Change of aesthetic and functional outcome over time and their relationship to quality of life after breast conserving therapy


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Abstract

Purpose
We analyzed changes in aesthetic and functional outcome over time after breast conserving therapy. Our special interest resides in the question of whether these aspects gain or loose their influence on quality of life (QoL) with temporal progress.

Patients and methods
This prospective single centre cohort study included 138 patients, treated with breast conserving surgery and consecutive radiotherapy. Patients completed two questionnaires one week and one year after surgery: the BCTOS (Breast Cancer Treatment Outcome Scale) to measure Functional, Aesthetic, and Breast Sensitivity Status and the EORTC (European Organisation for Research and Treatment of Cancer) C30-BR23 to assess QoL. We applied correlation and multiple regression analysis as statistical methods.

Results
Aesthetic and Functional Status did not change significantly over one year, whereas Breast Sensitivity Status and several QoL subscales showed significant improvement (p<0.0001). Correlations between BCTOS scales and EORTC subscales remain similar over time. Functional and Aesthetic Status kept a strong impact on global health (Spearman’s Rho = -0.28 to -0.45 depending on time of assessment). Increasing age and poorer Functional Status shortly after surgery are predictors of a decline in global health over one year (p<0.001).

Conclusion
Functional and aesthetic outcome after breast-conserving surgery maintain their impact on QoL over a one year follow-up period and are valuable predictors of QoL.
Keywords - MeSH

Breast Neoplasms, surgery
Breast conserving therapy, aesthetics
Breast conserving therapy, function
Quality of life
Introduction

The surgical treatment of breast cancer is not only an invasive physical intervention, but also can represent a deep incision in a woman’s body image. Several studies assessing objective and subjective measures of breast aesthetics demonstrate its influence on different aspects of Quality of Life (QoL) [1–2]. Moreover, functional disabilities such as breast and/or shoulder-arm morbidity, determined both by breast tissue resection and by axillary dissection, also influence QoL [3–4]. However, aesthetic and functional factors are not necessarily equally important over the course of time.

Of the published instruments to evaluate functional and aesthetic results, the Breast Cancer Treatment Outcome Scale (BCTOS) [5–6] is one of the most clearly structured and comprehensive. It addresses the most important dimensions of after-treatment morbidity with respect to aesthetic and functional outcome and is easy to administer. We hypothesize that the BCTOS subscales Aesthetic, Functional and Breast Sensitivity Status predict QoL in general across the year after surgery. To evaluate the patient’s QoL based on physical and psychological functioning, we used the European Organisation for Research and Treatment of Cancer (EORTC) questionnaire, consisting of a general module (C30) and a breast cancer specific questionnaire (BR23) [7–9].

Our work focuses on functional and aesthetic results and analyzes their impact on QoL with respect to the time of assessment. Generally, we would expect Functional Status, Aesthetic Status and Breast Sensitivity Status to improve with time as they are no longer impaired by the sequelae of the operation. Our special interest resides in the question of whether these aspects gain or loose their influence on QoL with temporal progress. We assume that the influence of the Aesthetic Status on QoL wins over the influence of the Functional Status one year postoperatively as we expect patients to focus on aesthetic aspects after having recovered from the physical distress of surgery. Therefore we hypothesize that the Aesthetic Status is of predictive value in assessing QoL one year postoperatively. Additionally, we try to assess whether other covariates such as the patient’s age have a predictive value on QoL one year postoperatively.
Evidence-based knowledge of predictors of QoL could, in the long run, create new perspectives in local breast cancer therapy as surgical and radiotherapeutic procedures may be influenced by these findings.
Patients and methods

Description of the study population

As a part of an exploratory, single institution, prospective cohort study, this analysis includes patients meeting the following inclusion criteria:

- Primary, unilateral, histologically proven breast cancer, treated conservatively
- Date of surgery between 7 September 2007 and 24 October 2008
- No secondary mastectomy in the first post surgical year
- ECOG performance Status <2,
- Adequate knowledge of German language.

Of 296 preoperatively screened patients, 270 patients gave informed consent to participate in the study. Shortly after surgery, 71 of these patients dropped out, 50 because of secondary surgeries, and 21 for individual reasons (patients dismissed of hospital without having completed the questionnaires or explicitly withdrew their informed consent). In total, 199 patients completed questionnaires within at mean 7 days after surgery, and 138 (69%) attended the one year follow-up visit.

On average, the 138 patients were 58 years old (SD 9.3; 95% CI 43-74). The mean body mass index was 25 (SD 4.2, 95% CI 18-37). The majority was postmenopausal and had a breast size of cup B. Most of the patients were diagnosed with unilateral invasive ductal carcinoma with a tumor size of less than two centimeters and were treated by a sentinel lymph node biopsy. All patients had a segmental resection of breast tissue (see Table 1). According to the German guidelines for the treatment of breast cancer 135 patients went through consecutive radiotherapy of the breast with 50,4 Gy for 28 days. In 96 cases a boost radiation of 16 Gy was additionally administered. As most of our patients were nodal negative (110 patients, 24 with only in situ carcinoma), only few patients (24 patients) received radiation of the nodal basins. The interspace between end of radiation and follow-up control was 3 to 9 months (median 7 months).
The study instruments: BCTOS and EORTC C30-BR23 questionnaires

The Breast Cancer Treatment Outcome Scale (BCTOS)
The BCTOS, constructed by Stanton et al. [5], contains 22 items. It was designed to assess women’s subjective evaluation of both the aesthetic and functional outcome after breast cancer treatment. Patients are instructed to rate each item of the BCTOS questionnaire on a four-point scale evaluating the differences between the treated and the untreated breast (1=no difference to 4=large difference). Recently, we showed [6] that the BCTOS is composed of the three internally consistent scales, which are defined as Functional Status (e.g. shoulder and arm movement, stiffness or pain), Aesthetic Status (e.g. breast size and texture, breast shape, scar tissue) and Breast Sensitivity Status (e.g. breast pain, breast tenderness and sensitivity). The score value of each scale is the mean of the ratings over all items belonging to this scale. A higher score reflects poorer status (i.e., larger difference between treated and untreated breast).

The EORTC C30-BR23 questionnaire
In order to measure the QoL in breast cancer patients, we chose the EORTC (EORTC Cancer Quality of Life Questionnaire number C30-BR23), as it is validated and approved for different languages [7] and for the German version specifically [9]. This questionnaire consists of a general module, the QLQ-C30 and a breast cancer specific questionnaire, the QLQ-BR23. Out of these two modules we use twelve scales: Global Health Status, Physical Functioning, Breast and Arm Symptoms, Emotional Functioning, Role Functioning, Social Functioning, Sexual Functioning, Sexual Enjoyment, Pain, Perspective for the Future and Body Image. A raw score was calculated as the average of all items of the scale, which was standardized by linear transformation (Likert method of summated scales). The scores range from 0 to 100, a higher score indicating a higher prevalence. For example, a high score for the global health status represents high QoL, but a high score for a symptom scale represents a high level of symptomatology [8].
Statistical methods

In order to analyze the relations of the three outcome variables (Aesthetic, Function, Breast Sensitivity Status) and QoL measured by the different BCTOS and EORTC subscales, we calculated correlation coefficients between the scales using Spearman’s Rho for both times of assessment. In order to assess the time stability of these relations, we applied a 2-sided normal-approximation test for comparing two correlation coefficients based on Fisher’s-z-transformation to assess the null hypothesis: Spearmans Rho(shortly after surgery)=Spearmans Rho(one year after surgery). To analyze absolute change in the BCTOS and EORTC scores over time, we performed two-sided paired t-tests. We also performed multiple regression analyses with the three BCTOS scales and age as predictors of the EORTC scales global health and body image, as these two subscales represent important dimensions of QoL in breast cancer patients after breast conserving therapy.
Results

Change in BCTOS scales and QoL over time

By comparing the means of the BCTOS and EORTC subscales over time (see Table 3) we discovered a significant improvement in some areas while others remain unchanged. Breast Sensitivity Status improved while the Functional and Aesthetic Status did not change significantly. Global health status also improved as well as the EORTC subscales physical functioning, role functioning and emotional functioning. Pain symptomatology declines over time, supporting the plausibility of the decline of the Breast Sensitivity Status. The breast and arm symptoms subscales of the EORTC do not show significant improvement over time, supporting the results for the BCTOS Functional and Aesthetic Status.

Impact of Functional and Aesthetic Status on QoL over time

The correlation analysis identified function, aesthetics and breast sensitivity as relevant correlates of the different aspects of QoL. Moreover, all correlation coefficients remain similar over time, so that function, aesthetics and breast sensitivity can be interpreted as important time independent influencing factors on QoL (cf. Table 3).

BCTOS Functional Status and age as predictors of QoL

The multiple regression analysis showed that the Aesthetic Status shortly after surgery was not associated significantly with the global health status after one year (p=0.2), meaning that the Aesthetic Status shortly after surgery does not predict the global health status one year after surgery. However, a poorer/better Functional Status shortly after surgery was significantly related to a poorer/better global health status one year after surgery (p=0.0002). Thus, the Functional Status is of higher importance than the Aesthetic Status in predicting QoL. In analyzing other potential covariates with an impact on QoL, we found that older patients tend to have a poorer global health status one year after surgery (p=0.003). With respect to body image, no BCTOS subscale shortly after surgery turned out to be a good predictor at one year.
Discussion

**Functional and Aesthetic Status did not change significantly with time**

Against our expectation, the BCTOS Aesthetic Status did not change significantly over time. Thus, postsurgical impairments such as hematomas or inflammable swellings which obviously improve with time seemed to be less important with respect to the aesthetic outcome. Constant factors as symmetry of size and shape seem to have more influence on aesthetic evaluation. Therefore the Aesthetic Status remains fairly stable through one year. Amichetti et al.[10] compared the postsurgical aesthetic results with the results 74 months later. They observed that patients’ satisfaction with cosmetic results was high at postsurgical assessment but tended to decline with time. At least for the first postsurgical year our data did not support this finding nor did an improvement occur as we hypothesized. Moreover, no significant changes occurred in BCTOS Functional Status and in the EORTC breast and arm symptoms scales. Montazeri et al. [11] reported similar findings: despite an overall improvement of global health status, the functional scores did not improve with time. Based on our clinical experience, that functional impairment improves very quickly and is thus relatively low even on the postsurgical control seven days after surgery, the results indicate that there is no significant further improvement over the first postsurgical year. Contrarily we would have expected that a possible transient functional impairment would decline over time which does not seem to be true. This statement might exclude patients with extensive axillary lymph node dissection and consecutive edema as described by Beaulac et al.[12]; those patients were very seldom in our cohort.

**BCTOS Breast Sensitivity Status and EORTC Global Health Status improve with time**

BCTOS Breast Sensitivity Status improved significantly over time. This might be due to the obvious circumstance that patients recover from the sequelae of the surgical intervention like narcosis, hematomas or even postsurgical psychological stress. Consequently, a temporary loss of sensitivity due to the sequelae of the intervention seems to diminish with time.
The EORTC global health status also improved over time, as did its subscales of physical functioning, role functioning, emotional functioning and social functioning. We assume that our patients, after having quit the hospital and their patient role, at least partly regained their former daily routine. In addition, as patients often undergo surgery only few days after having been diagnosed with breast cancer, they eventually had time to cope with the diagnosis which may have had a possible influence on their self-perception as well.

**Functional and Aesthetic Status are strong indicators of QoL over time; Functional Status shortly after surgery predicts global health one year after surgery**

We observed that the correlations of the different BCTOS and EORTC subscales remained equally strong and did not change with temporal progress. Hence, we might conclude that function and aesthetics are valuable indicators of QoL in general as they retain their impact over the course of time. In contrast to our expectations, Functional Status, but not Aesthetic Status, shortly after surgery was the strongest predictor of global health one year after surgery. The importance of the Functional Status with respect to QoL was also described by Krishnan et al. who reported that functional treatment outcomes are correlates to QoL with predictive validity even many years after patients underwent breast conserving therapy [13]. Therefore, the Functional Status seems to be of predominant importance in determining QoL and innovations in breast cancer therapy should respect these findings.

**Influence of radiotherapy**

It is well known that breast radiation has an influence on Functional, Aesthetic and Breast Sensitivity Status. Consequently, our results reflect the sequelae of breast irradiation and breast conserving surgery, together forming a breast conserving therapy. On average, our patients attended the follow-up control seven months after cessation of radiotherapy, hence short term side effects had time to recover. Patients seldom reported a slight darkening of the irradiated breast. Middle and long term effects did not occur. Various authors assessed the aesthetic outcome after breast irradiation though the results are difficult to compare due to different definitions of a good result and the respective method of
assessment. On average, they observed good to excellent results in 70 to 90% of the patients after radiotherapy [14-17]. Chie et al. [16] compared the postoperative aesthetic outcome with the outcome after radiotherapy and reported that the cosmetic results only deteriorated in patients who had received lymph node irradiation or who were exposed to heat after radiotherapy. Cardoso et al. [14] determined scar visibility and BMI to be the only factors significantly associated with aesthetic results in patients who received breast conserving surgery and consecutive irradiation. Hence, we might conclude that the cosmetic outcome is most closely associated with the surgery even though we cannot adjust our findings for the potential influence of radiotherapy.

**Study limitations**

Study limitations deserve mention. The less than optimal one year follow-up rate of 69% is explained by the fact that the aftercare is not done by our hospital but by general practitioners; thus, study participants had to visit our hospital only for study follow up. With over 50% of patients coming from more than 50 kilometers distance we additionally lost patients due to the related time and cost effort. Moreover the study cohort is relatively homogenous (one sided early breast cancer, treated conservatively) that the conclusion cannot easily be generalized to other breast cancer patients. We report findings reflecting the influence of breast conserving surgery and breast radiation on Aesthetic and Functional Status. Obviously it is not possible to quantify effects of surgery and radiotherapy separately for the results obtained at the one year follow-up visit.
Conclusion

Functional and aesthetic outcomes maintain their relations with QoL over a one year follow-up period and are valuable correlates of QoL. Beyond that, poorer functional outcome shortly after surgery predicts a decline in overall QoL one year later.
Conflict of interest statement

There are no conflicts of interests (e.g. employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding) by any of the authors with regard to that paper.

Funding source

There is no special funding source beside the Heidelberg medical school, employer of all authors.

Ethical Approval

The study was approved by the ethics commission of the University of Heidelberg Medical School. All patients gave their written informed consent to participate.
Literature


Table 1: Description of the study cohort

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menopause Status</td>
<td>138</td>
<td>100</td>
</tr>
<tr>
<td>- Premenopausal</td>
<td>25</td>
<td>18.1</td>
</tr>
<tr>
<td>- Perimenopausal</td>
<td>15</td>
<td>10.9</td>
</tr>
<tr>
<td>- Postmenopausal</td>
<td>98</td>
<td>71.0</td>
</tr>
<tr>
<td>Breast size = bra size</td>
<td>138</td>
<td>100</td>
</tr>
<tr>
<td>- Cup A</td>
<td>16</td>
<td>11.5</td>
</tr>
<tr>
<td>- Cup B</td>
<td>69</td>
<td>50.0</td>
</tr>
<tr>
<td>- Cup C</td>
<td>40</td>
<td>29.0</td>
</tr>
<tr>
<td>- Cup D-G</td>
<td>13</td>
<td>9.5</td>
</tr>
<tr>
<td>Tumour histology</td>
<td>138</td>
<td>100</td>
</tr>
<tr>
<td>- Ductal carcinoma in situ</td>
<td>24</td>
<td>17.4</td>
</tr>
<tr>
<td>- Invasive ductal carcinoma</td>
<td>83</td>
<td>60.1</td>
</tr>
<tr>
<td>- Invasive lobular carcinoma</td>
<td>16</td>
<td>11.6</td>
</tr>
<tr>
<td>- Others</td>
<td>15</td>
<td>10.8</td>
</tr>
<tr>
<td>Pathological T-stage</td>
<td>138</td>
<td>100</td>
</tr>
<tr>
<td>- T0</td>
<td>2</td>
<td>1.4</td>
</tr>
<tr>
<td>- Tis</td>
<td>24</td>
<td>17.4</td>
</tr>
<tr>
<td>- pT1a-1c</td>
<td>92</td>
<td>66.7</td>
</tr>
<tr>
<td>- pT2-3</td>
<td>20</td>
<td>14.5</td>
</tr>
<tr>
<td>Lymphonodectomy</td>
<td>138</td>
<td>100</td>
</tr>
<tr>
<td>- Sentinel node biopsy</td>
<td>97</td>
<td>70.3</td>
</tr>
<tr>
<td>- Classical axillary lymphonodectomy</td>
<td>25</td>
<td>18.3</td>
</tr>
<tr>
<td>- None</td>
<td>16</td>
<td>11.6</td>
</tr>
</tbody>
</table>
Table 2: Postoperative and follow up means of BCTOS and EORTC subscales

<table>
<thead>
<tr>
<th>Scale</th>
<th>Mean postoperative</th>
<th>Mean Follow up</th>
<th>p-value (*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCTOS sensitivity status</td>
<td>2.10</td>
<td>1.84</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BCTOS aesthetic status</td>
<td>1.82</td>
<td>1.90</td>
<td>0.21</td>
</tr>
<tr>
<td>BCTOS functional status</td>
<td>1.38</td>
<td>1.38</td>
<td>0.97</td>
</tr>
<tr>
<td>Global health status</td>
<td>57.29</td>
<td>70.66</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>78.72</td>
<td>87.35</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Role functioning</td>
<td>70.35</td>
<td>83.33</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Emotional functioning</td>
<td>58.88</td>
<td>74.83</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Social functioning</td>
<td>73.88</td>
<td>83.50</td>
<td>0.001</td>
</tr>
<tr>
<td>Pain</td>
<td>45.14</td>
<td>36.46</td>
<td>0.05</td>
</tr>
<tr>
<td>Sexual functioning</td>
<td>73.16</td>
<td>66.10</td>
<td>0.05</td>
</tr>
<tr>
<td>Sexual enjoyment</td>
<td>41.67</td>
<td>41.67</td>
<td>1.00</td>
</tr>
<tr>
<td>Perspective for the future</td>
<td>57.36</td>
<td>65.89</td>
<td>0.05</td>
</tr>
<tr>
<td>breast symptoms</td>
<td>37.93</td>
<td>35.45</td>
<td>0.45</td>
</tr>
<tr>
<td>arm symptoms</td>
<td>32.45</td>
<td>30.12</td>
<td>0.56</td>
</tr>
<tr>
<td>body image</td>
<td>83.77</td>
<td>81.02</td>
<td>0.21</td>
</tr>
</tbody>
</table>

(*)p-values correspond to a two sided paired t-test.
Table 3: Correlation coefficients (Spearman’s Rho) between the scales of the BCTOS and the EORTC: correlation of shortly postoperative (PO) and the one year follow-up (FU) results of BCTOS subscales with EORTC subscales on the correspondent time of assessment.

<table>
<thead>
<tr>
<th>EORTC status</th>
<th>Functional Status</th>
<th>Aesthetic Status</th>
<th>Breast Sensitivity Status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PO</td>
<td>FU</td>
<td>p (#)</td>
</tr>
<tr>
<td>Global Health Status</td>
<td>-0.28</td>
<td>-0.45</td>
<td>0.16</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>-0.38</td>
<td>-0.51</td>
<td>0.20</td>
</tr>
<tr>
<td>Role functioning</td>
<td>-0.29</td>
<td>-0.49</td>
<td>0.08</td>
</tr>
<tr>
<td>Emotional functioning</td>
<td>-0.27</td>
<td>-0.41</td>
<td>0.23</td>
</tr>
<tr>
<td>Social functioning</td>
<td>-0.18</td>
<td>-0.32</td>
<td>0.27</td>
</tr>
<tr>
<td>Body image</td>
<td>-0.19</td>
<td>-0.09</td>
<td>0.41</td>
</tr>
</tbody>
</table>

All listed correlation coefficients >(-)0.20 correspond to descriptive p-values < 0.05, 2-sided t-test with n-2 degrees of freedom for the null hypothesis: Saoerman’s Rho=0

(#: p-values correspond to a 2-sided normal-approximation test for comparing two correlation coefficients after Fisher’ S-z-transformation to assess the null hypothesis that Spearman Rho(shortly after surgery)=Spearman Rho(one year after surgery)