

Do Breast Implants Affect Breast Cancer Survival?

An Expert Interview With Jacques Brisson, MD, DSc

Linda Brookes, MSc, Jacques Brisson, MD, DSc

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The Study

Dr. Brisson is senior author of:

Lavigne E, Holowaty EJ, Pan SY, et al. Breast cancer detection and survival among women with cosmetic breast implants: systematic review and meta-analysis of observational studies. *BMJ*. 2013;346:f2399

About the Interviewee

Dr. Brisson is a Professor in the Department of Social and Preventive Medicine of the Faculty of Medicine at Laval University, Quebec, Canada, and Director of the Epidemiology Graduate Studies Program at Laval University, where he also directs the evaluation team of the Quebec Breast Cancer Screening Program (Programme Québécois de Dépistage du Cancer du Sein). His research interests include fundamental research in cancer epidemiology, investigating the possible causes of breast cancer (diet, vitamin D and calcium, growth hormones, genetic polymorphisms), and applied research in the evaluation of breast cancer screening and treatments.

Background to the Interview

Cosmetic breast augmentation is the most popular procedure performed by plastic surgeons worldwide, with 1,205,251 of these procedures reported in an international 2011 survey. The United States had the highest rates, followed by Brazil, China, Japan, and Mexico,^[1] and its popularity is increasing everywhere. In 2012, 330,631 breast augmentations were performed in the United States, a 227% increase since 1997. Of those performed, only 28% used saline implants and 72% used silicone.^[2]

Information is widely available on the risks and possible adverse outcomes associated with breast augmentation surgery; nonetheless, there is widespread concern about its possible long-term health effects. Epidemiologic studies have shown no increased risk for breast cancer in women with breast implants compared with those without them, but studies on survival after breast cancer diagnosis in women with implants have produced uncertain results.

To address whether consolidated data could show a difference between women with and without breast implants in terms of stage distribution at diagnosis of breast cancer and postdiagnosis survival, Canadian researchers led by Dr. Brisson and Eric Lavigne, PhD, at Laval University, Quebec, carried out a systemic review and quantitative meta-analysis of studies published up to September 2012.^[3] Their investigation was supported by funding from the Unité de recherche en santé des populations, Cancer Care Ontario, and the Public Health Agency of Canada.

Through a literature search of Medline, Embase, Global health, CINAHL, IPAB, and PsycINFO, the researchers identified 13 studies in women who had had cosmetic breast augmentation and in whom breast cancer was diagnosed that were eligible for inclusion in the meta-analyses. Most of the studies were done in the United States, and the rest in Canada or Northern Europe.

The first meta-analysis, based on 12 studies, identified a relative risk of 1.26 (95% confidence interval [CI], 0.99-1.60; $P=.058$) for a nonlocalized stage of breast cancer at diagnosis in women with implants vs women without implants.

This suggested that at diagnosis, women with cosmetic breast implants who are diagnosed with breast cancer tend to have later-stage tumors compared to cases diagnosed among women without implants.

The second meta-analysis, based on 5 of the studies, showed reduced survival after breast cancer among women who had implants compared with those who did not; the overall hazard ratio for breast cancer-specific mortality was 1.38 (95% CI, 1.08 to 1.75).

In the report of their study,^[3] Dr. Brisson and his colleagues pointed out limitations specific to their analyses overall, including the possibility of selection bias, misclassification bias, confounding bias that affected individual studies, and the small number of studies used in the second meta-analysis. As a result, "considering the gaps and limitations in the available literature," their results should be interpreted with caution, they said. However, their findings support other accumulating evidence, and consequently, they believe that "further investigations are warranted into the long-term effects of cosmetic breast implants on the detection and prognosis of breast cancer, adjusting for potential confounders."

Dr. Brisson spoke further about the study with Linda Brookes, MSc, for Medscape.

The Interview

Medscape: Canadian researchers, including those in your own group, seem to have taken particular interest in the long-term safety of cosmetic breast implants. Is that because of the number of breast augmentation procedures done in Canada?

Dr. Brisson: Breast augmentation is popular in Canada, as it is in the United States. Canadian physicians have been very aware of and sensitive to issues of safety associated with breast implants. Some of the initial epidemiologic studies way back in the 1990s concerning the possible carcinogenic effects of implants on breast cancer risk originated in Canada.^[4,5] In the 1990s, because of the concerns about breast implants and their possible health effects, including increased risk for cancers at different sites and immune effects, Health Canada -- which is responsible for regulating these devices -- realized that few studies had been conducted on the health effects of implants. This agency was therefore keen on supporting a major Canadian cohort study that would document the possible health effects of implants.^[6]

Medscape: Was that the Ontario and Quebec breast implant cohort, which was the basis for your earlier studies?

Dr. Brisson: Yes. On the basis of our Canadian cohort, we published a number of reports in the early 2000s,^[7,8] and then we had further follow-up.^[9-11] It was this second series of publications that finally

encouraged us to do a systematic review of the association of breast implants with breast cancer survival.

Medscape: I think that it is generally agreed that there is no evidence that breast implants are associated with an increased incidence of breast cancer?

Dr. Brisson: That is right, and it is important to remember that. This is the very basis from which we should start: that breast implants are not associated with an increased risk for breast cancer occurrence. A number of studies have evaluated the relationship between breast implants and subsequent breast cancer risk. In fact, most showed a slight *reduction* in the incidence of breast cancer among women with breast implants compared with women without implants.

Medscape: What would be the reasons for that?

Dr. Brisson: There are a number of possible reasons, but my own preferred hypothesis is that breast implants are most often implanted because the breasts are smaller in size, which may mean that there is less breast tissue at risk.

Medscape: In your latest study, you seemed to face several challenges in locating appropriate studies in women with breast implants and a breast cancer diagnosis to include in your meta-analyses. Why was that? Has there been a lack of research worldwide?

Dr. Brisson: Although breast cancer is perceived to be frequent, cohorts of women with implants that have been followed long enough to accrue a sufficient number of new breast cancer cases and study survival are relatively rare. Our Canadian cohort is the largest to date, not only in terms of the number of women who have had implants and have been followed, but also in terms of the number of new breast cancer cases that were identified and could be examined in terms of their stage and their survival. It is quite a challenge to assemble a cohort of women with implants, then to accrue among them a sufficient number of breast cancer cases to examine their stage, and then to follow up these cases for examining survival. Finally, in order to examine the possible association of implants with stage and survival, you need either a comparison cohort or other data that are appropriate for comparison to women with breast implants.

Medscape: Would the best comparison groups be women who had other cosmetic surgeries, or could you draw comparisons with any women in the general population with breast cancer?

Dr. Brisson: We think a comparison group of women who had other kinds of cosmetic surgeries are more likely to be comparable to women who have breast implants. For example, there are similarities in concerns about appearance and socioeconomic status.

Medscape: In the study under discussion,^[3] you and your colleagues performed 2 meta-analyses. Which do you think has the most far-reaching implications?

Dr. Brisson: Each meta-analysis addressed one of our questions. The first was whether breast cancer was diagnosed at a later stage in women with implants than in women with breast cancer following no-implant surgery, and we saw a slight increase in stage at diagnosis in women with implants.

The other meta-analysis addressed whether breast cancer survival was different among women with implants who developed this disease. We felt that this second meta-analysis, which was newer, was more important and needed to be examined and interpreted with care.

Medscape: Didn't this finding contradict the results of single studies, including one of your own previous studies?^[9]

Dr. Brisson: Actually, we did further follow-up of our cohort and reanalyzed survival. The results of this extended survival analysis were slightly different from the initial ones.^[11] They suggested that perhaps women with breast cancer following implants had reduced breast cancer survival, although this reduction was not statistically significant. So we concluded that it might be worthwhile to look at the bulk of the evidence on breast implants and breast cancer survival. When we put all the survival studies together, we saw a statistically significant increase in breast cancer-specific mortality rate in breast cancer patients with implants, which means reduced breast cancer survival.

Medscape: How should this result be considered by individual women looking at their personal risks? It must be difficult.

Dr. Brisson: You are right; hazard ratios are difficult to interpret. One point that needs to be taken into consideration is the relatively limited number of studies, which also have limitations themselves. So we have to be wary of the survival result, and that is why we call for additional studies. But while waiting for additional evidence, physicians need to consider this result and determine how they are going to use it.

One can try to translate the result into more familiar kinds of numbers. In our study, we reported an overall hazard ratio of 1.38 for breast cancer-specific mortality in women with cosmetic implants compared with women with no implants. So what does it mean in terms of breast cancer-specific survival? To give you a sense of it, the 5-year overall relative survival ratio for breast cancer in Canada right now is around 88%^[12] -- that is, the likelihood of surviving breast cancer 5 years after a diagnosis is about 88%. If the results of our study hold true, for a woman who has implants and then has a diagnosis of breast cancer, the 5-year breast cancer-specific survival after diagnosis, on average, would be approximately 84%. So, breast implants would be associated with a possible absolute 4% reduction in 5-year breast cancer-specific survival.

These numbers are very approximate, but they give us a sense of the overall absolute reduction in 5-year breast cancer-specific survival that goes with that hazard ratio of 1.38. Such a number could be useful to both physicians and women when they are trying to understand our results.

Medscape: Breast cancer survival rates vary among different countries. How does Canada rank?

Dr. Brisson: An 88% 5-year relative survival for breast cancer is close to what it is in the United States.^[13,14] Because most of the studies in our meta-analysis were done in the United States and Canada -- actually, the largest study was done in Canada^[11] -- our results and the above interpretation apply primarily to North America. Breast cancer survival seems to be a little lower in Europe.^[15] Therefore, a hazard ratio of 1.38 could translate into a somewhat larger average absolute reduction in survival there.

Medscape: Were you able to find any association between survival and the number of surgeries the women had had? We know that many women who have cosmetic implants need to have additional surgery^[16] -- and quite a high proportion need it within 5 years.

Dr. Brisson: Unfortunately, we don't have those data. But you are quite right; it would be very valuable information to have.

Medscape: The first meta-analysis you mentioned showed that disease was identified at a later stage in patients with breast implants. This was presumably related to the result about survival?

Dr. Brisson: Yes; I think that the finding about later stage at diagnosis, which is also important, probably does provide a reasonable explanation for the survival findings. In our own survival analysis, the lower breast cancer survival in patients with implants was almost entirely attributable to later stage at diagnosis.^[11]

Medscape: In your article, you stress the need for specialized radiographic techniques in women with breast implants having mammography.

Dr. Brisson: Special positioning techniques can be used to visualize as much breast tissue as possible during mammography when examining a woman with implants. Unfortunately, even with these techniques, a portion of breast tissue remains difficult to visualize.

Medscape: Do your findings reflect the fact that patients aren't seeking out mammographers who are experienced in this type of imaging? Is there any evidence that disease is being missed because of failure to have the proper imaging done? What is the evidence for using other imaging techniques, such as MRI?

Dr. Brisson: These are all important issues, but I do not know of a recent careful review of the literature on them. Given our meta-analysis, such a review would be useful.

Medscape: There don't seem to be any specific professional guidelines on this, although the American Society for Aesthetic Plastic Surgery^[17] and the American Cancer Society^[18] recommend that patients have implant displacement views done on mammography.

Dr. Brisson: That is right. Breast cancer screening recommendations for women with breast implants are usually not very much different from those for women without breast implants, except for the additional imaging techniques. Mammography is recommended at about the same ages and intervals, but the caveat is just to do additional imaging positioning techniques in women with implants in order to visualize as much breast tissue as possible. Our results should encourage breast imaging specialists to make sure that imaging guidelines for women with implants are appropriate and are followed.

Medscape: Has anything been learned about screening from studies on women who have had breast reconstructive surgery after mastectomy?

Dr. Brisson: The imaging challenges after breast reconstruction surgery are very different from those after implants for cosmetic purposes. Our results apply only to women who had implants for cosmetic purposes.

Medscape: Obviously, more studies are needed in patients with cosmetic breast implants, but how can these be done?

Dr. Brisson: I hope that all those who already have cohorts of women with breast implants will follow them further and gather additional information on stage at diagnosis and survival after breast cancer diagnosis. If other investigators can assemble additional cohorts by use of implant registries, or other means, that would also be helpful. It is a major task, but the information would be most valuable.

Medscape: Are you continuing to follow up on your Canadian cohort?

Dr. Brisson: Hopefully in a few years, we will be able to do further follow-up and add to the knowledge in this area.

Medscape: What would be your final thoughts on your results?

Dr. Brisson: One point that I'd like to make again and stress is that breast cancer incidence is not greater among women with breast implants.

The second point that should be emphasized is that the increase in breast cancer-specific mortality we saw applies to women diagnosed with breast cancer following implants. Breast cancer mortality among all women with implants is not increased. Like breast cancer incidence, breast cancer mortality among all women with implants tends to be slightly lower than that in the general population.^[7]

The final point I'd like to stress again is that these results should be taken into account by women and physicians but they are based on a small number of studies that had limitations. I look forward very much to seeing further studies on survival among women with implants and breast cancer from other investigators who already have cohorts of women with implants that they are following, so that we have better data on this important outcome for women with cosmetic breast implants.

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