



PII: S0959-8049(97)00312-2

## Original Paper

# Quality of Life of Early-stage Breast Cancer Patients Treated with Radical Mastectomy or Breast-conserving Procedures: Results of EORTC Trial 10801

D. Curran,<sup>1</sup> J.P. van Dongen,<sup>2</sup> N.K. Aaronson,<sup>2</sup> G. Kiebert,<sup>1</sup> I.S. Fentiman,<sup>3</sup> F. Mignolet<sup>1</sup> and H. Bartelink<sup>2</sup> on behalf of the European Organization for Research and Treatment of Cancer (EORTC), Breast Cancer Co-operative Group (BCCG)

<sup>1</sup>European Organization for Research and Treatment of Cancer (EORTC), Data Center, Avenue E. Mounier, 83, Bte 11, 1200 Brussels, Belgium; <sup>2</sup>The Netherlands Cancer Institute, Plesmanlaan 121, NL-1066 CX Amsterdam, The Netherlands; and <sup>3</sup>Guy's Hospital, ICRF Clinical Oncology Unit, St. Thomas Street, London SE1 9RT, U.K.

In 1980 the EORTC-BCCG initiated a multicentre randomised clinical trial comparing modified radical mastectomy (MRM) with breast-conserving therapy (BCT) in stage I and II breast cancer. The main endpoint of the trial was survival. A brief quality of life (QoL) questionnaire consisting of two multi-item scales (body image and fear of recurrence) and two single items (satisfaction with treatment and cosmetic result) was included in the trial. A cosmetic evaluation of the breast after conservative surgery was also performed. This report concentrates on the results of the QoL study and the cosmetic evaluation. Multitrait scaling analysis was employed to verify the hypothesised scale structure of the questionnaire. Treatment comparison of the QoL scores at 2 years post-treatment was performed using a stratified Wilcoxon rank sum test. Both patients' and doctors' ratings of the cosmetic result were documented on the clinical follow-up form. A multivariate analysis was performed to identify which factors influenced the cosmetic outcome. In total, 127 patients in the MRM arm and 151 in the BCT arm completed a QoL questionnaire at approximately 2 years after randomisation (months 25-36). The Cronbach's alpha coefficients were 0.79 and 0.73 for the body image and fear of recurrence scales, respectively. Significant benefit in body image and satisfaction with treatment was observed in the BCT patients. No significant difference was observed in fear of recurrence between the two groups. Ratings of cosmetic results decreased with time, in line with clinical observations of long-term side-effects of radiotherapy. Wide excision appeared to be the most important predictive factor for poor cosmetic result. In this multicentre randomised study, BCT helped to maintain the patients' body image, resulted in higher satisfaction with treatment and yielded no significant difference from MRM with respect to fear of recurrence. © 1998 Elsevier Science Ltd. All rights reserved.

**Key words:** quality of life, cosmetic outcome, breast cancer

*Eur J Cancer*, Vol. 34, No. 3, pp. 307-314, 1998

## INTRODUCTION

BREAST-CONSERVING therapy (BCT) is now a well-established alternative to mastectomy for the treatment of early-stage breast cancer. Several randomised clinical trials from Europe

and North America have confirmed that BCT and more radical procedures yield similar results for survival [1-6]. An overview, which included almost 5000 patients, demonstrated that the 10-year survival was approximately equivalent for the two treatment strategies [7]. Breast irradiation after lumpectomy reduces the risk of a recurrence of tumour in the breast [6]. In addition, contrary to the thinking of Halsted

Correspondence to D. Curran.

Received 17 Apr. 1997; accepted 29 May 1997.

[8], adjuvant chemotherapy has been confirmed to prolong disease-free survival and overall survival [9].

Since the first publication of clinical trials describing no difference between BCT and modified radical mastectomy (MRM) with respect to duration of survival [10, 11], the discussion of the physical, psychological, social, occupational, and sexual impact of the different modalities of treatment has continued. Initially, the general belief was that BCT would provide more benefits because of the physical and emotional importance a woman attaches to her breasts [12]. However, in reviews of the literature [13, 14], conflicting results regarding psychological well-being, fear of recurrence, social adjustment and physical dysfunction were reported for these two patient populations. An extensive overview of previous studies comparing BCT and MRM, which were limited by the relatively small numbers of patients included and by the percentage of non-randomised trials, has been previously published [13, 14]. These studies were primarily single-institution trials in which the selection of patients, eligibility criteria and surgical procedures were variable. In addition, most of the studies were retrospective evaluations with a wide range of instruments being used to assess quality of life (QoL).

In 1978 Pierquin and associates [15] and Calle and associates [16] demonstrated promising possibilities for BCT in both stage I and II breast cancer. Considering these results were shown in large tumours as well [15, 16], the European Organization for Research and Treatment of Cancer (EORTC) Breast Cancer Cooperative Group (BCCG) initiated a prospective, randomised, multicentre clinical trial (EORTC trial 10801) comparing mastectomy with BCT (lumpectomy, axillary clearance and radiotherapy of the breast: 50 Gy external irradiation in 5 weeks followed by boost with an iridium implant of 25 Gy) in patients with both stage I and II breast cancer. 902 patients were entered in the study between 1980 and 1986. To date, the survival duration and local recurrence rates are not significantly different for the two treatment arms. A detailed description of the study design, eligibility criteria, patient characteristics and clinical treatment comparisons have been previously published [4]. The purpose of this paper is to describe the experience of the EORTC-BCCG with respect to assessing QoL in this trial. The focus is mainly on body image, fear of recurrence of the disease, satisfaction with treatment and the cosmetic results as judged both by the patient and the physician.

## PATIENTS AND METHODS

Randomisation was carried out using the minimisation technique, stratifying patients according to their institution, stage and menopausal status [17]. Randomisation was performed centrally at the EORTC Data Center in Brussels. In the first two years, randomisation was done using a 1:2 ratio as it was planned to share the control arm (MRM) with another European study. After 1982 the study plans had to be modified and the randomisation ratio was changed to adjust further randomisation. The main endpoint of the study was survival. Additional endpoints included local control, disease-free survival, cosmetic results and QoL.

Mastectomy was performed according to the procedure of Halsted or Patey [18]. BCT comprised local excision of the tumour, dissection of the axilla and radiotherapy of the breast: 50 Gy external irradiation in 5 weeks followed by boost with an iridium implant of 25 Gy. One centre performed only local excision of the palpable tumour, whereas

the other centres preferred to have a macroscopic margin of 1 cm.

### *QoL assessment*

As this was a large-scale clinical trial, the investigators believed it was necessary to keep the QoL component of the trial as simple as possible, and thus a choice had to be made as to which QoL issues were to be investigated. It was hypothesised that BCT would preserve body image, but would result in a heightened fear of disease recurrence. Additionally, it was considered important to assess overall satisfaction with treatment, and the perceived quality of the cosmetic results obtained by BCT. A QoL questionnaire consisting of 10 items was constructed and made available in English (see Appendix 1) and Dutch. These questions were derived mainly from Avery and associates [19]. Variations of the questionnaire have also been used in other studies [12, 20, 21]. The hypothesised scale structure of the questionnaire included: a body image scale consisting of five questions (1, 3, 5, 6 and 8); a fear of recurrence scale composed of three questions (2, 4 and 7); a single item on satisfaction with treatment (question 9); and a single item (question 10) on cosmetic results (i.e., a comparison of the treated breast with the untreated breast) which was to be completed by the BCT patients only.

For the two multi-item scales, scores were calculated by averaging items within scales and transforming average scores linearly to a 0–100 scale, with higher scores representing a more positive body image and a higher fear of recurrence, respectively. In the presence of missing items within a scale, provided at least half of the items were completed, the scale score was calculated using the completed items which were present for that respondent [22, 23]. For presentation purposes, the two multi-item scales were subsequently collapsed into 10 levels.

Multitrait scaling analysis was employed to verify the hypothesised scale structure of these domains [21]. Evidence of item convergent validity was defined as a correlation of 0.40 or greater between an item and its own scale (corrected for overlap). A scaling success was defined as those cases in which an item correlated significantly higher with its own scale (corrected for overlap) than with other scales. The reliability (i.e., internal consistency) of the multi-item scales was assessed using Cronbach's alpha coefficient [24]. As recommended by Nunally, the minimal standards of reliability (Cronbach's alpha coefficient  $\geq 0.70$ ) were sought [25]. To evaluate the validity of the questionnaire, an examination of the correlations among the various scales was performed. It was expected that scales would not correlate substantially with one another (Spearman's  $r < 0.40$ ).

As specified in the protocol, patients' QoL should have been evaluated at 2 years (months 25–36) following the completion of therapy. If a patient completed more than one questionnaire in this time period, the questionnaire which was completed closest to the midpoint of this period was taken. For all the analyses related to the fear of recurrence scale, the number of patients was restricted to only those patients who did not have progression or evidence of a new tumour before completing the QoL questionnaire. A baseline QoL assessment was not requested as the items included in the questionnaire were specifically related to the patients' QoL after treatment (i.e., fear of recurrence, satisfaction with treatment and cosmetic result).

A two-sided Wilcoxon rank sum test stratifying for time since randomisation to completion of the QoL questionnaire (25–30 months versus 31–36 months) was used to compare QoL scores in the two treatment arms [26]. Exact *P* values were calculated using Stat Exact. The Kruskal–Wallis non-parametric statistical test was used to test the hypothesis of no group difference in QoL scores for categorical variables (e.g. menopausal status, nodal classification of regional lymph nodes, tumour side, etc.) [26].

#### Cosmetic evaluation

Patients visited the hospital for clinical follow-up assessments at regular time intervals. Both patients, and doctors, opinions of the cosmetic result of patients treated with BCT were documented on the follow-up form with possible response categories as follows: poor, acceptable, good and excellent. When more than one follow-up form was completed during one time period for the same patient, the form which was completed closest to the required date was taken.

An exact two-sided marginal homogeneity test was used to test the hypothesis of no difference in cosmetic rating provided by the patient and the doctor [27]. An analysis of prognostic factors was performed to investigate which variables were predictive of a poor cosmetic result. The worst cosmetic score as provided by the doctor was calculated over all assessments. The score was subsequently dichotomised into a binary score (low = poor/acceptable and high = good/excellent). A logistic regression model was used for both the univariate and multivariate prognostic factor analyses of the cosmetic result [28]. A two-sided test was used at the 5% significance level to test the prognostic value of each variable. A step-down variable selection procedure was used for building the multivariate model. The importance of a prognostic factor was expressed by the percentage of low scores observed in the patients presenting a specific value of the prognostic variable, odds ratio (OR: the odds of a response versus no response in patients with that specific value as compared to the odds in the reference category), its 95% confidence interval (95% CI) and the *P* value of the Chi-square statistic.

The analysis was performed on all eligible patients according to the 'intention-to-treat' principle. As the main endpoint of the study was survival, this analysis was seen as exploratory. Unlike the situation in confirmatory data analysis, an exploratory data analysis does not adjust the significance levels for multiple tests as the objective is to explore the data rather than to draw definitive conclusions from the results [29].

Software for the Management and Analysis of Randomized Trials (SMART) was used for data management and Statistical Analysis Software (SAS®) and STAT exact were used for the data analysis [30].

## RESULTS

Between May 1980 and May 1986, 902 patients were entered into EORTC trial 10801, 436 patients were randomised into the MRM arm and 466 into the BCT arm (local excision + axillary dissection with external irradiation and iridium implant). 29 patients were considered to be ineligible on review (equally distributed between both treatment arms), the main reasons being a too advanced tumour situation or an incorrect diagnosis. For 1 other patient we received no onstudy form.

In total, 278 patients (127 in the MRM arm and 151 in the BCT arm) filled out at least one QoL questionnaire at 2 years (median 30 months, range 25–36). For all analyses related to fear of recurrence (i.e., including only patients who did not have progression or evidence of a new tumour before completing the quality of life form), the sample size was 254 patients (117 in the MRM arm and 137 in the BCT arm). Comparing the characteristics of patients who were included in the QoL study with those who were not included, no statistically significant differences were observed. However, it was noticed that higher compliance rates of completion of QoL questionnaires were observed in South Africa (64%), Belgium (57%), The Netherlands (40%) as compared with the U.K. which had a compliance rate of 14%. Of the total number of patients randomised into the trial, 420 (47%) were from the U.K. The numbers of patients within each hospital contributing to the QoL analysis were similar in both treatment arms.

Patient characteristics at study entry are presented in Table 1. Of the 127 patients in the mastectomy arm, 41 (32%) and 79 (62%) had radical and modified mastectomy, respectively. Of the 151 patients in the BCT arm, 102 (68%) and 48 (32%) had a microscopically complete excision and

Table 1. Patient characteristics at entry for patients with completed onstudy forms

	Patients in QoL study		Patients not in QoL study	
	Mastectomy <i>n</i> = 127 <i>n</i> (%)	BCT <i>n</i> = 151 <i>n</i> (%)	Mastectomy <i>n</i> = 295 <i>n</i> (%)	BCT <i>n</i> = 299 <i>n</i> (%)
Age				
23–47	42 (33)	38 (25)	94 (32)	108 (36)
48–56	35 (28)	54 (36)	98 (33)	76 (25)
57–70	50 (39)	59 (39)	103 (35)	114 (38)
Unknown	0 (0)	0 (0)	0 (0)	1 (<1)
Menopausal status				
Premenopause	50 (39)	54 (36)	124 (42)	130 (44)
Postmenopause	65 (51)	92 (61)	158 (54)	155 (52)
Artificial menopause	12 (9)	5 (3)	13 (4)	13 (4)
Unknown	0 (0)	0 (0)	0 (0)	1 (<1)
Primary tumour				
T <sub>1</sub>	16 (13)	21 (14)	71 (24)	63 (21)
T <sub>2</sub>	111 (87)	130 (86)	224 (76)	235 (79)
Unknown	0 (0)	0 (0)	0 (0)	1 (<1)
Regional lymph nodes				
N <sub>0</sub>	97 (76)	104 (69)	218 (74)	216 (72)
N <sub>1A</sub>	17 (13)	16 (11)	16 (5)	22 (7)
N <sub>1B</sub>	13 (10)	29 (19)	61 (21)	59 (20)
N <sub>x</sub>	0 (0)	1 (1)	0 (0)	0 (0)
Unknown	0 (0)	1 (1)	0 (0)	2 (1)
Stage				
I	14 (11)	14 (9)	56 (19)	52 (17)
II	113 (89)	137 (91)	239 (81)	246 (82)
Unknown	0 (0)	0 (0)	0 (0)	1 (<1)
Tumour side				
Right	63 (50)	93 (62)	138 (47)	138 (46)
Left	64 (50)	58 (38)	155 (53)	160 (54)
Unknown	0 (0)	0 (0)	2 (1)	1 (<1)
Other concomitant diseases				
No	109 (86)	128 (85)	249 (84)	258 (86)
Yes	13 (10)	17 (11)	30 (10)	28 (9)
Unknown	5 (4)	6 (4)	16 (5)	13 (4)

BCT, breast-conserving therapy.

incomplete excision of the primary tumour, respectively, and 129 (85%) and 20 (13%) had discontinuous and continuous resection, respectively. The characteristics of the 278 patients included in the QoL study were similar in the two treatment arms with only tumour side showing a slight imbalance (see Table 1). No association between tumour side with any of the QoL scales was observed, even when stratifying for treatment. For the group of patients included in the QoL study, no significant difference was found in duration of survival between the two treatment arms.

#### Validity of the QoL instrument

The Cronbach's alpha reliability coefficients were 0.79 and 0.73 for the body image and fear of recurrence scales, respectively. All item-scale correlations (corrected for overlap) exceeded the 0.40 criterion for item-convergent validity for both multi-item scales. Scaling successes were observed in all cases, that is, all items correlated significantly higher with their own scale (corrected for overlap) than with other scales. While all interscale correlations were statistically significant, the correlations were moderate ( $r < 0.40$ ), indicating that the scales were assessing distinct components of quality of life.

Table 2. Quality of life scores by treatment arm

	Mastectomy n (%)	BCT n (%)	P value
Body image			
0-10	3 (2)	0 (0)	
11-20	2 (2)	0 (0)	
21-30	2 (2)	1 (1)	
31-40	3 (2)	1 (1)	
41-50	5 (4)	1 (1)	
51-60	8 (6)	5 (3)	
61-70	13 (10)	5 (3)	
71-80	18 (14)	9 (6)	
81-90	23 (18)	22 (15)	
91-100	49 (39)	104 (69)	0.001
Unknown	1 (1)	3 (2)	
Fear of recurrence			
0-10	19 (16)	26 (19)	
11-20	11 (9)	9 (7)	
21-30	14 (10)	15 (11)	
31-40	13 (11)	23 (17)	
41-50	33 (26)	43 (31)	
51-60	7 (6)	8 (6)	
61-70	7 (6)	8 (6)	
71-80	2 (2)	2 (1)	
81-90	4 (3)	2 (1)	
91-100	6 (5)	1 (1)	0.236
Unknown	1 (1)	0 (0)	
Satisfaction with treatment*			
Certainly not	8 (6)	1 (1)	
Probably not	7 (6)	2 (1)	
Probably	31 (24)	37 (25)	
Certainly	71 (56)	110 (73)	0.001
Unknown	10 (8)	1 (1)	
Breast comparison*			
Not at all		22 (15)	
A little		28 (19)	
Quite a bit		55 (36)	
Very much		40 (26)	
Unknown		6 (4)	

\*See Appendix 1 for the exact wording of the questions.

#### Missing data

Overall rates of non-response to individual items were less than 5%, except for the question concerning being self-conscious about being seen naked by a husband/partner, which had a non-response rate of 14% (39/280). The non-response rates were similar in both treatment arms for all the single items except for question number 4 ('I believe that the difficulties with my illness are over') which had 8 (6%) missing values in the MRM arm and only 1 (1%) in the BCT arm and for question number 9 ('If I should have to be treated again, I should like to have the same therapy') which had 10 (8%) missing values in the MRM arm and only 1 (1%) in the BCT arm.

#### Comparisons with respect to QoL

Table 2 indicates a significant advantage for the BCT arm with regard to body image. Level of fear of recurrence was not significantly different between the two treatment arms. However, in both treatment arms fear of recurrence varied with age, with younger patients having a higher fear of recurrence ( $P = 0.002$ ), and relatedly, premenopausal and artificial menopausal patients being more afraid of a recurrence than postmenopausal patients ( $P = 0.027$ ).

Patients' scores for the satisfaction with treatment question indicated significantly better results in the BCT arm. Even though the treated breast did not markedly resemble the untreated breast for 50 patients (Not at all/A little), 28 (56%) of these 50 patients indicated that they would certainly like to have the same therapy, and 20 (40%) indicated that they would probably like to have the same therapy if they had to be treated again. In the BCT arm a worse score for the comparison of the treated and untreated breasts was associated significantly with having a continuous resection ( $P = 0.016$ ) and having a wide excision ( $P = 0.001$ ).

#### Cosmetic results

Figures 1(a) and (b) display the proportion of BCT patients in each response category of the cosmetic rating scale

Table 3. Univariate prognostic factor analysis with respect to doctor's rating of cosmetic result

Prognostic factor	L/n	(%)	OR	95% CI	P value
Age (years)					
< 55*	110/226	(49)	1.00		
≥ 55	118/192	(61)	1.68	(1.14-2.49)	0.009
Menopausal status					
Premenopausal*	78/168	(46)	1.00		
Postmenopausal	141/233	(61)	1.77	(1.18-2.64)	0.005
Artificial menopausal	9/17	(53)	1.30	(0.48-2.64)	0.609
Size of primary tumour					
T <sub>1</sub> *	34/83	(41)	1.00		
T <sub>2</sub>	195/336	(58)	1.99	(1.22-3.25)	0.006
Resection					
Discontinuous*	190/360	(53)	1.00		
Continuous ( <i>en bloc</i> )	34/47	(72)	2.34	(1.20-4.58)	0.013
Number of needles					
≤ 7*	122/273	(45)	1.00		
> 7	81/114	(71)	3.04	(1.90-4.86)	< 0.001
Method of resection					
Lumpectomy*	83/203	(41)	1.00		
Wide excision	77/98	(79)	5.30	(3.04-9.26)	< 0.001

\*Reference category. L/n, number of patients with low score/number of patients. OR, odds ratio; CI, confidence interval.

at each assessment time point as judged by the clinician and the patient, respectively. At all of the 11 time points at which we studied the cosmetic results, the marginal homogeneity test indicated that the scores provided by the patients were significantly different from those provided by the doctors, with patients' ratings of cosmesis being more favourable.

Cosmetic results were available within 6 months of completion of the QoL questionnaire for 115 (76%) of the 151 patients included in the BCT arm of the QoL analysis. Only

weak correlations were observed between the doctors' evaluation of the cosmetic results with the QoL scales, body image ( $r = 0.08$ ), fear of recurrence ( $r = -0.09$ ) and satisfaction with treatment ( $r = 0.14$ ). Similar results were observed when looking at the correlations of the patients' evaluation of the cosmetic results with the QoL scales: body image ( $r = 0.10$ ), fear of recurrence ( $r = -0.13$ ) and satisfaction with treatment ( $r = 0.06$ ). However, correlations between the cosmetic results as rated by both the physicians and the

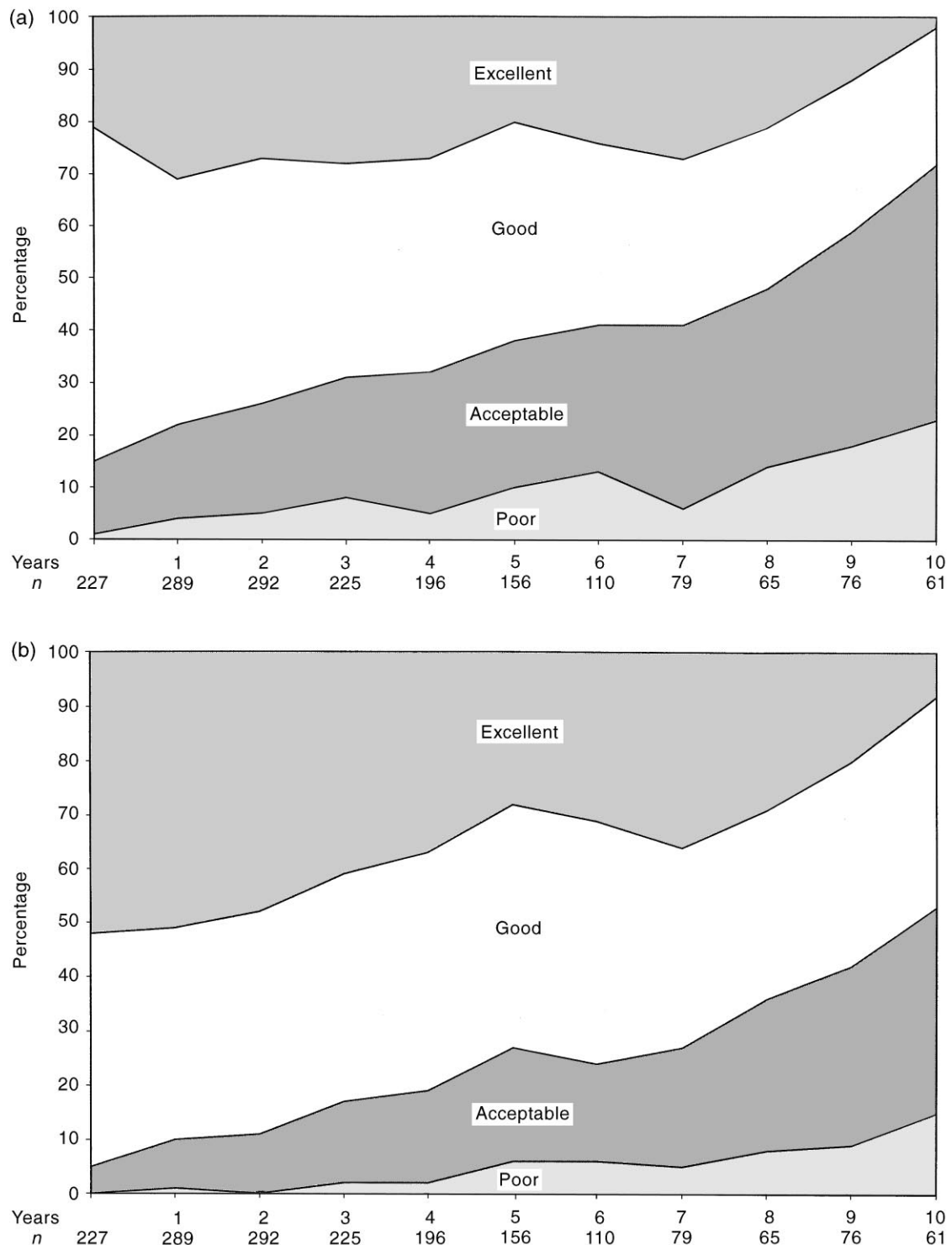


Figure 1. (a) Doctors' rating of cosmetic result. (b) Patients' rating of cosmetic result.

Table 4. Univariate prognostic factor analysis with respect to patient's rating of cosmetic result

Prognostic factor	L/n (%)	OR	95% CI	P value
Age (years)				
<55*	71/225 (32)	1.00		
≥55	72/191 (38)	1.31	(0.88–1.97)	0.189
Menopausal status				
Premenopausal*	52/167 (31)	1.00		
Postmenopausal	86/232 (37)	1.31	(0.85–1.99)	0.220
Artificial menopausal	5/17 (29)	0.92	(0.31–2.75)	0.884
Size of primary tumour				
T <sub>1</sub> *	24/83 (29)	1.00		
T <sub>2</sub>	119/334 (36)	1.36	(0.81–2.30)	0.250
Resection				
Discontinuous*	110/358 (31)	1.00		
Continuous ( <i>en bloc</i> )	31/47 (66)	4.37	(2.30–8.32)	<0.001
Number of needles				
≤7*	58/272 (21)	1.00		
>7	64/114 (56)	4.72	(2.95–7.56)	<0.001
Method of resection				
Lumpectomy*	29/203 (14)	1.00		
Wide excision	67/97 (69)	13.40	(7.48–24.0)	<0.001

\*Reference category. For abbreviations see legend to Table 3.

patients, and the patients' comparison of the breast with the untreated breast were significant ( $r=0.48$  and  $0.51$ , respectively).

Table 3 presents all of the factors which were identified in the univariate analysis as being of prognostic importance for cosmetic results (as judged by the clinician). The multivariate logistic regression analysis indicated that a worse cosmetic result was associated with postmenopausal status ( $P=0.043$ ) and having a wide excision ( $P=0.004$ ). When the univariate analysis was repeated, taking the patients' rating of cosmetic result as the dependent variable (Table 4), age, menopausal status and size of primary tumour were no longer significant. In the multivariate analysis the only variable which was retained in the model was method of resection ( $P<0.001$ ).

## DISCUSSION

In this paper we have reported the results of a QoL investigation carried out as part of a large, multicentre, randomised trial comparing BCT with MRM in the treatment of early-stage breast cancer. Specific QoL domains assessed included body image, fear of disease recurrence and overall treatment satisfaction. Additionally, ratings of the cosmetic results of BCT were elicited from both patients and clinicians. The low compliance rate of 33% observed for the QoL evaluation in this trial reflects the lack of acceptance of QoL as an integral part of clinical trials in the early 1980s. Nowadays, with the increasing interest in QoL, higher compliance rates can be expected. Nevertheless, this multicentre study is one of the largest QoL evaluations in early breast cancer. In addition, randomisation was performed stratifying for institution, stage and menopausal status. Thus, the number of patients within each hospital and the patient characteristics of the patients contributing to the QoL analysis were similar in both treatment arms.

Our data showed a significant benefit in body image for patients who received BCT over those who received MRM. This is in agreement with the majority of reviewed publications

[13, 14]. In the review of Kiebert and associates [13], 10 out of the 12 studies which investigated the effect of treatment on body image reported positive outcomes with respect to body image in the BCT group, i.e., 'patients felt more attractive and less ashamed, anxious, embarrassed or concerned about their body image'. In the review by Schover [14], 8 of the 12 studies reviewed found that women who had their breasts conserved had 'more positive feelings about their bodies, particularly their appearance in the nude, than do women after mastectomy'. In both of these reviews the remaining studies found no difference between the two treatment groups with respect to body image [13, 14].

Early concerns that the positive results of BCT in terms of preserved body image might be offset by fears that not all of the cancer had been radically removed have not been substantiated by our study or by previous reports [12–14]. In fact, in the review of Kiebert and associates [13], six out of the eight studies which investigated fear of recurrence and death showed no difference between the two treatment strategies and the remaining two trials found more fear of recurrence after MRM than after BCT. The review of Schover [14] included six studies which produced conflicting results with respect to fear of recurrence; two showed no difference, one favoured MRM and three favoured BCT. Thus, it appears that women who are treated with MRM continue to fear a recurrence of disease to at least the same degree as women who are treated with BCT. A possible explanation for this was provided by Aaronson and associates [21] who suggested that the physical mutilation associated with mastectomy may serve as a daily reminder of the threat of cancer. In our study we observed that younger women had a higher fear of recurrence of disease. Other authors reported associations between age and other factors related to fear of recurrence [14, 31], including Levy and associates [32] who reported that 'in the face of physical and biological challenge, younger patients were more vulnerable to mental health impairment'.

Among women treated with BCT, the cosmetic results of treatment may be of particular importance. Bartelink and associates [12] reported that the overall cosmetic ratings made by plastic surgeons are determined by a range of factors, including scars, breast shape, nipple placement, volume reduction and skin pigmentation, respectively. For practical reasons, in the current study, evaluation of cosmetic results was limited to a global assessment by both patients and clinicians. When asked to compare the appearance of their treated breast with that of the untreated breast, nearly two-thirds of the patients treated with BCT rated the differences as being small. Similarly, in the majority of cases, patients rated themselves and were rated by their physicians as having a good to excellent cosmetic result. Age, menopausal status, T-stage, dose and number of needles used during radiotherapy and the type and method of resection all influence the cosmetic result at the univariate level. In the multivariate logistic regression model, the factors which were the most important predictive factors were method of resection and menopausal status. Radiation dose was not studied in the multivariate analysis as the majority of patients received the complete protocol dose of radiotherapy. Importantly, the ratings of the cosmetic outcome appear to change over time, with the patients in the 'poor' and 'acceptable' categories increasing and the proportion of patients in the 'excellent' category decreasing. While these longitudinal data need to be

interpreted with some caution, in that the number of patients contributing to the analysis varied over time, they are in line with clinical observations that changes in the breast due to irradiation (e.g., fibrosis, skin changes and telangiectasis) increase with the passage of time [33]. A better cosmetic result may be observed with the lower boost doses applied in the ongoing EORTC trial 22881. Additionally, although not assessed in the current study, Ganz and associates [34] reported that women receiving BCT may require more intensive psychosocial intervention because of the added burden of primary radiation therapy.

Overall satisfaction with treatment was assessed indirectly by asking women if they would choose the same treatment if treatment were again necessary. Large differences were observed between the BCT and MRM groups, with nearly three-quarters of those treated with BCT stating that they would again choose BCT, whereas only approximately half of the MRM group would opt for the same treatment. These results, indicating a higher satisfaction with treatment in the BCT arm, are consistent with those reported previously by Bartelink and associates [12] and Aaronson and associates [21].

Studies comparing the QoL of patients undergoing BCT versus MRM have employed various methods for selecting patients for treatment [13, 14]. In some studies, patients self-selected their treatment under the guidance of their physician, in other studies strict randomisation procedures were employed, and in yet other studies a mix of self-selection and randomisation was used. Each of these methods has consequences for the internal and external validity of study results. In non-randomised studies, an array of factors may influence the choice of treatment, including not only the sociodemographic and clinical status of the patients (e.g., age, marital status, the extent of disease, the location of the tumour within the breast, the size of the breast), but also the anticipated psychological impact of treatment, concern with body image and cosmesis, and concern with disease recurrence, etc. For example, Fallowfield reported that 'women who chose mastectomy had firmer convictions about the benefits of mastectomy in terms of removing all of the cancer', whereas, women who choose lumpectomy 'thought that the fear of losing a breast was worse than that of having cancer' [35]. While the internal validity of non-randomised studies may be compromised due to the non-comparability of patient groups, the external validity (or generalizability of results to the 'real world' setting may be enhanced.

Conversely, it has been argued that in the randomised setting, although the comparability of the study arms may be optimised (i.e., high internal validity), there may be a selection bias in recruiting patients into the study, as the more independent woman will select her own treatment and will not be willing to have her future decided by chance. This, in turn, would restrict the generalisability of study results to the population of 'indecisive' women who do not have a clear treatment preference.

With these in mind, the most conservative approach would be to conclude that the results of the current, randomised study provide a valid picture of the psychosocial consequences of BCT versus MRM only for those women who do not have a clear preference for one treatment over the other. However, the fact that most of the findings of our study confirm earlier reports based on both randomised and non-randomised studies suggest that they reflect the relative impact

of BCT versus MRM on the larger population of patients with early-stage breast cancer.

The treatment of breast cancer has changed rapidly in the last two decades. Breast-conserving therapy has been shown to be an effective alternative to radical mastectomy. Breast-conserving surgery is now a more refined procedure, permitting smaller macroscopic margins and thus better cosmetic results. Additionally, the proliferation of breast cancer screening programmes has resulted in more patients presenting with smaller tumours amenable to treatment with BCT [36]. The results of this and other studies suggest that the increased use of BCT in the treatment of early-stage breast cancer will help preserve a positive body image, will not compromise patients' trust in efficacy of the treatment and will enhance patients' overall satisfaction with their treatment.

1. Sarazin D, Le MG, Arriagada R, *et al.* Ten year results of a randomized trial comparing a conservative treatment to mastectomy in early breast cancer. *Radiother Oncol* 1989, **14**, 177-184.
2. Veronesi U, Banfi A, Salvadori B, *et al.* Breast conservation is the treatment of choice in small breast cancer: long term results of a randomized trial. *Eur J Cancer* 1990, **26**, 668-670.
3. Blichert-Toft M, Rose V, Andersen JA, *et al.* Danish randomized trial comparing breast conservation therapy with mastectomy: six years of life table analysis. *JNCI Monogr* 1992, **11**, 19-25.
4. van Dongen JA, Bartelink H, Fentiman IS, *et al.* Factors influencing local relapse and survival and results of breast-conserving therapy in operable breast cancer: EORTC Trial 10801, Breast Conservation Compared With Mastectomy in TNM Stage I and II Breast Cancer. *Eur J Cancer* 1992, **28**, 801-805.
5. Jacobson JA, Danforth DN, Cowan KH, *et al.* Ten-year results of a comparison of conservation with mastectomy in the treatment of stage I and II breast cancer. *N Engl J Med* 1995, **332**, 907-911.
6. Fisher B, Anderson S, Redmond CK, *et al.* Reanalysis and results after 12 years of follow-up in a randomized clinical trial comparing total mastectomy with lumpectomy with or without irradiation in the treatment of breast cancer. *N Engl J Med* 1995, **333**, 1456-1461.
7. Early Breast Cancer Trialists' Collaborative Group. Effects of radiotherapy and surgery in early breast cancer: An overview of the randomized trials. *N Engl J Med* 1995, **333**, 1444-1455.
8. Halsted WS. The results of operations for the cure of cancer of the breast performed at the Johns Hopkins Hospital from June 1989 to January 1994. *Johns Hopkins Hosp Rep* 1994, **4**, 297-350.
9. Early Breast Cancer Trialists' Collaborative Group. Systemic treatment of early breast cancer by hormonal, cytotoxic, or immune therapy: 133 randomized trials involving 31,000 recurrences and 24,000 deaths among 75,000 women. *Lancet* 1992, **339**, 1-15, 71-85.
10. Veronesi U, Saccozzi R, Del Vecchio, *et al.* Comparing radical mastectomy with quadrantectomy, axillary dissection and radiotherapy in patients with small cancers of the breast. *N Engl J Med* 1981, **305**, 6-11.
11. Fisher B, Bauer M, Margolese R, *et al.* Five-year results of a randomized clinical trial comparing total mastectomy with segmental mastectomy with or without radiation in the treatment of breast cancer. *N Engl J Med* 1985, **312**, 665-673.
12. Bartelink H, van Dam F, van Dongen J. Psychological effects of breast conserving therapy in comparison with radical mastectomy. *Int J Radiat Oncol Biol Phys* 1985, **11**, 381-385.
13. Kiebert GM, de Haes JCJM, van de Velde CJH. The impact of breast-conserving treatment and mastectomy on the quality of life of early breast cancer patients: a review. *J Clin Oncol* 1991, **9**, 1059-1070.
14. Schover LR. The impact of breast cancer on sexuality, body image, and intimate relationships. *CA Cancer J Clin* 1991, **41**, 112-120.
15. Pierquin B, Mueller W, Baillet F, *et al.* Radical radiation therapy for cancer of the breast. The experience of Cr teil. *Front Radiat Ther Oncol* 1978, **12**, 150-161.

16. Calle R, Pilleron JP, Schlienger P, *et al.* Conservative management of operable breast cancer. *Cancer* 1978, **42**, 2045–2053.
17. Pocock SJ, Simon R. Sequential treatment assignment with balancing for prognostic factors in the controlled clinical trial. *Biometrics* 1975, **31**, 103–115.
18. De Vita VT, Hellmann S, Rosenberg SA. *Cancer: Principles and Practices of Oncology*, 2nd edn. Philadelphia, Lippincott, 1985.
19. Avery AD, Lelak T, Solomon NE, *et al.* *Quality of Medical Care Assessment Using Outcome Measures. Eight Disease Specific Applications*. Santa Monica, Rand, 1976.
20. Bergman RB, van Dam FSAM. *Borstreconstructie, psychologie & chirurgische aspecten (Breast Reconstruction Psychological and Surgical Aspects)*. Dissertation (Dutch), University of Amsterdam, 1981.
21. Aaronson NK, Bartelink H, van Dongen JA, *et al.* Evaluation of breast conserving therapy: clinical, methodological and psychosocial perspectives. *Eur J Surg Oncol* 1988, **14**, 133–140.
22. Ware JE, Snow KK, Kosinski M, *et al.* *SF-36 Health Survey; Manual and Interpretation Guide*. Boston, The Health Institute, New England Medical Center, 1993.
23. Morris J, Coyle D. Quality of life questionnaires in cancer clinical trials: imputing missing values. *Psycho-Oncology* 1994, **3**, 215–222.
24. Bravo G, Potvin L. Estimating the reliability of continuous measures with Cronbach's alpha or the intraclass correlation coefficient: toward the integration of two traditions. *J Clin Epidemiol* 1991, **44**, 381–390.
25. Nunally JC, Bernstein IH. *Psychometric Theory*. New York, McGraw-Hill, 1994.
26. Hollander M, Wolfe DA. *Nonparametric Statistical Methods*. New York, John Wiley, 1973.
27. Kuritz SJ, Landis JR, Koch GG. A general overview of Mantel-Haenszel methods: applications and recent developments. *Ann Rev Pub Health* 1988, **9**, 123–160.
28. Cox DR. *Analysis of Binary Data*. London, Chapman and Hall, 1970.
29. Campbell MJ, Machin D. *Medical Statistics: A Commonsense Approach*, 2nd edn. London, John Wiley & Sons, 1993.
30. SAS<sup>®</sup> Technical Report, *The PHREG Procedure, version 6*. North Carolina, SAS Institute Inc., 1991.
31. Ganz PA, Lee JJ, Sim MS, *et al.* Exploring the influence of multiple variables on the relationship of age to quality of life in women with breast cancer. *J Clin Epidemiol* 1992, **45**, 473–485.
32. Levy SM, Haynes LT, Herberman RB, *et al.* Mastectomy versus breast conservation surgery: Mental health effects at long-term follow-up. *Health Psychol* 1992, **11**, 349–354.
33. Whelan TJ, Levine MN, Gafni A, *et al.* Breast Irradiation Post-lumpectomy: Development and evaluation of a decision instrument. *J Clin Oncol* 1995, **13**, 847–853.
34. Ganz PA, Coscarelli Schag CA, Lee JJ, *et al.* Breast conservation versus mastectomy: Is there a difference in psychological adjustment or quality of life in the year after surgery? *Cancer* 1992, **69**, 1729–1738.
35. Fallowfield LJ, Hall A, Maguire GP, *et al.* Psychological outcomes of different treatment policies in women with early breast cancer outside a clinical trial. *Br Med J* 1990, **301**, 575–580.
36. de Koning HJ, van Dongen JA, van der Maas PJ. Changes in use of breast-conserving therapy in years 1978–2000. *Br J Cancer* 1994, **70**, 1165–1170.

**Acknowledgement**—The EORTC Data Center is grateful to the Parthenon Trust which provided support for this research.

## APPENDIX 1

### Quality of life questionnaire

	All of the time	Most of the time	Some of the time	Little of the time	None of the time
1. I feel self-conscious about my appearance	1	2	3	4	5
2. I am bothered by thoughts about the recurrence of cancer	1	2	3	4	5
3. I feel ashamed of my body	1	2	3	4	5
4. I believe that the difficulties with my illness are over	1	2	3	4	5
5. I feel self-conscious about being seen nude by husband/partner	1	2	3	4	5
6. I don't feel like myself	1	2	3	4	5
7. I feel uneasy about my future health	1	2	3	4	5
8. I don't feel as if my body belongs to me	1	2	3	4	5
9. If I should have to be treated again, I should like to have the same therapy	1	certainly			
	2	probably			
	3	probably not			
	4	certainly not			
10. The treated breast resembles the other one	1	very much			
	2	quite a bit			
	3	a little			
	4	not at all			