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Original Article

The Cambridge Breast Intensity-modulated Radiotherapy Trial: Comparison of Clinician- versus Patient-reported Outcomes

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Abstract

Aims: Breast radiotherapy-associated toxicity is often reported using clinical and photographic assessments. The addition of patient-reported outcome measures (PROMs) is becoming more common. This study investigated the concordance between clinician- and patient-reported outcomes.
Materials and methods: The Cambridge Breast Intensity-modulated Radiotherapy (IMRT) trial prospectively collected data on clinician assessment and PROMs at 2 and 5 years after breast radiotherapy. Clinician assessment included physical examination and photographic assessment. PROMs included European Organization for Research and Treatment of Cancer (EORTC) BR23 questionnaire and four breast radiotherapy-specific questions. The correlation between patient and clinician scores were analysed on an independent patient basis using percentage agreement, Cohen's kappa coefficient (k) and Bowker's test of symmetry. The analysis was repeated after stratifying patients based on age, baseline Hospital Anxiety and Depression Score (HADS) and baseline body image score.
Results: At 2 and 5 years, a weak level of concordance was seen between the clinician-based assessment and PROMS for all the five toxicity end points ($k = 0.05–0.21$), with individual patient-based agreement of 32.9–78.3% and a highly discordant Bowker's test of symmetry ($P < 0.001$). The most frequently reported moderate–severe toxicity by patients was change in breast appearance (14% at both 2 and 5 years), whereas it was breast induration (36% and 25% at 2 and 5 years, respectively) by the clinicians. The lack of concordance was not affected by patient's age, baseline HADS and baseline body image score.
Conclusions: This study found that moderate–severe toxicity reported by patients is low and the overall concordance between clinicians and patients is low. This could be due to methodological limitations or alternatively reflects the subjective nature of PROMs. Incorporation of a patient's perception on treatment-related toxicity will have important implications for treatment decisions and follow-up care.

Key words: Breast cancer; concordance; late treatment toxicity; radiotherapy

Introduction

Early cancer detection and the use of adjuvant therapies, including chemotherapy and radiotherapy, have significantly improved breast cancer survival rates. As the number of breast cancer survivors increases, efforts to reduce long-term treatment-related morbidity are paramount. While addressing this issue, it is imperative that the methodology of toxicity assessment is standardised.

Traditionally, breast radiotherapy-associated toxicity has been reported using clinician-based assessment tools, including physical examination and/or photographic assessment [1–3]. More recently, patient-reported outcome measures (PROMs) have been introduced as they provide patient perception of their own health condition and treatment toxicity. This raises the concept of PROMs replacing clinician-based assessments in clinical trials and

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therefore minimising the number of trial follow-up visits for patients.

The large Cambridge Breast Intensity-modulated Radiotherapy (IMRT) trial showed superior overall cosmesis and reduced skin telangiectasia with IMRT using clinician-based assessment, although the benefits of IMRT could not be shown using PROMs [4,5]. This report analysed the concordance between clinician- and patient-based assessment at 2 and 5 years after breast radiotherapy and investigated the factors that may explain the difference in outcome between clinicians and patients.

Materials and Methods

Patient Population

The Cambridge Breast IMRT trial opened in April 2003 and was closed to recruitment in June 2007 ($n = 1145$). The Cambridge Research Ethics Committee provided ethical approval for the study. Eligibility criteria included women with operable unilateral histologically confirmed invasive breast cancer (T1-3, N0-1, M0) or ductal carcinoma *in situ* requiring postoperative radiotherapy after tumour excision by breast-conserving surgery. The full details of the trial, including patient characteristics and treatment details have previously been published [6].

Clinician Assessment

The late breast tissue toxicity after radiotherapy was assessed by clinicians using serial photographs and clinical examination.

Photographic Assessment

Frontal photographs of both breasts were taken after primary surgery and before radiotherapy (baseline) and repeated at 2 and 5 years after radiotherapy. Two photographs were taken, one with the hands resting on the hips, the other with the arms raised above the head. These photographs were scored by a multidisciplinary panel of clinicians (three at any one time). The 2 and 5 year photographs were compared with postoperative baseline photograph for radiotherapy-associated breast shrinkage and scored on a validated three-point scale (none/minimal = 1, mild = 2, marked = 3). The panel also assessed overall cosmesis on photographs taken at 2 and 5 years and scored them using a three-point score (good, moderate and poor cosmesis). This method of scoring has been validated and shown to be quicker than using three independent scorers with re-scoring of discrepancies and final resolution through discussion [1]. The inter-observer variability of this assessment has previously been assessed [7].

Clinical Assessment

One clinician assessed the treated breast 2 and 5 years after radiotherapy for breast oedema, skin telengiectasia and palpable induration. Each of these end points was graded 0–3 (none, a little, quite a bit, very much) on the scale used in the START trials [2,3]. An oncologist (CEC) assessed the first 70 patients at 2 years and trained the breast research radiographer (JW), who then assessed the remaining patients.

Patient-reported Outcome Measure

All patients enrolled in the trial were offered participation in the PROMs study. Patients completed validated quality of life questionnaires (European Organization for Research and Treatment of Cancer [EORTC] QLQ-C30, BR23 and Body Image Scale [8]) before starting radiotherapy and then at 6 months, 2 years and 5 years after radiotherapy completion. Four additional questions were added to the questionnaire to record the patient's assessment of breast tissue toxicity and graded 1–4 (none, a little, quite a bit, very much): change in skin appearance of affected breast, overall change in breast appearance, breast shrinkage and breast hardness/firmness.

Comparison of Clinician- versus Patient-reported Outcomes

Each clinician-assessed toxicity end point was paired with a PROM for comparison (Table 1 for toxicity items and Table 2 for score system). Both assessments were carried out at the same time point. The agreement between patient and clinician scores was analysed on an individual patient basis using measures of agreement, including percentage agreement, Cohen's kappa coefficient (k) and Bowker's test of symmetry. A zero-weight row or column was used in calculating the kappa statistics (by using the ZEROS option in SAS) when no patients were in a particularly grouped category. A k value of <0.4 was considered weak, 0.4–0.75 as fair to good and >0.75 as excellent concordance [9].

The analysis was also carried out by stratifying patients based on age (<50 or ≥ 50 years), baseline Hospital Anxiety and Depression Score (HADS) (normal, baseline and cases) and baseline body image score (BIS) (≤ 3 or >3) to investigate whether these factors had an effect on the degree of concordance.

Results

Clinician-based toxicity assessments were available for 80.4% (921/1145) and 52.2% (598/1145) of patients at 2 and 5 years, respectively. The PROMs were available for 78.7% (901/1145) and 56.3% (645/1145) of patients at 2 and 5 years, respectively.

At 2 years, a weak level of concordance was seen between the clinician-based assessment and PROMS for all the five toxicity end points ($k = 0.05$–0.21), with individual patient-based agreement of 32.9–58.6% and a highly discordant Bowker's test of symmetry ($P < 0.001$) (Table 3). Clinicians consistently reported higher treatment toxicity as compared with patients, except for breast shrinkage (Figure 1). Clinicians scored 23% of patients

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