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Oncological safety and patient-related outcomes of autologous fat grafting in breast reconstruction after breast cancer surgery

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Oncological safety and patient-related outcomes of autologous fat grafting in breast reconstruction after breast cancer surgery [Rekonstruktion med fettransplantation efter bröstcancer – onkologiskt utfall]

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1. Abbreviations

AFG	Autologous Fat Grafting (synonyms: lipofilling, lipotransfer, adipose tissue grafting)
AMSTAR	Assessment of Multiple SysTemAtic Reviews
BCS	Breast Conserving Surgery
BRAVA	Brava Breast Enhancement and Shaping System
DCIS	Ductal cancer in situ
DHRPS	Department of Hand and Reconstructive Surgery, Sahlgrenska University Hospital
DIEP	Deep Inferior Epigastric artery Perforator flap
LD	Latissimus Dorsi musculocutaneous flap
LTD	Lateral ThoracoDorsal flap
MRM	Modified Radical Mastectomy
HRQoL	Health Related Quality of Life
RT	Radiotherapy

2. Abstract

Background

Breast reconstruction after breast cancer surgery attempts to restore symmetry thus giving functional as well as aesthetic advantages that may improve health related quality of life. Different reconstructive procedures, including implants and flap techniques, are currently offered worldwide and are selected depending on the extent of surgery and irradiation treatment. Autologous fat grafting, or lipo-filling, is a method that can be used as a sole procedure or as an adjunct to other reconstructions. Questions have been raised whether stem cells in the fat graft could trigger cancer recurrence or even de novo tumors.

Objective

To study whether autologous fat grafting affect risk of recurrence and new tumor and patient-related outcomes in women operated for breast cancer or for increased risk for breast cancer.

Methods

A systematic literature search was conducted in PubMed, Embase, the Cochrane Library, and a number of HTA-databases. At least two persons independently screened titles, abstracts and full-text articles for inclusion and extracted data. The certainty of evidence was graded according to the Grade system.

Main results

One systematic review (SR), three subsequently published cohort studies and four case series were included in the report. There were no publications specifically on patients operated for increased risk of breast cancer.

Oncological outcomes:

Recurrence

The risk ratio (RR) was 1.33 (95% CI 0.43; 4.09) comparing autologous fat grafting with other methods, when three cohort studies were pooled. Local, regional and distant recurrence had a similar variation in groups with and without lipo-filling (ranging from 0.95 to 3.3% vs from 0 to 2.6%) in two additional cohort studies. Statistical analysis was not reported.

Survival

Similar survival rates at five years in groups with and without lipo-filling (90% vs 92%) were reported in one study. Statistical analysis was not reported.

Conclusion: It is uncertain whether there is any difference in recurrence or survival after breast reconstruction with lipo-filling compared with no lipo-filling in women operated for breast cancer. Low certainty of evidence (GRADE ⊕○○○).

Aesthetic result

Overall aesthetic analysis showed statistically significantly higher rating after combined fat grafting and implant compared with the separate procedures, 4.5 vs 3.8 and 3.6 (scale 1-5), reported in one study. Low certainty of evidence (GRADE ⊕○○○).

Complications

The overall complication rate after fat grafting was 7.3% in 2543 cases in the SR. Low grade complications, mostly fat necrosis, accounted for 86%. A specific method (BRAVA) had five cases of pneumothorax.

Concluding remarks

Autologous fat grafting for breast reconstruction after breast cancer is an evolving method for which concern has been raised regarding oncological safety. It is uncertain whether there is any difference in oncological outcomes comparing autologous fat grafting with other methods without fat grafting. The present literature is not sufficient for evaluation of the oncological risks.

3. Svensk sammanfattning – Swedish summary

Bakgrund

Rekonstruktion efter bröstcancerkirurgi avser att återskapa symmetri och förbättra estetik och hälsorelaterad livskvalitet. Olika rekonstruktiva metoder används, inkluderande användning av implantat och lambåtekniker. Val av metod beror på omfattningen av den primära kirurgin och om patienten strålbehandlats. Autolog fettransplantation kan användas som enda metod eller i kombination med andra metoder. Stamceller i fettransplantatet skulle teoretiskt kunna öka risken för återfall och nya tumörer.

Syfte

Att studera huruvida autolog fettransplantation påverkar risken för återfall av bröstcancer eller uppkomst av nya tumörer hos patienter som är opererade för bröstcancer eller profylaktiskt för ökad bröstcancerrikt.

Metoder

Systematisk litteratursökning gjordes och artiklar relevanta för frågeställningen granskades enligt mall och data extraherades. Evidensgradering av slutsatser gjordes enligt GRADE.

Resultat

En systematisk översikt, samt tre kohortstudier och fyra fallserier publicerade efter denna inkluderades i rapporten. Alla artiklar avsåg bröstrekonstruktion efter operation för bröstcancer och ingen efter profylaktisk operation.

Onkologiska utfall:

Återfall:

I den systematiska översikten presenterades en meta-analys: Relativ risk var 1,33 och 95 % konfidensintervall 0,46; 4,09, när autolog fettransplantation jämfördes med andra metoder. De efterföljande två kohortstudierna visade liknande variation mellan autolog fettransplantation och andra metoder när lokalt återfall, spridning till lymfkörtlar och fjärrmetastasering jämfördes (range 0,9-3,3% jämfört med 0-2,6%).

Överlevnad:

Fem-årsöverlevnad i grupper med eller utan autolog fettransplantation var 90% jämfört med 92% i en kohortstudie.

Konklusion:

Det är osäkert huruvida det är någon skillnad i återfallsfrekvens eller överlevnad efter bröstrekonstruktion med eller utan autolog fettransplantation hos kvinnor opererade för bröstcancer. Otillräckligt vetenskapligt underlag (GRADE ⊕○○○).

Estetiskt resultat

I en kohortstudie skattades estetiskt resultat i tre olika operationsgrupper av en panel. De som opererats med kombinerad autolog fettransplantation och implantat skattades (skala 1-5) högre än de med enbart autolog fettransplantation respektive implantat (4,5, 3,8 respektive 3,6).

Konklusion:

Det är osäkert huruvida det är någon skillnad i estetiskt resultat efter bröstrekonstruktion med eller utan autolog fettransplantation.

Otillräckligt vetenskapligt underlag (GRADE ⊕○○○).

Komplikationer

I den systematiska översikten var total komplikationsfrekvens 7,3% vid autolog fettransplantation hos 2543 patienter. Den vanligaste komplikationen (86%) var fettnekros. Pneumothorax var den allvarligaste komplikationen och förekom i fem fall.

Sammanfattande bedömning

Autolog fettransplantation är en av flera metoder för bröstrekonstruktion efter bröstcancerkirurgi. Det finns teorier att stamceller i fettväven skulle kunna öka risken för förnyad cancerutveckling i bröstet. Denna rapport visar att det vetenskapliga underlaget är otillräckligt för att bedöma den onkologiska säkerheten.

The above summaries were written by HTA-centrum and approved by the Regional board for quality assurance of activity-based HTA. The Regional Health Technology Assessment Centre (HTA-centrum) Region Västra Götaland, Sweden has the task to make statements on HTA reports carried out in Region Västra Götaland. The English summary is a concise summary. The Swedish summary addresses the question at issue, results and quality of evidence regarding efficacy and risks, and economical and ethical aspects of the particular health technology that has been assessed in the report, and includes a concluding remark from HTA-centrum.

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4. Summary of Findings (SoF-table)

Outcomes	Study design Number of studies Total number of patients	Relative effect (95%CI)	Absolute effect (autologous fat grafting vs other reconstruction)	Certainty of evidence GRADE
Survival	1 cohort study 211 vs 422	Not presented	90% vs 92% at 5 years	⊕○○○ Very low ¹
Recurrence	1 SR including 3 cohort studies 448 vs 1572 + 2 cohort studies 313 vs 871	SR: RR 1.33 95% CI 0.43; 4.09	SR: 2.3% vs 1.9% annually	⊕○○○ Very low ²
Aesthetic result	1 SR including 2 cohort studies and 14 case series + 1 cohort study 3 +16 vs 4		SR: No summary results Mean score overall analysis 4.5 and 3.8 vs. 3.6 (scale 1-5, 5 superior)	⊕○○○ Very low ³

SR= systematic review, RR= risk ratio, CI=confidence interval

¹ Serious study limitations due to uncertainties in the analysis and reporting. Serious imprecision; few events and no confidence intervals presented.

² Serious study limitations due to poor description of controls. Serious indirectness due to unclear selection of patients, variable and short periods of follow-up. Serious imprecision due to few events.

³ Serious study limitations, indirectness due to previous breast reconstruction and imprecision.

High certainty
⊕⊕⊕⊕

We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty
⊕⊕⊕○

We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty
⊕⊕○○

Confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

Very low certainty
⊕○○○

We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

5. Background

Breast cancer surgery

Reconstruction of the breast after cancer surgery attempts to restore symmetry with the purpose to give functional and aesthetic improvement. It may improve health related quality of life (HRQoL) (Kim et al. 2015), although breast reconstruction is probably not the main factor determining HRQoL after breast cancer surgery (Harcourt 2003).

Prevalence and incidence of breast cancer surgery and breast reconstructions

About one in ten Swedish women will be diagnosed with breast cancer. Improved multimodal treatment during the last decades has improved long term survival. The five-year survival rate during 2006-2010 was 87% in Region Västra Götaland (VGR), a similar rate as national data for Sweden (Socialstyrelsen 2014). In VGR 1200-1400 women are annually diagnosed with breast cancer. About 700 of them undergo mastectomy, and 500-700 have breast conserving surgery. An increasing number of breast cancer patients request breast reconstruction to improve function, well-being and cosmetics.

Approximately 350 breast reconstructions after cancer surgery are currently performed each year at the Department of Hand- and Reconstructive Plastic Surgery at Sahlgrenska University Hospital (Regionalt medicinskt vårdprogram 2014). Twenty to 30 immediate reconstructions are performed after prophylactic mastectomy in women at increased risk of breast cancer. It is expected that the demand for breast reconstructions will increase with an increased awareness of available techniques among patients.

Current use of breast reconstruction after cancer surgery

Breast cancer surgery causes asymmetry of the breast. This may trigger compensatory changes in posture and muscular tension, and may also cause social and psychological stigmata.

Many different breast reconstructive procedures have been described. A breast reconstruction can be performed during the same session as the oncological surgery (immediate reconstruction) or later (delayed reconstruction). There is presently no consensus regarding which procedure is optimal. Thus, the surgeon's and the patient's preferences are crucial in the decision-making.

Currently, the majority of patients are offered one of four different types of reconstruction at the Department of Hand- and Reconstructive Plastic Surgery at Sahlgrenska University Hospital. In patients who undergo mastectomy but not postoperative radiotherapy one of two different procedures are used. Either a reconstruction with a two-stage subpectoral tissue expander to a permanent implant or a lateral thoracodorsal flap with an implant are used. Patients treated with radiotherapy are usually not offered implant-only procedures since this has been shown to increase the risk of complications (Kronowitz et al. 2009). Patients receiving postoperative radiotherapy have had either a modified radical mastectomy or breast conserving surgery (BCS). They are recommended pedicled- or free flap procedures (latissimus dorsi musculocutaneous flap with an implant or deep inferior epigastric artery perforator flap). Patients with breast conserving surgery are usually offered a contralateral breast reduction to improve symmetry. In selected cases other procedures related to the irradiated breast are performed.

Commonly, additional surgical corrections are needed to improve functional and aesthetic results of a breast reconstruction. Autologous fat grafting can be useful to improve these results and is currently used for corrective procedures in selected cases.

The oncological safety of autologous fat grafting has not yet been established. In 1987 the American Society of Plastic and Reconstructive Surgeons issued a cautionary statement regarding its use (ASPRS Ad-Hoc Committee 1987; Snyderman 1988). The concern was that radiological anomalies secondary to the fat grafting could interfere with the detection of recurrent cancer in the breast. This issue was largely resolved as subsequent studies did not find any major disadvantages in this regard. However, new concerns were raised about the possibility that stem cells in the fat graft could trigger cancer recurrence or even de novo tumors. In vitro studies have been inconclusive and this issue is still debated.

The normal pathway through the health care system and current wait time for treatment

Delayed breast reconstructions are usually performed after a minimum of one year of recurrence free survival after initial surgery or completion of any adjuvant therapy. The wait time vary for the different methods (see above), but is currently more than three months and for deep inferior epigastric artery perforator flap more than six months.

Number of patients per year who undergo breast reconstruction

During 2014, 103 patients were treated with expanders as stage one of their breast reconstruction and 236 received permanent implants as second stage procedure in Region Västra Götaland. Latissimus Dorsi musculocutaneous flap (LD) flap was performed in 41 and Deep Inferior Epigastric artery Perforator flap (DIEP) in 25 patients. Various procedures to correct previous breast reconstructions were performed in 69 patients, a majority due to capsular contracture. Autologous fat grafting was performed 78 times during 2014 as adjunct to previous reconstructions.

Present recommendations from medical societies or health authorities

There is no international or national consensus regarding how, and when, breast reconstruction after cancer surgery should be performed. Region Västra Götaland has recommended that autologous fat grafting should only be used in controlled studies until further documentation of this method is available.

6. Autologous fat grafting

Fat grafting is a well-established procedure for reconstructive as well as aesthetic surgery. Autologous fat tissue is harvested by liposuction and injected at a chosen location. Many of the adipocytes will not survive, and therefore several treatments may be needed to achieve an acceptable result. Numerous techniques and various equipment are used, and optimal methods are not defined. The harvested tissue will also contain vascular stromal stem cells. It has been proposed that these stem cells are the actual source of the added tissue volume of the breast, while other authors suggest that the added tissue volume is due to surviving grafted adipocytes. Inconclusive in vitro studies have raised questions whether stem cells in the fat graft may trigger cancer recurrence or even increase the risk of de novo tumors. There have been previous concerns that radiological anomalies secondary to fat grafting could potentially interfere with cancer detection in the breast. However, no major disadvantages in radiological follow-up after autologous fat grafting have been detected.

Question at issue

How does autologous fat grafting affect the risk of recurrence of cancer and the risk of a new tumor, the health related quality of life, the patient satisfaction, the aesthetic result, and the need for follow-up in women who have had breast cancer surgery?

PICO P= Patients, I= Intervention, C= Comparison, O=Outcome

P	Patients operated for breast cancer or for increased risk of breast cancer
I	Breast reconstruction with autologous fat grafting
C	Breast reconstruction without autologous fat grafting
O	<u>Critical for decision making</u> Recurrence of breast cancer De novo tumor risk Survival <u>Important but not critical for decision making</u> Health related quality of life Patient satisfaction Aesthetic result <u>Not important for decision making</u> Extra follow-up procedures generated Total operating time to achieve final result (number of procedures x time for procedure) <u>Complications/Risks</u>

7. Methods

Systematic literature search (Appendix 1)

During February 2015 two authors (TS, KF) performed systematic searches in PubMed, Embase, the Cochrane Library, and a number of HTA-databases. Reference lists of relevant articles were also scrutinised for additional references. Search strategies, eligibility criteria and a graphic presentation of the selection process are presented in Appendix 1. These authors conducted the literature searches, selected studies, and independently of one another assessed the obtained abstracts and made a first selection of full-text articles for inclusion or exclusion. Any disagreements were resolved in consensus. The remaining articles were sent to all the participants of the project group. They also read the articles independently of one another and it was finally decided in a consensus meeting which articles should be included in the assessment.

Critical appraisal and certainty of evidence

The included studies and their design and patient characteristics are presented in Appendix 2. The excluded studies and the reasons for exclusion are presented in Appendix 3. The included studies have been critically appraised using checklists from SBU (Swedish Council on Health Technology Assessment) and a checklist for assessment of case series, modified from Guo et al (2013) by HTA-centrum. The results and the assessed quality of each article have been summarised per outcome in Appendix 4. A summary result and the certainty of evidence are presented in a Summary-of-findings table (page 8). The certainty of evidence was graded according to the Grade system (Atkins et al, 2004; GRADE Working group).

Ongoing research

A search in Clinicaltrials.gov (2015-03-13) using the search terms (*lipofilling OR lipostructuring OR lipotransfer OR lipomodelling OR autograft* OR autotransplant* OR graft* OR transplant OR transplantat* OR injection* OR transfer*) AND (*Adipose Tissue OR fat OR fatty tissue*) AND (*mammoplast* OR mammaplast* OR breast*) identified 25 trials. Two of them were relevant for the question at issue.

8. Results

Literature search (Appendix 1)

The literature search identified 114 articles after removal of duplicates. Ninety articles were excluded after reading the abstracts. Another 10 articles were excluded by two of the authors after reading the articles in full text. The remaining 14 articles were sent to all participants of the project group, and eight (one SR, three cohort studies and four case series) were finally included in the assessment (Appendix 2). All of them included patients who had undergone surgery for breast cancer and not prophylactic surgery in patients with increased risk of breast cancer.

Critical outcomes

Recurrence of breast cancer (Appendix 4.1)

One systematic review (SR) from 2015 of high methodological quality, two retrospective cohort studies with major study limitations, and two case series reported the incidence of recurrent breast cancer. The data on the controls was very limited, and the tumor stage was reported in only one study (Gale et al. 2015). Furthermore, it was not always clear whether the fat grafting was performed as the sole reconstructive procedure or as an adjunct to previous surgery. The SR presented data on recurrence for 2428 patients, of which 1928 were reported in case series and 500 in cohort studies. A meta-analysis of data from three cohort studies in the SR demonstrated a moderate heterogeneity between studies and a pooled risk ratio (RR) of 1.33, 95% confidence interval 0.43; 4.09.

In the non-randomised controlled studies (the cohort studies), the recurrence rate (including local, regional and distant location) in patients who had undergone autologous fat grafting varied between 0.9% and 3.3%, compared with 0.9% to 2.6% in those without fat grafting. The largest available case series reported 0.7% recurrences among 488 patients who had undergone mastectomy and secondary breast reconstruction (Khouri et al. 2014).

Conclusion: It is uncertain whether there is any difference in the recurrence of breast cancer after breast reconstruction with autologous fat grafting compared with no fat grafting in women operated for breast cancer. Low certainty of evidence (GRADE ⊕○○○).

Survival (Appendix 4.2)

Only one retrospective, cohort study with matched controls reported long-term survival. It had major study limitations. Estimations from the published Kaplan-Meier curve yielded a five-year disease-free survival rate of 90% in patients with and 92% in patients without autologous fat grafting.

Conclusion: It is uncertain whether there is any difference in survival after breast reconstruction with autologous fat grafting compared with no fat grafting in women operated for breast cancer. Low certainty of evidence (GRADE ⊕○○○).

De novo tumor risk

No study has reported the incidence of de novo tumor development.

Important outcomes

Aesthetics and patient satisfaction (Appendix 4.3)

The aesthetic outcome was reported in three groups of women in one cohort study. All women had previously had autologous flap reconstruction. The secondary augmentation was either autologous fat grafting or implant insertion, or both. The results were evaluated by a panel. The overall judgments of the aesthetic results showed a statistically significantly higher rating after a combined fat grafting and implant insertion compared with each procedure separately, 4.5 versus 3.8 and 3.6 (scale 1-5).

Conclusion: It is uncertain whether there is any difference in aesthetic result after breast reconstruction with autologous fat grafting compared with no fat grafting.

Very low certainty of evidence (GRADE ⊕○○○).

Health related quality of life

No study reported on health related quality of life.

Outcomes not important for decision making (see PICO above)

No study reported on the need for extra follow-up procedures or the total operating time necessary to achieve a final surgical result (number of procedures x time for procedure).

Complications (Appendix 4.4)

The systematic review reported an overall complication rate of 7.3% after autologous fat grafting in 2543 cases. Eighty-six per cent of these complications were low grade complications, mostly fat necrosis. Two cohort studies and four case series have reported complication rates varying between 1 % and 17.9%. The most commonly reported complication was fat necrosis. In the case series published by Khouri et al. (2014), five patients were reported to have had a pneumothorax.

9. Ethical consequences

Ethical consequences

Further research is needed to determine the effect of autologous fat grafting on breast cancer survival and recurrence. If the effect of AFG on breast cancer recurrence is small, high level of evidence will be practically impossible to obtain due to the large number of participants required. The procedure has an acceptable rate of surgical complications and can be offered to selected patients who have undergone mastectomy, provided that the patient is fully informed. The uncertainty of evidence necessitates guidelines for follow-up and motivates a prospective register. If patients treated with breast conserving surgery undergo AFG, the very low certainty of evidence requires close monitoring of this group. AFG allows breast reconstructions in patients who previously would not be considered, thus potentially increasing the number of women who can be offered the procedure. Fat grafting in breast reconstruction has several potential benefits for the patient, and denying access to these procedures while awaiting higher certainty evidence may lead to the use of more invasive procedures, increasing surgical risk without certain positive effects on oncological risk.

10. Organisational aspects of breast reconstruction with autologous fat grafting

Time frame for the putative introduction

The method at issue is already in use for selected cases of breast reconstruction at the Department of Hand- and Reconstructive Plastic Surgery at Sahlgrenska University Hospital. It is normally used as a touch-up procedure after a reconstruction with another method, but a small number of patients get autologous fat grafting as the sole reconstructive procedure after cancer surgery.

Present use in other hospitals in Region Västra Götaland

No other surgical department in the region uses autologous fat grafting.

Consequences for personnel

Surgeons who perform breast reconstruction are generally plastic surgeons and thus familiar with fat grafting procedures for various other reconstructive procedures. If new equipment is necessary the surgeons and the staff of the operating room will need further training. Nurses at the Department of Hand- and Reconstructive Plastic Surgery at Sahlgrenska University Hospital may need more information of the fat grafting procedures to be able to inform an expected increased number of patients.

Consequences for other clinics or supporting functions at the hospital or in the Region Västra Götaland

The departments of surgery, radiology and cytology will all be affected. The fat grafting procedures will increase the number of extra check-up visits due to palpable masses, and most probably lead to uncertainties regarding interpretation of some radiological or ultrasound findings. To resolve these uncertainties a biopsy will be required in some patients. It is difficult to estimate the magnitude of these needs, but an initial increase of approximately 10% of interim diagnostic procedures in fat grafted patients seems likely (Agha et al. 2015).

11. Economy aspects

Present costs of currently used technologies

Today, AFG is utilized mainly as an adjuvant procedure to other forms of breast reconstruction in our department. It is most commonly used for secondary corrections of smaller defects. The cost of AFG is SEK 22 000 if performed under general anesthesia with no other treatments given. This amount is based on a series of three patients who had only AFG. However, 78 AFG procedures were performed in women who had previous breast reconstructions and the average cost was SEK 25 973, indicating that patients usually receive other corrective measures in the same session. When AFG is performed as a complement to another procedure, the cost of AFG itself is not known today. However, the average cost of one corrective procedure without AFG is SEK 39 926.

A two-stage breast reconstruction with expander and permanent implant costs SEK 39 000 for stage one and SEK 38 607 for stage two, a total of SEK 77 607 per patient. This does not include outpatient clinic visits to fill the expander, generally three to seven visits are required. DIEP flaps cost SEK 194 507 per patient, and LD flap SEK 81 027. In 2014, the total cost for breast reconstruction procedures (including corrections but excluding AFG) was SEK 18 794 360, while the total cost for lipofilling was SEK 2 025 861. The total cost for all breast reconstructions is almost 23 million SEK.

Costs for sick leave are not included above. In general, expander or implant surgery requires two to four weeks off work per procedure, a two-stage breast reconstruction thus generating up to eight weeks of sick-leave. None of the three patients who had AFG alone had more than one week off work, two of them returned to work within three days.

Expected costs of the new health technology

Smaller volume defects may be reconstructed with one session of lipofilling, but it is likely that most patients will need two or more sessions. This may generate an increase in the number of procedures required for breast reconstruction. As the AFG procedures generally are less time consuming than other reconstructions, the total operating time may decrease. In some instances it will be possible to perform lipofilling under local instead of general anesthesia. Each time AFG can be used instead of other corrections, the potential saving is about SEK 15 000. However, the tendency to correct previous reconstructions with lipofilling may increase and post-BCS patients that were previously not considered for reconstruction may now be offered a procedure. Lipofilling procedures are generally performed as day surgery cases, potentially decreasing the need for in-patient care. If lipofilling is used instead of other corrective procedures or as the sole method of breast reconstruction, it is likely that the number of days patients need to stay home from work will decrease.

A two session AFG will generate a cost of SEK 44 000. A corresponding result achieved by more invasive measures would cost SEK 39 226. However, the AFG carries a lower risk of complications and the associated sick-leave is shorter. As the AFG procedures will be performed in day surgery, ward occupancy may decrease.

Total change of cost

Our department already uses several different systems for lipofilling. New equipment for more effective harvesting of injectable fat was recently procured (BodyJet). No further investments are necessary at this time. Change in cost is difficult to estimate, as some patients would undergo AFG instead of other corrective procedures and short repeat procedures may be less costly than single, more time-consuming ones. If AFG is used to reconstruct an entire breast in a woman who has not received radiotherapy, three to five sessions of lipofilling will be needed according to Khouri et al. (2014). However, this requires use of the BRAVA procedure which will add cost for the external expansion and various pre-treatments used in that method. At present, it is not possible to determine how costs will be affected. It is likely that costs for work absence per corrective procedure will decrease if AFG is used.

Possibility to adopt and use the new technology within the present budget

Autologous fat grafting is already in use in selected cases.

Available analyses of health economy or cost advantages or disadvantages

No analyses of health economy were available.

12. Discussion

No definitive conclusions concerning the effectiveness and safety of fat grafting and breast cancer recurrence can be made from findings published to date. There is a demand for breast reconstruction to achieve aesthetic and functional improvement after breast cancer surgery. Well established reconstructive methods include flap procedures, implants or combination of these. The use of autologous fat grafting has increased since the concern about radiological difficulties in follow-up was resolved. The question whether stem cells in the fat graft may trigger cancer recurrence, particularly after breast conserving surgery, is a major concern. Large studies with adequate follow-up are needed to evaluate the oncological safety of the procedure. National prospective registries would be valuable for the long-term follow-up and for the possibility of evaluating factors like estrogen receptor status.

13. Future perspective

Scientific knowledge gaps

Both the safety concerns and the aesthetic results of breast reconstruction with autologous fat grafting need further clarification.

Ongoing research

A search in clinicaltrials.gov yielded two relevant controlled trials. One is a French study (GRATSEC NCT01035268) that is not currently recruiting patients. The other is a newly registered randomised, controlled trial from the Netherlands (BREAST NCT02339779) that has not yet started recruitment. Both studies have the objective to compare the risk for recurrence of breast cancer and de novo tumor development in patients with or without autologous fat grafting. The expected study completion dates are 2026 and 2022, respectively. A prospective Finnish study is currently recruiting patients, investigating AFG without external expansion (personal communication from chief investigator Dr. Kauhanen, Helsinki University).

Interest at the clinic to start studies within the research field at issue

There are currently several ongoing research projects in breast reconstruction at the Department of Hand- and Reconstructive Plastic Surgery at Sahlgrenska University Hospital. Evaluating the use of autologous fat grafting is in line with the research profile of the department. We are interested in designing a study to compare outcomes after whole breast reconstructions using AFG with current standard care, primarily two-stage implant procedures. The study will be designed with a statistical power to detect effects on breast cancer recurrence as well as other outcomes, but the effect on risk of recurrence that we will be able to detect will likely be limited to two- or threefold. Detection of smaller risk differences will likely require thousands of participants.

14. Participants in the project

The question was nominated by

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Participants from the clinical departments

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Conflicts of interest

None of the authors has any conflict of interest to declare.

Project time

HTA was accomplished during the period of 2015-02-04 – 2015-05-29

Literature searches were made in February 2015.

Appendix 1, Search strategy, study selection and references

Question(s) at issue:

How does autologous fat grafting affect the risk of recurrence of cancer and the risk of a new tumor, the health related quality of life, the patient satisfaction, the aesthetic result, and the need for follow-up in women who have had breast cancer surgery?

PICO: (*P=Patient I=Intervention C=Comparison O=Outcome*)

P = Patients operated for breast cancer or for increased risk of breast cancer
I = Breast reconstruction with autologous fat grafting
C = Breast reconstruction without autologous fat grafting
O = <u>Critical for decision making</u> Recurrence De novo tumor risk Survival <u>Important but not critical for decision making</u> Health related quality of life Patient satisfaction Aesthetic result <u>Not important for decision making</u> Extra follow-up procedures generated Total operating time to achieve final result (number of procedures x time for procedure)) <u>Complications/Risks</u>

Eligibility criteria

Study design:

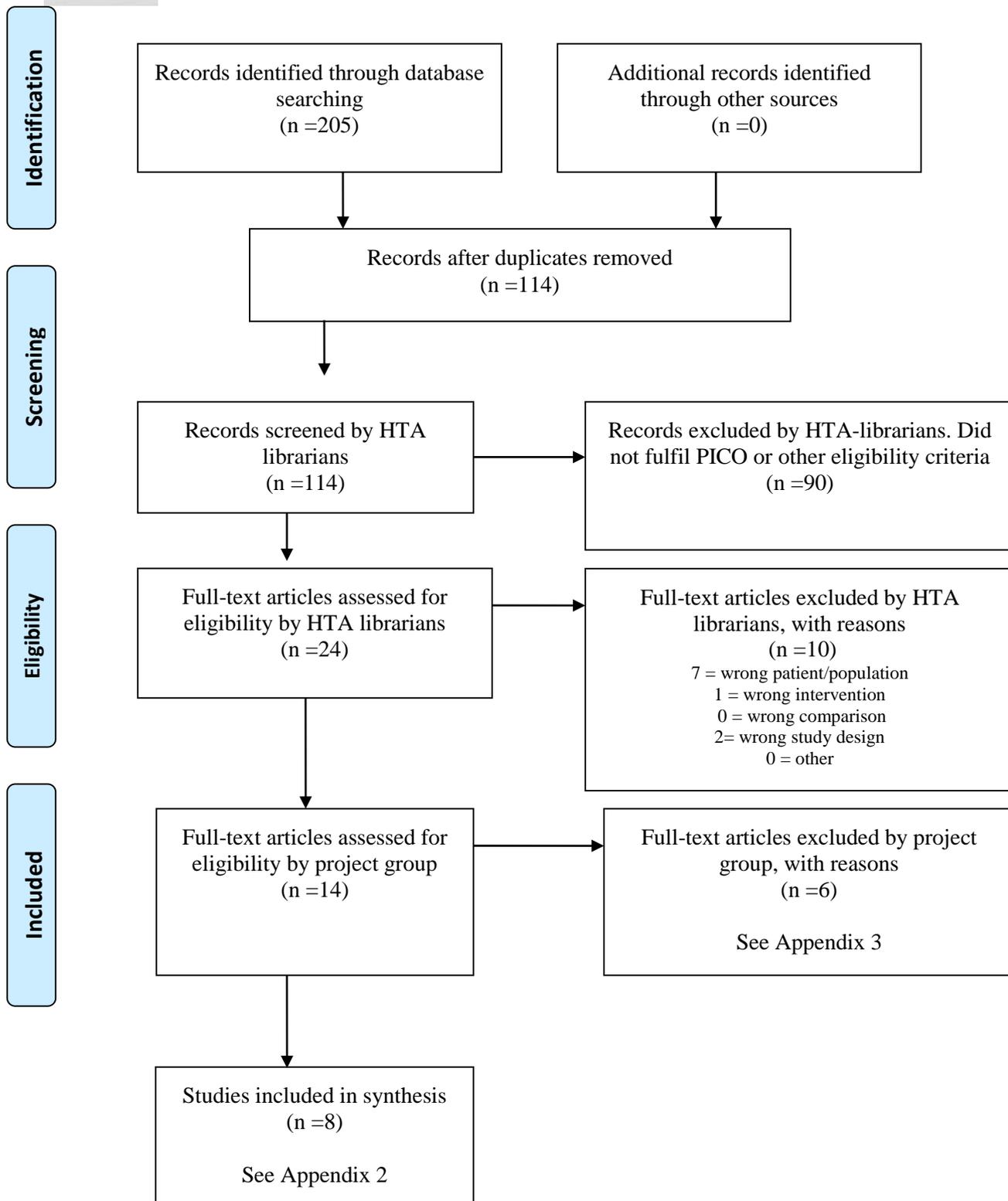
Randomised controlled trials
Non-randomised controlled studies
Case series etc. if ≥ 50 patients

Language:

English, Swedish, Norwegian, Danish

Publication date: The literature search is based on a systematic review with last search date March 31, 2014. We searched for everything published after January 1, 2014.

Selection process – flow diagram



Search strategies

Database: PubMed

Date: 2015-02-10

No of results: 76

Search	Most Recent Queries	Results
#23	Search #15 NOT #19 Filters: Publication date from 2014/01/01	76
#20	Search #15 NOT #19	560
#19	Search #16 OR #17 OR #18	6210297
#18	Search (Editorial[ptyp] OR Letter[ptyp] OR Comment[ptyp])	1377288
#17	Search ((child[mh]) NOT (child[mh] AND adult[mh]))	973700
#16	Search ((animals[mh]) NOT (animals[mh] AND humans[mh]))	3972537
#15	Search #3 AND #13 AND #14	646
#14	Search mammoplast* OR mammaplast* OR mammaplasty[mesh] OR breast reconstruction OR breast reconstructed OR breast augmentation OR breast enlargement OR (breast[tiab] AND surg*[tiab])	48875
#13	Search #11 OR #12	1254260
#12	Search lipofilling OR lipostructuring OR lipotransfer OR lipomodelling OR autograft* OR autotransplant* OR graft* OR transplant[tiab] OR transplantat*[tiab] OR injection*[tiab] OR transfer[tiab] OR adipose tissue/transplantation[mesh]	1253835
#11	Search ("Transplants"[Mesh:NoExp]) OR "Autografts"[Mesh]	2476
#3	Search "Adipose Tissue"[Mesh] OR fat OR adipose tissue OR fatty tissue	257541

Database: EMBASE (OVID SP)

Date: 2015-02-10

No of results: 36

#	Searches	Results
1	exp adipose tissue/	109644
2	(fat or adipose tissue or fatty tissue).ti,ab.	254794
3	1 or 2	277307
4	transplantation/ or autograft/ or autotransplantation/	149985
5	(lipofilling or lipostructuring or lipotransfer or lipomodelling or autograft\$ or autotransplant\$ or graft\$ or transplant or transplantat\$ or injection\$ or transfer).ti,ab.	1420324
6	4 or 5	1457985
7	exp breast reconstruction/	14502
8	(mammoplast\$ or mammaplast\$ or (breast adj3 reconstruction) or (breast adj3 reconstructed) or (breast adj3 augmentation) or (breast adj3 enlargement) or (breast adj3 surg\$)).ti,ab.	26569
9	7 or 8	31047
10	3 and 6 and 9	594
11	(animal not (animal and human)).sh.	1199151
12	10 not 11	593
13	limit 12 to yr="2014 -Current"	47
14	limit 13 to (article or conference paper or note or "review")	36

Database: CINAHL (EBSCO)

Date: 2015-02-10

No of results: 4

#	Searches	Results
S12	S3 AND S7 AND S10	4
S11	S3 AND S7 AND S10	29
S10	S8 OR S9	3793
S9	TI (Mammoplasty* or mammoplast* or (breast N3 reconstruction) or (breast N3 reconstructed) or (breast N3 augmentation) or (breast N3 enlargement) or (breast N3 surg*)) OR AB (Mammoplasty* or mammoplast* or (breast N3 reconstruction) or (breast N3 reconstructed) or (breast N3 augmentation) or (breast N3 enlargement) or (breast N3 surg*))	3228
S8	(MH "Breast Reconstruction")	1,291
S7	S4 OR S5 OR S6	99,055
S6	(MH "Transplantation+")	35,761
S5	(MH "Grafts+") OR (MH "Autografts+")	14,551
S4	TI (lipofilling or lipostructuring or lipotransfer or lipomodelling or autograft* or autotransplant* or graft* or transplant or transplantat* or injection* or transfer) OR AB (lipofilling or lipostructuring or lipotransfer or lipomodelling or autograft* or autotransplant* or graft* or transplant or transplantat* or injection* or transfer)	78,136
S3	S1 OR S2	29,787
S2	TI (fat OR adipose tissue OR fatty tissue) OR AB (fat OR adipose tissue OR fatty tissue)	25,265
S1	(MH "Adipose Tissue+")	10,370

Database: PsycInfo

Date: 2015-02-10

No of results: 63

#	Searches	Results
S7	TI (Mammoplasty* or mammoplast* or (breast N3 reconstruction) or (breast N3 reconstructed) or (breast N3 augmentation) or (breast N3 enlargement) or (breast N3 surg*)) OR AB (Mammoplasty* or mammoplast* or (breast N3 reconstruction) or (breast N3 reconstructed) or (breast N3 augmentation) or (breast N3 enlargement) or (breast N3 surg*))	63
S6	S3 AND S4 AND S5	1
S5	TI (Mammoplasty* or mammoplast* or (breast N3 reconstruction) or (breast N3 reconstructed) or (breast N3 augmentation) or (breast N3 enlargement) or (breast N3 surg*)) OR AB (Mammoplasty* or mammoplast* or (breast N3 reconstruction) or (breast N3 reconstructed) or (breast N3 augmentation) or (breast N3 enlargement) or (breast N3 surg*))	697
S4	TI (lipofilling or lipostructuring or lipotransfer or lipomodelling or autograft* or autotransplant* or graft* or transplant or transplantat* or injection* or transfer) OR AB (lipofilling or lipostructuring or lipotransfer or lipomodelling or autograft* or autotransplant* or graft* or transplant or transplantat* or injection* or transfer)	74348
S3	S1 OR S2	10889
S2	TI (fat OR adipose tissue OR fatty tissue) OR AB (fat OR adipose tissue OR fatty tissue)	10699
S1	DE "Body Fat"	991

Database: The Cochrane Library

Date: 2015-02-10

No of results: 26*

Cochrane reviews 7

Other reviews 13

Technology assessments 2

Economic evaluations 4

*This is the number of results retrieved from the databases *Cochrane reviews*, *Other reviews*, *Technology assessments* and *Economic evaluations* for search #4.

No results were identified in *Clinical trials* for publication year 2014-2015 with a narrower search, #5.

ID	Search	Hits
#1	adipose tissue or fat or fatty tissue:ti,ab,kw (Word variations have been searched)	16586
#2	lipofilling or lipostructuring or lipotransfer or lipomodelling or autograft* or autotransplant* or graft* or transplant or transplantat* or injection* or transfer:ti,ab,kw (Word variations have been searched)	76768
#3	Mammoplasty* or mammoplast* or (breast near/3 reconstruction) or (breast near/3 reconstructed) or (breast near/3 augmentation) or (breast near/3 enlargement) or (breast near/3 surg*):ti,ab,kw (Word variations have been searched)	2304
#4	Mammoplasty* or mammoplast* or (breast near/3 reconstruction) or (breast near/3 reconstructed) or (breast near/3 augmentation) or (breast near/3 enlargement) or (breast near/3 surg*):ti,ab,kw Publication Year from 2014 to 2015 (Word variations have been searched)	152
#5	#1 and #2 and #3 Publication Year from 2014 to 2015	0

Reference lists

A comprehensive review of reference lists brought no new records

Reference lists

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[centrum/Hj%c3%a4lpmedel%20under%20projektet/Granskningsmall%20f%c3%b6r%20fallserier%202015-03-25.docx](https://www2.sahlgrenska.se/upload/SU/HTA-centrum/Hj%c3%a4lpmedel%20under%20projektet/Granskningsmall%20f%c3%b6r%20fallserier%202015-03-25.docx)

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Report: Oncological safety and patient-related outcomes of autologous fat grafting in breast reconstruction after breast cancer surgery

Appendix 2 – Characteristics of included studies

Author, Year, Country	Study Design	Study Duration (years)	Study Groups; Intervention vs control	Patients (n)	Mean Age (years)	Outcome variables
Agha, 2015, UK	Systematic review meta-analysis	1981- 2014	Mastectomy BCS	3624 overall 2428 oncological	(21-86) range in included studies	Recurrence Complications Aesthetics
Gale, 2015, UK	Cohort	2007-2013	BCS	211	52.2 (30-76)	Recurrence
Kim, 2014, Korea	Cohort	2005-2013	Mastectomy	102	46.3 (22-63)	Recurrence Complications
Lakhiani, 2014, USA	Cohort	2008-2011	Mastectomy	24	51.7 (35.8-62.7)	Complications Aesthetics
Brenelli, 2014, Brazil	Case series	2005-2008	BCS	59	50.0 +/-8.5	Recurrence Complications
Kaoutzanis, 2014, USA	Case series	2008-2013	Mastectomy	108	48 (22-71)	Recurrence Complications
Khouri, 2014, USA	Case series	7 years	Mastectomy	488	Not reported	Recurrence Complications
Semprini, 2014, Italy	Case series	2004-2012	BCS	151	40-72	Recurrence

BCS= breast conserving surgery

Appendix 3. Excluded articles

Study (author, publication year)	Reason for exclusion
Canadian Agency for Drugs and Technologies in Health 2014	Systematic review with lower AMSTAR-score than Agha et al. 2015
Cuomo, 2014	Not concurrent with PICO. Studies post-mastectomy pain.
Maione, 2014	Not concurrent with PICO. No relevant outcomes.
Maione, 2015	Not concurrent with PICO. No separate data for breast cancer patients.
Small, 2014	Not concurrent with PICO. Volume retention as outcome.
Tsoi, 2014	Systematic review. Not concurrent with PICO. No lipofilling procedures.

Project: Autologous fat grafting in breast reconstruction after breast cancer surgery

Appendix 4.1

Outcome variable: Recurrence

* + No or minor problem
 ? Some problems
 - Major problems

Author, year, country	Study design	Number of patients n=	Oncological procedure	Follow-up after oncological procedure	Follow-up after fat grafting	Recurrence after fat grafting	Recurrence in controls	Directness*	Study limitations	Precision
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Agha 2015 UK	Systematic review w meta-analysis	2428	Mastectomy or BCS	n/a	Median 22.6 months	2.5% annually (all studies) 2.3% annually in 3 controlled studies MA: RR 1.33, 95%CI 0.43; 4.09	1.9% annually in 3 controlled studies.			
Gale 2015 UK	Cohort-retrospective w matched controls	211 with 422 matched controls	Mastectomy 83.4% BCS 16.6%	Mean 88 months	Mean 32 months	Local 0.95% Regional 0.95% Distant 3.32%	Local 1.90%, p=0.32 Regional 0%, p=0.16 Distant 2.61%, p=0.69	+?	-	?
Kim 2014 Korea	Cohort-retrospective w controls	102 w 449 controls	Mastectomy	Mean 12.5 (3.2-62.2) + 6 months	6 months	Locoregional 0.9% (1)	Locoregional 2% (9) n.s.	-	-	-
Brenelli 2014 Brazil	Case series - prospective	59	BCS	Mean time from oncological procedure to FG 76.6+/-30.9 months	34.4+/-15.3 months	Local 5.1% (3) Metastasis 1.7%(1)	n/a	-	-	-
Kaoutzani 2014 USA	Case series - retrospective	108	Mastectomy	Not reported	15.5 (6.3-57.4) months	0	n/a	-	-	-
Khoury, 2014 USA	Case series - retrospective	488	BCS 20% Mastectomy 80%	Not reported	30 (6-84) months	3 (0.7%) 12.5% dropouts	n/a	-	-	-
Semprini, 2014 Italy	Case series - retrospective	151	BCS	69 (27-100) months	45 (17-76) months	0	n/a	-	-	-

BCS=breast conserving surgery, FG=fat grafting, MA= meta-analysis, RR= risk ratio, CI= confidence interval, n.s.=non significant, n/a=not applicable

Project: Autologous fat grafting in breast reconstruction after breast cancer surgery

Appendix 4.2

Outcome variable: Survival

* + No or minor problem
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	Oncological procedure	Follow-up after oncological procedure	Follow-up after fat grafting	Survival after fat grafting	Survival in controls	Directness*	Study limitations	Precision
Gale et al 2015, UK	Cohort-retrospective w matched controls	211 with 422 matched controls	Mastectomy 83.4% BCS 16.6%	Mean 88 months	Mean 32 months	90% at 5 years evaluated from K-M curve	92 %	+?	-	?

Project: Autologous fat grafting in breast reconstruction after breast cancer surgery

Appendix 4.3

Outcome variable: Aesthetic result

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	Results			Comments	* Directness	* Study limitations	* Precision
			Intervention	Control					
Lakhiani 2014 USA	Retrospective cohort study	24	Fat grafting + implant n=3 4.5 p=0.01	AFG only n=16 3.8	Implant only n=8 3.6	Previous postmastectomy free flap reconstruction. Secondary augmentation was the study intervention. A panel evaluated aesthetic result. Scale 1-5 (5 superior outcome). Final average score from the overall analysis is presented	-	-	-

AFG= autologous fat grafting

Project: Autologous fat grafting in breast reconstruction after breast cancer surgery

Appendix 4.4

Outcome variable: Complications (reported for intervention groups only)

Author year country	Study design	Number of patients n=	Times fat grafted	Complication rate	Type of complication	Radiological abnormalities	Comments
Agha 2015 UK	Systematic review	2543	Mean 1.9 (1-5)	7.3% (207)	Grade 1 (Clavien-Dindo scale) 86% Fat necrosis 62% of all complications	323/1979 (14.5%) 263 had interval examination (11.5%) 60/1979 proceeded to biopsy (2.7%)	
Kim 2014 Korea	Cohort- retrospective with controls	102 w 449 controls	29 had more than one	17.6% (18)	10/18 fat necrosis 8/18 cystic lesion	3/18 proceeded to biopsy	
Lakhiani 2014 USA	Cohort - retrospective with internal controls	24	FG only: 1.8 (1-5) FG+implant 1.4 (-2)	(2)	2 fat necrosis	n/a	Touch-up FG of previous breast reconstruction
Brenelli 2014 Brazil	Case series - prospective	59	16.8% had more than one session	4% (3)	2 fat necrosis 1 cellulitis	15 (20%) 6/15 proceeded to biopsy 10.6% had no radiological follow-up	
Kaoutzanis 2014 USA	Case series - retrospective	108	Not reported	0.9% (1)	1 wound infection	7.4% (8) biopsy rate 36.1% had radiologic follow-up	
Khoury 2014 USA	Case series - retrospective	488	2-4.9	Not reported	5 pneumothorax 18 abscess	Not reported	BRAVA method
Semprini 2014 Italy	Case series - retrospective	151	30% had 2 14% had 3	0	3 ecchymoses on donor site	0	

FG=fat grafting, n/a=not applicable

Appendix 5

Etiska hänsyn

Finns en ökad risk för återfall?

Lipofilling kan användas på rekonstruktioner som tidigare varit omöjliga att utföra utan mer omfattande ingrepp. I synnerhet kan det vara tillämpligt på kvinnor som har substansdefekter efter bröstbevarande kirurgi. Likaledes finns det data som talar för att lipofilling kan minska smärta och stramhet från strålningsutlöst fibros och ärr. Lipofilling kan användas för att rekonstruera ett helt bröst efter mastektomi och på så vis ge en autolog rekonstruktion till patienter som tidigare endast kunnat bli erbjudna implantat. Fettransplantation kan användas för att korrigera eller förbättra resultatet kombinerat med bröstrekonstruktion med annan metod. Ingreppet är relativt snabbt, i vissa fall kan det utföras i lokalanestesi med eller utan sedation. Postoperativ vård kan ofta polikliniseras, vilket kan minska totalt antal inläggande vård dygn vid bröstrekonstruktion. Sjukskrivningsbehovet efter lipofilling förefaller att vara lägre än efter annan bröstkirurgi.

In vitro-studier har visat motstridiga resultat huruvida lipofilling påverkar risken för bröstcancerrecidiv. Kliniska studier, inklusive de som ingår i denna rapport, visar även de motstridiga resultat, men det finns ingen studie som med säkerhet kan påvisa ökad risk för återfall i bröstcancer efter lipofilling och de flesta studier hittar ingen skillnad i risk. I det material som hittills publicerats, är kvinnor som blivit mastektomerade och sedan fått lipofilling den till antalet största gruppen. Gruppen som genomgått bröstbevarande kirurgi med efterföljande fettransplantation är avsevärt mindre.

I vår rapport anges en återfallsrisk på 2,3-2,5 % per år efter operation för bröstcancer. Denna relativt låga siffra försvårar möjligheterna att skaffa säkrare kunskap. Idag finns inte någon studie som analyserar statistisk power, men det skulle krävas ett stort antal deltagare (flera tusen) för att en studie skall kunna utesluta att det föreligger någon ökad risk för återfall i bröstcancer vid bröstrekonstruktion med fettransplantation. Dessutom är det angeläget att studera subgrupper, baserat på typen av terapi mot bröstcancern (mastektomi, bröstbevarande kirurgi, radioterapi).

Fettransplantation vid bröstrekonstruktion efter bröstcancer kan ge patientnytta i form av förbättrad estetik och funktion, men det är osäkert om denna åtgärd påverkar återfallsrisken. Det är troligt att evidensläget inte kommer att förbättras nämnvärt i framtiden på grund av de svårigheter i studiedesign som beskrivs ovan. Det kan komma att dröja många år innan kunskapen är tillräcklig och patienter kommer sannolikt att efterfråga ingreppet. Behovet av prospektiv registrering i nationella kvalitetsregister är tydligt.

Om metoden skall användas i VG-regionen bör man välja ut patienter med försiktighet och vara beredd att följa upp dem. Med tanke på att kunskapsläget är som sämst för patienter som genomgått bröstbevarande kirurgi, kan det vara motiverat att följa dem i en studie. Kirurgen bör informera patienten om det oklara bevisläget.

Är metoden säker ur kirurgiskt perspektiv?

Komplikationsfrekvensen vid autolog fettransplantation är relativt låg, huvuddelen av komplikationerna är lindriga. Ingreppet kan ibland utföras i lokalanestesi, vilket ytterligare förbättrar säkerheten.

Vid mammografi kan man se förändringar sekundärt till lipofilling och emellanåt kan patienten själv känna knölar i bröstet efter fettransplantation. Ofta kan radiologerna särskilja dessa postoperativa förändringar från malignitet, men i en andel av fallen krävs biopsi. Vissa patienter kommer alltså att uppleva en period av ovisshet innan man kan konstatera om en

självupptäckt knöl i bröstet är ett återfall i bröstcancer eller en bieffekt av tidigare lipofilling. Mammografienheter och cytologlaboratorier kan komma att behöva utföra fler åtgärder, vilket kan påverka tillgången på diagnostik för övriga patienter.

Metoden har en acceptabel kirurgisk säkerhet, men kommer att skapa ett ökat behov av uppföljningsåtgärder.

Skapar metoden undanträngningseffekter?

Fettransplantation är tekniskt relativt lätt att utföra och går snabbt, det finns en risk för indikationsglidning vilket skulle kunna öka antalet patienter på väntelistan och eventuellt förlänga köerna till andra ingrepp. Å andra sidan kan man ofta göra ingreppet i dagkirurgi och sannolikt krävs kortare sjukskrivningsperioder, vilket kan spara vårddygnet och sjukförsäkringskostnader.

Vilket värde för patienten tillför metoden?

Troligen kommer det att bli mindre krävande för patienten att få korrigeringar för att förbättra slutresultatet av tidigare rekonstruktion. Nya grupper kan bli aktuella för behandling, vilka tidigare inte kunnat erbjudas annat än kontralateral bröstreduktion. I vissa fall kan man eventuellt erbjuda autologa rekonstruktioner till kvinnor som tidigare varit hänvisade till protesrekonstruktion, vilket ökar patientinflytandet. Kortare sjukfrånvaro och kortare vårdtid är fördelar jämfört med alternativa ingrepp. Alla kvinnor som är i behov av korrigeringar efter bröstrekonstruktion kommer dock inte att kunna behandlas uteslutande med fettransplantation, inte heller kommer alla rekonstruktioner att kunna göras med enbart fett. Idag finns dock ingen tillförlitlig kunskap som säger om patienterna verkligen blir mer nöjda.

Metoden kan potentiellt öka patientnöjdhet men inga säkra bevis för detta finns.

Konsekvenser för eventuella forskningsprojekt

Framtida forskningsprojekt inom området behöver konstrueras för att kunna besvara om patienternas risk för återfall eller nyinsjuknande påverkas av lipofilling. Stora fallserier från den estetiska kirurgin har använt sig av fettransplantation för bröstförstoring på kosmetisk indikation utan att kunna påvisa någon ökad andel av nyinsjuknande i bröstcancer. För kvinnor som redan genomgått behandling för bröstcancer kan det vara återfallsrisken som utgör huvudproblemet. En förändring av den relativa risken för återfall med 10% i en population med en grundrisk för återfall på 2,5% kommer att kräva mycket stort deltagarantal för att kunna detekteras med säkerhet – dvs om absolut risk ökar från 2,5% till 2,75%. Prospektiv registrering i nationella kvalitetsregister skulle bidra med kunskap.

Sammanfattning

Lipofilling vid bröstrekonstruktion har flera fördelar för patienten. Kunskapsläget avseende risken för återfall och dödlighet i bröstcancer är osäkert. I avvaktan på fler studier och ett förbättrat evidensläge är det rimligt att informera patienterna kring kunskapsläget, överväga särskilda uppföljningsprotokoll och prospektiva register samt bedriva forskning för att förbättra kunskapsläget. Man bör också överväga vilka patienter som skulle erbjudas behandlingen; att okritiskt göra fettransplantationer på kvinnor som genomgått sektorresektion är diskutabelt.

Region Västra Götaland, HTA-centrum

Health Technology Assessment
Regional activity-based HTA



HTA

Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the quality of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High quality of evidence	= (GRADE ⊕⊕⊕⊕)
Moderate quality of evidence	= (GRADE ⊕⊕⊕○)
Low quality of evidence	= (GRADE ⊕⊕○○)
Very low quality of evidence	= (GRADE ⊕○○○)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

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