Annals of Epidemiology 24 (2014) 376–382

Contents lists available at ScienceDirect

Annals of Epidemiology

journal homepage: www.annalsofepidemiology.org

Original article

Reproductive windows, genetic loci, and breast cancer risk

Shaneda Warren Andersen PhD [a,b,*], Amy Trentham-Dietz PhD [a,b], Ronald E. Gangnon PhD [b], John M. Hampton MS [a], Jonine D. Figueroa PhD [c], Halcyon G. Skinner PhD [b], Corinne D. Engelman PhD [b], Barbara E. Klein MD [d], Linda J. Titus PhD [e], Kathleen M. Egan ScD [f], Polly A. Newcomb PhD [a,g]

[a] University of Wisconsin Carbone Cancer Center, Madison
[b] Department of Population Health Sciences, University of Wisconsin School of Medicine and Public Health, Madison
[c] Division of Cancer Epidemiology & Genetics, National Cancer Institute, Bethesda, MD
[d] Department of Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health, Madison
[e] Norris Cotton Cancer Center, Geisel School of Medicine at Dartmouth, Lebanon, NH
[f] Division of Cancer Prevention and Control, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
[g] Cancer Prevention Program, Fred Hutchinson Cancer Research Center, Seattle, WA

ARTICLE INFO

Article history:
Received 26 September 2013
Accepted 12 February 2014
Available online 2 March 2014

Keywords:
Breast neoplasms
Epidemiology
Menarche
Menopause
Genetic loci
Histology

ABSTRACT

Purpose: The reproductive windows between age at menarche and age at first birth (standardized age at first birth) and from menarche to menopause (reproductive lifespan) may interact with genetic variants in association with breast cancer risk.

Methods: We assessed this hypothesis in 6131 breast cancer cases and 7274 controls who participated in the population-based Collaborative Breast Cancer Study. Risk factor information was collected through telephone interviews, and DNA samples were collected on a subsample (N= 1484 cases, 1307 controls) to genotype for 13 genome-wide association study-identified loci. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated, and P values for the interaction between reproductive windows and genotypes were obtained by adding cross-product terms to statistical models.

Results: For standardized age at first birth, the OR was 1.52 (CI, 1.36–1.71) comparing the highest quintile with the lowest quintile. Carrier status for rs10941679 (5p12) and rs10483813 (*RAD51B*) appeared to modify this relationship ($P = .04$ and $P = .02$, respectively). For reproductive lifespan, the OR comparing the highest quintile with the lowest quintiles was 1.62 (CI, 1.35–1.95). No interactions were detected between genotype and reproductive lifespan (all $P > .05$). All results were similar regardless of ductal versus lobular breast cancer subtype.

Conclusions: Our results suggest that the reproductive windows are associated with breast cancer risk and that associations may vary by genetic variants.

© 2014 Elsevier Inc. All rights reserved.

Introduction

Reproductive and menstrual exposures such as the age at menarche, age at first birth (AFB), and age at menopause have been consistently, but modestly, associated with breast cancer risk. The windows defined by these reproductive experiences have also been associated with risk [1–3]. Specifically, the length of time between the initiation of menarche and AFB, termed the “standardized AFB” [1] has been proposed to represent the number of ovulatory cycles a woman experiences with undifferentiated breast tissue, which is hypothesized by Russo and Russo [4] to be more susceptible to the proliferative effects of ovarian hormones.

Epidemiologic studies have produced findings consistent with this hypothesis [1,2]. In one study, postmenopausal nulliparous women and women with 15 years or more between menarche and AFB had an increased breast cancer risk when compared with women with an interval of fewer than 10 years (nulliparous relative risk = 2.0; 95% confidence interval [CI], 1.0–3.8; ≥15 years relative risk = 2.4; CI, 1.3–4.3) [1].

A second reproductive window possibly linked to breast cancer risk is defined as the “reproductive lifespan” and comprises the time between ages at menarche and natural menopause. Several studies report an association between longer reproductive lifespan and increased breast cancer risk, particularly when comparing extremes of the risk factor’s spectrum [2,3,5]. Approaches to estimate the reproductive lifespan have varied, with some investigators

Disclaimer/Conflict of Interest: The authors have no conflicts of interest to disclose.

* Corresponding author. University of Wisconsin Carbone Cancer Center, 610 Walnut St, WARF Room 307, Madison, WI 53726.
E-mail address: snandersen@uwalumni.com (S. Warren Andersen).

1047-2797/$ – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.annepidem.2014.02.007

removing anovulatory phases from the calculation of reproductive lifespan (e.g., time during pregnancy, lactation, or exogenous hormone use) [2,5] and other investigators including these phases [1]. A small case-control study assessed the role of reproductive lifespan excluding time for pregnancy, lactation, and hormone use on postmenopausal breast cancer risk and found a 1-year increase in reproductive lifespan was associated with a 10% increased odds of breast cancer risk (CI, 2%–19%) [5]. However, at least one study found no association between reproductive lifespan and breast cancer risk [6]. Further research is needed to confirm the associations between reproductive windows and breast cancer risk.

Reproductive windows may have stronger associations in certain subgroups identified by genetic factors. Many of these single nucleotide polymorphisms (SNPs) identified in genome-wide association studies (GWAS) act through unknown mechanisms but epidemiologic evidence suggests that certain breast cancer susceptibility loci modify the effects of hormonal risk factors on breast cancer risk [7–9]. We assessed the relationships between reproductive windows, top GWAS-identified loci, and their interactions in relation to invasive breast cancer risk in a population-based case-control study.

Methods

Study sample

The study data arise from the Collaborative Breast Cancer Study, a previously described population-based case-control study [10–12]. Eligible participants were selected from English-speaking women residents of MA, NH, or WI. Cases were women aged 20–69 years with an incident invasive breast cancer reported to a state cancer registry between 1995 and 2000. Community controls were randomly selected in each state from lists of licensed drivers (aged <65 y) or Medicare beneficiaries (aged ≥ 65 y) and were frequency matched to approximate the age distribution of the cases within 5-year age strata. Participants gave informed consent during study enrollment. This study was conducted with the approval of the University of Wisconsin Health Sciences Institutional Review Board.

Data collection

Telephone interviews were used to obtain detailed information on reproductive and menstrual experiences. Participant interviews were conducted on average 1 year after a specified reference date, which was defined as the date of cancer diagnosis for the cases. A comparable reference point for control participants was calculated based on their 5-year age strata and date of interview [12]. Among eligible participants, approximately 80% ($N = 6421$) of cases and 76% ($N = 7673$) of controls completed the interview.

Information about the histology and stage of breast cancer was obtained from each state's cancer registry. Cases were grouped by histology using International Classification of Diseases for Oncology codes (ICD-10), ductal (code 8010, 8012, 8021, 8140, 8310, 8323, 8410, 8500, 8502, 8530, 8560, and 8571), lobular (code 8520), and mixed ductal-lobular (code 8521, 8522, and 8523) [13]. All other individual tumor subtypes were excluded from histologic specific analyses ($N = 463$).

DNA extraction and genotyping

For a selected sample interviewed between the years 2000 and 2001, participants were asked to donate a buccal cell sample for genetic analyses. Seventy percent ($N = 1717$) of approached cases and 61% ($N = 1524$) of approached controls agreed to donate a sample.

Samples were sent by participants through the mail directly to a National Cancer Institute–affiliated laboratory under the direction of Dr. Montserrat Garcia-Closas for processing. DNA collection, isolation, and storage were conducted according to previously described protocols [10]. DNA was quantitated from frozen aliquots and plated for the genotyping assays. Top significant results from GWAS and follow-up studies were used to identify candidate loci for this analysis [7,14–17]. In total, 13 SNPs were genotyped: rs4973768, rs10941679, rs2981582, rs3817198, rs3803662, rs13281615, rs11249433, rs889312, rs2046210, rs17468277, rs10483813, rs13387042, and rs6504950. Genotyping was conducted using TaqMan nuclease assay (TaqMan) with reagents designed by Applied Biosystems (http://www.appliedbiosystems.com/) as Assays-by-Design and performed using the ABI PRISM 7900HT, 7700, or 7500 Sequence Detection Systems according to the manufacturer's instructions.

To reduce the possibility of population stratification and maintain a study sample with similar ancestry to the GWAS in which the loci were identified, all analyses were limited to participants self-identified as White/Caucasian in race (95.1% of participants). Quality control measures were taken to remove poor quality genetic data. SNPs missing greater than 20% of values or individual participants with a call rate less than 80% for genotypic data were excluded from the analysis. All 13 SNPs passed quality control measures. One hundred seventy eight cases and 174 controls were removed from genetic analyses because of a high percent of missing genotype data for a total of 1484 breast cancer cases and 1307 community controls with a viable DNA sample for study analyses.

Reproductive window definitions

The first reproductive window, standardized AFB, was defined as the interval between age at menarche and AFB in which duration of oral contraceptive use before a first pregnancy was subtracted from the interval. Participants with negative standardized AFB values were set to zero ($N = 5$). A secondary variable was created where the time when participants used oral contraceptives before first pregnancy was included in the interval. Among postmenopausal nulliparous women, standardized AFB was defined as the difference between age at menarche and menopause. Premenopausal nulliparous women ($N = 446$ cases and 414 controls) were excluded from this analysis.

The second reproductive window examined was the reproductive lifespan and restricted to postmenopausal women. Participants were considered postmenopausal if they reported their menstrual cycles had stopped for at least the last 6 months before reference date. The postmenopausal participants were categorized into two groups: participants with natural menopause and a second group defined as postmenopausal due to other causes. The primary definition of reproductive lifespan was the time between age at menarche and age at natural menopause excluding phases of pregnancy, lactation, and oral contraceptive use. A secondary definition was established in which these phases were included in the window. A third reproductive lifespan analysis was conducted among all postmenopausal women irrespective of menopause type.

Population for analysis

A total of 6131 white breast cancer cases and 7274 white controls were included in this analysis. Of these, 1484 cases and 1307 controls were involved in the genetic analyses. Participants with missing data from a component of the reproductive windows (age at menarche $N = 146$, oral contraceptive duration $N = 162$, parity

Download English Version:

https://daneshyari.com/en/article/3444412

Download Persian Version:

https://daneshyari.com/article/3444412

Daneshyari.com