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SHORT REPORT

Cancer among Scandinavian women with cosmetic breast implants: A pooled long-term follow-up study

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No increased risks of specific types of cancer following breast implantation have been consistently reported, but data on risk beyond 15 years are limited. We have pooled the results of 2 nationwide cohort studies of 3,486 Swedish and 2,736 Danish women who underwent cosmetic breast implantation between 1965 and 1993. Cancer incidence through 2002 was ascertained through nationwide cancer registries. Standardized incidence ratios (SIRs) and 95% confidence intervals (CIs) were calculated to compare cancer incidence among women with implants with women in the general population. Mean duration of follow up was 16.6 years (range 0.1–37.8 years). Over 50% of women were followed for 15 years or more after breast implantation and 13.3% for at least 25 years. There was a reduced incidence of breast cancer (SIR = 0.73; 95% CI 0.58–0.90), whereas lung cancer was above expectation (SIR = 1.64; 95% CI 1.10–2.36). The increased risk of lung cancer is expected due to the high prevalence of smoking among the women with implants in our study. With respect to other site-specific cancers, no significantly increased or decreased SIR was observed. This study, which includes women followed for almost 4 decades, represents the longest follow up of women with cosmetic breast implants to date. The results provide no evidence of an association between breast implants and any type of cancer.

Key words: breast implants; cancer incidence; epidemiology; cohort study

Based on the results of numerous epidemiologic studies and independent scientific reviews,[1–6] there is no evidence for an association between cosmetic breast implants and the occurrence of breast cancer. In fact, women with cosmetic breast implants consistently have a lower than average risk for breast cancer. Concerns about other types of cancer have been raised by reports of silicone-induced plasmacytomas in genetically susceptible mice,[7] and by anecdotal reports of lymphoma and multiple myeloma in women with cosmetic breast implants.[8–11] However, no increased risks of specific types of cancer have been consistently reported in epidemiologic studies.

We pooled the results of 2 nationwide cohort studies of women with cosmetic breast implants in Sweden[12] and Denmark.[13] This analysis based on 6,222 women with over 100,000 person-years of follow up, including women followed for more than 37 years after implantation, represents the longest follow up of women with cosmetic breast implants published to date, thus allowing us to present risk estimates for numerous additional cancer sites with too few cases to be included in the original reports.

Material and methods

Breast implant cohorts

Details about study cohorts and methods have been presented elsewhere.[12,13] Briefly, the studies were conducted in Sweden and Denmark using essentially complete nationwide population- and health care registers, including Hospitalization Registers, Cancer Registers, Death Registers, Migration Registers, and Population Registers. Unique personal identifiers assigned to each Swedish and Danish resident encode gender and date of birth and allow record linkage among these registers with few losses to follow up. The studies were approved by relevant regional Ethics Committees in Sweden and Denmark.

The Swedish National Patient Register (NPR), established in 1964 and becoming nationwide by 1987, records information on all hospital discharges.[14] Through the NPR, we identified a cohort of 3,486 Swedish women who underwent cosmetic breast implantation (*i.e.,* excluding reconstruction after breast cancer) for the first time between 1965 and 1993. The Danish implant cohort consisted of 2,736 women who underwent breast implant surgery for cosmetic reasons at public hospitals between 1977 and 1992, as recorded in the Danish National Hospital Register,[15] or at 8 private clinics of plastic surgery between 1973 and 1995. Thus, the present combined analysis is based on 6,222 women who received cosmetic breast implants in Denmark or Sweden between 1965 and 1995. At least 80% of implants in our study were silicone-gel filled.

Follow up

Through linkages to the Registers listed earlier, women in the breast implant cohorts were followed for the occurrence of cancer from the date of first cosmetic breast implantation (Denmark) or from 30 days after the date of first cosmetic breast implantation (Sweden) until date of emigration, date of death or December 31, 2002, whichever occurred first. Information on cancer diagnoses (ICD-7) was obtained from the Swedish and Danish Cancer Registers, which have recorded cases of cancer on a nationwide basis since 1958 and 1943, respectively and have virtually complete ascertainment of cancer cases.[16,17]

Statistical analyses

The number of cancer cases observed among women with breast implants was compared with the number expected in the general female populations of Sweden and Denmark. Age-, sex-, and calendar year-specific person-years were multiplied by the corresponding cancer incidence rates for Sweden and Denmark to determine expected numbers. Standardized incidence ratios (SIRs), *i.e.,* the ratios of observed to expected numbers of cancer cases, and exact 95% confidence intervals (CIs) were calculated for total cancers and for specific sites assuming a Poisson distribution for observed cancer cases.[18]

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TABLE I – CHARACTERISTICS OF THE COHORTS OF SWEDISH AND DANISH WOMEN WITH COSMETIC BREAST IMPLANTS

Characteristic	Swedish implant cohort (1965–1993)[1]	Danish implant cohort (1973–1995)[1]
Total number of women	3,486	2,736
Mean age at breast implant surgery (SD), years	32 (8.6)	32.2 (7.9)
Total person-years of follow up	64,271	39,294
Mean duration of follow up (range), years	18.4 (0.1–37.8)	14.4 (0.1–29.2)
Duration of follow up, *N* (%)		
<5 years	70 (2.0)	62 (2.3)
5–9 years	272 (7.8)	512 (18.7)
10–14 years	889 (25.5)	1,081 (39.5)
15–19 years	900 (25.8)	583 (21.3)
20–24 years	614 (17.6)	412 (15.1)
≥25	741 (21.2)	86 (3.1)
Year of implantation, N (%)		
≤1976	763 (21.9)	2 (0.1)
1977–1981	629 (18.0)	469 (17.1)
1982–1986	854 (24.5)	528 (19.3)
1987–1995	1240 (35.6)	1,737 (63.5)

[1]Calendar years of breast implant surgery.

TABLE II – SIRs AND 95% CIs[1] FOR SELECTED CANCER SITES AMONG 6,222 SWEDISH AND DANISH WOMEN WITH COSMETIC BREAST IMPLANTS, 1965–2002

Cancer (ICD-7)	Observed	Expected	SIR (95% CI)
All sites (140–209)[2]	288	303.59	0.95 (0.84, 1.07)
Buccal Cavity (140–148)	4	4.14	0.97 (0.26, 2.47)
All Digestive (150–159)	27	33.73	0.80 (0.53, 1.16)
Stomach (151)	2	3.67	0.54 (0.07, 1.97)
Colon (153)	5	12.97	0.39 (0.13, 1.13)
Rectum (154)	6	7.10	0.85 (0.31, 1.84)
Liver/Billiary (155–156)	7	3.87	1.81 (0.73, 3.73)
Pancreas (157)	4	4.09	0.98 (0.27, 2.50)
All Respiratory (160–164)	30	18.72	1.60 (1.08, 2.29)
Lung (162–163)	29	17.64	1.64 (1.10, 2.36)
Breast (170)	84	115.62	0.73 (0.58, 0.90)
Female Genital (171–176)	52	52.43	0.99 (0.74, 1.30)
Cervix (171)	19	18.48	1.03 (0.62, 1.61)
Corpus Uterus (172)	10	13.56	0.74 (0.35, 1.36)
Ovary (175)	21	16.57	1.27 (0.78, 1.94)
All Urinary (180–181)	8	8.85	0.90 (0.39, 1.78)
Kidney (180)	3	4.23	0.71 (0.15, 2.08)
Bladder (181)	5	4.63	1.08 (0.35, 2.52)
Melanoma (190)	20	19.09	1.05 (0.64, 1.62)
Brain/CNS (193)	17	14.12	1.20 (0.70, 1.93)
Thyroid (194)	8	4.94	1.62 (0.70, 3.19)
Endocrine (195)	3	5.46	0.55 (0.11, 1.61)
Connective Tissue (197)	2	1.77	1.13 (0.14, 4.08)
Lymphohematopoietic (200–205)	16	15.98	1.00 (0.57, 1.63)
NHL (200, 202)	9	7.36	1.22 (0.56, 2.32)
Hodgkin's Lymphoma (201)	2	1.74	1.15 (0.14, 4.16)
Leukemia (204)	4	4.89	0.82 (0.22, 2.09)

[1]SIR, standardized incidence ratio; CI, confidence interval.–[2]Excluding nonmelanoma skin cancer.

Results

Characteristics of the Swedish and Danish women with cosmetic breast implants are presented in Table I. The average age at implant surgery was 32 years in both cohorts. The combined mean duration of follow up was 16.6 years (range 0.1–37.8 years). Over 50% (n = 3,336) of women in the combined cohort were followed for 15 years or more after implantation, and 13.3% (n = 827) were followed for at least 25 years.

Table II presents SIRs for total and specific types of cancer (other than nonmelanoma skin cancer) with 2 or more observed cases in the combined cohort. We observed 288 cancers overall, compared with 303.59 expected based on general population rates, yielding a SIR of 0.95 (95% CI 0.84–1.07) (Table II). There was a significantly reduced incidence of breast cancer among women with implants, with 84 cases observed compared with 115.62 expected (SIR = 0.73; 95% CI 0.58–0.90). Incidence of lung cancer was significantly above expectation, with a SIR of 1.64 (95% CI 1.10–2.36) based on 29 observed cases.

For other site-specific cancers, no significantly increased or decreased SIR was observed in the cohort (Table II). In particular, the SIR for brain and nervous system cancer was 1.20 (95% CI 0.70–1.93) based on 17 observed cases. The SIR for non-Hodgkin's lymphoma was 1.22 (95% CI 0.56–2.32); none of the 9 observed cases had primary origin in or near the breast. Only 1 case with multiple myeloma was observed among women with implants, compared with 1.99 expected. Fewer sarcomas were observed (n = 3) than expected, and none was located in or near the breast.

Table III presents SIRs for total cancer and for breast, brain and lung cancer, stratified by time since breast implantation. Approximately 55% of the observed cancers occurred among cohort members followed for at least 15 years after implantation, with almost

TABLE III – SIRs AND 95% CIs[1] FOR SELECTED CANCER SITES AMONG 6,222 DANISH AND SWEDISH WOMEN WITH COSMETIC BREAST IMPLANTS, STRATIFIED BY DURATION OF FOLLOW UP

Cancer	Duration of follow up (years)											
	<5		5–9		10–14		15–19		20–24		25+	
	Obs[1]	SIR (95% CI)	Obs	SIR (95% CI)	Obs	SIR (95% CI)	Obs	SIR (95% CI)	Obs	SIR (95% CI)	Obs	SIR (95% CI)
Total[2]	46	0.99 (0.7–1.3)	71	1.05 (0.8–1.3)	64	0.88 (0.7–1.1)	63	1.07 (0.8–1.4)	26	0.66 (0.4–1.0)	18	0.99 (0.6–1.6)
Breast	11	0.69 (0.3–1.1)	21	0.82 (0.5–1.3)	21	0.73 (0.4–1.1)	19	0.82 (0.5–1.3)	9	0.60 (0.3–1.1)	3	0.44 (0.1–1.3)
Brain	3	1.13 (0.2–3.3)	5	1.43 (0.5–3.3)	3	0.89 (0.2–2.6)	5	2.03 (0.7–4.7)	0	0.00 (0.0–2.0)	1	1.58 (0.1–8.8)
Lung	3	1.66 (0.3–4.8)	3	0.88 (0.2–2.6)	6	1.39 (0.5–3.0)	10	2.52 (1.2–4.6)	3	1.06 (0.2–3.1)	4	3.24 (0.9–8.3)

[1]SIR, standardized incidence ratio; CI, confidence interval.–[2]Excluding nonmelanoma skin cancer.

25% occurring among women followed for at least 20 years. The only statistically significantly increased SIR was for lung cancer among women followed for 15–19 years after implantation. Breast cancer SIRs were nonsignificantly reduced throughout the follow-up period. Among the 1,853 women (30% of the cohort) with 20 or more years of follow up, there was 1 brain cancer observed compared with 1.26 expected.

Discussion

This pooled analysis of 2 large, nationwide cohorts is the longest follow-up study of cancer incidence among women with cosmetic breast implants published to date. It is the only published incidence study to include women followed for at least 25 years (and up to 37 years) after implantation and includes over 3,300 women followed for 15 years or more after implantation. Thus, we were able to present for the first time risk estimates for many cancer types with high statistical precision. In addition to the long follow up, the strengths of our study include the cohort design, the population-based approach and the almost complete follow up obtained by computerized linkage of cohort members to nationwide Cancer and Population Registers in Denmark and Sweden.

Consistent with previous large-scale epidemiologic studies, the incidence of cancer overall among women with breast implants in our study was close to expectation, whereas the incidence of breast cancer was below expectation, with a statistically significant 30% reduction in risk compared with the general population. The corresponding SIR for breast cancer in a recent, large Canadian study was 0.57 among 24,558 women with implants.[19] The consistently observed reduced incidence of breast cancer among women with breast implants may be explained by a higher prevalence of patient characteristics which may put them at a lower risk for breast cancer; these characteristics include younger age at first birth, higher parity and lower body mass index,[20–23] all of which have been reported among Danish and Swedish women in the present cohort,[20,21] compared with women in the general population or women with other types of cosmetic surgery. Most studies of breast cancer among women with breast implants did not have information on reproductive characteristics of the women. In a separate analysis of the Danish women with implants included in this report, the reduction in breast cancer risk persisted even after adjustment for age at first birth and number of children,[13] suggesting that reproductive factors may not have a major influence. It is also plausible that women seeking cosmetic breast implantation may be diagnosed with breast cancer during preoperative screening. Exclusion of these women whose breast cancers would have ultimately been diagnosed during follow up could lead to decreased incidence of breast cancer among women with cosmetic breast implants compared with women in the general population, although these effects are unlikely to explain the persistent risk reduction with long-term follow up.

We observed no statistically significant excess risk for brain cancer among women with implants, either overall or in any follow-up period, consistent with numerous large-scale incidence and mortality studies.[19,24–28] In the most recent update of the single original study reporting a brain cancer excess,[29,30] no additional deaths from brain cancer were observed (SMR = 1.4; 95% CI 0.8–2.5).[31]

Concerns about multiple myeloma are not supported by epidemiologic studies. One woman in our study developed multiple myeloma and 3 developed sarcomas (none in or near the breast), both below expected numbers based on population cancer incidence rates. In the large Canadian study,[19] 3 cases of multiple myeloma were observed (SIR = 0.46; 95% CI 0.09–1.33). Similarly, in the US breast implant cohort[29] and a recent Finnish study of 2,171 women with cosmetic breast implants,[24] no multiple myeloma was observed (compared with 1.73 and 0.2 expected, respectively).

The 60% excess of lung cancer seen in our data showed no clear pattern with increasing duration of follow up. A greater than 2-fold higher prevalence of cigarette smoking has previously been reported among the Swedish and Danish women in this cohort.[20,21] These differences in smoking habits are the most likely explanation for the excess lung cancer risk among the Scandinavian women in the present study. No increased risk for lung cancer was observed in the recent Canadian implant study.[19] In the US study, lung cancer risk was not elevated among women with implants when compared with the general population, but when compared with other plastic surgery patients, lung cancer was the only site-specific malignancy for which a statistically significant elevation was observed.[29]

In summary, the results of this analysis of 6,222 women, followed for up to 37 years after breast implantation, are consistent with all other large-scale incidence studies in providing reassurance that there is no credible evidence of an association between breast implants and cancer.

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