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Original article

Early life growth, socioeconomic status, and mammographic breast density in an urban US birth cohort

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ABSTRACT

Purpose: Rapid infant and childhood growth has been associated with chronic disease later in life, including breast cancer. Early life socioeconomic status (SES) influences childhood growth, but few studies have prospective measures from birth to consider the effects of early life growth and SES on breast cancer risk.
Methods: We used prospectively measured early life SES and growth (percentile weight change in height and weight between each pair of consecutive time points at birth, 4 months, 1 and 7 years). We performed linear regression models to obtain standardized estimates of the association between 1 standard deviation increase in early life SES and growth and adult mammographic density (MD), a strong risk factor for breast cancer, in a diverse birth cohort ($n = 151$; 37% white, 38% black, 25% Puerto Rican; average age at mammogram = 42.4).
Results: In models adjusted for race/ethnicity, prenatal factors, birthweight, infant and childhood growth, and adult body mass index, percentile weight change from 1 year to 7 years was inversely associated with percent MD (standardized coefficient (Stdβ) = −0.28, 95% CI: −0.55 to −0.01), and higher early life SES was positively associated with percent MD (Stdβ = 0.24, 95% CI: 0.04–0.43). Similar associations were observed for dense area, but those estimates were not statistically significant.
Conclusions: These results suggest opposite and independent effects of early life SES and growth on MD.

Introduction

Emerging evidence supports the role of early life growth in risk of breast cancer [1–7]. Notably, rapid growth *in utero* reflected through birthweight may influence breast cancer risk, as this is a critical life period when the mammary tissue is rapidly developing [8,9]. Birthweight is affected by genetics and environmental factors during the intrauterine period and has been positively associated with breast cancer. The influence of birthweight on breast cancer risk may depend on the rate of growth after birth, including rapid growth in childhood [7,10,11]. However, results of studies evaluating these associations have been mixed, likely due to lack of prospective measures of growth during infancy and childhood in addition to birth characteristics.

Birth and childhood growth, as well as breast cancer risk, are influenced by parental socioeconomic status (SES) [12,13]. Although babies born to lower SES parents have on average lower birthweights than babies of higher SES parents, they experience rapid childhood growth and are more likely to be overweight in childhood [14,15]. The association between early life SES, measured through parental education and/or income, and breast cancer incidence later in life has been examined in a few studies [16,17]. In these studies, higher early life SES was significantly associated with increased breast cancer incidence after adjusting for adult reproductive and lifestyle characteristics, providing evidence for a direct role of early life SES on breast cancer risk [16,17]. Early life SES may increase breast cancer risk through changes occuring during the development and differentiation of mammary tissue in the critical window of early life, which may involve early life body size and growth [17]. Most studies to date have lacked data on prospective early life SES and growth measures to tease apart the independent effects of these factors on breast cancer risk.

Mammographic density (MD), one of the strongest risk factors for breast cancer, reflects the amount of dense fibroglandular tissue present in the breast as seen on mammograms [18–21]. As prospective collection of early life data in breast cancer studies is difficult and costly, researchers interested in examining early life

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determinants of breast cancer risk have often examined MD as a marker of risk that can be assessed in all women through mammography. Yochum et al. [22] reviewed the results of nine studies examining birthweight [23–31] and nine studies examining body size in childhood through adolescence in relation to adult MD [23–26,32–36]. Three studies found positive associations between birthweight and MD [27–29], and seven studies found inverse associations between childhood body size and MD [23–26,33–35], with the remainder of the studies observing mostly null associations. Only a few studies have simultaneously assessed birthweight, childhood growth, and early life SES in relation to MD [23,24], and none has used prospective data on all these factors.

We address these limitations by using comprehensive and prospectively collected early life data to measure growth from the prenatal period to the age of 7 years and multidimensional SES based on parental income, education, and occupation at birth. We focused on a cohort of racially/ethnically diverse population of premenopausal and perimenopausal women to investigate the association between prospectively assessed early life growth in relation to MD and whether the observed associations were independent of early life SES.

Materials and methods

Study population

We used data from the New York Women's Birth Cohort, a follow-up study of women enrolled at birth in the New York City site of the National Collaborative Perinatal Project (NYC NCPP). Study details have been published elsewhere [37–39]. Briefly, the NYC NCPP study included 1026 female children born at Columbia University Medical Center between 1959 and 1963. Of the 841 (82%) of the infants who were followed until the age of 7 years and eligible for the adult follow-up, we traced 44% as adults and enrolled 70% of the traced participants ($n = 262$). We obtained institutional review board approval from the Columbia University Medical Center.

Perinatal and childhood data

The NCPP recruited mothers into the study during their second and third trimesters [37,40]. At the initial study visit, clinical coordinators prospectively recorded maternal information including current age, age at menarche, race, and smoking behavior, pregnancy conditions, and anthropometric factors. We calculated maternal weight gain using maternal pre-pregnancy weight and maternal weight just before birth and calculated maternal body mass index (BMI) using self-reported pre-pregnancy weight and height. We used a validated continuous index for measuring parental SES, which uses a combination of parental education, income, and occupation data for the head of household or main wage earner. The SES index ranged from 0 to 100 with higher scores indicating higher SES (see for detailed background information on this measure [41]). We obtained prospective height and weight measures at birth and at the ages of 4 months, 1 year, and 7 years at clinical visits using a standardized protocol. Due to differences in participant's age for each height and weight follow-up measures (i.e., not all participants attended the clinic at exactly 4 months, 1 year, and 7 years of age), we used individual cubic splines to interpolate the data for each participant at the target times (4 months, 1 year, and 7 years). We did this for all measures except for birth measurements, which were measured for all participants at the time of their birth. To measure growth, we calculated the differences in height and weight between measures taken at each pair of consecutive time points; that is, between birth and 4 months, between 4 months and 1 year, and between 1 year and 7 years.

Adult follow-up and mammogram data

Between 2001 and 2006, 262 women enrolled in the adult follow-up study (New York Women's Birth Cohort) provided detailed epidemiologic data, including data on adult body size (current height and weight) and availability of mammogram. Of this sample, 228 (87%) women had received a prior mammogram, and 166 (73%) provided a medical release form for accessing their mammograms. We requested recent mammograms from the radiological facilities where participants had been screened and obtained films on 163 women. We excluded data from 11 participants due to poor mammogram quality and for one participant whose mammogram was taken after breast cancer diagnosis [39].

For each participant, we selected the mammogram that was taken closest to the date of completion of adult follow-up questionnaire. We used the craniocaudal mammogram views of the left breast for all participants, as breast densities in left and right breasts are strongly correlated [42,43]. We digitized mammograms using a Kodak Lumisys Film Digitizer (Kodak LS85) and assessed MD using Cumulus, a computer-assisted thresholding program that allows readers to measure the size of the total breast area and dense areas and identify the number of pixels within the areas. We calculated the size of breast area and dense area by converting the number of pixels to cm^2 and calculated percent MD (%MD) by taking the ratio of the dense area to the breast area and multiplying that by 100. A single reader, trained in the MD assessment using Cumulus software, read all mammograms arranged in random order, while blinded to exposure status, and repeated reading for a random 10% of all films. We obtained a Pearson correlation coefficient of 0.93 for dense area and 0.90 for %MD for the repeated readings.

Statistical analyses

We examined the associations of prenatal, birth, and childhood characteristics and early life SES with %MD and dense area. We further investigated the same associations with nondense area (total breast area-dense area) as the outcome. We modeled postnatal growth as standard deviation (SD) increases in percentile-rank changes in height and weight during three growth periods: birth to 4 months, 4 months to 1 year, and 1 year to 7 years. The use of percentile rank changes allows for the assessment of growth rates without adjustment for age-dependent measurement scales [44]. For example, a participant at 20th percentile for birthweight and 35th percentile for weight at 4 months would have a value of 0.15 for percentile weight change from birth to 4-month growth period [44–46]. We used partial regression plots to examine for the linearity of associations between the main exposures and MD. We generated standardized (Std) beta estimates of the associations between early life growth and SES and MD from linear regression models; this allowed us to compare the magnitude of the association for variables with different units in multivariable analysis (Supplementary Tables 2 and 3 present results of unstandardized estimates, and Supplementay Table 1 presents descriptive statistics for early life growth and SES and MD measures). We assessed for confounding of these associations by prenatal and birth variables selecting those that changed the estimates of the associations between childhood growth or SES at birth and MD by >10%. Next, we conducted linear regression models to examine the associations between early life SES, early life height and weight changes at the ages of 4 months, 1 year, and 7 years, and MD. All models were adjusted for age at mammogram and race/ethnicity. Additionally, Model 1 included all birth and growth variables, model 2 included SES at birth, model 3 included SES at birth, and birth and growth variables, and model 4 included all the previous variables in addition to adult BMI to account for the strong correlation of this