

Birth weight and mammographic density among postmenopausal women in Sweden

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Birth weight is a significant predictor of breast cancer risk in adult life and mammary gland mass could be an intermediate stage in this long process. We have studied the association of birth size measurements with mammographic density, a marker of mammary gland mass. For a population-based sample of 893 postmenopausal women without previous cancer in Sweden, we retrieved information on birth size from birth records and their most recent mammography. Film mammograms of the medio-lateral oblique view were digitized and the Cumulus software was used for computer-assisted semi-automated thresholding of mammographic density. Results were analyzed using generalized linear models controlling for possible confounders. Mean percent mammographic density increased when comparing the extreme categories of birth weight (from 15.6% to 18.6%) and head circumference (from 15.5% to 20.4%), and the corresponding linear trends were statistically significant (*p* values 0.02 and 0.007, respectively). The associations were particularly strong when the cutoff for high versus low mammographic density was set at the relatively high value of 50%. Compared to women weighing 3001–3500 grams at birth, women with birth weights >4000g were at almost 3-fold risk of developing high mammographic density (odds ratio: 2.9, 95% confidence interval 1.1 to 7.9). No association with mammographic density was evident with respect to birth length which, however, is known to be less accurately measured. These results indicate that adult breast density, a powerful predictor of breast cancer risk, has intrauterine roots, as reflected in birth size.

Several investigators have implicitly postulated that perinatal factors are associated with breast cancer risk in the offspring, but the hypothesis that endocrine exposures *in utero* may affect breast cancer risk several decades later was formally articulated in 1990.¹ More than 30 studies have evaluated this hypothesis, most of them focusing on birth weight as an important correlate of intrauterine exposures. Recent meta-analyses have concluded that birth weight is a significant predictor of breast cancer risk in adult life.^{2–4}

Key words: birth weight, mammographic density, mammography, breast cancer, birth size

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The mechanism(s), however, linking intrauterine endocrine exposures and, thus, birth weight to breast cancer risk in later life are not apparent. It has been postulated that mammary gland growth and eventually mass may be a critical manifestation of the early life processes that modulate risk of this disease in adult life.⁵ An important test of the validity of the postulated chain of causation—linking intrauterine influences to mammary gland mass to breast cancer risk—would be through evaluation of the association between birth size and mammary gland mass as assessed through mammographic density. Ever since Wolfe published his first report of an association between breast density and breast cancer risk,⁶ studies have confirmed relative risks in the 4-fold range when comparing the highest to the lowest mammographic density categories.^{7–9}

Few studies have investigated the association between aspects of birth size and mammographic patterns and, collectively, their results have been inconclusive.^{10–14} To our knowledge, however, no study has evaluated this association using at the same time, birth size data from records (as opposed to self recall), and computer-assisted mammographic density thresholding methods (as opposed to the more subjective categorical classifications of mammographic density).

In a population-based sample of postmenopausal women in Sweden, we have studied the association of aspects of birth