Comparison of skin-sparing mastectomy versus non-skin-sparing mastectomy for breast cancer: a meta-analysis of observational studies

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CRD summary
This review found that there were no differences in local breast cancer recurrence between women who received a skin-sparing mastectomy and women who received a non skin-sparing mastectomy. The authors’ conclusions reflected the evidence presented, but weaknesses in the evidence base and the inclusion of retrospective non-randomised studies made their reliability unclear.

Authors’ objectives
To evaluate differences in outcomes of patients with breast cancer undergoing either skin-sparing mastectomy (SSM) or non skin-sparing mastectomy (NSSM).

Searching
MEDLINE, EMBASE and The Cochrane Library databases and Ovid Google Scholar search engines were searched to April 2009 for relevant studies; search terms were reported. The related articles function was used to broaden the search. References of the retrieved articles were checked to identify additional studies. There were no language restrictions.

Study selection
Comparative studies in which SSM with immediate reconstruction was compared to NSSM in patients with breast cancer and where tumour characteristics were adequately described were eligible for inclusion. Additional inclusion criteria were that the studies reported at least one of the outcomes: local tumour recurrence (primary outcome); distant relapse or development of metastatic disease; severe post-operative complications; and other outcomes (included quality of life). Studies that compared only non-oncological outcomes were excluded.

The included studies were conducted in USA, Germany, Japan and Australia. Patients with Stages I II and III cancers were included in the studies. Median age of patients at presentation ranged from 47 to 59 years.

Two reviewers independently performed study selection. Inter-reviewer agreement for study selection was assessed using the Maxwell test and generalised McNemar statistic evaluation.

Assessment of study quality
Two reviewers independently assessed methodological quality using the Newcastle-Ottawa scale in terms of selection criteria and compatibility of study groups and outcomes in the individual studies. Star ratings on a nine-point scale were assigned to each study; studies that attained six points or higher were deemed to be high quality. Any disagreements were resolved by discussion.

Data extraction
Two reviewers independently extracted data to calculate odds ratios (OR) and 95% confidence intervals (CI) for each outcome. Any disagreements were resolved by discussion.

Methods of synthesis
Pooled odds ratios and 95% CIs were calculated using a Mantel-Haenszel fixed-effect model. Statistical heterogeneity was evaluated using the $I^2$ statistic. Where significant heterogeneity was evident, a random-effects model was used to combine the data. Meta-regression analyses were performed to examine the effects of quality scores, stage of disease at presentation and proportion of in situ disease between the two groups among the studies. The reviewers evaluated publication bias using funnel plots and the Egger’s weighted regression test.

Results of the review
Nine retrospective non-randomised studies (n=3,739, SSM 1,104 and NSSM 2,635) were included in the review. The Maxwell test statistic was not significant, which indicated high levels of agreement between reviewers and the McNemar test result showed an even spread of agreement. Median follow-up ranged from 15.6 to 67 months. Seven studies attained a score of six or more stars on the Newcastle-Ottawa scoring system, which indicated higher quality studies. In studies that reported on tumour grade, SSM was performed less often for patients with higher tumour grades than NSSM.

There were no significant differences observed between SSM and NSSM groups in local recurrence (OR 1.25, 95% CI 0.81 to 1.94; seven studies, n=3,436). There were no significant differences observed in postoperative complications between SSM and NSSM groups (OR 0.81, 95% CI 0.57 to 1.16; three studies, n=789).

There were significantly fewer incidences of distant relapse observed for patients who received SSM compared to those who received NSSM (OR 0.67, 95% CI 0.48 to 0.94; five studies, n=2,122). There were no significant differences observed when patients who received nipple-sparing SSM were compared to those who received NSSM (OR 0.83, 95% CI 0.45 to 1.52; two studies, n=401).

There were no significant differences between SSM and NSSM groups for disease stage and axillary lymph node status. Meta-regression analyses showed that study quality scores, differences in presentation stage and proportion of in situ disease did not influence local recurrence or distant relapse.

The was no statistically significant heterogeneity reported across the studies for any outcome. There was no evidence of publication bias from the funnel plots.

Authors’ conclusions
There were no statistically significant differences in rates of local tumour recurrence in patients with breast cancer who received a skin-sparing mastectomy and reconstruction compared to patients who received a non skin-sparing mastectomy.

CRD commentary
The review addressed a clear question. Criteria for the inclusion of studies were generally clear. Criteria for study design were not explicitly stated. Appropriate electronic databases were searched with no language restrictions. Unpublished studies were not included in the search, so there was a risk of publication bias. Steps were taken to minimise errors and bias at most stages of the review process. Pooling results of non-randomised studies may not have been appropriate given that results from such studies are associated with a number of biases and confounding factors. The authors investigated differences between the groups and between studies as part of the meta-analysis.

The authors acknowledged several limitations of the included studies, particularly the non-comparability of the two groups and selection bias from a tendency to perform SSM for less extensive and lower grade tumours. The authors’ conclusions reflected the evidence presented, but weaknesses in the evidence base mean that the conclusions should be interpreted with some caution.

Implications of the review for practice and research
**Practice:** The authors stated that in well-selected patients with a clear indication for mastectomy, skin-sparing mastectomy may be an attractive alternative to non skin-sparing mastectomy as it shares similar morbidity and recurrence rates with better cosmetic results and potentially less psychological morbidity. These recommendations were only partly derived from the review, as it did not investigate cosmetic or psychological outcomes.

**Research:** The authors stated that long term follow-up was required to confirm the findings of the meta-analysis. Although a randomised trial would provide a higher level of evidence, the authors stated that such a trial was unlikely to occur.

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