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Breast-specific factors determine cosmetic outcome and patient satisfaction after breast-conserving therapy

Results from the randomised COBALT study



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ABSTRACT

Introduction To identify breast-specific factors and the role of tumour, treatment and patient-related items in influencing patient opinion on cosmesis and satisfaction after breast-conserving therapy (BCT).

Methods Data from the randomised COBALT study were used. At 3, 12 and 36 months, 128 patients with T1-T2 breast cancer completed a questionnaire on breast-specific factors and overall cosmetic outcome and patient satisfaction, using a 4-point Likert scale.

Results There was a strong positive correlation between breast-specific factors, overall cosmetic outcome and satisfaction at all time-points. Excellent/good cosmetic outcomes and satisfaction decreased during follow-up. A shift was noted in the degree of influence of the various breast-specific factors. At three years, symmetry factors such as size, shape and nipple position largely determined a patient's opinion on the final cosmesis, followed by firmness. The risk of an unacceptable outcome was associated with young age and large excision volumes.

Conclusion A questionnaire including breast-specific questions provides important information on final cosmetic results and satisfaction after BCT. These outcomes can also be of great value as quality indicators and pre-operative counseling. The major role of breast-specific factors influencing asymmetry underlines the importance of achieving optimal excision volume at the initial procedure.

INTRODUCTION

Breast-conserving therapy (BCT) is the treatment of choice for stage I and II breast cancer.¹ BCT consists of lumpectomy, with or without axillary surgery, followed by radiation therapy of the breast. The primary goal of local treatment is removal of the tumour, with tumour-free resection margins crucial to avoiding a local recurrence. Due to the growing number of survivors, secondary goals such as the cosmetic outcome, a patient's perception of breast appearance and quality of life (QOL) are now receiving increased attention.

Questionnaires are now commonly used to gauge a patient's own perception of breast appearance after BCT.²⁻¹⁸ In early studies, breast-specific questions on cosmesis were incorporated in validated quality of life forms. However, many of the included questions broadly reflected the consequences of routinely performed axilla lymph node dissection (ALDN) in breast cancer patients, such as lymphedema and limited arm/shoulder movement. The Breast Cancer Treatment Outcome Scale (BCTOS), developed by Stanton et al. in 2001, contains only six questions that can be regarded as breast-specific in our opinion. These include size, texture, nipple appearance, shape, elevation and scar tissue.^{2,3} As was apparent from the results of Stanton and colleagues, the serious morbidity associated with ALND overrides any judgments of treatment-related cosmetic results.³ The subsequent introduction of the sentinel node procedure completely changed the morbidity of breast cancer surgery and comparisons with results from the ALND-era should therefore be avoided.

Nowadays, studies of patient opinion on cosmetic results are generally based on institutional questionnaires that focus on breast-specific factors, although the number and type of questions may vary.⁴⁻⁸ Historically, many authors have used a 4-point Likert scale (excellent/good/fair/poor) to rate breast-specific factors. Patient-reported cosmetic outcomes have been based on only one question comparing the treated breast with the contralateral breast^{12, 13, 15, 19} or on (more reliable) questionnaires with up to nine questions on breast-specific factors.^{2, 7, 9, 11, 14, 16-18} An example of the latter is a study by Waljee et al. in which the authors extracted all eight questions from the BCTOS questionnaire, including six questions on breast-specific factors,¹¹ with data averaged to generate an overall asymmetry score. In a recent (2016) study from Dahlback et al., patients

were asked to rate their satisfaction with aesthetic outcome, symmetry between the breasts, shape and size of the operated breast, as well as appearance of the scar.⁷

Since both satisfaction and cosmetic outcome are considered to be important individual components of a patient's perception of breast appearance, we conducted a long-term analysis of both of these secondary outcomes in relation to breast-specific factors. The current study offers the opportunity to determine which specific factors are decisive for satisfaction and cosmetic outcome and may therefore allow better information prior to treatment and suggestions for improvements in secondary outcomes after BCT.

METHODS

Trial design and patient population

In the current study, patients from the Cosmetic Outcome of the Breast After Lumpectomy Treatment (COBALT) trial were included. The COBALT trial is a multicenter, comparative, two-arm, randomised controlled trial undertaken in six Dutch hospitals. Patients eligible to participate were diagnosed with a palpable early-stage (T1-T2, N0-1) invasive breast cancer scheduled to undergo BCT. Women were randomised to undergo either ultrasound-guided surgery (USS) or palpation-guided surgery (PGS). Primary endpoints were resection volume and margin status, while secondary endpoints included oncological follow-up, cosmetic outcome and QOL.^{20,21} The COBALT trial was performed in accordance with the Declaration of Helsinki, guidelines for Good Clinical Practice, and the CONSORT statement.²²

In total, 134 patients were included in the COBALT trial. Six patients were excluded from follow-up analyses: five of these patients underwent a mastectomy for tumour-involved margins, and one patient refused to participate in follow-up. During follow-up, another five patients were excluded because a mastectomy was eventually performed for reasons other than tumour-involved margins (reasons included refusal of radiation therapy, BRCA mutation, a persisting non-healing radiation ulcer and deformity of the breast [n = 2]). A brief overview of patient and tumour characteristics is provided in Table 1.

Characteristics (n = 128)	Total
N	128
Palpation guided surgery	63 (49.2%)
Ultrasound guided surgery	65 (50.8%)
T-stage	
T1	68 (53.1%)
T2	60 (46.9%)
Axillary surgery	
Sentinel lymph node only	102 (79.7%)
Axillary dissection	26 (20.3%)
Location of carcinoma	
Upper outer quadrant	78 (60.9%)
Upper inner quadrant	18 (14.1%)
Lower outer quadrant	23 (18.0%)
Lower inner quadrant	9 (7.0%)
Re-excision	
No	124 (96.9%)
Yes	4 (3.1%)
Radiotherapy boost	
None	15 (11.7%)
Because of involved margins	17 (13.3%)
Because of individual risk factors	96 (75.0%)
Excision volume (cm ³)	45.5 (30.5, 7 – 165)
Age (years)	55 (9.9, 38 – 78)
Body mass index (kg/m ²)	26.4 (4.8, 19 – 48)
Bra cup size	
A/B	52 (40.6%)
C/D	58 (45.3%)
E/F/G	17 (13.3%)
Missing	1 (0.8%)

Average, standard deviation and range are shown for continuous variables. The number of patients with percentages are illustrated for categorical variables.

Table 1 Patient and tumour characteristics and primary outcomes of the COBALT study

Patient follow-up

All patients received standard follow-up according to national guidelines, with mammography performed at yearly intervals. Follow-up conform study protocol has been described elsewhere.²¹ Briefly, follow-up was performed at 3, 12 and 36 months after the initial surgery. During these visits women filled out a questionnaire that consisted of questions related to six breast-specific factors including the scar, breast size, breast shape and breast firmness, the position of the nipple-areola complex (NAC) and skin color. Additionally, two concluding questions concerning overall cosmetic outcome of the breast in comparison to the healthy breast and overall satisfaction with the operated breast, were completed during a hospital visit. The questions were scored on a 4-point Likert scale (excellent/good/fair/poor).¹⁴ Those patients who did not appear for their regular visits were actively approached for study purposes.

Statistical analysis

Descriptive statistics were used to report patient demographics. The course of patient-reported cosmetic outcome and satisfaction change over time was investigated using trend tests. The correlation between breast-specific factors and cosmetic outcome or satisfaction, and the correlation between cosmetic outcome and satisfaction were analyzed using Spearman's correlation with the 4-point Likert scale outcomes. Logistic regression models were used to study effects of the six breast-specific factors, patient and tumour characteristics on cosmetic outcome and satisfaction, with both outcomes dichotomized as good (excellent or good) or poor (fair or poor). The tumour/treatment items included as covariates in models were T-stage (T1/T2), excision method (PGS/USS), axillary surgery (sentinel lymph node/axillary dissection), location of the tumour (upper outer/upper inner/lower outer/lower inner quadrant), re-excision, boost radiation (standard in high risk patients or due to irradicality), excision volume, and the patient-related items age, BMI and cup size. As our previous study defined the cut-off of 40cc for the excision volume to define low/risk group of poor outcome, a subanalysis of these subgroups of patients was therefore carried out.²³

All p-values were two-sided and a significance level of 5% was used. Statistical analyses were performed using SPSS software, version 22.

RESULTS

The overall response rate for the patient questionnaire was 86% (n = 110/128) at 3 months, 90% (n = 112/124) at 12 months and 91% (n = 112/123) at 36 months.

The rating of both cosmetic outcome and patient satisfaction declined significantly during the three years of follow-up ($p_{\text{trend}} = 0.001$ for both outcomes): the proportion of excellent/good cosmetic outcomes decreased with time during follow-up (78.0% at 3 months, 77.5% at 1 year and 70.3% at 3 years follow-up, respectively), and the proportion of satisfied/very satisfied patients also decreased (90.0% at 3 months, 89.2% at 1 year, and 74.1% at 3 years follow-up). Only one patient reported an improvement in satisfaction during follow-up, while 19 patients who were initially very satisfied/satisfied eventually became dissatisfied/very dissatisfied.

The correlation between cosmetic outcome and satisfaction during follow-up was strongly positive (Spearman correlation 0.637 at 3 months, 0.537 at 12 months, 0.725 at 36 months, all $p < 0.001$). Despite this strong correlation, there were differences at the individual level. During the follow-up period, 11.8% of patients were satisfied with breast appearance despite judging the cosmetic outcome as fair/poor. However, satisfaction despite a fair/poor cosmetic outcome decreased during the post-operative period, from 13.9% at 3 months to 8.1% at 36 months.

Figure 1 shows the evaluations of the six breast-specific factors scored by all patients during follow-up. The shift of most factors towards a more negative outcome is readily apparent. For the factors size and shape in particular, negative scores exceed 30% at 36 months. An exception was the scores of skin color of the treated breast which, as expected, improve during follow-up as a consequence of recovery from early radiation effects. The logistic regression model at 3 years indicates that cosmetic outcome is significantly influenced by shape, while satisfaction is influenced by the appearance of the scar and breast firmness.

Patients with fair/poor overall results

At 36 months, 38 patients scored fair/poor on either cosmetic outcome or satisfaction or on both. Differences in scores between cosmetic outcome and satisfaction were apparent for 23 of these patients, although differ-

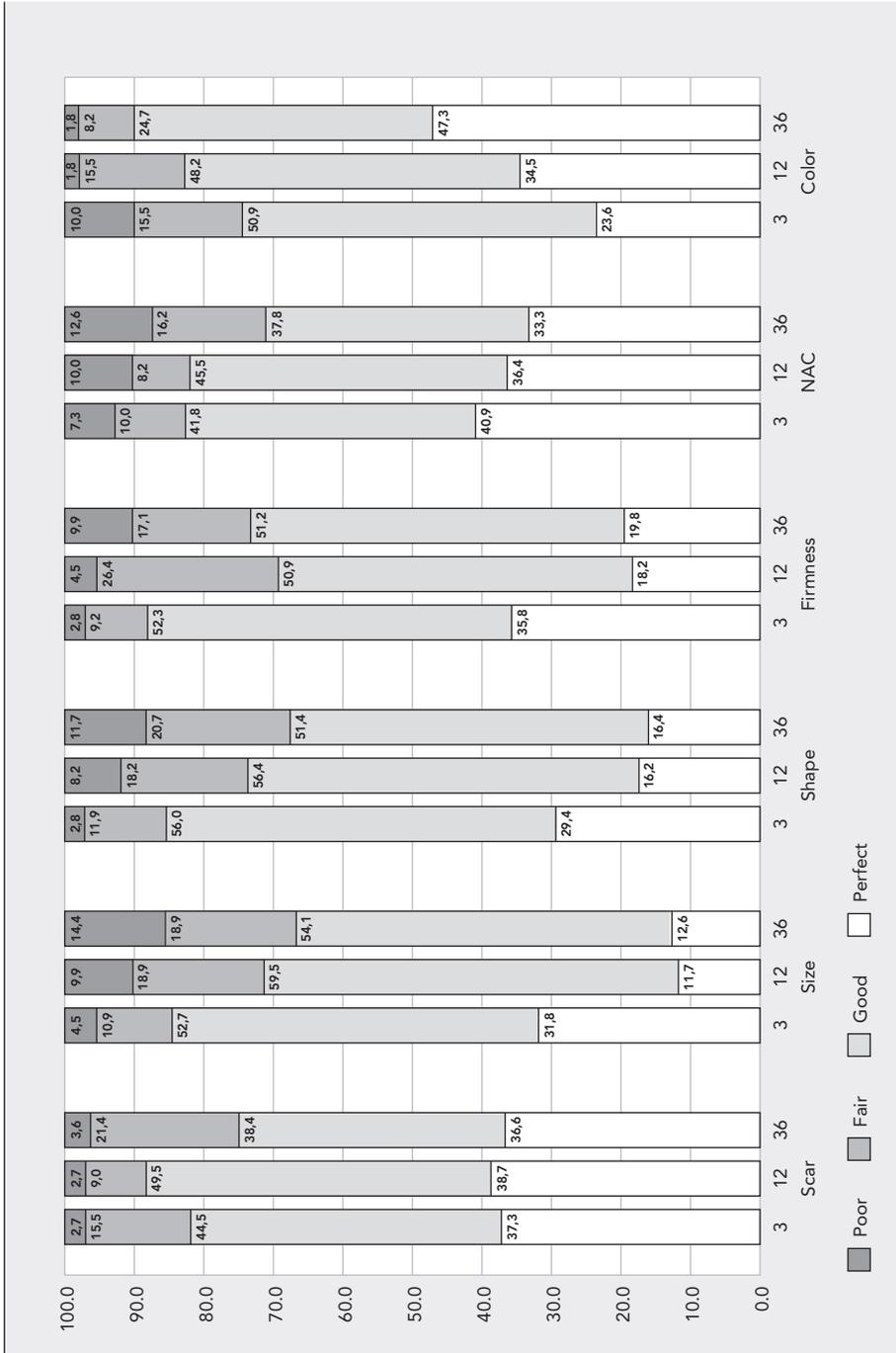


Figure 1 Rating of scar, size, shape, firmness, position of NAC and skin color for all patients at 3, 12 and 36 months follow-up (in percentages).

ences remained within one point on the Likert-scale. In 19 cases patient satisfaction scored better than cosmesis.

Figure 2 illustrates the scores for the six breast-specific factors for all patients who scored fair/poor on cosmetic outcome and/or satisfaction. Unacceptable results on overall cosmetic outcome and satisfaction were predictable based on the results for breast-specific factors. Only two patients had excellent/good scores for all six items, with an overall perception of fair. In addition, all patients in the fair/poor overall group after 3 years also scored fair/poor on at least one breast-specific item (mean 4 out of 6 items). Closer examination of poor scores on breast-specific factors revealed that the influence of the scar and skin color on the final result was limited, in contrast to scores for size and shape of the breast, which had a major impact on the fair/poor overall outcome.

Table 2 separately illustrates results for all patients with a fair/poor cosmetic outcome or fair/poor satisfaction at 36 months. It is clear that all breast-specific factors show a significant correlation with cosmetic outcome and satisfaction at 3 years follow-up, with size, shape and firmness showing the highest correlation with the cosmetic outcome, while size, shape and NAC show the highest correlation with satisfaction.

Breast-specific Factor	Cosmetic outcome Fair/poor N = 34	Satisfaction Fair/poor N = 29	Spearman's correlation of cosmetic outcome	Spearman's correlation of satisfaction
Scar	58.8%	72.4%	0.531*	0.602*
Size	91.2%	86,2%	0.753*	0.692*
Shape	94.1%	79.3%	0.798*	0.654*
Firmness	76.5%	72.4%	0.729*	0.620*
Position of NAC	67.6%	79.3%	0.562*	0.645*
Skin color	29.4%	31.0%	0.471*	0.404*

The percentages represent the amount of fair/poor scores on breast-specific items. Spearman's correlation is applied for breast-specific items and cosmetic outcomes or satisfaction. * p < 0.001.

Table 2 Patients with fair/poor cosmetic outcomes and satisfaction

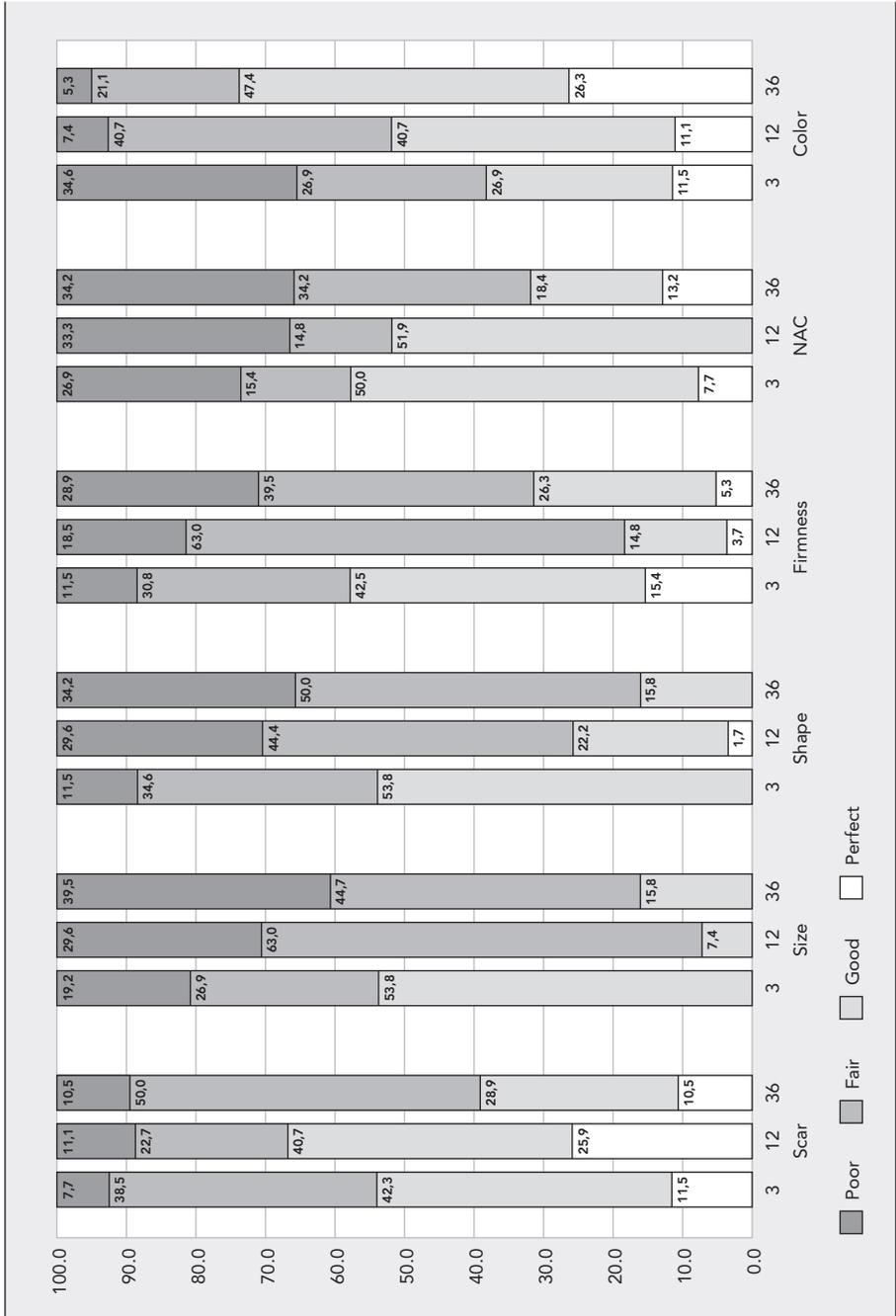


Figure 2 Rating of scar, size, shape, firmness, position of NAC and skin color for patients with fair/poor cosmetic outcome and/or satisfaction at 3, 12 and 36 months follow-up (in percentages).

Items influencing cosmetic outcome and satisfaction at 36 months

The tumour/treatment-related items including T-stage, excision method, axillary surgery, location of the tumour, re-excision, application of a radiotherapy boost, and the patient-related items BMI and cup size did not show a significant influence on cosmetic outcome or satisfaction. Only the treatment-related item excision volume and patient-related item age influenced cosmetic outcome and satisfaction at 36 months; increased age and decreased excision volume improved cosmetic outcome (OR 2.1 per 10 years, $p = 0.027$; OR 0.64 per 10cc, $p = 0.002$) and satisfaction (OR 2.2 per 10 years, $p = 0.023$; OR 0.76 per 10cc, $p = 0.022$).

Of the 39 patients with excision volumes $> 40\text{cc}$, cosmetic outcome was rated fair or poor in 20 patients after three years. Size, shape or NAC were fair or poor in 70% of these patients, compared to 30% in patients with excision volumes $< 40\text{cc}$. For firmness, the fair/poor outcomes were 40% versus 20%, respectively.

DISCUSSION

As an increasing number of successfully treated patients now have to deal with the results of local treatment on a daily basis, self-reported cosmetic outcome and satisfaction have both become critical endpoints of BCT.²⁴

Our study demonstrates that the use of a questionnaire containing multiple breast-specific questions provides an adequate evaluation of a patient's perception of breast appearance. In addition, evaluation of scores for breast-specific factors provides the surgeon with a tool to improve quality of care and discuss outcome expectations with individual patients before treatment. As expected, breast-specific factors were the starting point for assessment of overall patient perception of breast appearance. Completion of the questionnaire at three points during follow-up revealed a shift in factor ratings during the first three postoperative years. However, a positive rating of breast-specific factors was associated with a good overall rating of cosmetic outcome and satisfaction at all time points. It is important to realize that unacceptable overall outcomes of BCT are mainly caused by the combination of abnormal size, shape, nipple position and firmness of the breast.

Cosmetic outcome and satisfaction were negatively influenced by the treatment-related item volume and the patient-related item age. This result underlines the importance of achieving adequate low excision volumes

and, for the surgeon, avoiding resection of excess healthy breast tissue (the primary measure for avoidance of a poor cosmetic outcome).

The importance of a woman's perception of the appearance of her breast after BCT is reflected in the numerous questionnaires that have been developed and the growing number of studies incorporating patient self-evaluation.⁵⁻⁷ These questionnaires are designed to identify failures of BCT and to identify the breast-specific factors, patient and tumour-related items that are responsible for unacceptable outcomes.

Breast-specific factors as we know them today were first described in 1985 by Patterson et al. These authors asked patients for their opinion on cosmetic outcomes and their degree of satisfaction. Patients were also asked to describe, in their own words, which aspect of the operated breast was subjectively important in determining cosmetic outcome.⁹ The factors mentioned by patients in that study, including breast size, breast firmness, breast elevation and skin color changes have been used ever since in many different questionnaires.^{14, 16, 25, 26}

In early studies from the axillary lymph node dissection era, functional status predominated over cosmetic results in determining patient satisfaction. Since the introduction of standard axillary staging using the sentinel node (SN) procedure, patient satisfaction has been based on cosmetic results and is no longer overshadowed by the serious morbidity associated with ALND. This development has also allowed greater factual insight into the importance of breast-specific factors on the final cosmetic result. Waljee et al. (2008) were the first to report the use of the BCTOS questionnaire in the SN era. These investigators extracted the breast-specific questions from the cosmetic subscale of the BCTOS questionnaire, added a question on skin color, and defined 'asymmetry' on a summative score of these ratings. This breast-specific questionnaire showed that overall pronounced asymmetry was negatively associated with the patient's feeling of satisfaction after BCT.¹¹

In 2009, the Breast-Q-BCT questionnaire for breast-conserving therapy was developed at the Memorial Sloan Kettering Cancer Center. This questionnaire has great potential since it addresses modern surgery-specific issues. It encompasses six domains that cover satisfaction with breasts, effect of radiation therapy, physical, psychological wellbeing, sexual wellbeing and satisfaction with the information provided and staff interactions.²⁷ The questions of the "satisfaction of the breast domain" and "effect of ra-

diation therapy domain” are comparable with the content of the questionnaire used in our study. In 2016, O’Connell et al. were the first to report the application of this questionnaire and found that a high BMI, delayed wound healing and axillary surgery were all risk factors for decreased patient satisfaction.²⁷

Over the past ten years, several authors have included breast-specific factors in questionnaires that recorded overall good/excellent cosmetic outcome or satisfaction at rates of 76-84%.^{6-8, 11, 27} In 2014, Parvez et al. stated that one third of patients reported a large to moderate difference in breast size and shape three years after surgery. In addition, scar appearance was rated fair or poor in only 22% of the patients.⁸ A study by Dahlback et al. found that 12% of patients were dissatisfied with the size and shape of their breast 16 months after surgery.⁷ Similarly to Waljee and colleagues, Hennigs et al. also created a summative score from the cosmetic subscale of the BCTOS. In agreement with our results, we found that the incidence of poor cosmetic outcomes increases during long-term follow-up and that patients experiencing poor cosmetic outcomes after BCS are likely to remain unsatisfied over time.⁶

Summarizing the recent literature, and consistent with our results, avoidance of asymmetry should be a primary objective.^{6-8, 11, 27, 28} Asymmetry is mainly influenced by size, shape and nipple position. The value of these items as part of a questionnaire is now proven, since all patients with unacceptable outcomes score fair/poor on at least one symmetry item.

Our results establish beyond dispute the strong correlation between the perception of cosmetic outcome and feelings of satisfaction in breast cancer patients. However, 11.8% of patients are satisfied despite a fair or poor cosmetic outcome, an incongruity which is also observed in many other studies.^{10, 14, 26, 29} This discordance in favor of satisfaction might be related to prior expectations, with some patients perhaps not expecting that the treated breast will remain unchanged. In the long term, scoring of cosmetic outcomes and breast factors does not seem to have greatly improved over the past 30 years, even though we are inclined to believe that the cosmetic outcomes of BCS have improved over this period.

This effect might be due to expectations specific to a given period, with judgment of treatment outcomes dependent on alternative treatment options. In the previous era, knowledge of the recent change from mastectomy to BCT may have encouraged women to be satisfied with their cosmetic outcome because the alternative was no breast at all. Nowadays, BCT is the

standard of care in early stage breast cancer and a good cosmetic outcome is understood by patients to be a priority of this approach.

Evaluating to what extent patients are satisfied with their treatment outcomes is clinically relevant, as satisfied patients are more likely to comply with treatment and take an active role in their own care.³⁰ In addition, health professionals can benefit from satisfaction questionnaires that identify areas for improvement. Moreover, for optimal shared decision making, patients require meaningful data about how other women have perceived the outcome of surgery.

It is clear from the current study that differences between cosmetic outcome and satisfaction decrease over time. We hypothesize that breast cancer patients are initially less concerned with their cosmetic outcome than with their oncological outcome. After several years their focus may increasingly shift to the cosmetic outcome when it is clear that oncological treatment has been effective. As suggested by O'Connell et al, expectation of treatment outcomes, including the identification of factors determining a poor cosmetic outcome, are very important and have to be adequately addressed with the patient before surgery.²⁷

There are many patient, tumour and treatment-related items that influence cosmetic outcome and satisfaction. The most frequently reported items that cannot be influenced are younger age^{10,28}, tumour site within the breast^{10, 28, 31-33}, large tumour size^{23, 28, 31, 32}, axillary dissection^{7, 27}, infectious complications⁷, high BMI^{7, 23, 27} and breast size.³¹

Most of these factors are predictable by surgeons, and thereby surgeons could better inform their patients pre-operatively of what to expect post-operatively. It is well known that many breast cancer patients feel to be insufficiently informed about the impact of treatment modalities on their quality of life.³⁴ Moreover, accumulating evidence suggests that expectations substantially influence treatment outcome.^{35,36} Optimizing expectation management regarding the secondary outcomes of breast conserving therapy could thereby contribute to improved overall satisfaction.

The two main treatment modalities that contribute to poor cosmetic outcome and low patient satisfaction that can be influenced are inaccurate surgery and adjuvant radiotherapy

The need for continual improvements in breast appearance is now mandatory and will only be achieved through a focus on obtaining the most symmetrical breast possible. This can be accomplished by improvements

in surgical techniques that result in lower excision volumes and through a reduction in the burden of radiotherapy, as the latter is primarily responsible for long-term tissue changes.

The decisive impact of large resection volumes on cosmetic outcomes was suggested in the late 1980's and this negative influence has been observed by many others since.^{6-8, 18, 19, 23, 31, 33, 37} In the COBALT study, the rate of cosmetic failure was strongly related to lumpectomy specimens exceeding 40cc.²³ By three years, more than half of patients with excision volumes exceeding 40cc had an unacceptable cosmetic outcome, compared to less than twenty percent in patients with resection volumes < 40cc.

Since the initial studies in the 1990's, substantial evidence has accumulated which supports the superiority of USS over other localization techniques in reducing the amount of positive margins as well as excision volumes in non-palpable and palpable tumours.^{21, 23, 38-49}

Due to the low excision volumes achievable with USS, the wide excision of normal healthy breast tissue involved in oncoplastic breast surgery (OPBS) means that the utility of OPBS is now questionable. In early stage breast cancer, the efficacy of OPBS in achieving fewer involved margins and improved cosmetic outcome is still unsupported by data, since published results are based on poorly designed and underpowered studies.⁵⁰ Plastic surgeons can certainly contribute to improvements in cosmetic outcome by increasing awareness amongst surgical oncologists regarding the general reconstructive principles applied in cosmetic breast surgery. Perioperative recognition of the anatomical landmarks of the breast, with the patient placed in a semi-sitting position, ensure that the natural position of the breast is foremost.⁵¹

The goal of adjuvant radiotherapy is to prevent locoregional recurrence, and thanks to excellent results in achieving this goal, radiotherapy is an important part of breast-conserving treatment. Unfortunately, radiation therapy has a negative impact on skin color (especially in the first year), and gradually increasing fibrosis negatively influences breast firmness as well as symmetry of the operated breast.^{19, 31, 32} In the EORTC "Boost versus No Boost" trial, the application of a boost to the tumour bed was shown to increase the rate of moderate to severe fibrosis in particular (from 13% to 28%).³¹ The development of fibrosis is an ongoing process that continues for years after irradiation. The negative effect of radiotherapy on cosmetic outcome could be reduced by identifying those patients in whom radio-

therapy can be omitted or the total dose and/or the targeted volume can be lowered. Selective omission of radiotherapy can be indicated in elderly women treated with endocrine therapy.⁵² Future efforts will be aimed at developing personalized radiation schedules through prediction of radiosensitivity in individual patients.⁵³

Again, the role of the surgeon is extremely important, since the marked area of the excised breast tissue after BCT is the target area for the highest radiation dose. By lowering excision volumes, the burden of radiation therapy will also be lowered.

In conclusion, optimizing both the cosmetic outcomes and satisfaction of women with breast cancer after BCT is crucial. Questionnaires offer the opportunity to identify the shortcomings of current treatment strategies and can stimulate improvement. It is striking that hospitals are judged on a range of quality indicators such as waiting time for surgery, whereas posttreatment evaluations of esthetic outcomes and determining items (excision volume) have not yet been instituted as a standard of care or used to assess the performance of surgical teams. Questionnaires not only help patients and clinicians make better decisions, they also enable the comparison of individual and institutional performance regarding cosmetic outcome and satisfaction. Furthermore, the adoption of patient questionnaires in breast cancer care is a quality indicator in itself, as it can stimulate the changes necessary to improve a healthcare organization and the quality of breast cancer care.

Optimal symmetry, minimal visible scarring and minimal changes in firmness should be the goals for breast appearance after BCT, and further progress will require improvement of current surgical techniques to the level where radical surgery can be efficiently combined with minimal excision volumes.

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