Research article

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Breast implants following mastectomy in women with early-stage breast cancer: prevalence and impact on survival

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Received: 16 Jul 2004 Revisions requested: 10 Sep 2004 Revisions received: 25 Oct 2004 Accepted: 16 Nov 2004 Published: 23 Dec 2004

Breast Cancer Res 2005, 7:R184-R193 (DOI 10.1186/bcr974)

See related Commentary: http://breast-cancer-research.com/content/7/2/61

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Abstract

Background Few studies have examined the effect of breast implants after mastectomy on long-term survival in breast cancer patients, despite growing public health concern over potential long-term adverse health effects.

Methods We analyzed data from the Surveillance, Epidemiology and End Results Breast Implant Surveillance Study conducted in San Francisco–Oakland, in Seattle–Puget Sound, and in Iowa. This population-based, retrospective cohort included women younger than 65 years when diagnosed with early or unstaged first primary breast cancer between 1983 and 1989, treated with mastectomy. The women were followed for a median of 12.4 years (n=4968). Breast implant usage was validated by medical record review. Cox proportional hazards models were used to estimate hazard rate ratios for survival time until death due to breast cancer or other causes for women with and without breast implants, adjusted for relevant patient and tumor characteristics.

Results Twenty percent of cases received postmastectomy breast implants, with silicone gel-filled implants comprising the most common type. Patients with implants were younger and more likely to have *in situ* disease than patients not receiving implants. Risks of breast cancer mortality (hazard ratio, 0.54; 95% confidence interval, 0.43–0.67) and nonbreast cancer mortality (hazard ratio, 0.59; 95% confidence interval, 0.41–0.85) were lower in patients with implants than in those patients without implants, following adjustment for age and year of diagnosis, race/ethnicity, stage, tumor grade, histology, and radiation therapy. Implant type did not appear to influence long-term survival.

Conclusions In a large, population-representative sample, breast implants following mastectomy do not appear to confer any survival disadvantage following early-stage breast cancer in women younger than 65 years old.

Keywords: breast implants, epidemiology, mastectomy, Surveillance, Epidemiology, and End Results, survival

Introduction

Over the past 30 years, an estimated 1.5–2 million women have received breast implants in the United States [1]. Starting in the 1980s, widespread public health concern arose regarding their potential adverse health effects [2]. Numerous epidemiologic investigations have focused on systemic complications, particularly cancer and connective tissue disease, but have found no significantly increased short-term risk for these diseases [3,4].

Approximately 20% of breast implants are used for reconstruction in breast cancer patients following mastectomy [1]. In this population, however, the use of breast implants, while increasing, has not been well documented [5]. Furthermore, little research has addressed long-term survival, although the few studies conducted suggest that use of implants for breast reconstruction does not impact patient survival [6-9]. However, these studies were limited by comprising clinic-based samples not necessarily representative of all patients, by small sample sizes, by lack of information on type of implant, and by short durations of follow-up.

In 1993, the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute implemented the Breast Implant Surveillance Study to document and validate postmastectomy breast implant usage in a population-based series of young, early-stage breast cancer cases. Since the SEER program also monitors patient vital status for life, survival up to 17 years exists in the study cohort. The purpose of the current analysis was to describe the use of breast implants and to examine the impact of breast implants on survival after breast cancer in this cohort.

Methods

Breast Implant Surveillance Study

The Breast Implant Surveillance Study was conducted during the period 1993–1994 in the United States. Patients were identified through the population-based SEER cancer registries in San Francisco–Oakland, CA, in Seattle–Puget Sound, WA, and in the state of Iowa. Eligible patients included the 5862 females diagnosed younger than age 65 with early-stage or unstaged first primary breast cancer in 1983, 1985, 1987, or 1989 and treated with mastectomy during their first course of therapy.

Participation involved completing a standardized questionnaire inquiring about implant status (right breast only, left breast only, both breasts, no implant, or unknown) and implant type (silicone gel, saline, double lumen [consisting of silicone gel and saline], other, and unknown type), and providing signed consent for release of medical records for validation of implant usage and implant type. Patients in the Seattle-Puget Sound region and the state of lowa were mailed a self-administered questionnaire, and nonrespondents were contacted for a telephone interview. Women from the San Francisco-Oakland region were administered questionnaires by telephone.

Next-of-kin were asked about the deceased patient's implant status and for consent for medical record review. For women reporting breast implants, a medical record review of breast implant usage (including the date and type of implant received, and removal and replacement status) was conducted by trained abstractors for women who reported having a breast implant. Patient and tumor characteristics at diagnosis, including age, race/ethnicity, year, stage, histology, grade, radiation treatment, vital status, and cause of death, were obtained from the SEER database.

Although socioeconomic status (SES) is not routinely collected by SEER, we were able to assign census block group level measures of SES to a subset of subjects (1989 San Francisco Bay Area patients). Using data from the 1990 US Census, we examined the impact of living in census block groups characterized by low education, by poverty, and by occupation (median income, < 20% below

poverty versus \geq 20% below poverty; education, no high school diploma versus high school graduate; and occupation, blue collar versus nonblue collar [10]).

Patients who reported a breast implant were classified as having a particular type of implant if they had a unilateral implant, or if they had bilateral implants of the same type. Nineteen women with bilateral implants and discordant information about implant type were excluded from analyses stratified by the type of implant. An additional 133 women reporting implants but lacking implant information were excluded from all analyses requiring detailed implant information. The vital status (obtained annually through patient contact, death records, motor vehicle departments, voters' registration records, and Social Security files) was determined from the December 1999 SEER Public Use Tape. The outcome variables were death due to breast cancer and death due to nonbreast cancer causes, as routinely ascertained by SEER and as defined by the International Classification of Disease, Ninth Revision, codes 174.0-174.9 for deaths occurring between 1983 through 1998, and by the International Classification of Disease, 10th Revision, code C509 for deaths occurring in 1999. Survival time was calculated from the date of diagnosis to the earliest date: death, last known to be alive, or 31 December 1999 (study cutoff date).

Statistical analysis

For descriptive analyses, women with breast implants were compared with those without implants on characteristics at diagnosis (SEER region of residence, age, year, race/ethnicity, marital status, stage, grade, and histology), using chisquare tests and Fisher's exact test to assess differences. Two-sided P < 0.05 was considered statistically significant.

Of the 5862 patients eligible for the study, 4968 (84.7% of those eligible) patients participated in the study. After restricting the sample to women with primary invasive breast cancer and known survival time, a final sample size of 4385 patients were used for all survival analyses. Survival estimates were computed using the Kaplan–Meier method, and differences in survival were compared using the two-sided log-rank test. To adjust for patient and tumor characteristics, the risks of nonbreast cancer mortality and death due to breast cancer were modeled using Cox proportional hazards regression after censoring deaths from other or unknown causes. The assumption of proportionality was tested and met for all covariates used in the Cox analysis. All analyses were performed using SAS Version 8.02 (SAS Institute, Inc., Cary, NC, USA).

Table 1

Characteristics of mastectomy-treated breast cancer patients in the Surveillance, Epidemiology, and End Results (SEER) Breast Implant Surveillance Study, 1983–1989

| Characteristic | | All eligible | patients (n = | 5862) | | Study responders only ($n = 4968$) | | | | | |
|-----------------------------------|------------|---------------|---------------|--------------|---------|---|------|-------------------------|--------------------------|---------|--|
| | Nonrespond | ers (n = 894) | Responders | s (n = 4968) | P value | Women with breast implants $(n = 1018)$ | | Women wit implants (| hout breast n = 3950) | P value | |
| | n | % | n | % | | n | % | n | % | _ | |
| SEER region | | | | | | | | | | | |
| San Francisco-Oakland | 468 | 52.4 | 1853 | 37.3 | 0.0001 | 416 | 40.9 | 1437 | 36.4 | 0.0001 | |
| Seattle-Puget Sound | 190 | 21.3 | 1663 | 33.5 | | 374 | 36.7 | 1078 | 27.3 | | |
| lowa | 236 | 26.4 | 1452 | 29.2 | | 228 | 22.4 | 1435 | 36.3 | | |
| Year of diagnosis | | | | | | | | | | | |
| 1983 | 246 | 27.5 | 1102 | 22.2 | 0.0001 | 176 | 17.3 | 926 | 23.4 | 0.0003 | |
| 1985 | 241 | 27.0 | 1152 | 23.2 | | 244 | 24.0 | 908 | 23.0 | | |
| 1987 | 230 | 25.7 | 1405 | 28.3 | | 319 | 31.3 | 1086 | 27.5 | | |
| 1989 | 177 | 19.8 | 1309 | 26.3 | | 279 | 27.4 | 1030 | 26.1 | | |
| Age at diagnosis | | | | | | | | | | | |
| <35 years | 59 | 6.6 | 175 | 3.5 | 0.0001 | 88 | 8.6 | 87 | 2.2 | 0.0001 | |
| 35-44 years | 231 | 25.8 | 919 | 18.4 | | 334 | 32.8 | 585 | 14.8 | | |
| 45-54 years | 256 | 28.6 | 1545 | 31.1 | | 370 | 36.4 | 1175 | 29.8 | | |
| 55-64 years | 348 | 38.9 | 2329 | 46.9 | | 226 | 22.2 | 2103 | 53.2 | | |
| Mean age at diagnosis (years) | 49.9 | - | 52.1 | - | 0.0001 | 46.7 | - | 53.4 | - | 0.0001 | |
| Race/ethnicity | | | | | | | | | | | |
| Non-Hispanic White | 670 | 74.9 | 4444 | 89.5 | 0.0001 | 959 | 94.2 | 3485 | 88.2 | 0.0001 | |
| Non-Hispanic Black | 78 | 8.7 | 150 | 3.0 | | 13 | 1.3 | 137 | 3.5 | | |
| Hispanic | 38 | 4.3 | 131 | 2.6 | | 20 | 2.0 | 111 | 2.8 | | |
| Asian/Pacific Islander | 86 | 9.6 | 179 | 3.6 | | 16 | 1.6 | 163 | 4.1 | | |
| Other/unknown | 22 | 2.5 | 64 | 1.3 | | 10 | 1.0 | 54 | 1.4 | | |
| Stage at diagnosis | | | | | | | | | | | |
| In situ | 78 | 8.7 | 567 | 11.4 | 0.04 | 199 | 19.6 | 368 | 9.3 | 0.0001 | |
| Localized | 562 | 62.9 | 3141 | 63.2 | | 601 | 59.0 | 2540 | 64.3 | | |
| Regional | 241 | 27.0 | 1209 | 24.3 | | 211 | 20.7 | 998 | 25.3 | | |
| Unstaged | 13 | 1.5 | 51 | 1.0 | | 7 | 0.7 | 44 | 1.1 | | |
| Histology | | | | | | | | | | | |
| Infiltrating ductal | 687 | 76.9 | 3638 | 73.2 | 0.04 | 695 | 68.3 | 2943 | 74.5 | 0.0001 | |
| Lobular | 44 | 4.9 | 364 | 7.3 | | 106 | 10.4 | 258 | 6.5 | | |
| Infiltrating ductal and lobular | 35 | 3.9 | 195 | 3.9 | | 54 | 5.3 | 141 | 3.6 | | |
| Not otherwise specified/ other | 128 | 14.3 | 771 | 15.5 | | 163 | 16.0 | 608 | 15.4 | | |
| Grade | | | | | | | | | | | |
| Well differentiated | 17 | 1.9 | 150 | 3.0 | 0.02 | 29 | 2.9 | 121 | 3.1 | 0.91 | |
| Moderately differentiated | 128 | 14.3 | 712 | 14.3 | | 137 | 13.5 | 575 | 14.6 | | |
| Poorly differentiated | 144 | 16.1 | 824 | 6.6 | | 169 | 16.6 | 655 | 16.6 | | |
| Undifferentiated | 17 | 1.9 | 185 | 3.7 | | 39 | 3.8 | 146 | 3.7 | | |
| Unknown grade | 588 | 65.8 | 3097 | 62.3 | | 644 | 63.3 | 2453 | 62.1 | | |

Table 1 (Continued)

Characteristics of mastectomy-treated breast cancer patients in the Surveillance, Epidemiology, and End Results (SEER) Breast Implant Surveillance Study, 1983–1989

| Number of primary tumors | | | | | | | | | | |
|--|-----|------|------|------|--------|-----|------|------|------|--------|
| One primary only | 771 | 86.2 | 4001 | 80.5 | 0.0001 | 867 | 85.2 | 3134 | 79.3 | 0.0001 |
| Two or more primaries | 123 | 13.8 | 967 | 19.5 | | 151 | 14.8 | 816 | 20.7 | |
| Radiation therapy during first course of treatment | | | | | | | | | | |
| No | 814 | 91.1 | 4626 | 93.1 | 0.03 | 969 | 95.2 | 3657 | 92.6 | 0.01 |
| Yes | 80 | 9.0 | 333 | 6.7 | | 48 | 4.7 | 285 | 7.2 | |
| Unknown | 0 | 0 | 9 | 0.2 | | 1 | 0.1 | 8 | 0.2 | |
| Vital status ^a | | | | | | | | | | |
| Alive | 538 | 60.2 | 3696 | 74.4 | 0.0001 | 867 | 85.2 | 2828 | 71.6 | 0.0001 |
| Dead | 356 | 39.8 | 1272 | 25.6 | | 151 | 14.8 | 1122 | 28.4 | |

^aFinal date of follow-up, December 1999.

Results

Study population

Eighty-five percent of study-eligible women completed the interview. Responders were slightly older compared with nonresponders. They also were more often non-Hispanic white, were diagnosed with *in situ* cancers, were less likely to have more than one primary tumor and were more likely to have lived until the end of the study period (Table 1).

Among the responders, 20% received a breast implant (Table 1). Their mean age at diagnosis was 47 years, and they were younger, on average, than women without implants. Somewhat higher proportions of women with implants were of non-Hispanic white race/ethnicity, resided in the San Francisco-Oakland region, were diagnosed in the late 1980s, and had tumors of lobular histology than women without implants. The percentage of women with *in situ* breast cancer was twice as high in women with breast implants as in nonimplanted women. In addition, women with implants were less likely to receive radiation therapy or to be diagnosed with more than one primary tumor.

Implant characteristics and usage

Implant information was obtained for 866 women; these women were slightly older and more likely to be living than women with unknown implant information. Among the 1143 breast implants received (Table 2), the most common types were silicone gel and double lumen. The majority of women (67%) received a unilateral implant a median of 9.6 months after breast cancer diagnosis. Approximately one-third of the women had an implant removed; the majority of these women chose to have the implant replaced. Saline-filled implants were removed for 48% of women, although saline-filled tissue expanders (temporary implants) may be incorrectly included in this category. Fifty-four percent of women with 'other' implants had them removed, and 49% had them replaced.

Survival

At the end of the follow-up period, 231 (5.3%) patients did not have complete follow-up. Twenty-eight percent of all patients died, with nearly two-thirds of these deaths due to breast cancer (Table 3). Women with implants had a similar distribution of causes of death to those without implants (Table 3), except for a significantly larger proportion of deaths due to suicide – although this was based on a small number of deaths (0.4% versus 0.03% of all patients, respectively; P=0.02). Among the 4385 patients with invasive breast cancer and known survival time, the 817 (19%) receiving a breast implant experienced better survival than women without implants, after adjustment for age at diagnosis (Fig. 1).

The multivariate Cox proportional hazards model showed that implant status was a significant factor associated with improved survival for deaths due to breast cancer and for nonbreast cancer mortality (Table 4). Risk of breast cancer death in women with implants was approximately one-half of that for women without implants, after adjustment for multiple clinical and sociodemographic factors. Age at diagnosis, stage, grade, histology, and radiation therapy were significant predictors of breast cancer death in this cohort, as they were for women without implants. With the exception of age, results were similar when modeled for nonbreast cancer mortality, although hazard rate ratios for women with implants were slightly higher overall. Among women with implants, the type of breast implant did not significantly impact survival, although women receiving saline implants had marginally lower risks than women receiving silicone gel implants.

For the subsample of 384 San Francisco Bay Area study subjects for whom we were able to assign census-level SES indicators, risk of death among women with breast implants compared with that among women without

Table 2

Characteristics of breast implants in mastectomy-treated breast cancer patients in the Surveillance, Epidemiology, and End Results Breast Implant Surveillance Study, 1983–1989 (n = 866)^a

| | Silicone gel ($n = 333$) | | Saline (<i>n</i> = 149) | | Double lumen ($n = 314$) | | Other $(n = 33)$ | | Unknown ($n = 37$) | | P value |
|----------------------------|----------------------------|------|--------------------------|------|----------------------------|------|------------------|------|----------------------|------|---------|
| | n | % | n | % | n | % | n | % | п | % | |
| Prevalence of type | | 38.4 | | 17.2 | | 36.3 | | 3.8 | | 4.3 | |
| Implant removal status | | | | | | | | | | | |
| No known removal | 244 | 73.3 | 77 | 51.7 | 216 | 64.9 | 15 | 45.5 | 25 | 67.6 | 0.0001 |
| Removed | 89 | 26.7 | 72 | 48.3 | 98 | 31.2 | 18 | 54.5 | 12 | 32.4 | |
| Implant replacement status | | | | | | | | | | | |
| No known replacement | 262 | 78.7 | 87 | 58.4 | 237 | 75.4 | 17 | 51.5 | 26 | 70.3 | 0.0001 |
| Replaced | 71 | 21.3 | 62 | 41.6 | 77 | 24.5 | 16 | 48.5 | 11 | 29.7 | |

^aExcludes 133 patients with missing implant information and 19 patients with bilateral implants of disordant types

implants continued to be reduced (hazard ratio, 0.50; 95% confidence interval, 0.20–1.25) after adjustment for census block-group level SES variables.

Discussion

In this large population-based study of breast cancer patients treated with mastectomy, risks of breast cancer death and nonbreast cancer mortality were lower in women with implants than in women without implants, after adjustment for potential confounders. Postmastectomy breast implants were used by one-fifth of patients who were slightly younger at diagnosis and were more likely to be of white race/ethnicity and to have *in situ* disease than women without implants. The silicone gel-filled implant was the most common type of implant received.

Although breast reconstruction has been shown to provide psychosocial benefits to breast cancer survivors [11-13], concerns have been raised that breast implants may increase the risk of local complications and systemic diseases, including certain cancers and autoimmune diseases [2,3,14,15]. Breast implants have been suggested to interfere with mammography, thereby facilitating delayed detection of breast tumors, and, consequently, decreased survival [16]. Despite recent Institute of Medicine recommendations to continue monitoring women with breast implants and to evaluate the potential long-term health effects [1], few research studies have addressed long-term health outcomes in this group. Moreover, these studies were often conducted on small, nonrepresentative samples without detailed information on implant type and history of use.

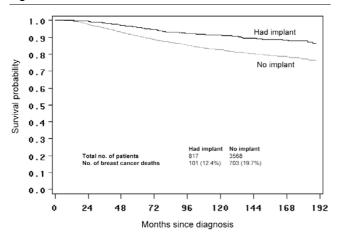
Georgiade and colleagues found that the survival time for 101 women undergoing breast reconstruction with breast implants was nonsignificantly better than that for 377 women without reconstruction, after adjustment for tumor grade, histology, lymph node involvement, and age at diag-

nosis, and after a median of 3 years of follow-up [6]. With a median of 13 years of follow-up, Petit and colleagues found that the risk of breast cancer death was marginally lower in 146 women who underwent breast reconstruction with silicone gel-filled implants than in a matched group without implants (relative risk, 0.6; 95% confidence interval, 0.3-1.1) [7]. Vandeweyer and colleagues compared 49 women who received saline-filled breast implants following mastectomy with a matched group of women who did not. They found no difference in the number of breast cancer deaths between the two groups [8]. In a matched analysis of 176 women with a mean of almost 6 years of follow-up, Park and colleagues found that women with breast implants after mastectomy had approximately a 70% reduced risk of death compared with women without implants (relative risk, 0.33; 95% confidence interval, 0.11-0.92) [9].

Our finding of better survival in women with breast implants is consistent with most of this research [6-8]. However, our study has the substantial advantages of being population-based, being large, having a long follow-up (median, 12.4 years), and including information on implant type and the implant removal and replacement. It is thus well suited to address public health concerns regarding the long-term survival and use of breast implants in women with early-stage, mastectomy-treated breast cancer. Such concerns have recently been re-evaluated in conjunction with the Food and Drug Administration hearings regarding the safety of silicone gel breast implants and their availability for the general market [17,18].

One explanation for our finding of reduced mortality in patients with breast implants may relate to self-selection rather than to a causal role of implants. Although most women who receive mastectomy are eligible to receive breast implants as part of breast reconstruction, surgeons may not recommend this surgery to women with health con-

Figure 1



Age-adjusted breast cancer survival curve by breast implant status, 1983–1989.

ditions such as obesity or a recent history of smoking that may contribute to postoperative complications, and may thus impact on survival [19,20]. In our data, the possibility of self-selection based on smoking is supported by the higher proportions of deaths from respiratory cancers and chronic obstructive pulmonary diseases in women without breast implants (Table 3). Further investigation is warranted for lifestyle factors (e.g. smoking, diet) and for comorbidities that may account for the survival advantage seen in women with breast implants.

In the present study, women with breast implants had a significant excess proportion of deaths due to suicide compared with women without implants. This finding, albeit based on small numbers, is consistent with observations from studies conducted in cosmetic breast implant patients [21,22] and suggests psychiatric consultation should also be considered for breast cancer patients seeking reconstructive surgery with breast implants. In any case, future studies with larger sample sizes are needed to confirm this finding in the breast reconstruction population.

An important bias of common concern in retrospective cohort studies is loss to follow-up. A total 231 (5.3%) of the 4385 patients included in the survival analysis did not have complete follow-up at the end of the study period. However, because of the relatively small percentage of patients lost to follow-up, we know that bias due to loss to follow-up has little impact on our survival findings since we found no substantial change in hazards ratios when we assumed the worst-case scenario that all patients lost to follow-up had all died or assumed that all patients lost to follow-up all lived until the end of the study period.

Furthermore, although our response rate was relatively high, differences between nonresponders and responders on several patient and tumor characteristics could have biased our findings. Although we were able to adjust for reported patient and tumor characteristics in our multivariate analyses, 356 women (nearly 40% of study-eligible patients) who did not participate in the study were deceased. In the unlikely event that all 356 deceased women had received breast implants, it is possible that the exclusion of these cases from our analysis could bias our results towards and beyond the null, and thereby overestimate the protective effects.

Although our survival analyses were adjusted for various demographic and clinical characteristics, our finding of better survival in women with breast implants could reflect uncontrolled confounding by social class, medical care, and psychological factors related to implant usage and survival. Among breast cancer patients treated with mastectomy, those choosing to have breast reconstruction have been shown to differ from women without breast reconstruction on SES, which may be an important factor affecting survival [23,24]. In a convenience sample of more than 200,000 breast cancer patients undergoing mastectomy between 1985 and 1995, Morrow and colleagues found that patients with a family income of \$40,000 or more were twice as likely as patients with a family income of less than \$40,000 to receive postmastectomy breast reconstruction [25]. Higher income may be a predictor of better survival after breast cancer, as women with higher incomes may have better access to cancer care and treatment. In the present study, SES did not alter the effect of implants on survival in the subset of women for whom SES measures were available. Differences in these area-level measures of SES are thus not likely to contribute substantially to the survival differences between breast cancer patients with and without implants in this study.

Additional unmeasured confounders related to the increased medical care of women with breast implants could explain the protective association of breast implants with cancer survival. Because women with breast implants may be more closely followed in their medical care, they may have recurrences diagnosed and treated earlier; thus they may experience better survival than women without implants. Although our study lacked information on breast cancer recurrence, we were able to examine the impact of subsequently diagnosed primary breast tumors. We observed that the proportion of women with two or more primary breast tumors was lower in women with breast implants than in women without (15% and 21%, respectively).

To address the possibility that a higher incidence of subsequently diagnosed primary breast tumors impacted survival in women without breast implants, we limited survival analyses to women with only one primary tumor (n = 3535) and

Table 3

Distribution of living and deceased patients by breast implant status in the Surveillance, Epidemiology, and End Results Breast Implant Surveillance Study, 1983–1989 (n = 4385)

| | Women with breast implant $(n = 817)$ | | | breast implants 3568) | Total $(n = 4385)$ | | P value ^a |
|---------------------------------------|---------------------------------------|------|------|--------------------------|--------------------|------|----------------------|
| | n | % | n | % | n | % | = |
| Alive | 676 | 82.3 | 2498 | 70.0 | 3174 | 72.4 | < 0.0001 |
| Deceased | | | | | | | |
| All malignant cancers | | | | | | | |
| Digestive system | 2 | 0.2 | 32 | 0.9 | 34 | 0.8 | 0.08 |
| Respiratory | 3 | 0.4 | 51 | 1.4 | 54 | 1.2 | 0.01 |
| Breast | 101 | 12.4 | 703 | 19.7 | 804 | 18.3 | < 0.0001 |
| Female genital | 4 | 0.5 | 20 | 0.6 | 24 | 0.5 | 0.80 |
| Kidney | - | - | 2 | 0.1 | 2 | 0.2 | - |
| Brain | - | - | 7 | 0.2 | 7 | 0.2 | - |
| Melanoma | 1 | 0.1 | 2 | 0.1 | 3 | 0.1 | 0.46 |
| Multiple myeloma | - | - | 3 | 0.1 | 3 | 0.1 | - |
| Non-Hodgkin's lymphoma | - | - | 3 | 0.1 | 3 | 0.1 | - |
| Leukemia | 2 | 0.2 | 2 | 0.1 | 4 | 0.1 | 0.16 |
| Diabetes mellitus | 2 | 0.2 | 13 | 0.4 | 15 | 0.3 | 0.60 |
| Circulatory system | | | | | | | |
| Heart disease | 4 | 0.5 | 65 | 1.8 | 69 | 1.6 | 0.01 |
| Cerebrovascular disease | 2 | 0.2 | 14 | 0.4 | 16 | 0.4 | 0.75 |
| Atherosclerosis | - | - | 3 | 0.1 | 3 | 0.1 | - |
| Respiratory disease | | | | | | | |
| Pneumonia/influenza | 1 | 0.1 | 10 | 0.3 | 11 | 0.3 | - |
| Chronic obstructive pulmonary disease | 2 | 0.2 | 23 | 0.6 | 25 | 0.6 | 0.21 |
| Digestive system disease | | | | | | | |
| Stomach/duodenal ulcers | - | - | 3 | 0.1 | 3 | 0.1 | - |
| Chronic liver disease | 1 | 0.1 | 7 | 0.2 | 8 | 0.2 | - |
| Nephritis | - | - | 7 | 0.2 | 7 | 0.2 | - |
| All external causes | | | | | | | |
| Accidents | - | - | 4 | 0.1 | 4 | 0.3 | - |
| Suicides | 3 | 0.4 | 1 | 0.03 | 4 | 0.3 | 0.02 |
| Other cause of death | 5 | 0.6 | 38 | 1.1 | 43 | 3.6 | 0.26 |
| Unknown cause of death | 7 | 0.9 | 32 | 0.9 | 39 | 3.2 | 0.91 |

Sum of deaths will not add to overall total since data are only shown for causes with at least two deaths in either group of women. ^aP value for chi-square test or, where appropriate, Fisher's Exact Test.

found a consistently reduced risk of breast cancer death associated with breast implant usage (hazard ratio, 0.54; 95% confidence interval, 0.42–0.68), after adjusting for similar prognostic factors. Our findings also are consistent with results from studies showing a reduced risk of death in augmentation mammoplasty patients with at least 10 years of follow-up compared with the general population [26-29]. Furthermore, psychological factors underlying a

woman's decision to obtain breast implants [30,31], including body image concerns and self-esteem, may play a role in lifestyle behaviors relevant to survival, although the extent to which they directly impact survival is unclear.

Several biological mechanisms have been proposed to explain how breast implants may influence survival outcomes [16,26,32,33]. Breast implants may stimulate a

Table 4

Proportional hazards regression model: hazard ratio and 95% confidence interval (CI) for mastectomy-treated breast cancer patients in the Surveillance, Epidemiology, and End Results (SEER) Breast Implant Surveillance Study, 1983–1989 (n = 4385)^a

| Covariate | Distributio | n of sample | Breast car | ncer mortality | Non-breast cancer mortality | | |
|----------------------------------|-------------|-------------|--------------|----------------------------|-----------------------------|----------------------------|--|
| | n | % | Hazard ratio | 95% confidence interval | Hazard ratio | 95% confidence interval | |
| Implant status | | | | | | | |
| No (referent) | 3568 | 81.4 | 1.00 | - | 1.00 | - | |
| Yes | 817 | 18.6 | 0.54 | 0.43-0.67 | 0.59 | 0.41-0.85 | |
| Age at diagnosis | | | | | | | |
| < 35 years | 163 | 3.7 | 1.95 | 1.42-2.69 | 0.24 | 0.09-0.66 | |
| 35-44 years | 805 | 18.4 | 1.29 | 1.07-1.56 | 0.19 | 0.12-0.30 | |
| 45-54 years | 1332 | 30.4 | 1.02 | 0.86-1.20 | 0.35 | 0.26-0.46 | |
| 55-64 years (referent) | 2085 | 47.6 | 1.00 | - | - | - | |
| Race/ethnicity | | | | | | | |
| Non-Hispanic White (referent) | 3915 | 89.3 | 1.00 | - | 1.00 | - | |
| Non-Hispanic Black | 131 | 3.0 | 0.90 | 0.58-1.39 | 1.58 | 0.93-2.68 | |
| Hispanic | 120 | 2.7 | 1.37 | 0.93-2.04 | 1.22 | 0.64-2.33 | |
| Non-Hispanic Asian | 160 | 3.7 | 0.86 | 0.57-1.31 | 0.68 | 0.33-1.39 | |
| Other/unknown | 59 | 1.4 | 0.75 | 0.37-1.50 | 1.36 | 0.60-3.07 | |
| Stage at diagnosis | | | | | | | |
| Local (referent) | 3126 | 71.3 | 1.00 | - | 1.00 | - | |
| Regional | 1208 | 27.6 | 2.28 | 1.97-2.63 | 1.86 | 1.65-2.09 | |
| Unstaged | 51 | 1.2 | 3.80 | 2.41-5.99 | 3.35 | 2.28-4.92 | |
| SEER region | | | | | | | |
| San Francisco-Oakland (referent) | 1624 | 37.0 | 1.00 | - | 1.00 | - | |
| Seattle-Puget Sound | 1423 | 34.1 | 1.10 | 0.91-1.32 | 1.17 | 0.91-1.51 | |
| lowa | 1268 | 28.9 | 1.15 | 0.96-1.38 | 0.86 | 0.66-1.13 | |
| Year of diagnosis | | | | | | | |
| 1983 (referent) | 1037 | 23.7 | 1.00 | - | 1.00 | - | |
| 1985 | 1003 | 22.9 | 1.06 | 0.88-1.29 | 0.96 | 0.73-1.27 | |
| 1987 | 1232 | 28.1 | 0.97 | 0.80-1.18 | 1.05 | 0.78-1.40 | |
| 1989 | 1113 | 25.4 | 0.84 | 0.68-1.04 | 1.12 | 0.80-1.56 | |
| Grade | | | | | | | |
| Well differentiated (referent) | 142 | 3.2 | 1.00 | - | 1.00 | - | |
| Moderately differentiated | 695 | 15.9 | 2.16 | 1.13-4.13 | 0.75 | 0.42-1.34 | |
| Poorly differentiated | 817 | 18.6 | 3.45 | 1.82-6.53 | 0.79 | 0.44-1.40 | |
| Undifferentiated | 182 | 4.2 | 4.97 | 2.52-9.78 | 1.23 | 0.60-2.52 | |
| Unknown | 2549 | 58.1 | 2.41 | 1.28-4.52 | 0.85 | 0.50-1.45 | |
| Histology | | | | | | | |
| Ductal (referent) | 3253 | 74.2 | 1.00 | - | 1.00 | - | |
| Lobular | 279 | 6.4 | 1.09 | 0.82-1.44 | 1.26 | 0.88-1.81 | |
| Mixed ductal and lobular | 167 | 3.8 | 1.06 | 0.74-1.53 | 0.66 | 0.32-1.33 | |
| Other | 686 | 15.6 | 0.71 | 0.57-0.89 | 1.01 | 0.76-1.34 | |

Table 4 (Continued)

Proportional hazards regression model: hazard ratio and 95% confidence interval (CI) for mastectomy-treated breast cancer patients in the Surveillance, Epidemiology, and End Results (SEER) Breast Implant Surveillance Study, 1983-1989 (n = 4385)^a

| Radiation therapy | | | | | | |
|-------------------------------------|------|------|------|------------|------|------------|
| No (referent) | 4047 | 92.3 | 1.00 | - | 1.00 | - |
| Yes | 329 | 7.5 | 1.43 | 1.15-1.78 | 0.84 | 0.54-1.30 |
| Unknown | 9 | 0.2 | 4.68 | 1.74-12.60 | - | - |
| Type of breast implant ^b | | | | | | |
| Silicone gel (referent) | 274 | 39.8 | 1.00 | - | 1.00 | - |
| Saline | 118 | 17.1 | 1.01 | 0.44-2.34 | 1.75 | 0.29-10.39 |
| Double lumen | 240 | 34.8 | 1.49 | 0.83-2.70 | 3.13 | 0.91-10.78 |
| Other | 26 | 3.8 | 1.11 | 0.24-5.03 | - | - |
| Unknown | 31 | 4.5 | 2.03 | 0.71-5.79 | 6.59 | 1.17-37.06 |

^aAdjusted for age, year, stage at diagnosis, race/ethnicity, SEER region, tumor grade, histology, and radiation therapy.

local immune response in which cancer cells are more likely to be destroyed [34]. Breast implants may compress breast tissue, reducing the flow of blood and thereby slowing the rate of cell or tumor growth. Breast implants may decrease the temperature of the breast by separating the breast tissue from the body, thereby decreasing the metabolic rate and slowing the growth rate of residual breast cancer cells [35]. These mechanisms may provide important clues in cancer prevention and warrant further investigation.

Conclusions

With a median of more than 12 years of follow-up on patients, our population-based study shows that the risk of breast cancer mortality in patients with breast implants following mastectomy is about one-half of that for patients without implants, after adjustment for prognostic characteristics. Although patients in our study received implants in the 1980s and early 1990s, breast implants continue to be an integral part of breast reconstruction in breast cancer patients and have not changed dramatically in design. Thus, despite an overall decrease in implant use among breast cancer patients, breast implants remain an important and commonly used option for women considering reconstruction. Certainly, further research is needed to explain the survival differential in women with breast implants and those without, by examining potentially explanatory factors such as SES, comorbidity, smoking, or other lifestyle factors. However, based on this large, representative sample of breast cancer patients with extensive follow-up, we found that breast implants following mastectomy do not appear to confer any survival disadvantage following earlystage breast cancer in women younger than 65 years old.

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

SLG, DWW, JLS, and CFL implemented the study and acquired the data. GML, SLG, and CDO participated in the design and conceptualization of the study. GML performed the statistical analysis and drafted the manuscript. GML, SLG, CDO, and THMK participated in the analysis and interpretation of the data. All authors read and approved the final manuscript.

Acknowledgements

Data for the SEER Breast Implant Surveillance Study were collected by the Northern California Cancer Center (contract N01-CN-05224 Modification Number 12), Seattle-Puget Sound Cancer Registry (contract N01-CN-05230), and Iowa Cancer Registry (contract N01-CN-05229 Modification Number 11) with support of the National Cancer Institute, National Institutes of Health. The content of this publication does not necessarily reflect the views or policies of the US Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government.

References

- Bondurant S, Ernster V, Herdman R, Eds: Safety of silicone breast implants (Report of the Committee on the Safety of Silicone Breast Implants, Division of Health Promotion and Disease Prevention, Institute of Medicine). In Book Safety of Silicone Breast Implants (Report of the Committee on the Safety of Silicone Breast Implants, Division of Health Promotion and Disease Prevention, Institute of Medicine) Washington, DC: National Academy Press: 2000.
- Brown SL: Epidemiology of silicone-gel breast implants. Epidemiology 2002, 13:S34-S39.
- Silverman BG, Brown SL, Bright RA, Kaczmarek RG, Arrowsmith-Lowe JB, Kessler DA: Reported complications of silicone gel breast implants: an epidemiologic review. Ann Intern Med 1996, 124:744-756.
- Janowsky EC, Kupper LL, Hulka BS: Meta-analyses of the relation between silicone breast implants and the risk of connective-tissue diseases. N Engl J Med 2000, 342:781-790.
- Polednak AP: How frequent is postmastectomy breast reconstructive surgery? A study linking two statewide databases. Plast Reconstr Surg 2001, 108:73-77.
- Georgiade GS, Riefkohl R, Cox E, McCarty KS, Seigler HF, Georgiade NG, Snowhite JC: Long-term clinical outcome of immedi-

bModel (n = 689) restricted to women with implant-specific information and concordant bilateral implants

- ate reconstruction after mastectomy. Plast Reconstr Surg 1985, **76**:415-420.
- Petit JY, Le MG, Mouriesse H, Rietjens M, Gill P, Contesso G, Lehmann A: Can breast reconstruction with gel-filled silicone implants increase the risk of death and second primary cancer in patients treated by mastectomy for breast cancer? Plast Reconstr Surg 1994, 94:115-119.
- Vandeweyer E, Hertens D, Nogaret JM, Deraemaecker R: Immediate breast reconstruction with saline-filled implants: no interference with the oncologic outcome? Plast Reconstr Surg 2001. 107:1409-1412.
- Park AJ, Chetty U, Watson ACH: Silicone breast implants and breast cancer. Breast 1998, 7:22-26.
- O'Malley CD, Le GM, Glaser SL, Shema SJ, West DW: Socioe-conomic status and breast carcinoma survival in four racial/ethnic groups: a population-based study. Cancer 2003, 97:1303-1311.
- Harcourt DM, Rumsey NJ, Ambler NR, Cawthorn SJ, Reid CD, Maddox PR, Kenealy JM, Rainsbury RM, Umpleby HC: The psychological effect of mastectomy with or without breast reconstruction: a prospective, multicenter study. Plast Reconstr Surg 2003, 111:1060-1068.
- Cederna PS, Yates WR, Chang P, Cram AE, Ricciardelli EJ: Post-mastectomy reconstruction: comparative analysis of the psy-chosocial, functional, and cosmetic effects of transverse rectus abdominis musculocutaneous flap versus breast implant reconstruction. *Ann Plast Surg* 1995, 35:458-468.
- Alderman AK, Wilkins EG, Lowery JC, Kim M, Davis JA: Determinants of patient satisfaction in postmastectomy breast reconstruction. Plast Reconstr Surg 2000, 106:769-776.
- Nahabedian MY, Tsangaris T, Momen B, Manson PN: Infectious complications following breast reconstruction with expanders and implants. Plast Reconstr Surg 2003, 112:467-476.
- Gabriel SE, Woods JE, O'Fallon WM, Beard CM, Kurland LT, Melton LJ 3rd: Complications leading to surgery after breast implantation. N Engl J Med 1997, 336:677-682.
- Hoshaw SJ, Klein PJ, Clark BD, Cook RR, Perkins LL: Breast implants and cancer: causation, delayed detection, and survival. Plast Reconstr Surg 2001, 107:1393-1407.
- Ault A: Silicone breast implants may be close to US approval [news]. Lancet 2003, 362:1384.
- Moynihan R: Safety concerns about breast implants persist [news]. BMJ 2003, 327:947.
- Lin KY, Johns FR, Gibson J, Long M, Drake DB, Moore MM: An outcome study of breast reconstruction: presurgical identification of risk factors for complications. Ann Surg Oncol 2001, 9:588-591
- Yeh KA, Lyle G, Wei JP, Sherry R: Immediate breast reconstruction in breast cancer: morbidity and outcome. Am Surg 1998, 64:1195-1199.
- Brinton LA, Lubin JH, Burich MC, Colton T, Brown SL, Hoover RN: Breast cancer following augmentation mammoplasty (United States). Cancer Causes Control 2000, 11:819-827.
- Koot VC, Peeters PH, Granath F, Grobbee DE, Nyren O: Total and cause specific mortality among Swedish women with cosmetic breast implants: prospective study. Br Med J 2003, 326:527-528.
- Dayal HH, Power RN, Chiu C: Race and socio-economic status in survival from breast cancer. J Chronic Dis 1982, 35:675-683.
- Gordon NH, Crowe JP, Brumberg DJ, Berger NA: Socioeconomic factors and race in breast cancer recurrence and survival. Am J Epidemiol 1992, 135:609-618.
- Morrow M, Scott SK, Menck HR, Mustoe TA, Winchester DP: Factors influencing the use of breast reconstruction postmastectomy: a National Cancer Database study. J Am Coll Surg 2001, 192:1-8.
- Deapen DM, Bernstein L, Brody GS: Are breast implants anticarcinogenic? A 14-year follow-up of the Los Angeles Study. Plast Reconstr Surg 1997, 99:1346-1353.
- Brinton LA, Lubin JH, Burich MC, Colton T, Hoover RN: Mortality among augmentation mammoplasty patients. Epidemiology 2001, 12:321-326.
- Deapen D, Hamilton A, Bernstein L, Brody GS: Breast cancer stage at diagnosis and survival among patients with prior breast implants. Plast Reconstr Surg 2000, 105:535-540.

- Birdsell DC, Jenkins H, Berkel H: Breast cancer diagnosis and survival in women with and without breast implants. Plast Reconstr Surg 1993, 92:795-800.
- Reaby LL: Reasons why women who have mastectomy decide to have or not to have breast reconstruction. Plast Reconstr Surg 1998, 101:1810-1818.
- 31. Sarwer DB, LaRossa D, Bartlett SP, Low DW, Bucky LP, Whitaker LA: **Body image concerns of breast augmentation patients.** *Plast Reconstr Surg* 2003, **112**:83-90.
- Brinton LA, Malone KE, Coates RJ, Schoenberg JB, Swanson CA, Daling JR, Stanford JL: Breast enlargement and reduction: results from a breast cancer case-control study. Plast Reconstr Surg 1996, 97:269-275.
- Dreyfuss DA, Singh S, Dowlatshahi K, Krizek TJ: Silicone implants as an anticarcinogen. Surg Forum 1987, 38:587-588.
- Su CW, Dreyfuss DA, Krizek TJ, Leoni KJ: Silicone implants and the inhibition of cancer. Plast Reconstr Surg 1995, 96:513-518. discussion 519–520
- Ramasastry SS, Weinstein LW, Zerbe A, Narayanan K, LaPietra D, Futrell JW: Regression of local and distant tumor growth by tissue expansion: an experimental study of mammary carcinoma 13,762 in rats. Plast Reconstr Surg 1991, 87:1-7. discussion 8–9