	1.00			159	1.00		
1–6/week	40	1.22	0.81	1.85	84	1.50	1.11	2.02
≥7/week	13	1.56	0.82	2.96	16	1.09	0.63	1.89
Past	28	1.16	0.73	1.85	72	0.94	0.70	1.27

ER, estrogen receptor; OR, odds ratio; CI, confidence interval; BMI, body mass index ORs are adjusted for menopausal status; estrogen plus progestin use (for age ≥50 years only); age at menarche; recency of oral contraceptive use; family history of breast cancer; parity; age at first birth; lactation; BMI at age 18; current waist-to-hip ratio; age (5-year categories); study; geographic region; and time period.

[a] Among parous women only.

[b] Adjusted for all variables listed above, except age at first birth.

[c] Adjusted for all variables listed above, except waist-to-hip ratio.

associated exclusively with invasive breast cancer. Breast cancers that arise in younger women tend to be more aggressive. Therefore, earlier-onset DCIS may be more likely to share common risk factors with invasive breast cancers [30,43]. We found some evidence that certain risk factor associations were stronger for women diagnosed with DCIS before age 50, notably family history of breast cancer, recent OC use, and older age at first birth.

Some limitations of this analysis are worth considering. First, we lacked information on mode of detection of breast cancer, and symptomatic vs. screen-detected DCIS may reflect different pathways of carcinogenesis. However, the vast majority of DCIS tumors are identified through routine screening mammography [40]. Results of sensitivity analyses restricted to a screening-eligible population were similar to overall results. Second, while study investigators confirmed cases through review of pathology reports, misclassification of small invasive tumors as DCIS is possible [71]; however, upgrades from DCIS to invasive cancer by secondary pathology review are rare [72,73]. Third, we lacked information on tumor grade for DCIS. Previous studies of comedo (high-grade) and non-comedo (low/moderate grade) DCIS have generally found that associations did not differ [49,60,74]; however, others reported somewhat stronger associations of risk factors for comedo DCIS

than for non-comedo DCIS [48,63]. We lacked adequate statistical power to evaluate associations for ER− DCIS (n = 81); results may not be generalizable among subtypes of DCIS. However, restricting analyses to ER+ disease reduced the potential for length bias [75] and also minimized the impact of tumor heterogeneity in observed associations. Finally, we relied on self-report for risk factor assessment. Thus, measurement error is a possible limitation; however, the risk factors evaluated are generally reported with high accuracy and findings are unlikely to be strongly influenced by measurement error.

To the best of our knowledge, this is the first study to report associations of risk factors for DCIS separately in AA women. Given that the majority of DCIS diagnoses are screen-detected and ER+, restriction of analyses to ER+ breast cancers ensured a direct comparison of risk factors between DCIS and invasive tumors. Some previous studies, mostly based in populations of European ancestry, have suggested that specific risk factors may be more strongly associated with invasive disease than with DCIS [27,29–31,41], though others found the opposite [26–28,31]. Our findings suggest that risk factor associations for ER+ DCIS and invasive cancer in AA women are similar in magnitude and support a common etiology and pathogenesis between these tumor types. Additional research to elucidate predictors of recurrence and mortality after DCIS in this population is warranted.

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Compliance with ethical standards

Conflict of interest

The authors declare that they have no conflicts of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committees of participating studies and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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