Breast Implants and the Risk of Breast Cancer: A Meta-Analysis of Cohort Studies

Eline C. Noels, MD; Oren Lapid, MD, PhD; Jan H.N. Lindeman, MD, PhD; and Esther Bastiaannet, PhD

Abstract

Background: The popularity of cosmetic breast augmentation and the incidence of breast cancer have been increasing worldwide. It has been hypothesized that the risk of breast cancer may be greater among patients who have undergone cosmetic breast implantation.

Objectives: The authors performed a meta-analysis of the available literature on the risk of breast cancer among women with cosmetic breast implants.

Methods: The study was designed as a meta-analysis of observational studies. A systematic search of the English literature (published by August 28, 2013) was conducted in PubMed and EMBASE. Eligible reports were those that included relative risk (RR; the increased or decreased risk of breast cancer associated with breast implants) or the standardized incidence ratio (SIR) of the observed number of cases of breast cancer to the expected number of cases among patients that previously underwent cosmetic breast augmentation.

Results: Seventeen studies representing 7 cohorts were selected. Some of these were follow-up reports of previously published studies; in such cases, only the most recent reports were included in the meta-analysis. Summary SIR and RR rates and the corresponding 95% confidence intervals (CIs) were calculated with a random-effects (SIR) or fixed-effects (RR) model. The overall SIR estimate was 0.69 (95% CI, 0.56-0.85), and the overall RR, based on 4 studies, was 0.63 (95% CI, 0.56-0.71).

Conclusions: Finding of this meta-analysis suggest that women who have undergone cosmetic breast implantation do not have an increased risk of breast cancer.

Accepted for publication May 22, 2014.
Meta-Analyses (PRISMA) statement for reporting systematic reviews and meta-analyses.²

Publication Search

A literature search was performed in PubMed and EMBASE on August 28, 2013, for English-language articles published in all years. Articles not yet indexed for Medline were included. The search strategy for both databases included terms for exposure (breast implant, breast prosthesis, breast augmentation) and for outcome (breast cancers, breast neoplasm, mammary carcinoma, and mammary neoplasm). (Search criteria appear in Appendix A, which is available online at www.aestheticsurgeryjournal.com.) The search results included epidemiologic studies, case reports, literature reviews, and letters. The references in relevant literature were checked for possible additional articles. The search strategy was reviewed by a reference librarian. Initially, the titles and abstracts of the publications were retrieved.

Inclusion Criteria

Screening of the titles and abstracts was performed by 2 authors (E.C.N. and O.L.). Any articles that raised inclusion concerns were discussed with a third author (E.B.). Studies were required to meet the following inclusion criteria: (1) cohort design, (2) exposure of interest was breast implants, (3) outcome of interest was breast cancer, and (4) data on standardized incidence ratio (SIR) or relative risk (RR) with 95% confidence intervals (CIs). There were no restrictions for patient age or duration of follow-up. Update reports for similar study populations were permitted. Cohort studies on patients receiving breast implants for reconstructive purposes were excluded.

Relative Risk and Standardized Incidence Ratio

The RR indicates the increased or decreased risk of disease associated with exposure to the factor of interest. An RR of 1 indicates that the risk is similar for the exposed and unexposed groups. RR > 1 indicates that the exposed group has an increased risk compared with the unexposed group, and RR < 1 indicates that the exposed group has a reduced risk of disease. The SIR is the ratio of the observed number of cases to the expected number of cases. For both risk estimates, 95% CIs were calculated; P values were 2-sided.

Data Extraction

The following data were extracted (by E.C.N.) from each study: first author’s surname, publication year, geographic location of study, data resources, mean follow-up time, sample size, average age of cohort, percentage of patients with silicone implants, and estimated effects with 95% CIs. Also noted were the exclusion criteria for each study and adjustment factors. Additional extracted information included the setting of the cohort (private plastic surgery practice or public hospital) and whether an induction period was applied.

Statistical Methods

Meta-analyses were performed separately for reports that included SIR and those that included RR. Summary SIR and RR rates for breast cancer after breast augmentation mammoplasty with breast implants and the corresponding 95% CIs were calculated with STATA/SE, version 12.0 (Stata Corp, College Station, TX) from as-reported data. Pooled SIRs and RRs and 95% CIs were calculated, using a random-effects (SIR) or fixed-effects (RR) model, depending on the number of included studies and the amount of heterogeneity observed. Some authors presented an update of other studies or an update of their previous analyses. Meta-analysis was performed only on the most recent results of those studies if they were from the same cohort i.e. the same study population described in the original publication (sensitivity analysis). Cochran’s Q and I² were calculated as measures of heterogeneity. Cochran’s Q denotes the weighted sum of the squared differences between individual studies and the pooled effect across studies, with the weights being those of the pooling method; I² denotes the percentage of total variation across studies that is due to heterogeneity rather than chance. A funnel plot was used to assess publication bias.

RESULTS

Literature Search

The full search strategy is listed in Appendix A (available at www.aestheticsurgeryjournal.com). Based on the terms for exposure and outcome, 2063 titles were identified. Subsequently, 1062 articles were eliminated based on the exclusion criteria. Another 126 articles were excluded when the additional filter of “English” for “Languages” was applied (Figure 1). After removal of duplicates, 760 articles remained and underwent primary screening. After screening the titles and abstracts for relevance, 17 full-text reports were selected. After consultation with the third author, 3 of the 17 studies were eliminated. One of these studies included a pooled analysis of 2 previous studies, another had been re-analyzed and republished due to possible errors noted shortly after the initial publication, and the third report contained an unrelated outcome measure. Three other articles were added after reviewing the references of eligible articles. (The latter 3 articles did not appear in our initial search results because the term “breast cancers” rather than “breast cancer” was applied; we recommend including the wild card “breast cancer*” for future research.)
Characteristics of the 17 included studies are reported in Table 1. Some articles were follow-up reports of previously published studies; in such cases, only the most recent reports were included.

**Meta-Analysis**

We performed a meta-analysis to obtain pooled risk data. The overall SIR and 95% CI showed a statistically significant inverse association between breast implants and breast cancer. For articles that included SIRs, the summary SIR was 0.69 (95% CI, 0.56-0.85; Figure 2). For reports with RRs, the summary RR was 0.63 (95% CI, 0.56-0.71; Figure 3).

In all the included reports, except the 1997 publication by Friis et al, the SIR was < 1, indicating that the risk of breast cancer is lower for women with breast implants than for the general population. However, the difference was statistically significant only in the Canadian and Los Angeles cohorts. The RR was < 1 in all 5 reports in which RR was documented, indicating that women with breast implants have a lower risk of subsequent development of breast cancer compared with the control group. The difference was statistically significant only in the Canadian cohorts described by Brisson et al and Pan et al.

**Risk of Bias**

The main risk of bias within these cohort studies would be the result of confounding by indication and loss to follow-up, particularly because of migration, as most studies linked records at a local level. Potential confounders are the exclusion of women with a history of cancer at sites other than breast (eg, the study by Brisson et al) and the cohort setting. This is due to differences in factors such as socioeconomic status, reproductive history, lifestyle, and past medical history. Although some authors corrected for these factors by matching of control cohorts, a residual bias may remain.

No statistically significant heterogeneity was detected in the meta-analysis of studies with RR estimates. However, statistically significant heterogeneity was observed in the meta-analysis of studies with SIR estimates; the funnel plots demonstrated considerable asymmetry (Figures 4 and 5).

**DISCUSSION**

In this review, we investigated the association of breast cancer with previous breast implant surgery by performing a meta-analysis of 7 cohort studies. To our knowledge, there is no literature report of a statistically significant increased risk of breast cancer in patients who received breast implants. However, some previous studies have been subject to heterogenicity in that they have included non-augmentation indications for breast implants. In contrast, we included augmentation patients exclusively; reconstruction indications for the use of implants were excluded. The overall results show no increased risk of breast cancer associated with previous breast augmentation with implants, and even suggest that the incidence of breast cancer among these patients is lower than would be expected. This meta-analysis also confirms the results of previous reviews. Furthermore, no statistically
### Table 1. Characteristics of Studies in the Meta-Analysis

<table>
<thead>
<tr>
<th>Study Authors (y)</th>
<th>Country</th>
<th>Setting</th>
<th>Inclusion Age, y</th>
<th>Induction Period</th>
<th>Implantation Period</th>
<th>Last Follow-Up Date</th>
<th>Patients, n</th>
<th>Mean Age at Implantation, y</th>
<th>Patients, n</th>
<th>Cancer Cases, n</th>
<th>SIR Estimates</th>
<th>RR Estimates</th>
<th>Controls, n</th>
<th>Cancer Case Controls, n</th>
<th>RR</th>
<th>95% CI</th>
<th>External Rate, n</th>
<th>SIR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brinton et al20 (2000)</td>
<td>US</td>
<td>PC</td>
<td>NK</td>
<td>1 y</td>
<td>1962-1988</td>
<td>1996</td>
<td>13,488</td>
<td>34.8</td>
<td>136</td>
<td>152.2</td>
<td>0.89</td>
<td>0.80-1.10</td>
<td>3936</td>
<td>60</td>
<td>0.79</td>
<td>0.60-1.10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bryant37 (1995)</td>
<td>CA</td>
<td>NK</td>
<td>20-64</td>
<td>0/1/5/10 y</td>
<td>1973-1986</td>
<td>1991</td>
<td>10,835</td>
<td>NK</td>
<td>NK</td>
<td>NK</td>
<td>0.76</td>
<td>0.55-1.02</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deapen et al30 (1986)</td>
<td>US</td>
<td>PC</td>
<td>NK</td>
<td>NK</td>
<td>1953-1980</td>
<td>1981</td>
<td>3112</td>
<td>31.4</td>
<td>9</td>
<td>15.7</td>
<td>0.57</td>
<td>0.26-1.09</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deapen and Brody29 (1992)</td>
<td>US</td>
<td>PC</td>
<td>NK</td>
<td>NK</td>
<td>1953-1980</td>
<td>1986</td>
<td>3112</td>
<td>31.4</td>
<td>21</td>
<td>31.7</td>
<td>0.66</td>
<td>0.41-1.01</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deapen et al28 (1997)</td>
<td>US</td>
<td>PC</td>
<td>NK</td>
<td>NK</td>
<td>1953-1980</td>
<td>1991</td>
<td>3182</td>
<td>31.4</td>
<td>31</td>
<td>49.2</td>
<td>0.63</td>
<td>0.43-0.90</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deapen et al21 (2007)</td>
<td>US</td>
<td>PC</td>
<td>NK</td>
<td>NK</td>
<td>1953-1980</td>
<td>1994</td>
<td>3139</td>
<td>31.4</td>
<td>43</td>
<td>62.6</td>
<td>0.69</td>
<td>0.50-0.93</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deapen and Brody14 (2012)</td>
<td>US</td>
<td>PC</td>
<td>NK</td>
<td>NK</td>
<td>1953-1980</td>
<td>2006</td>
<td>3139</td>
<td>31.4</td>
<td>59</td>
<td>99.0</td>
<td>0.60</td>
<td>0.45-0.77</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Friis et al11 (1997)</td>
<td>DK</td>
<td>PH</td>
<td>13-64</td>
<td>NK</td>
<td>1977-1992</td>
<td>1993</td>
<td>1135</td>
<td>31.0</td>
<td>8</td>
<td>7.8</td>
<td>1.00</td>
<td>0.40-2.00</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mellemkjaer et al33 (2000)</td>
<td>DK</td>
<td>PC, PH</td>
<td>&lt;55</td>
<td>NK</td>
<td>1973-1995</td>
<td>1995</td>
<td>2767</td>
<td>31.0</td>
<td>16</td>
<td>17.3</td>
<td>0.90</td>
<td>0.50-1.50</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Friis et al19 (2006)</td>
<td>DK</td>
<td>PC, PH</td>
<td>&lt;55</td>
<td>NK</td>
<td>1973-1995</td>
<td>2002</td>
<td>2736</td>
<td>31.0</td>
<td>31</td>
<td>43.8</td>
<td>0.70</td>
<td>0.50-1.00</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Friis et al18 (2006)</td>
<td>DK</td>
<td>PC</td>
<td>&lt;55</td>
<td>NK</td>
<td>1973-1995</td>
<td>2001</td>
<td>1653</td>
<td>21.0</td>
<td>15</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1736</td>
<td>29</td>
<td>0.70</td>
<td>0.40-1.30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McLaughlin et al13 (1994)</td>
<td>DK</td>
<td>PH</td>
<td>NK</td>
<td>NK</td>
<td>1977-1989</td>
<td>1989</td>
<td>824</td>
<td>32.0</td>
<td>1</td>
<td>4.2</td>
<td>0.24</td>
<td>0.00-1.31</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McLaughlin et al12 (1995)</td>
<td>S</td>
<td>PH</td>
<td>NK</td>
<td>NK</td>
<td>1965-1983</td>
<td>1989</td>
<td>1756</td>
<td>NK</td>
<td>7</td>
<td>11.2</td>
<td>0.63</td>
<td>0.30-1.30</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McLaughlin38 (1996)</td>
<td>S</td>
<td>PH</td>
<td>NK</td>
<td>30 d</td>
<td>1965-1993</td>
<td>1993</td>
<td>3473</td>
<td>30.0</td>
<td>18</td>
<td>25.0</td>
<td>0.70</td>
<td>0.40-1.10</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McLaughlin et al22 (2006)</td>
<td>S</td>
<td>PH</td>
<td>NK</td>
<td>30 d</td>
<td>1965-1993</td>
<td>2002</td>
<td>3486</td>
<td>32.0</td>
<td>53</td>
<td>71.9</td>
<td>0.70</td>
<td>0.60-1.00</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brison et al6 (2006)</td>
<td>CA</td>
<td>PC</td>
<td>&gt;18</td>
<td>1 y</td>
<td>1974-1989</td>
<td>1997</td>
<td>24,558</td>
<td>31.3</td>
<td>188</td>
<td>331.6</td>
<td>0.57</td>
<td>0.49-0.65</td>
<td>15893</td>
<td>206</td>
<td>0.64</td>
<td>0.53-0.79</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pan et al15 (2012)</td>
<td>CA</td>
<td>PC</td>
<td>&gt;18</td>
<td>1 y</td>
<td>1974-1989</td>
<td>2007</td>
<td>24,558</td>
<td>32.2</td>
<td>414</td>
<td>NK</td>
<td>0.54</td>
<td>0.49-0.59</td>
<td>15893</td>
<td>457</td>
<td>0.60</td>
<td>0.53-0.69</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kern39 (1997)</td>
<td>US</td>
<td>PH</td>
<td>NK</td>
<td>NK</td>
<td>1980-1993</td>
<td>1993</td>
<td>680</td>
<td>34.0</td>
<td>4</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1022</td>
<td>9</td>
<td>0.67</td>
<td>0.20-2.17</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Seventeen studies were identified in the search, some of which were follow-up reports of previously published studies. In such cases, only the most recent reports were included. The highlighted studies represent the 7 cohorts included in the meta-analysis. CA, Canada; CI, confidence interval; DK, Denmark; NA, not applicable; NK, not known; PC, private clinic; PH, public hospital; RR, relative risk; SIR, standardized incidence ratio; US, United States; S, Sweden.
significant increased risk was observed for attained age,\textsuperscript{14,19–21} years of exposure,\textsuperscript{14,16,19,21,22} or type of implant.\textsuperscript{16,20} From the data available, it was not possible to discern the histologic types of the diagnosed breast cancers.

In contrast to earlier reviews by Hoshaw et al\textsuperscript{5} and Deapen,\textsuperscript{18} we omitted studies\textsuperscript{23–26} for which full text was not available and studies that included women who received breast implants for reconstructive purposes. (Such women have a potentially higher risk of local recurrence or developing cancer in the contralateral breast.\textsuperscript{27}) We did not perform quantitative analysis on case-control studies, which had been done by Hoshaw et al.\textsuperscript{5} We found no new case-control studies.

An interesting aspect of the cohorts published by Deapen et al\textsuperscript{14,21,28–30} is the inclusion of patients starting in 1953. Because silicone implants were first introduced in 1962, we assume that the implants placed in earlier studies were of another type, which may have influenced their results.\textsuperscript{31} Because Deapen et al\textsuperscript{30} were not authorized to contact patients to obtain additional information, the inability to adjust risk estimates for known breast cancer risk factors was a possible confounder in their study.

The results also may be influenced by more generic factors, such as record-linkage design, which can miss patients who migrate or travel from distant locations for surgery. The large variation in sample size also should be considered, which ranged from 680 patients in the smallest cohort to 24,558 patients in the largest.

In the present meta-analysis, studies that included RR data showed a more pronounced inverse association than studies in which SIR was documented. This effect may be explained by the fact that the general population may differ from patients seeking cosmetic augmentation mammoplasty in regard to risk factors for breast cancer,
including demographics, lifestyle, reproductive history, and medical characteristics. However, such differences also apply to women with breast implants vs women who have undergone other cosmetic surgery, as was compared in the studies by Brinton et al, Brisson et al, Friis et al, Mellemkjaer et al, and Pan et al. In addition, the general population cohorts were biased in that they supposedly represented the unexposed cohort but inevitably also included an unknown (albeit small) percentage of women with breast implants.

Only 2 cohorts showed a statistically significant lower SIR or RR. This could be due to bias (primarily selection bias, or insufficiently adjusting for confounders). However, it could also be an actual association with a lower
incidence of breast cancer in women with breast implants, which is difficult to ascertain from observational studies. Therefore, we may conclude that there was no increased risk and no association between breast implants and breast cancer. Another potential confounder could be body mass index (BMI) and breast size. Given that many breast augmentation patients have lower BMIs and smaller breasts, it may be suggested that women with implants have a smaller risk of breast cancer because they have less breast tissue. However, this is not the case. It has been shown that BMI and breast size do not differ significantly between women with breast cancer and women in the general population.34

The interference of breast implants with the detection of breast cancer by imaging also may be a factor; however, the methodology of our study and of the studies included in the meta-analysis does not provide information on the necessary surveillance for patients with previous breast augmentation.35,36

An issue not mentioned in the examined studies is the possibility that patients who underwent explantation were included in the cohorts. The study designs do not allow for this assessment. Therefore, we refer to the original exposure of implantation, although we may assume that the majority of the patients kept their implants.

Additional biases include the applied language restriction (English literature only) and publication bias. However, in reviewing the references of eligible articles, no additional publications in a language other than English were found. Therefore, we believe that this bias is limited. Part of our search strategy was erroneous because we used the term “breast cancers” (rather than “breast cancer”), which explained why 3 relevant articles were missed initially. A subsequent search revealed that this mistake did not influence the results of our review. However, we recommend that the wild card “breast cancer*” be applied in future research.

Publication bias might explain some of the risk we observed, as suggested by the asymmetric shape of the funnel plot. However, the overall RR estimate (of reports that included it) was homogenous. Therefore, we maintain that women who undergo breast augmentation have a lower risk of subsequent breast cancer compared with women who undergo other types of surgery. This may indicate that breast implants have a protective effect against breast cancer.

**CONCLUSIONS**

The overall results of this meta-analysis, which focused exclusively on patients who underwent cosmetic breast augmentation, show no increased risk of breast cancer associated with previous implant breast augmentation. Rather, the findings suggest that the incidence may be lower than expected. Future research should focus on possible explanations for these phenomena.

**Disclosures**

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

**Funding**

The authors received no financial support for the research, authorship, and publication of this article.

**REFERENCES**


