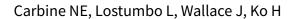


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Risk-reducing mastectomy for the prevention of primary breast cancer (Review)



Carbine NE, Lostumbo L, Wallace J, Ko H. Risk-reducing mastectomy for the prevention of primary breast cancer. *Cochrane Database of Systematic Reviews* 2018, Issue 4. Art. No.: CD002748. DOI: 10.1002/14651858.CD002748.pub4.

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[Intervention Review]

Risk-reducing mastectomy for the prevention of primary breast cancer

Nora E Carbine¹, Liz Lostumbo², Judi Wallace³, Henry Ko^{4,5}

¹Translational Breast Cancer Research Consortium (TBCRC), Georgetown University Lombardi Cancer Center, Washington, D.C., USA. ²Gaithersburg, Maryland, USA. ³Baltimore, Maryland, USA. ⁴NHMRC Clinical Trials Centre, University of Sydney, Camperdown, Australia. ⁵Centre for Health Services Research, SingHealth, Academic Medicine Research Institute, Duke-NUS Graduate Medical School, Singapore, Singapore

Contact: Nora E Carbine, Translational Breast Cancer Research Consortium (TBCRC), Georgetown University Lombardi Cancer Center, Washington, D.C., 20007, USA. necarbine@comcast.net.

Editorial group: Cochrane Breast Cancer Group.

Publication status and date: Stable (no update expected for reasons given in 'What's new'), published in Issue 1, 2019.

Citation: Carbine NE, Lostumbo L, Wallace J, Ko H. Risk-reducing mastectomy for the prevention of primary breast cancer. *Cochrane Database of Systematic Reviews* 2018, Issue 4. Art. No.: CD002748. DOI: 10.1002/14651858.CD002748.pub4.

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ABSTRACT

Background

Recent progress in understanding the genetic basis of breast cancer and widely publicized reports of celebrities undergoing risk-reducing mastectomy (RRM) have increased interest in RRM as a method of preventing breast cancer. This is an update of a Cochrane Review first published in 2004 and previously updated in 2006 and 2010.

Objectives

(i) To determine whether risk-reducing mastectomy reduces death rates from any cause in women who have never had breast cancer and in women who have a history of breast cancer in one breast, and (ii) to examine the effect of risk-reducing mastectomy on other endpoints, including breast cancer incidence, breast cancer mortality, disease-free survival, physical morbidity, and psychosocial outcomes.

Search methods

For this Review update, we searched Cochrane Breast Cancer's Specialized Register, MEDLINE, Embase and the WHO International Clinical Trials Registry Platform (ICTRP) on 9 July 2016. We included studies in English.

Selection criteria

Participants included women at risk for breast cancer in at least one breast. Interventions included all types of mastectomy performed for the purpose of preventing breast cancer.

Data collection and analysis

At least two review authors independently abstracted data from each report. We summarized data descriptively; quantitative meta-analysis was not feasible due to heterogeneity of study designs and insufficient reporting. We analyzed data separately for bilateral risk-reducing mastectomy (BRRM) and contralateral risk-reducing mastectomy (CRRM). Four review authors assessed the methodological quality to determine whether or not the methods used sufficiently minimized selection bias, performance bias, detection bias, and attrition bias.

Main results

All 61 included studies were observational studies with some methodological limitations; randomized trials were absent. The studies presented data on 15,077 women with a wide range of risk factors for breast cancer, who underwent RRM.

Twenty-one BRRM studies looking at the incidence of breast cancer or disease-specific mortality, or both, reported reductions after BRRM, particularly for those women with BRCA1/2 mutations. Twenty-six CRRM studies consistently reported reductions in incidence of



contralateral breast cancer but were inconsistent about improvements in disease-specific survival. Seven studies attempted to control for multiple differences between intervention groups and showed no overall survival advantage for CRRM. Another study showed significantly improved survival following CRRM, but after adjusting for bilateral risk-reducing salpingo-oophorectomy (BRRSO), the CRRM effect on all-cause mortality was no longer significant.

Twenty studies assessed psychosocial measures; most reported high levels of satisfaction with the decision to have RRM but greater variation in satisfaction with cosmetic results. Worry over breast cancer was significantly reduced after BRRM when compared both to baseline worry levels and to the groups who opted for surveillance rather than BRRM, but there was diminished satisfaction with body image and sexual feelings.

Seventeen case series reporting on adverse events from RRM with or without reconstruction reported rates of unanticipated reoperations from 4% in those without reconstruction to 64% in participants with reconstruction.

In women who have had cancer in one breast, removing the other breast may reduce the incidence of cancer in that other breast, but there is insufficient evidence that this improves survival because of the continuing risk of recurrence or metastases from the original cancer. Additionally, thought should be given to other options to reduce breast cancer risk, such as BRRSO and chemoprevention, when considering RRM.

Authors' conclusions

While published observational studies demonstrated that BRRM was effective in reducing both the incidence of, and death from, breast cancer, more rigorous prospective studies are suggested. BRRM should be considered only among those at high risk of disease, for example, BRCA1/2 carriers. CRRM was shown to reduce the incidence of contralateral breast cancer, but there is insufficient evidence that CRRM improves survival, and studies that control for multiple confounding variables are recommended. It is possible that selection bias in terms of healthier, younger women being recommended for or choosing CRRM produces better overall survival numbers for CRRM. Given the number of women who may be over-treated with BRRM/CRRM, it is critical that women and clinicians understand the true risk for each individual woman before considering surgery. Additionally, thought should be given to other options to reduce breast cancer risk, such as BRRSO and chemoprevention when considering RRM.

PLAIN LANGUAGE SUMMARY

Women should be aware of their true risk of developing breast cancer and the limitations of current evidence when considering risk-reducing mastectomy

Review question

We reviewed the evidence on whether risk-reducing mastectomy (RRM) reduces death rates from any cause in women who have never had breast cancer and in women who have a history of breast cancer in one breast. Also, we reviewed the effect of RRM on other endpoints, including breast cancer incidence, breast cancer mortality, disease-free survival, physical morbidity, and psychosocial outcomes.

Background

Recent progress in understanding the genetic basis of breast cancer and widely publicized reports of celebrities undergoing RRM have increased interest in it as a method of preventing breast cancer.

Study characteristics

Sixty-one studies presented data on 15,077 women with a wide range of risk factors for developing breast cancer, who underwent RRM. Risk-reducing mastectomy could include either surgically removing both breasts to prevent breast cancer (bilateral risk-reducing mastectomy or BRRM), or removing the disease-free breast in women who have had breast cancer in one breast to reduce the incidence of breast cancer in the other breast (contralateral risk-reducing mastectomy or CRRM). The evidence is current to July 2016.

Key results

The BRRM studies reported that it reduced the incidence of breast cancer or the number of deaths or both, but many of the studies have methodological limitations. After BRRM, most women are satisfied with their decision, but reported less satisfaction with cosmetic results, body image, and sexual feelings. One of the complications of RRM was the need for additional unanticipated surgeries, particularly in women undergoing reconstruction after RRM. However, most women also experienced reduced worry of developing and dying from breast cancer along with diminished satisfaction with body image and sexual feelings

In women who have had cancer in one breast, removing the other breast (CRRM) may reduce the incidence of cancer in that other breast, but there is insufficient evidence that this improves survival because of the continuing risk of recurrence or metastases from the original cancer.



While published observational studies demonstrated that BRRM was effective in reducing both the incidence of, and death from, breast cancer, more rigorous prospective studies are suggested. BRRM should be considered only among those at high risk of disease, for example, carriers of mutations in the breast cancer genes, BRCA1 and BRCA2. CRRM was shown to reduce the incidence of contralateral breast cancer (CBC), but there is insufficient evidence that CRRM improves survival, and studies that control for multiple variables that can affect results are recommended. It is possible that selection bias in terms of healthier, younger women being recommended for or choosing CRRM produces better overall survival numbers for CRRM.

Quality of evidence

Just over half of the studies were found to have a low risk of selection bias, that is, studies adjusting for systematic differences in prognosis or treatment responsiveness between the groups, and similarly, 60% had a low risk of detection bias, that is, studies considered systematic differences in the ways the outcomes were measured and detected. The primary cause for both selection bias and detection bias was not controlling for all major confounding factors, e.g., risk factors or having bilateral risk-reducing salpingo-oophorectomy (BRRSO - surgery to remove fallopian tubes and ovaries) in the subject and control groups. Performance bias (validation of the risk-reducing mastectomy) was not problematic, as most studies were based on surgical reports; three relied on self-reports and eight were unclear because of multiple sources of data and/or broad timeframe. Attrition bias was at high risk or unclear in approximately 13% of the studies. The mean or median follow-up period reported was from 1 - 22 years.

Conclusions

Given the number of women who may be over-treated with BRRM/CRRM, it is critical that women and clinicians understand the true risk for each individual woman before considering surgery. Additionally, thought should be given to other options to reduce breast cancer risk, such as BRRSO and chemoprevention, when considering RRM.