

Autologous versus prosthetic reconstruction for women with breast cancer who will undergo post-reconstruction radiotherapy

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Abstract

Introduction

Radiotherapy is frequently used after breast reconstruction in patients with locally advanced breast cancer or metastases in axillary lymph nodes. However, there might be differences between autologous and prosthetic reconstruction in terms of effectiveness and safety of post-reconstruction radiotherapy.

Methods

To answer this question we searched in Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others. We extracted data from the systematic reviews, reanalyzed data of primary studies, conducted a meta-analysis and generated a summary of findings table using the GRADE approach.

Results and conclusions

We identified five systematic reviews including nine primary studies overall, of which all were observational studies. We concluded that in patients who will undergo post reconstructive radiotherapy, autologous breast reconstruction could reduce reoperations due to general complications compared to prosthetic breast reconstruction. However, it probably increases the risk of skin or flap necrosis. It is not clear whether there are differences in other outcomes as the certainty of evidence has been assessed as very low.

Problem

In 2017, 252,710 women were diagnosed with invasive breast cancer in the United States. It is estimated that over a third would undergo a total mastectomy, and 32% of them to breast reconstruction surgery¹⁻³. There are two main techniques for breast reconstruction: autologous breast reconstruction with pedicled myocutaneous flaps or microsurgical free flaps, and prosthetic reconstruction, either with tissue expanders or definitive implants⁴. Once breast reconstruction has been conducted in locally advanced breast cancer or with metastatic involvement of axillary lymph nodes, it is common practice to apply radiotherapy, since it would reduce loco-regional recurrence and increase disease-free survival⁵. However, this can also negatively affect the results of breast reconstruction, with worse aesthetic results, need for post-radiation reoperation and even failure of breast reconstruction [6]. So, it has been proposed that depending on the type of breast reconstruction conducted prior to radiotherapy, different results could be obtained in relation to the final aesthetic reconstruction.

Key messages

- Autologous breast reconstruction compared to prosthetic breast reconstruction could reduce reoperations for general complications in patients that will undergo post-reconstruction radiotherapy (low certainty evidence).
- Autologous breast reconstruction compared to prosthetic breast reconstruction probably increases skin or flap necrosis in patients that will undergo post-reconstruction radiotherapy.
- We are uncertain whether autologous breast reconstruction compared to prosthetic breast reconstruction reduces breast reconstruction failure, surgical site infection, wound dehiscence or presence of hematoma or seroma, as the certainty of evidence has been assessed as very low.

Methods

We searched in Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others, to identify systematic reviews and their included primary studies. We extracted data from the identified reviews and re-analyzed data from primary studies included in those reviews. With this information, we generated a structured summary denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos) using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies when it is possible, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

About the body of evidence for this question

<p>What is the evidence. See evidence matrix in Epistemonikos later</p>	<p>We found five systematic reviews⁶⁻¹⁰ that included nine primary studies overall¹¹⁻¹⁹, of which all corresponded to observational studies.</p> <p>Three non-comparative studies were excluded from this summary^{12,16,18}.</p> <p>This table and general summary are based in six observational studies^{11,13-15,17,19} as no randomized trials were found that answered the question of interest.</p>
<p>What types of patients were included*</p>	<p>The effect of radiotherapy on breast reconstruction was evaluated for both groups. Six studies evaluated patients with post reconstructive radiotherapy^{11,13-15,17,19} and two of these studies also included patients with pre reconstruction radiotherapy^{11,15}, whose subgroup was not considered for the analysis.</p> <p>No study described the average dose of radiotherapy used in patients.</p> <p>Two studies reported confusing potential variables such as body mass index, smoking habit or diabetes^{11,15}, while four did not report it.</p>
<p>What types of interventions were included*</p>	<p>In relation to breast reconstruction, three studies included patients with primary breast reconstruction^{11,15,19} and three studies did not specify it^{13,14,17}.</p> <p>In relation to type of reconstruction, six studies compared tissue expander/implant against autologous tissue. Of the latter, one study included autologous reconstruction with pedicled transverse rectus abdominis myocutaneous (TRAM) flap¹⁵, two studies included TRAM flap not specified^{11,19} and three studies did not reported the type of autologous reconstruction^{13,14,17}.</p>

What types of outcomes were measured	All studies and the review reported survival as main outcome. Average follow-up was 10.6 years, with a range of seven to 16 years. Only one of them reported the number of patients with R0 borders after surgery.
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* The information about primary studies is extracted from the systematic reviews identified, unless otherwise specified.

Summary of findings

The information on the effects of autologous breast reconstruction versus prosthetic reconstruction in women with breast cancer who will undergo post reconstructive radiotherapy is based on six observational cohort studies including 478 patients in total. One study reported the outcome reconstruction failure (48 patients)¹⁵, five studies reported surgical site infection (337 patients)^{11,13-15,17,19}, two studies reported wound dehiscence (98 patients)^{15,19}, three studies reported skin or flap necrosis (183 patients)^{11,15,19}, one study reported hematoma or seroma (50 patients)¹⁹ and five studies reported reoperation due to general complications (428 patients)^{11,13,14,15,17}.

The summary of findings is as follows:

- We are uncertain whether autologous breast reconstruction compared to prosthetic breast reconstruction reduces breast reconstruction failure in patients who underwent post reconstructive radiotherapy, as the certainty of the evidence has been assessed as very low.
- We are uncertain whether autologous breast reconstruction compared to prosthetic breast reconstruction reduces surgical site infection in patients who underwent post reconstructive radiotherapy, as the certainty of the evidence has been assessed as very low.
- We are uncertain whether autologous breast reconstruction compared to prosthetic breast reconstruction reduces wound dehiscence in patients who underwent post reconstructive radiotherapy, as the certainty of the evidence has been assessed as very low.
- Autologous breast reconstruction compared to prosthetic breast reconstruction probably increases skin or flap necrosis in patients who underwent post reconstructive radiotherapy (moderate certainty of evidence).
- We are uncertain whether autologous breast reconstruction compared to prosthetic breast reconstruction reduces hematoma or seroma in patients who underwent post reconstructive radiotherapy, as the certainty of the evidence has been assessed as very low.
- Autologous breast reconstruction compared to prosthetic breast reconstruction may reduce reoperations due to general complications in patients who underwent post reconstructive radiotherapy (low certainty of evidence).

Autologous reconstruction compared to prosthetic reconstruction				
Patients	Women with breast cancer who will undergo post reconstruction radiotherapy.			
Intervention	Autologous reconstruction.			
Comparison	Prosthetic reconstruction.			
Outcome	Absolute effect*		Relative effect (95% CI)	Certainty of evidence (GRADE)
	WITH prosthetic reconstruction	WHIT autologous reconstruction		
	Difference: patients per 1000			
Breast reconstruction failure	111 per 1000	13 per 1000	RR 0.12 (0.01 to 2.42)	⊕○○○ ^{1,2,3} Very low
	Difference: 98 patients less (Margin of error: 110 less to 158 more)			
Surgical site infection	163 per 1000	70 per 1000	RR 0.43 (0.17 to 1.07)	⊕○○○ ^{1,2} Very low
	Difference: 93 patients less (Margin of error: 135 less a 11 more)			
Wound dehiscence	91 per 1000	16 per 1000	RR 0.18 (0.02 to 1.49)	⊕○○○ ^{1,2,3} Very low
	Difference: 75 patients less (Margin of error: 89 less a 45 more)			
Skin or flap necrosis	48 per 1000	368 per 1000	RR 7.67 (1.43 to 41.22)	⊕⊕⊕○ ^{1,2,4} Moderate
	Difference: 320 patients more (Margin of error: 21 to 1000 more)			
Hematoma or seroma	38 per 1000	14 per 1000	RR 0.36 (0.02 to 8.43)	⊕○○○ ^{1,2} Very low
	Difference: 24 patients less (Margin of error: 38 less a 286 more)			
Reoperations due to general complications	299 per 1000	93 per 1000	RR 0.31 (0.20 to 0.50)	⊕⊕○○ ^{1,2,4} Low
	Difference: 206 patients less (Margin of error: 150 to 239 less)			

Margin of error: 95% confidence interval (CI).
RR: Risk ratio.
GRADE: Evidence grades of the GRADE Working Group (see later).

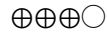
*The risk WITH prosthetic reconstruction is based on the risk in the control group of the trials. The risk WITH autologous reconstruction (and its margin of error) is calculated from relative effect (and its margin of error).

¹ Observational design.
² The certainty of evidence was downgraded for risk of bias, since attrition bias was identified and there was no adjustment for confounding variables.
³ The certainty of evidence was downgraded for imprecision, since each extreme of the confidence interval would lead to different conclusions. In the case of hematoma or seroma outcomes, two levels of certainty of evidence were reduced for this factor.
⁴ Considering that the effect is of great magnitude and there are no confounding variables, we increased the certainty of the evidence in two levels for skin or flap necrosis and in one level for reoperation due to general complications. The expected effect is plausible, which reinforces the decision.

About the certainty of the evidence (GRADE)*



High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.



Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate.



Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.



Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

* This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision

Other considerations for decision-making

To whom this evidence does and does not apply

The evidence presented applies to patients that will undergo post reconstructive radiotherapy, whether with autologous reconstruction with pedicled or free transverse rectus abdominis myocutaneous (TRAM) flap or prosthetic reconstruction.

Although the studies did not evaluate patients with other types of flaps such as the latissimus dorsi myocutaneous flap or deep inferior epigastric artery perforator flap, in the absence of direct evidence, it is reasonable to extrapolate the evidence to these cases.

The evidence presented is not aimed to patients undergoing radiotherapy prior to breast reconstruction, so it is not reasonable to extrapolate the results to this population.

About the outcomes included in this summary

There are no standardized outcomes to report breast reconstruction results²⁰. The outcomes selected in the table are those considered critical for decision-making according to the opinion of the authors of this summary, which coincide in general with those presented in the systematic reviews identified.

The outcome breast reconstruction failure is defined in the case of prosthetic reconstruction as prosthetic extrusion or implant rupture¹⁵. In autologous reconstruction it was defined as flap failure without specifying its cause¹⁵.

The outcome skin or flap necrosis is also stated as skin or 'fat' necrosis in one systematic review, making interpretation difficult. It is not clear if it is considering partial, total necrosis or both. On the other hand, of the included primary studies, no events were found in the comparison group for this outcome, which led us to extrapolate the proportion of skin or flap necrosis events without radiotherapy for this group.

The outcomes capsular contracture and fibrosis were not analyzed because they occur separately, either in prosthetic reconstruction or autologous reconstruction respectively.

Balance between benefits and risks, and certainty of the evidence

It is difficult to determine the balance between benefits and risks between autologous and prosthetic breast reconstruction in patients who will undergo post reconstructive

radiotherapy because, for most outcomes, the certainty of evidence was very low.

While autologous reconstruction seems to have fewer complications overall than prosthetic reconstruction, it probably increases the risk of skin or flap necrosis.

Resource considerations

None of the systematic reviews considered an economic analysis for each intervention. In addition, considering the poor level of certainty of the evidence, it is not appropriate to analyze this aspect until the benefits of one technique are proven over the other.

What would patients and their doctors think about this intervention

Although the decision is discussed and individualized for each patient, prosthetic reconstruction is currently performed more frequently due to reduced surgical times, hospitalization length and recovery time. However, it usually requires a second operation and several tissue expansions.

It is unlikely that the evidence presented would modify clinical decisions, since their level of certainty is very poor. However, based on individual values and preferences, especially those related with skin or flap necrosis, some patients or clinicians might prefer one intervention over the other.

Differences between this summary and other sources

Four of the systematic reviews concluded in favor of autologous breast reconstruction^{5,7,8,10}, while only one coincides with the results presented here [9]. However, systematic reviews that favor autologous breast reconstruction recognize the limitation of the primary studies and the lack of standardization in the report of outcomes used to obtain their conclusions.

There are no international clinical guidelines that address the type of breast reconstruction. However, an up-to-date review article recommends autologous reconstruction over prosthetic reconstruction²¹.

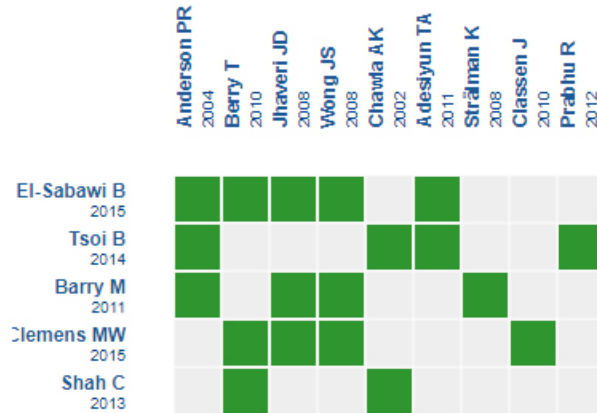
Could this evidence change in the future?

The likelihood of future research changing the conclusions of this summary is high, due to the limitations of existing evidence.

We did not identify systematic reviews or ongoing trials evaluating this question in PROSPERO or in the International Clinical Trials Registry Platform of the World Health Organization.

How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



An evidence matrix is a table that compares systematic reviews that answer the same question. Rows represent systematic reviews, and columns show primary studies. The boxes in green correspond to studies included in the respective revisions. The system automatically detects new systematic reviews including any of the primary studies in the matrix, which will be added if they actually answer the same question.

Follow the link to access the **interactive version**: [Autologous reconstruction versus prosthetic reconstruction in women who will undergo radiotherapy post reconstruction](#).

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Notes

The upper portion of the matrix of evidence will display a warning of “new evidence” if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier.

After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

This article is part of the Epistemonikos Evidence Synthesis project. It is elaborated with a pre-established methodology, following rigorous methodological standards and internal peer review process. Each of these articles corresponds to a summary, denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos), whose main objective is to synthesize the body of evidence for a specific question, with a friendly format to clinical professionals. Its main resources are based on the evidence matrix of Epistemonikos and analysis of results using GRADE methodology. Further details of the methods for developing this FRISBEE are described here (<http://dx.doi.org/10.5867/medwave.2014.06.5997>)

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database

www.epistemonikos.org.

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