Research Article

Cancer Prevention Research

Benign Breast Disease and the Risk of Subsequent Breast Cancer in African American Women

Michele L. Cote[1,3], Julie J. Ruterbusch[1,3], Barra Alosh[2], Sudeshna Bandyopadhyay[2], Elizabeth Kim[1], Bassam Albashiti[2], Bashar Sharaf Aldeen[3], Derek C. Radisky[4], Marlene H. Frost[5], Daniel W. Visscher[6], Lynn C. Hartmann[7], Hind Nassar Warzecha[8], and Rouba Ali-Femhi[2]

Abstract

Benign breast disease (BBD) is an established risk factor for breast cancer among Caucasian women but less is known about BBD in African American women. As African American women suffer from disproportionate mortality due to breast cancer, special focus on pathologic characteristics that may influence disease risk is warranted.

Benign breast biopsies from African American women were identified by the University Pathology Group (Detroit, MI). African American women of ages 20 to 84 years, who underwent a breast biopsy from 1997 to 2000, were eligible for the study. Subsequent breast cancers were identified through a linkage with the Detroit Surveillance Epidemiology and End Results (SEER) program. The first biopsy was reviewed by the pathologist, and lesions were classified following Dupont and Page criteria along with involution and other histologic features. Logistic regression was used to estimate the risk of developing a subsequent breast cancer with the histologic characteristics of BBD.

A total of 1,406 BBD biopsies from African American women were included in this study with a median follow-up of 10.1 years. The majority (68%) showed nonproliferative disease, 29% had proliferative disease without atypia, and 3% had proliferative disease with atypia. Subsequent incident breast cancers occurred in 55 women (3.9%). Women whose biopsies showed proliferative disease with atypia were more than threefold more likely to develop breast cancer as compared with women who had nonproliferative disease [relative risk (RR) 3.29, 95% confidence interval (CI) 1.21–8.93].

Better characterization of the risk of breast cancer among women with BBD, considering both ethnicity and detailed molecular findings, can lead to better surveillance, earlier diagnosis, and potentially improved survival. *Cancer Prev Res; 5(12); 1375–80. ©2012 AACR.*

Introduction

Breast cancer is the most common cancer diagnosed in women in the United States and the second leading cause of cancer-related deaths (1). Racial disparities exist in both incidence and survival. In particular, African American women are at significantly greater risk of developing early-onset breast cancer (<35 years at diagnosis) and have poorer survival when compared with Caucasian women (1). The survival disparity can be partially explained because of a larger proportion of African American women being diagnosed at advanced stages of disease, with hormone receptor negative tumors, and tumors that display an aggressive histology type (2). There is a need to better understand the risk factors that may be unique to the African American population and that can identify high-risk women who might benefit from closer surveillance, earlier diagnosis, and, ultimately, improved survival.

It is well established that Caucasian women with a history of benign breast disease (BBD) are at an increased risk for developing breast cancer (3–7), but less is known about the risk of breast cancer associated with BBD in African American women. Further classification of BBD show that there are distinct pathologic features associated with higher breast cancer risk. The classification system developed by Dupont and Page (8) is commonly used to examine BBD and breast cancer risk, and consists of 3 categories: nonproliferative disease, proliferative disease without atypia, and proliferative disease with atypia, with the latter being associated with the highest risk of developing breast cancer. Additional

Authors' Affiliations: Departments of [1]Oncology and [2]Pathology, Wayne State University School of Medicine; [3]Population Studies and Health Disparities Program, Karmanos Cancer Institute, Detroit, Michigan; [4]Department of Pathology, Johns Hopkins Hospital, Baltimore, Maryland; [5]Division of Biochemistry/Molecular Biology, Mayo Clinic in Jacksonville, Jacksonville, Florida; [6]Women's Cancer Program, Departments of [7]Laboratory Medicine and Pathology, and [8]Oncology, Mayo Clinic, Rochester, Minnesota

Note: Supplementary data for this article are available at Cancer Prevention Research Online (http://cancerprevres.aacrjournals.org/).

Hind Nassar Warzecha and Rouba Ali-Femhi have contributed equally to the study.

Corresponding Author: Michele L. Cote, Wayne State University School of Medicine, 4100 John R. Mailcode: MM04EP, Detroit, MI 48201. Phone: 313-578-4204; Fax: 313-578-4306; E-mail: cotem@karmanos.org

doi: 10.1158/1940-6207.CAPR-12-0175

©2012 American Association for Cancer Research.

Downloaded from http://aacrjournals.org/cancerpreventionresearch/article-pdf/5/12/1375/2250545/1375.pdf by guest on 20 July 2024

pathologic features, such as columnar alterations, sclerosing adenosis, radical scars, lobular involution, and intraductal papillomas have also been associated with breast cancer risk to varying degrees in mostly Caucasian populations (9–15).

The African American and Caucasian populations differ with respect to several established risk factors for breast cancer. African American women tend to have an increased body mass index (BMI), higher rates of obesity, higher parity, earlier age at first birth, and lower rates of breast feeding than Caucasian women (2, 12). These differences are hypothesized to affect the amount and duration of estrogen exposure, which may be linked to aggressive disease and poorer survival. It follows that risk factor differences might also play a role in the characteristics and development of BBD. The goal of this study is to determine if BBD is a similar risk factor for African American women, it will increase our understanding of how breast cancer develops in this population, and may help identify high-risk women who could benefit from increased surveillance.

Materials and Methods

After receiving the local Institutional Review Board's approval, benign breast biopsies from African American women were identified from a database maintained by the University Pathology Group (UPG; Detroit, MI). The UPG provides pathology services to 8 general or specialty hospitals in the region, including those in the center of the city: Detroit Receiving Hospital (Detroit, MI), Harper University Hospital (Detroit, MI), Hutzel Women's Hospital (Detroit, MI), Sinai Grace Hospital (Detroit, MI), and Karmanos Cancer Institute (Detroit, MI). African American women of age 20 to 84 years, who underwent a breast biopsy at one of these institutions from 1997 to 2000, were eligible for the study. Exclusion criteria included: a history of invasive or *in situ* breast carcinoma before, or within 6 months, of the BBD biopsy, unilateral or bilateral mastectomy before or at diagnosis, prior breast reduction surgery, lipoma, fat necrosis, epidermal cysts, hematoma, accessory structure, phyllodes tumor, or a lymph node biopsy with no breast tissue.

Histology review

The first biopsy, either core, excisional, or lumpectomy, with a diagnosis of BBD was reviewed by a blinded study pathologist (R. Ali-Femhi or H. Warzecha) using the original hematoxylin and eosin (H&E) slides. The study pathologist reviewed any questionable cases with the collaborating pathologist at the Mayo Clinic, Rochester, MN (D.W. Visscher), as well as a random sample of cases, with 10% of all cases receiving double review and discussion until consensus was reached. Lesions were classified on the basis of the criteria developed by Dupont and Page (8) into 3 categories: nonproliferative disease, proliferative disease without atypia, or proliferative disease with atypia. The presence or absence of the following pathologic features were also assessed for each biopsy: apocrine metaplasia, ductal hyperplasia, lobular hyperplasia, evidence of cysts, duct ectasia, fibrosis, intraductal papilloma, sclerosing adenosis, mucocele-like tumor, and columnar alteration. In addition, the degree of atrophy was classified into 3 categories: none, 1% to 74% of the sample (partial involution), and 75% or more (complete involution).

Follow-up

Information on the subsequent development of breast cancer was obtained from the Metropolitan Detroit Cancer Surveillance System (MDCSS), part of the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) program. The MDCSS is a population-based cancer registry that collects incidence and follow-up information on all cancer cases diagnosed in the metropolitan Detroit area (Macomb, Oakland, and Wayne counties). The MDCSS catchment area covers the same geographic region that the UPG serves. Name, date of birth, and social security number were used to match records between the data sources, and follow-up data were available through the end of 2009. Follow-up information was also gathered by matching case information to the UPG's database. This database houses information on all specimens sent to the UPG, and contains detailed information on pathologic findings.

Statistical analysis

The distribution of pathologic characteristics of the breast biopsies was described using percentages. Associations between the histologic characteristics of BBD and the risk of developing a subsequent breast cancer were estimated using logistic regression to calculate relative risk ratios and 95% confidence intervals (CI). Models were adjusted for age and year at biopsy and then stratified by age at biopsy (age less than 50 years vs. age 50 years and more). In addition, standardized incidence ratios (SIR) and 95% CI limits were calculated using data from the MDCSS database for African American women with breast cancer as reference, taking into account age at biopsy (in 5-year age groups) and calendar year. These analyses were completed using SAS statistical software, version 9.2 (SAS Institute Inc.).

The pathologic characteristics of BBD in our study were compared with those reported in the Mayo Clinic BBD cohort, which was originally described by Hartmann and colleagues (3). This cohort now includes 9,087 primarily Caucasian women who were diagnosed with BBD between the years 1967 and 1991 and were followed for a median duration of 18.7 years for a subsequent diagnosis of breast cancer. Differences in the distribution of age at biopsy, involution, and overall impression between these 2 cohorts were assessed by using the 2-sample test for equality of proportions with a continuity correction (prop.test function) in the R statistical package (R version 2.8.0).

Results

A total of 1,406 eligible women were included in this study. The mean age at biopsy was 48.6 years and approximately half the samples were from excisional biopsies ($N = 685$, 49%). On the basis of the rereview, 945 (68%) showed nonproliferative disease, 405 (29%) had proliferative

Downloaded from http://aacrjournals.org/cancerpreventionresearch/article-pdf/5/12/1375/2250545/1375.pdf by guest on 20 July 2024

Table 1. Clinical characteristics of benign breast biopsies among African Americans from the UPG (Detroit, MI) from 1997 to 2000

Characteristic	*N* (%)
Age at biopsy	
<40	304 (22%)
40–49	497 (35%)
50–59	321 (23%)
60–69	173 (12%)
70+	111 (8%)
Biopsy type[a]	
Excisional	685 (49%)
Core/needle	717 (51%)
Apocrine metaplasia[b]	
No	965 (69%)
Yes	439 (31%)
Ductal hyperplasia[c]	
None	964 (69%)
Atypical	18 (1%)
Mild	218 (16%)
Moderate	198 (14%)
Lobular hyperplasia	
No	1,384 (98%)
Yes	22 (2%)
Presence of cysts[d]	
No	837 (60%)
Yes	567 (40%)
Duct ectasia	
No	1,346 (96%)
Yes	60 (4%)
Fibrosis[e]	
No	526 (40%)
Yes	617 (47%)
Marked	163 (12%)
Intraductal papilloma[f]	
No	1,268 (90%)
Single	123 (9%)
Multiple	14 (1%)
Sclerosing adenosis[g]	
No	1,314 (94%)
Yes	91 (6%)
Columnar alteration[h]	
No	1,167 (83%)
Yes	222 (16%)
Atypia	15 (1%)
Mucocele-like tumor[j]	
No	1,402 (100%)
Yes	3 (0%)
Atrophy[j]	
None	248 (21%)
Partial	727 (60%)
Complete	230 (19%)

Table 1. Clinical characteristics of benign breast biopsies among African Americans from the UPG (Detroit, MI) from 1997 to 2000 (Cont'd)

Characteristic	*N* (%)
Overall impression[k]	
Nonproliferative disease	945 (68%)
Proliferative disease without atypia	405 (29%)
Proliferative disease with atypia	44 (3%)

Unknown values:
[a]4; [b]2; [c]8; [d]2; [e]100; [f]1; [g]1; [h]2; [i]1; [j]201; [k]12.

disease without atypia, and 44 (3%) had proliferative disease with atypia (Table 1). Subsequent incident breast cancers for 55 women (3.9%) were reported in the MDCSS database. The mean age at cancer diagnosis was 59.5 years, and the mean time from biopsy to breast cancer diagnosis was 6.4 years. Overall, there was approximately a 50% increase in risk for developing a subsequent breast cancer for the entire cohort compared with other African American women in the MDCSS (SIR = 1.55, 95% CI 1.14–1.99, data not shown).

Table 2 describes the association between pathologic characteristics of the benign breast biopsies and subsequent breast cancer development. Women whose biopsies were classified as having proliferative disease with atypia were more than 3 times more likely to develop a subsequent breast cancer as compared with women who had nonproliferative disease [relative risk (RR) = 3.29, 95% CI 1.21–8.93]. In addition, women with biopsies that displayed columnar alterations were associated with an increased risk for developing a subsequent breast cancer (RR = 1.84, 95% CI 0.99–3.39), although this risk was only marginally statistically significant (P = 0.05). Degree of involution was associated with a non-statistically significant reduction in risk of breast cancer (RR = 0.75, 95% CI: 0.37–1.55 for partial involution and RR = 0.84, 95% CI: 0.34–2.07 for complete involution). When stratified by age at biopsy, proliferative disease with atypia for both age groups remained elevated but was no longer statistically significant (Supplementary Table S1). Women who were less than 50 years of age at biopsy and had columnar alterations (RR = 2.26, 95% CI: 0.99–5.17) or cysts (RR = 2.22, 95% CI: 1.02–4.85) were associated with an increased risk for developing a subsequent breast cancer, whereas women of age 50 years and more were not (RR = 1.30, 95% CI: 0.51–3.32 and RR = 0.77, 95% CI: 0.34–1.72, respectively).

Compared with the women in the Mayo Clinic BBD cohort, African American women in the Detroit cohort were younger at biopsy and had less lobular involution (for the category complete involution, 19.1% in Detroit vs. 21.9% in Mayo Clinic, P = 0.03). Yet African American women had similar percentages of proliferative disease with atypia (3.2% in Detroit vs. 3.7% in Mayo Clinic, P = 0.35; Table

Downloaded from http://aacrjournals.org/cancerpreventionresearch/article-pdf/5/12/1375/2250545/1375.pdf by guest on 20 July 2024

Table 2. The association between pathologic characteristics of benign breast biopsies and subsequent breast cancer risk in African American women in Detroit, MI

	Breast cancer status			
	Negative	Positive	Relative risk[a] (95% CI)	*P* value
Apocrine metaplasia				
No	927	38	1.0 (Ref.)	
Yes	422	17	0.93 (0.52–1.67)	0.80
Ductal hyperplasia				
None	928	36	1.0 (Ref.)	
Yes	415	19	1.14 (0.64–2.01)	0.66
Lobular hyperplasia				
No	1,330	54	1.0 (Ref.)	
Yes	21	1	1.08 (0.14–8.21)	0.94
Cyst				
No	809	28	1.0 (Ref.)	
Yes	540	27	1.41 (0.82–2.42)	0.21
Duct ectasia				
No	1,294	52	1.0 (Ref.)	
Yes	57	3	1.33 (0.40–4.41)	0.64
Fibrosis				
No	505	21	1.0 (Ref.)	
Yes	749	31	0.97 (0.55–1.71)	0.91
Intraductal papilloma				
None	1,220	48	1.0 (Ref.)	
1 or more	130	7	1.26 (0.55–2.84)	0.59
Sclerosing adenosis				
No	1,266	48	1.0 (Ref.)	
Yes	84	7	2.20 (0.96–5.01)	0.06
Columnar alteration				
No	1,127	40	1.0 (Ref.)	
Yes	222	15	1.84 (0.99–3.39)	0.05
Atrophy				
None	237	11	1.0 (Ref.)	
Partial	700	27	0.75 (0.37–1.55)	0.44
Complete	218	12	0.84 (0.34–2.07)	0.71
Overall impression				
Nonproliferative disease	912	33	1.0 (Ref.)	
Proliferative disease without atypia	388	17	1.16 (0.64–2.12)	0.62
Proliferative disease with atypia	39	5	3.29 (1.21–8.93)	0.02

[a]Adjusted for age and year at biopsy.

3). The median time from BBD diagnosis to breast cancer was 6.1 years for African Americans in Detroit, less than the 10.7 years in the mostly Caucasian Mayo Clinic BBD cohort, although this may be a function of fewer years of follow-up time in Detroit versus a true biologic difference.

Discussion

We report an association between BBD and an increased risk for developing a subsequent breast cancer in African American women. Women who had proliferative disease with atypia were at the greatest risk, and the magnitude of this association is similar to those reported in primarily Caucasian populations (3, 6, 13). Biopsies showing columnar alterations were also associated with an increased risk of breast cancer, primarily among younger African American women. Although there are conflicting reports about columnar alterations as a risk factor for breast cancer, the current findings agree with results from studies done in primarily Caucasian populations (6, 10). Because columnar alterations are highly correlated with proliferative disease, it would be ideal to examine independent effects. Unfortunately, there were not enough cases in this study to stratify by the presence of atypia. Unlike other reports (3, 6, 13), we did not see an association for proliferative disease without

Downloaded from http://aacrjournals.org/cancerpreventionresearch/article-pdf/5/12/1375/2250545/1375.pdf by guest on 20 July 2024

Table 3. Comparison of BBD characteristics between the Detroit, African American cohort and the Mayo Clinic cohort

	Detroit (*N*, %)	Mayo (*N*, %)	*P* value
Age at biopsy, y			
<40	304, 21.6%	1,603, 18.3%	<0.01
40–49	497, 35.4%	2,446, 28.0%	<0.01
50–59	321, 22.8%	2,109, 24.1%	0.30
60–69	173, 12.3%	1,600, 18.3%	<0.01
70+	111, 7.9%	978, 11.2%	<0.01
Atrophy/involution[a]			
None	248, 20.6%	1,627, 18.6%	0.11
Partial	727, 60.3%	5,197, 59.5%	0.60
Complete	230, 19.1%	1,912, 21.9%	0.03
Overall impression[b]			
Nonproliferative disease	945, 67.8%	5,736, 65.7%	0.13
Proliferative disease without atypia	405, 29.1%	2,677, 30.6%	0.24
Proliferative disease with atypia	44, 3.2%	323, 3.7%	0.35

[a]Unknown for 201 Detroit cases.
[b]Unknown for 12 Detroit cases.

atypia and subsequent breast cancer risk, but this may be a function of sample size versus a true null association.

Our findings among African American women with prior benign breast biopsies and incident breast cancers suggest that results from the Mayo Clinic BBD cohort study are likely to apply to African American populations. In fact, the SIR of 1.55 identified in our cohort is nearly identical to the findings reported by Hartmann and colleagues (RR = 1.56, 95% CI: 1.45–1.68; ref. 3). These findings also support previous work by Worsham and colleagues (16, 17) that showed the association between BBD and breast cancer risk did not vary by race. African American women in our study were significantly younger when diagnosed with BBD and had less lobular involution than other reports of BBD in Caucasian populations. This is consistent with the epidemiology of breast cancer in African American women, where breast cancer is diagnosed at a younger age. Because involution is in part a function of the aging process (18), it follows that there would be a smaller degree of involution in this population as well. Despite the younger ages at the time of the biopsy, the proportion of cases with proliferative disease was very similar for both populations. This suggests that breast changes happen at an accelerated rate in African American women or are modified by other factors (e.g., BMI or parity) that we could not evaluate in this study.

The distribution of cases within the 3 Dupont and Page categories, were nearly identical between the Detroit cohort and the Mayo Clinic cohort. In comparison, the proportion of nonproliferative disease and proliferative disease without atypia between the Detroit cohort and the Henry Ford Health system cohort reported by Worsham and colleagues (16) differed (nonproliferative disease: 67.8% in the Detroit cohort vs. 38.5% in the Henry Ford cohort). The difference may be due to pathologic interpretation, which is reduced in the Detroit and Mayo Clinic cohorts because of joint training and discussion of a subset of cases. It may also be due to differences in the years included in the cohort and the indication for biopsy. The Henry Ford Health system cohort included biopsies between 1981 and 1994, whereas the Detroit cohort was from 1997 to 2000, when more needle biopsies were being conducted.

The association with breast cysts and the development of subsequent breast cancer in younger African American women may be unique to the African American population. While most published literature suggests cysts are nonproliferative lesions that are not associated with future breast cancer risk (9, 19), the report from Worsham and colleagues (17), in a racially diverse population, also showed the presence of cysts to be associated with a significant increase in breast cancer risk. This finding warrants further investigation among African American women.

Aside from lack of behavioral risk factor information, there are other limitations in this work that should be considered. The logistic regression results used women with nonproliferative disease as the reference group. Because women with nonproliferative disease are at an increased risk of breast cancer (3), the relative risks presented are likely an underestimate of the risk compared with the general population. This study is also limited by the small number of subsequent breast cancer events. A larger cohort of BBD in African American women is needed to fully examine risk stratified by age and to examine some of the less frequent pathologic categories. In addition, this study lacked breast density data, which would allow for a more detailed assessment of the independent effects of BBD.

This study does have some notable strengths, including an adequate sample size to estimate risk of breast cancer after a diagnosis of BBD in African American women. In addition,

Downloaded from http://aacrjournals.org/cancerpreventionresearch/article-pdf/5/12/1375/2250545/1375.pdf by guest on 20 July 2024

the pathologic characterization was standardized with the Mayo Clinic cohort, allowing us to compare study populations. There was standardized pathology review using up-to-date criteria, and including less described features, such as involution, and the original pathologist working with the Mayo Clinic cohort (D.W. Visscher) trained the Detroit pathologists (R. Ali-Femhi, H. Warzecha) during their residencies and has continued to provide consultation over the last decade. Finally, follow-up continues in this cohort and will be expanded to additional BBD cases.

In conclusion, we report risk estimates for African American women with benign breast biopsies showing proliferative disease with atypia and increased breast cancer risk. While these pathologic characteristics seem to result in similar risk profiles as those seen among Caucasian women, it is likely other factors vary with respect to predictive potential. For example, while the Breast Cancer Risk Assessment tool has been integrated into clinical practice, the Women's Contraceptive and Reproductive Experiences (CARE) model seems to be more appropriate for African American women. The CARE model used data from 3,283 African American women enrolled in a case–control study and race-specific SEER rates to estimate relative and population-attributable risks, and was validated using data from African American women in the Women's Health Initiative (for postmenopausal women) and the Study of Tamoxifen and Raloxifene trial (20). While the CARE model is reported to provide a better risk assessment for African American women, it underestimates the risk associated with previous breast biopsies in this population (20). Better characterization of the risk of breast cancer among women with BBD, considering both ethnicity and detailed molecular findings, can lead to better surveillance, earlier diagnosis, and ultimately, improved survival.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: M.L. Cote, B.S. Aldeen, M.H. Frost, D.W. Visscher, L.C. Hartmann, R. Ali-Femhi

Development of methodology: M.L. Cote, B.S. Aldeen, M.H. Frost, D.W. Visscher, L.C. Hartmann, R. Ali-Femhi

Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): S. Bandyopadhyay, B.S. Aldeen, H. Warzecha, D.W. Visscher, R. Ali-Femhi

Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): M.L. Cote, J.J. Ruterbusch, B.S. Aldeen, H. Warzecha, M.H. Frost, D.W. Visscher, L.C. Hartmann, R. Ali-Femhi

Writing, review, and/or revision of the manuscript: M.L. Cote, J.J. Ruterbusch, E. Kim, D.C. Radisky, M.H. Frost, D.W. Visscher, L.C. Hartmann, R. Ali-Femhi

Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): M.L. Cote, J.J. Ruterbusch, B. Alosh, B. Albashiti, B.S. Aldeen, M.H. Frost, D.W. Visscher, L.C. Hartmann, R. Ali-Femhi

Study supervision: H. Warzecha, D.W. Visscher, R. Ali-Femhi

Review of H and E slides: S. Bandyopadhyay

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received April 19, 2012; revised July 27, 2012; accepted August 23, 2012; published OnlineFirst October 19, 2012.

References

1. Howlader N, Noone AM, Krapcho M, Neyman N, Aminou R, Waldron W, et al. SEER cancer statistics review, 1975–2008. Bethesda, MD: National Cancer Institute; 2011. Available from: http://seer.cancer.gov/csr/1975_2008/≤/csr/1975_2008/≥, based on November 2010 SEER data submission.
2. Morris GJ, Mitchell EP. Higher incidence of aggressive breast cancers in African-American women: a review. J Natl Med Assoc 2008;100:698–702.
3. Hartmann LC, Sellers TA, Frost MH, Lingle WL, Degnim AC, Ghosh K, et al. Benign breast disease and the risk of breast cancer. N Engl J Med 2005;353:229–37.
4. Connolly JL, Schnitt SJ. Benign breast disease. Resolved and unresolved issues. Cancer 1993;71:1187–9.
5. Goldacre MJ, Abisgold JD, Yeates DG, Vessey MP. Benign breast disease and subsequent breast cancer: English record linkage studies. J Public Health (Oxf) 2010;32:565–71
6. Kabat GC, Jones JG, Olson N, Negassa A, Duggan C, Ginsberg M, et al. A multi-center prospective cohort study of benign breast disease and risk of subsequent breast cancer. Cancer Causes Control 2010;21:821–8.
7. Dupont WD, Parl FF, Hartmann WH, Brinton LA, Winfield AC, Worrell JA, et al. Breast cancer risk associated with proliferative breast disease and atypical hyperplasia. Cancer 1993;71:1258–65.
8. Dupont WD, Page DL. Risk factors for breast cancer in women with proliferative breast disease. N Engl J Med 1985;312:146–51.
9. Pearlman MD, Griffin JL. Benign breast disease. Obstet Gynecol 2010;116:747–58.
10. Aroner SA, Collins LC, Schnitt SJ, Connolly JL, Colditz GA, Tamimi RM. Columnar cell lesions and subsequent breast cancer risk: a nested case-control study. Breast Cancer Res 2010;12:R61.
11. Bunting DM, Steel JR, Holgate CS, Watkins RM. Long term follow-up and risk of breast cancer after a radial scar or complex sclerosing lesion has been identified in a benign open breast biopsy. Eur J Surg Oncol 2011;37:709–13.
12. Palmer JR, Boggs DA, Wise LA, Ambrosone CB, Adams-Campbell LL, Rosenberg L. Parity and lactation in relation to estrogen receptor negative breast cancer in African American women. Cancer Epidemiol Biomarkers Prev 2011;20:1883–91.
13. Marshall LM, Hunter DJ, Connolly JL, Schnitt SJ, Byrne C, London SJ, et al. Risk of breast cancer associated with atypical hyperplasia of lobular and ductal types. Cancer Epidemiol Biomarkers Prev 1997;6:297–301.
14. Radisky DC, Hartmann LC. Mammary involution and breast cancer risk: transgenic models and clinical studies. J Mammary Gland Biol Neoplasia 2009;14:181–91.
15. Milanese TR, Hartmann LC, Sellers TA, Frost MH, Vierkant RA, Maloney SD, et al. Age-related lobular involution and risk of breast cancer. J Natl Cancer Inst 2006;98:1600–7.
16. Worsham MJ, Abrams J, Raju U, Kapke A, Lu M, Cheng J, et al. Breast cancer incidence in a cohort of women with benign breast disease from a multiethnic, primary health care population. Breast J 2007;13:115–21.
17. Worsham MJ, Raju U, Lu M, Kapke A, Botttrell A, Cheng J, et al. Risk factors for breast cancer from benign breast disease in a diverse population. Breast Cancer Res Treat 2009;118:1–7.
18. Henson DE, Tarone RE. On the possible role of involution in the natural history of breast cancer. Cancer 1993;71(6 Suppl):2154–6.
19. Venta LA, Kim JP, Pelloski CE, Morrow M. Management of complex breast cysts. AJR Am J Roentgenol 1999;173:1331–6.
20. Gail MH, Costantino JP, Pee D, Bondy M, Newman L, Selvan M, et al. Projecting individualized absolute invasive breast cancer risk in African American women. J Natl Cancer Inst 2007;99:1782–92.

Downloaded from http://aacrjournals.org/cancerpreventionresearch/article-pdf/5/12/1375/2250545/1375.pdf by guest on 20 July 2024