Null Results in Brief

Maternal Pelvic Size Not Predictive of Daughter's Breast Cancer or Ovarian Cancer in a Large Swedish Cohort

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Abstract

Recent studies from Finland reported that maternal pelvic size predicted daughters' breast and ovarian cancer, possibly because maternal pelvic size is a marker for *in utero* hormone exposure. We sought to replicate this association in 3,845 women born between 1915 and 1929 in Uppsala, Sweden, and followed from 1960 to 2002. Archived obstetric records provided the standard measures of maternal pelvic size (intercristal distance, interspinous distance, the intercristal-interspinous difference, and the external conjugate distance). The Swedish Cancer Registry ascertained cancer incidence, with 273 cohort members developing primary breast cancer, and 52 developing primary ovarian cancer during the follow-up period. There was no evidence ($P > 0.1$) of an association between any measure of maternal pelvic size and incidence of either breast or ovarian cancer. This was true both before and after adjustment for various characteristics of the women and their mothers, and in analyses stratified by age at diagnosis (<50 versus ≥50 years of age, as a proxy for premenopausal and postmenopausal ages). There was also no evidence of an association in subgroup analyses restricted specifically to those groups in which the Finnish data found the greatest effect. Our study is of comparable size to the Finnish studies and was highly powered (>99%) to detect effects of the magnitude they reported. Our nonreplication therefore casts doubt on the link between maternal pelvic size and risk of breast and ovarian cancer in the offspring. (Cancer Epidemiol Biomarkers Prev 2009;18(8):2333–5)

Introduction

Barker et al. recently reported that maternal pelvic size predicted breast and ovarian cancer in 4,102 Finnish women born between 1934 and 1944, and followed from 1971 to 2003 (1, 2). They investigated four standard measures of maternal pelvic size: intercristal distance (the maximal distance between the iliac crests), interspinous distance (distance between the anterior-superior iliac spines), the difference between the intercristal and interspinous distances, and external conjugate distance (distance from the front of the pubic bone to the fifth lumbar vertebrae). Two hundred and six of their cohort members developed primary breast cancer, with higher incidence among women whose mothers had a larger intercristal distance and a larger interspinous-intercristal difference. Thirty-nine developed primary ovarian cancer, with higher incidence among women whose mothers had a larger interspinous distance. Barker et al. hypothesize that pelvic size is a marker for the mother's hormone profile, and that this *in utero* exposure increases the daughter's risk.

Materials and Methods

Sample. The Uppsala Birth Cohort Multigenerational Study (UBCoS Multigen) has been described previously (3-5). Briefly, the cohort comprises all live births between 1915 and 1929 in the Uppsala Academic Hospital, Sweden. Archived obstetric records provided information about cohort members and their mothers at birth, and record linkage provided data from routine registers up to 2002. This included the Swedish Cancer Registry, which was established on January 1, 1960.

Of the 6,781 females live births, 751 died before 1960, 63 emigrated before 1960, and 202 were never traced. Of the remainder, 3,845 of 5,765 (66.7%) had maternal pelvic measurements, and these women comprise the starting population for our analyses. Pelvic measurements were more complete after 1924 (31.7-50.1% with data pre-1924 versus ≥93.4% after) and for primiparous women (72.1% with data versus 63.2% for multiparous). There was no evidence ($P > 0.05$) that missing pelvic measurements predicted breast or ovarian cancer in daughters.

Statistical Methods. We fitted Cox proportional hazards models, running separate models for breast and ovarian cancer. Follow-up started on January 1, 1960

Received 5/26/09; accepted 6/1/09; published online 8/6/09.

Grant support: The UBCoS Multigen study is supported by grants from the Swedish Council for Working Life and Social Research (grant no. 2007-1010) and the Swedish Research Council (grant no. 2006-7498). A. Goodman conducted this research while funded by the UK Economic Social and Research Council; I. Koupil is currently funded by the Swedish Council for Working Life and Social Research; and I. dos Santos Silva is a member of the Cancer Research UK Epidemiology and Genetics Group.

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doi:10.1158/1055-9965.EPI-09-0505

and continued until the date of death, emigration, diagnosis with any primary cancer, or until December 31, 2002. The woman's age defined the time scale. To adjust for possible cohort or period effects, we divided birth years into three bands (1915-1919, 1920-1924, and 1925-1929) and included this as a categorical variable in all models. We used the same cutoffs as Barker et al. for categorizing pelvic measurements and we also present analyses using the continuous measurements.

We then assessed the effect of adjusting for each potential confounder listed in Table 1 individually, and of adjusting for all of them, simultaneously. We banded the continuous confounders into between five and eight categories of approximately equal size, and modeled these as categorical variables.

Barker et al. report that the effect of intercristal distance on breast cancer was greatest in multiparous mothers and infants born at ≥40 weeks, and that the effect of interspinous distance on ovarian cancer was greatest in mothers who had menarche before age 14 and were <160 cm tall. We conducted sensitivity analyses restricting our analyses to these subgroups, except for mother's height, which was not recorded for our cohort. To assess whether the effect of maternal pelvic size was modified by menopausal status, we also conducted separate analyses for ages <50 and ≥50 years, using these as proxies for premenopausal and postmenopausal ages.

Results

The characteristics of the study population and their mothers are summarized in Table 1. Among our 3,845 study members, 273 developed primary breast cancer and 52 developed primary ovarian cancer by December 31, 2002 (total person-years at risk, 142,826.3).

Table 2 presents the hazard ratios for breast and ovarian cancer for each of the pelvic measures. In no case was there evidence of an association ($P > 0.1$); this remained true when entering the pelvic measurements as categorical variables or with quadratic terms. There was likewise no evidence at the 5% level of an association after adjusting for any potential confounder listed in Table 1, after stratifying our analyses between women ages <50 and those ages ≥50 years, or after restricting our analyses to the subgroups in which Barker et al. report the greatest effect.

Discussion

The Uppsala Birth Cohort Multigenerational Study provides a unique opportunity to test the hypotheses proposed by Barker et al. (1, 2). Unlike their findings from Finland, our Swedish cohort provided no evidence that maternal pelvic size predicts daughters' breast or ovarian cancer. This is despite a close similarity in our methods, and a close similarity between our study populations in terms of pelvic sizes and cancer incidence. Our null findings were robust to adjustment for confounders and sensitivity analyses, including analyses restricted to the subgroups in which Barker et al. report the largest effect. The one subgroup analysis we did not have the data to replicate was restricting the analysis of interspinous distance and ovarian cancer to shorter mothers. However, we found no evidence ($P = 0.17$) for this effect in the whole population, whereas in the Finnish cohort the whole-population P value was 0.008 (1).

This nonreplication cannot be attributed to insufficient power. Our cohort is of a similar size to the Finnish cohort (3,854 versus 4,201 females) and, because of the longer follow-up, contains somewhat more cancer cases (273 versus 206 breast cancers, 52 versus 39 ovarian cancers). For example, Barker et al. report a hazard ratio for breast cancer of 1.23 per 1 cm increase in the intercristal-interspinous difference. With 273 cancers among 3,845 women, and a SD of 1.3, our cohort would have 99.4% power to detect this at the 5% significance level. This nonreplication likewise cannot be attributed to poor measurement of exposure or outcome, as both have previously shown positive findings in

Table 1. Characteristics of the study population and their mothers (*N* = 3,845)

	No. with data	Mean (SD) or proportion	Range
Pelvic measurements of mother			
Intercristal distance (cm)	3,845	28.3 (1.6)	20-35
Interspinous distance (cm)	3,845	25.3 (1.7)	17.5-39
Intercristal minus interspinous distance (cm)	3,845	2.9 (1.3)	−10 to 9
External conjugate (cm)	3,332	20.1 (1.5)	10-34
Cancer incidence of daughter			
Age at breast cancer diagnosis (y)	273	61.9 (11.1)	36.4-85.4
Age at ovarian cancer diagnosis (y)	52	60.3 (12.0)	36.6-86.3
Potential confounders			
Mother's characteristics			
Mother's age at menarche (y)	3,811	14.7 (1.5)	11-22
Mother's age at child's birth (y)	3,845	28.1 (6.5)	15-47
Mother's parity at child's birth	3,845	2.6 (2.3)	1-16
Daughter's characteristics at birth			
Birth weight (g)	3,822	3,367.8 (521.5)	1,180-5,350
Birth length (cm)	3,838	50.2 (2.3)	38-59
Head circumference (cm)	3,744	34.3 (1.5)	23-46
Gestational age (wk)	3,713	39.6 (2.1)	29-47
Daughter's adult characteristics			
Post-elementary education	3,791	4.3%	—
Had at least one child	3,845	83.6%	—
Number of children among those who had at least one child	3,214	2.3 (1.3)	1-13
Age at first birth among those who had at least one child (y)	3,214	24.1 (4.6)	17-41

Table 2. Hazard ratios for breast and ovarian cancer by maternal pelvic measurements

	Breast cancer			Ovarian cancer		
	Hazard ratio (95% CI)	No. of cases (N = 273)	No. of women (N = 3,845)*	Hazard ratio (95% CI)	No. of cases (N = 52)	No. of women (N = 3,845)
Intercristal distance (cm)						
≤28.0	1	145	2,122	1	28	2,122
28.5-30.0	1.18 (0.92-1.51)	111	1,391	1.05 (0.59-1.89)	19	1,391
≥30.5	0.76 (0.46-1.26)	17	332	1.20 (0.46-3.11)	5	332
P for heterogeneity	0.16			0.93		
Change per 1 cm increase	1.00 (0.93-1.07)	273	3,845	1.05 (0.89-1.24)	52	3,845
P for linear trend	0.96			0.55		
Interspinous (cm)						
≤28.0	1	72	1,037	1	10	1,037
28.5-30.0	1.11 (0.83-1.48)	141	1,933	1.69 (0.81-3.53)	28	1,933
≥30.5	1.03 (0.73-1.47)	60	875	1.92 (0.84-4.42)	14	875
P for heterogeneity	0.77			0.27		
Change per 1 cm increase	0.98 (0.92-1.05)	273	3,845	1.11 (0.96-1.29)	52	3,845
P for linear trend	0.60			0.17		
Intercristal minus interspinous (cm)						
≤2.0	1	84	1,228	1	20	1,228
2.5	1.21 (0.76-1.92)	23	268	0.99 (0.37-2.65)	5	268
3.0	0.87 (0.63-1.19)	74	122	0.66 (0.33-1.30)	15	122
≥3.5	1.16 (0.85-1.58)	92	1,129	0.54 (0.25-1.15)	12	1,129
P for heterogeneity	0.25			0.35		
Change per 1 cm increase	1.03 (0.94-1.13)	273	3,845	0.90 (0.74-1.09)	52	3,845
P for linear trend	0.53			0.27		
External conjugate distance (cm)						
≤19.0	1	72	1,000	1	14	1,000
19.5-21.0	0.99 (0.74-1.32)	129	1,831	0.81 (0.41-1.61)	20	1,831
≥21.5	1.08 (0.72-1.60)	38	501	0.92 (0.35-2.41)	6	501
P for heterogeneity	0.90			0.83		
Change per 1 cm increase	1.02 (0.94-1.11)	239	3,332	0.98 (0.79-1.22)	40	3,332
P for linear trend	0.64			0.88		

NOTE: All analyses adjust for birth year with age defining the time scale.
*Five hundred and thirteen women had missing data on external conjugate distance, giving a total of 3,332.

other studies. For example, larger maternal pelvic size does protect against stroke in our cohort (6), in a way which replicates findings from the Finnish cohort (7). Similarly, breast cancer in our cohort is predicted by birth size (3), in a way consistent with the existing literature (8).

In summary, this cohort provides no evidence that maternal pelvic size predicts daughters' incidence of breast or ovarian cancers. This therefore casts doubt on a relationship between these factors.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Acknowledgments

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We thank Rawya Mohsen and Bitte Modin for their contribution to data preparation, to Richard Silverwood for help with statistical power calculations, and to Amal Khanolkar and Flaminia Chiesa for comments during the preparation of this manuscript.

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