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Factors associated with patient-reported cosmetic outcome in the Young Boost Breast Trial

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ABSTRACT

Purpose: To investigate which factors are related to patient reported cosmetic outcome (PRCO) after breast conserving therapy.
Methods: From 2004 to 2011, 2421 cT1-2N0-2a breast cancer patients were randomised in the Young Boost Trial between a 16 and a 26 Gy boost to the tumour bed. Cosmesis was scored subjectively by the patient and physician, and objectively using BCCT.core, at baseline, one and four years after treatment. Presence of fibrosis, QoL and rib pain at four years were also scored. Data were complete for 864 patients. The relation between the separate components was investigated using a proportional odds model.
Results: Of the 7 BCCT.core parameters, the distance from nipple to inframammary fold and the length of the breast contour were significantly related to the overall PRCO at four years. Patients with more fibrosis and poorer QoL scored their cosmesis worse, while rib pain was not related. The agreement between the different scores was low (kappa 0.26–0.42).
Conclusion: The distance from nipple to inframammary fold, the length of the breast contour and the severity of fibrosis were the main factors related to patient-reported cosmetic outcome. Patients with better QoL scored their cosmesis better.
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The EORTC boost-no boost trial showed that adding a 16 Gy boost to the primary tumour bed after 50 Gy whole breast irradiation, reduces the local recurrence rate (LRR) with 35% [1]. Nevertheless, even after a boost, the LRR in young patients (⩽50 years of age) remained higher than 1% per year. Therefore, in 2004, the Young Boost trial (YBT) was launched (NCT00212121), with the primary aim to investigate whether a higher boost dose of 26 Gy would further reduce the LRR in young patients. Since the boost-no boost trial showed that the boost led to a worse cosmetic outcome [2], cosmetic outcome was an important secondary endpoint in the YBT.

Scoring cosmesis is difficult and often considered as controversial, because of its subjective nature. For example: Mukesh et al. found that physicians judged cosmetic outcome to be superior after Intensity Modulated Radiotherapy (IMRT) compared to l 2D radiotherapy, whereas the patient reported cosmetic outcome (PRCO) showed no benefit of IMRT [3,4]. A recent analysis of the START trials showed that despite a low agreement between different scoring methods of cosmetic outcome, each scoring method could sufficiently discriminate different fractionation schedules [5]. In most studies different scoring methods are reported, including patient questionnaires, scoring by professionals (or a panel) and/or a photographic assessment using objective and reproducible software programs, such as BCCT.core [6] or BAT [7].

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Although the objective methods seem to be the most attractive due to their good reproducibility, they are mainly based on measures to quantify asymmetry, assuming that symmetry is the most important determinant for PRCO. However, if that were true, a much better correlation between PRCO and objective measures would be expected than described in literature. We hypothesised that specific aspects of symmetry (e.g. nipple-position) are more important for patients than other aspects (e.g. breast size), and that other factors such as pain or palpable firmness of the breast also influence PRCO. The aim of the current paper was therefore to prospectively investigate which objective cosmetic factors are associated with PRCO in the YBT. We also analysed the relation between fibrosis, pain and quality of life (QoL) with PRCO.

Patients and methods

Patient population and treatment

Patients younger than 51 years with non-metastatic, histologically proven invasive breast cancer, pT1-2pN0-2a [8], with an Eastern Cooperative Oncology Group (ECOG) performance scale [9] $\leqslant$2, were eligible for the trial. Tumours were completely removed by wide local excision, although focally involved margins were allowed, defined as: "tumour (ductal carcinoma in situ or invasive carcinoma) on ink in an area of less than 4 mm". Sentinel lymph node biopsy and/or axillary lymph node dissection had to be performed. No neoadjuvant systemic treatment was allowed. No previous history of malignant disease, except adequately treated carcinoma in situ of the cervix or basal cell carcinoma of the skin was allowed.

Patients were randomised to a standard 16 Gy or a high 26 Gy boost to the tumour bed after 50 Gy whole breast irradiation. Other fractionation schemes, including simultaneous integrated boost techniques were allowed as well, as long as the biologically equivalent dose, calculated with an α/β of 10 for tumour, was similar. Stratification factors were age (<>40 yr), pathological tumour size (<>3 cm), oestrogen receptor status, nodal status, interstitial/external boost and institute. Patients were stratified at the time of randomisation using a "randomisation by minimisation" technique.

The study was centrally approved by the medical ethical committee of the Netherlands Cancer Institute and by the local medical ethics committees. All patients gave their written informed consent to participate. The study was registered at https://clinicaltrials.gov/show/NCT00212121.

Cosmetic outcome

Cosmesis was scored prior to radiation therapy, at one year and four years of follow-up.

BCCT.core software [6,10]:

Digital photographs in anterior-posterior view were analysed using the BCCT.core software program, resulting in an objective score for the overall cosmetic outcome: excellent, good, fair or poor. This score is based on symmetry, skin colour and scar visibility (Fig. 1). The seven features of symmetry in the BCCT.core program are:

- breast retraction assessment (BRA)
- level of lower breast contour (LBC)
- upward nipple retraction (UNR)
- breast compliance evaluation (BCE; distance from nipple to inframammary fold)
- breast contour difference (BCD)
- breast area difference (BAD)
- breast overlap difference (BOD)

For all symmetry features a relative value was calculated by the program resulting in a pBRA, pLBC etcetera. An example of these relative values is shown in Fig. 1.

Physician's score

Physicians scored using the Harris scale on overall cosmetic outcome: excellent, good, fair or poor [11].

Patient's questionnaire

The PRCO was determined by asking patients to complete the questionnaire developed by Sneeuw et al. [12]. In this validated questionnaire (see Appendix) overall cosmetic outcome was rated on a five-point scale: very satisfied, satisfied, not dissatisfied, dissatisfied and very dissatisfied. The patients were also asked to rate the difference between the treated breast and the untreated breast in terms of scar visibility, difference in size, shape, colour, nipple position, and firmness on a four-point scale: no difference, small difference, quite a lot difference, or a large difference.

Other variables

At the same time points fibrosis (whole breast) was scored by the physician on a four-point scale. The presence of rib pain was scored separately (yes/no).

At four years, quality of life (QoL) was scored using the EORTC QLQ C-30 questionnaire [13]. The global QoL was measured on a scale from 1 to 7. Emotional functioning was measured on a multi-item scale ranging from 0 to 100. The parameter value was calculated for a difference of 10 points. Depression was measured at a scale from 1 to 4. A higher score on the functional scale and global QoL implies better score, while a higher score on the depression scale implies more symptoms.

Analysis

First, we analysed the correlation of overall cosmetic outcome between the three scoring methods, and between fibrosis scored by the physician and firmness of the breast scored by the patient.

Secondly, we analysed the seven features of BCCT.core in a proportional odds model, to investigate which parameters were related to the PRCO at four years. Also, we analysed whether fibrosis, presence of rib pain or QoL was related to the PRCO.

To evaluate the correlation between the different factors and overall cosmetic outcome, we defined two categories: satisfactory overall cosmetic outcome and unsatisfactory overall cosmetic outcome. Excellent and good as well as very satisfied and satisfied were grouped as 'satisfactory'; fair and poor, not dissatisfied, dissatisfied, and very dissatisfied were grouped as 'unsatisfactory'.

Statistics

Agreement between the three different scoring systems was calculated by Cohen's kappa statistics. The kappa coefficient (k) is a common measure for agreement [14]. The overall cosmetic outcome was evaluated on a five-point scale by the patient's questionnaire but on a four-point scale by the BCCT.core software and physician. Therefore, the agreement of the overall cosmetic outcome was assessed using the grouped dichotomised outcome variable as described above. For the agreement on individual (separate) cosmetic outcome parameters, all three used a four point scale and therefore a weighted kappa (wk) was used, where the weights were chosen quadratic. A value of 0–0.2 for k indicates a slight agreement, 0.2–0.4 indicates a fair agreement, 0.4–0.6 indicates a moderate agreement, 0.6–0.8 indicates a substantial agreement and a value of 0.8–1.0 indicates an almost perfect agreement.

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