Breast cancer detection and survival among women with cosmetic breast implants: systematic review and meta-analysis of observational studies

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CRD summary
This review evaluated the impact of previous cosmetic breast augmentation on cancer stage at diagnosis and survival in women subsequently diagnosed with breast cancer. The authors concluded that research indicated poorer survival in these women compared to women without implants, but advised caution because many primary studies did not consider confounding factors. These conclusions are likely to be reliable.

Authors' objectives
To determine whether the distribution of stages in breast cancer diagnoses differed between women with cosmetic breast implants and women without these implants; and to evaluate whether previous cosmetic breast augmentation was a predictor of post-diagnosis survival in breast cancer.

Searching
Seven databases including MEDLINE, EMBASE and CINAHL were searched up to September 2012. Search terms were reported. Reference lists of identified studies and relevant reviews were checked, and experts were contacted for additional studies. Only peer-reviewed studies published in English or French were eligible for inclusion.

Study selection
Case-control, cohort and cross-sectional studies which included women with a diagnosis of breast cancer after previous cosmetic augmentation mammaplasty were eligible. Comparison groups could be women with a breast cancer diagnosis who had previous common elective cosmetic surgical procedures, or women from the general population of breast cancer patients.

Studies that assessed association of breast implants with stage distribution needed to report data for both exposed and non-exposed women at each breast cancer stage, for nodal status or metastases status, or a combination of these. Studies that assessed survival needed to provide hazard ratios for exposed and non-exposed women, or to show Kaplan-Meier curves for both groups.

Included studies used three different staging systems. Data on breast cancer were obtained mainly from cancer registries or medical records, data on augmentation surgeries from hospital/surgeons records or medical records. Most comparison groups were women from the general population; a minority had other cosmetic surgical procedures. A minority of studies reported adjusted analyses.

Two authors were involved in selecting the studies for the review.

Assessment of study quality
Studies were assessed using the Newcastle-Ottawa scale; it was not clear how many reviewers performed the assessment.

Data extraction
Two reviewers independently extracted data to permit the calculation of odds ratios or hazard ratios. Only data on invasive breast cancers was included in the review. Breast cancer stages were divided into non-localised cancer (regional or distant spread) and localised cancer. Discrepancies were resolved through discussion.

Methods of synthesis
A random-effects DerSimonian and Laird model was used to calculate pooled odds ratios with 95% confidence intervals for the stages of breast cancer at diagnosis in women with and without implants. A random-effects model was also used to calculate the pooled HR for survival in exposed versus non-exposed women. Heterogeneity between studies was assessed using $X^2$ and $I^2$. The impact of a range of variables on measured association was assessed for the studies of
stage distribution using meta-regression. Publication bias in studies that reported stage distribution was assessed using a funnel plot and Egger's test.

**Results of the review**

Twenty-two studies with a total of 28,924 women were included for the evaluation of stage distribution. Seven studies with 18,026 women were included for the evaluation of survival. These figures were based on the review text; there were discrepancies between the text and the tables and the number of patients included in the meta-analyses was unclear. The authors stated that all studies were of acceptable quality and this was supported by the brief reporting of the quality assessment. Mean follow-up ranged from 6.4 to 16.1 years where reported.

**Stage distribution:** Twelve cross-sectional studies were combined in a meta-analysis. There was a trend for women with implants to be more likely to have non-localised breast cancer at diagnosis (OR 1.26, 95% CI 0.99 to 1.60; I²=35.6%). Sensitivity analysis excluding one outlier removed statistical heterogeneity (I²=0%) and produced a statistically significant estimate (OR 1.42, 95% CI 1.19 to 1.68). No other sensitivity analysis materially altered the estimate. The results of meta-regression analyses were also reported. Notably these indicated a stronger effect in studies providing an analysis adjusted for variables such as age at diagnosis.

**Survival:** Five cohort studies were combined in a meta-analysis. Survival was statistically significantly poorer in women with breast implants compared to women without implants (HR for breast cancer mortality 1.38, 95% CI 1.08 to 1.75; I² = 0%).

There was no evidence of publication bias in either analysis

**Authors' conclusions**

Published research suggested that cosmetic breast augmentation has a negative impact on the survival of women if they were subsequently diagnosed with breast cancer. These findings should be interpreted with caution because some studies included in the analysis did not adjust for potential confounding factors.

**CRD commentary**

This review had a clear research question supported by explicit inclusion criteria and a thorough search. The authors reported using methods designed to reduce reviewer bias and error in selection and data extraction of studies. Discrepancies between the text and tables meant that the numbers of patients in the statistical analyses were unclear. Studies were quality assessed using an appropriate scale but only limited details of the results were reported. The synthesis was appropriate and included methods designed to investigate differences between studies. The authors’ conclusions were conservative and took into account the methodological limitations of the included studies. They are likely to be reliable.

**Implications of the review for practice and research**

The authors stated that further investigations were warranted into the long-term effects of cosmetic breast implants on the detection and prognosis of breast cancer; these should adjust for potential confounders.

**Funding**

Unite de Recherche en Sante des Populations; Cancer Care Ontario; Public Health Agency of Canada.

**Bibliographic details**


**DOI**

10.1136/bmj.f2399

**Indexing Status**

Subject indexing assigned by CRD
MeSH
Breast Implants; Breast Neoplasms; Humans; Diagnosis; Survival

Accession Number
12013023560

Date bibliographic record published
02/05/2013

Date abstract record published
09/05/2013

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.