



# Quality of life in breast cancer patients aged over 70 years, participating in the EORTC 10850 randomised clinical trial

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## Abstract

Mastectomy and breast-conserving treatment have proven equally effective in terms of survival in early breast cancer, but studies continue to provide evidence that patients undergoing breast-conserving procedures have a better quality of life (QOL). Age is not considered to be a contraindication for breast-conserving treatment, but retrospective studies have indicated that elderly patients are less likely to be treated conservatively. In the present study, survival, QOL and treatment preference have been investigated in a multicentre, randomised clinical trial of elderly patients with early breast cancer undergoing mastectomy or tumour excision plus tamoxifen. Eligible patients were aged 70 years or more and had histologically- or cytologically-confirmed operable breast cancer. A QOL questionnaire consisting of 36 items was constructed covering 9 scales assessing different QOL domains. Patients completed their assessment between 2 and 12 months after randomisation. 136 patients (65 in the mastectomy arm and 71 in the local excision arm) from six centres filled out a QOL form during the first year of follow-up. No significant difference in the duration of survival between the two treatment arms was observed when including patients included in the QOL sub-study ( $P=0.33$ ). Patients undergoing tumour excision and tamoxifen did not differ from those undergoing mastectomy in terms of fatigue, emotional functioning, fear of recurrence, social support, physical functioning and leisure time activities. However, conservatively treated patients reported fewer arm problems ( $P=0.04$ ) and a shift, although borderline significant, in the direction of a benefit in body image ( $P=0.06$ ). As QOL seems to be better after conservative treatment, such treatment is to be preferred in both elderly and younger patients.

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## 1. Introduction

The choice of surgical treatment for breast cancer continues to interest both surgeons and patients. Mastectomy and breast-conserving treatment have proven equally effective in terms of survival, even after loco-regional recurrence of breast cancer [1]. At the same time, studies continue to provide evidence showing that patients undergoing breast-conserving procedures have

a better quality of life (QOL), especially in terms of body image, in the short- as well as the long-term [2–4].

Age alone need not be a factor that modifies a cancer treatment plan [5,6]. Even though age is not considered to be a contraindication for breast-conserving treatment [7], several retrospective studies have indicated that elderly patients are less likely to be treated conservatively [8–11]. It is unclear why this is the case. Surgical treatment may be selected for elderly patients for arbitrary reasons rather than based on empirical evidence [12]. This might occur because little empirical evidence supporting treatment policy in these patients is available: they are generally excluded from clinical trials

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[13] and few trials have specifically addressed the effectiveness of cancer treatments among elderly patients.

In the present study, survival, QOL and treatment preference have been investigated in a multicentre, randomised clinical trial of elderly patients with early breast cancer undergoing mastectomy or tumour excision plus tamoxifen. The results of the trial may support evidence-based decision-making in the surgical treatment of elderly breast cancer patients.

## 2. Patients and methods

### 2.1. Study design

This multicentre, randomised study comparing mastectomy and tumour excision plus tamoxifen in breast cancer patients over 70 years was conducted by the European Organization for Research and Treatment of Cancer (EORTC) Breast Cancer Cooperative Group (10850). The endpoints of the study were survival, QOL and treatment preference. Randomisation was by the minimisation technique [14], stratifying patients according to their institution and TNM stage.

Eligible patients were aged 70 years or more and had histologically- or cytologically-confirmed operable breast cancer (T1, T2, T3a, N0, N1a, N1b, M0). Informed consent was sought as required by the Ethical Committees of the individual institutions. Excluded from the trial were patients with prior malignancies, more than one breast primary, or evidence of metastatic disease. To be eligible, patients had to be fit, physically and mentally, as judged by the clinician. Prior to entry, all patients had staging investigations comprising full blood count, biochemical screen, chest X-ray, bilateral mammograms and radio-isotopic bone scan. The diagnosis of breast cancer was made by fine needle aspiration cytology or histologically from a needle core or excision biopsy. Patients randomised to receive tamoxifen were given a dose of 20 mg daily on a permanent basis or until there was evidence of relapse of disease. If relapse occurred within the breast, providing that the disease was operable, a salvage modified radical mastectomy was performed.

Six out of 11 centres involved in the trial collected QOL data in consecutive patients giving consent. Patients originated from South Africa, UK, The Netherlands and Greece.

### 2.2. Instruments

Based on previous QOL studies of the EORTC and clinical experience with breast cancer patients, a QOL questionnaire consisting of 36 items was constructed covering nine scales assessing different QOL domains. The emotional functioning scale used was a shortened, eight-item version of the Hospital Anxiety and Depres-

sion Scale [15]. The body image and fear of recurrence items were adapted from an earlier study by Bartelink and colleagues [16]. The social support items were formulated on an *ad hoc* basis.

For the questions included in the physical functioning and leisure time activity scale, patients were asked to respond on a dichotomous (i.e. yes/no) response scale. For the question on treatment preference (“If a friend or daughter became ill with the same breast disease, would you recommend the same medical treatment that you have received?”), the patient could select one of the following categories: definitely not, probably not, probably yes, definitely yes. For the remaining scales, four-point response categories were available as follows: not at all, a little, quite a bit, very much.

### 2.3. Statistical considerations

The analysis was performed on all patients according to the ‘intention-to-treat’ principle.

Duration of survival curves was estimated using the Kaplan–Meier technique [17] and compared using the logrank test. As specified in the protocol, patients’ QOL should have been evaluated at 6 months, 12 months and yearly thereafter. However, the time-points at which patients completed QOL questionnaires was heterogeneous. To include as many patients as possible in the analysis it was decided to concentrate on just one assessment of QOL. As most patients completed their first assessment between 2 and 12 months after randomisation it was decided to focus on this time period. Some patients completed more than one questionnaire in this time period. For those patients, the questionnaire which was completed closest to 7 months after randomisation (the midpoint of this period) was taken. Table 1 shows the time since randomisation to the completion of the QOL form. All scales were linearly transformed to a 0–100 scale, with higher scores representing a higher level of functioning or fewer symptoms. For presentation

Table 1

Time in months since randomisation to completion of form after mastectomy ( $N=65$ ) or breast conserving treatment ( $N=71$ )

Months	Mastectomy $N$ (%)	Tumorectomy plus tamoxifen $N$ (%)
2	2 (3%)	0
3	0	1 (1%)
4	2 (3%)	0
5	5 (8%)	10 (14%)
6	22 (34%)	16 (23%)
7	17 (26%)	10 (14%)
8	4 (6%)	4 (6%)
9	5 (8%)	10 (14%)
10	1 (2%)	8 (11%)
11	4 (6%)	3 (4%)
12	3 (5%)	9 (13%)

purposes, all scales, except for the treatment preference scale, were subsequently collapsed into five levels (0–25, 26–50, 51–70, 71–90, 91–100). The reliability (internal consistency) of the multi-item scales was assessed using Cronbach's  $\alpha$  coefficient (see Table 2) and found to be acceptable. The fear of recurrence scale was shortened from three to two items to improve reliability.

A two-sided stratified Wilcoxon rank sum test [18] stratifying for age and time since randomisation to completion of QOL forms was used to compare QOL scores in the two treatment arms. Exact  $P$  values were calculated using Stat Exact. No adjustment for multiple comparisons was performed.

### 3. Results

#### 3.1. Patients

Between September 1985 and October 1991, 236 patients from 11 centres were entered into EORTC trial 10850; 120 patients were randomised into the radical mastectomy arm and 116 into the local excision + tamoxifen arm. For 5 patients, no on-study form or any follow-up data were received (4 in the mastectomy arm and 1 in the local excision + tamoxifen arm). In total, 136 patients (65 in the mastectomy arm and 71 in the local excision arm) from six centres that collected QOL data, filled out at least one QOL form during the first year of follow-up.

Patient characteristics at entry are presented in Table 3. The distribution of patient characteristics of the 136 patients included in the QOL sub-study were similar in the two arms with only age, tumour site and 'other concomitant diseases' showing some imbalance between the two treatment arms. No association between the tumour site or 'other concomitant diseases' with any of the QOL scales was observed though, even when stratifying for treatment. Weak associations were observed between age and some QOL scales. Because of this, all treatment comparisons were performed stratifying by age and time since randomisation to completion of QOL forms (<7 months,  $\geq 7$  months). Table 3

suggests that the patients who were included in the QOL study were representative of the overall population with no obvious evidence of systematic bias in the recruitment of patients for the QOL study.

#### 3.2. Survival

We did not observe any significant difference in the duration of survival between the two treatment arms when including patients who were included in the QOL sub-study ( $P=0.33$ ) (see Fig. 1).

#### 3.3. Quality of life

As shown in Table 4, patients undergoing tumour excision and tamoxifen did not differ from those undergoing mastectomy in terms of fatigue, emotional functioning, fear of recurrence, social support, physical functioning and leisure time activities. However, conservatively treated patients reported fewer arm problems ( $P=0.04$ ) and a shift, although borderline significant, in the direction of a benefit in body image ( $P=0.06$ ), as compared with those who had undergone a mastectomy.

#### 3.4. Treatment preference

No significant difference was observed between the two treatment arms in treatment preference ( $P=0.19$ ), although patients undergoing conservative treatment seem to be somewhat more favourable towards their own therapy. 62% of patients undergoing mastectomy and 72% of patients undergoing breast-conserving treatment favoured their own therapy.

### 4. Conclusions

Few clinical trials have been undertaken to establish the level of effectiveness of treatment in elderly breast cancer patients. As a result, these patients may be treated for arbitrary reasons. In the present trial, the effect of conservative breast cancer surgery and radical mastectomy was compared and it was found that survival was similar after the two procedures. QOL thus becomes the main endpoint to support decision-making. As QOL seems to be better after conservative treatment, on the basis of this trial's results, the treatment of choice would be tumour excision followed by tamoxifen.

However, some limitations of the study presented should be considered. At the time this trial was undertaken, no standard QOL assessment instrument was available within the EORTC. In addition, clinicians were less familiar with QOL measurement and some of the institutions involved in the trial did not participate in the QOL data collection. Moreover, the selection of patients into the QOL study and the analysis was based

Table 2  
Reliability of scales

Scale	Number of items	Cronbach's $\alpha$
Arm problems	2	0.67
Fatigue and malaise	5	0.74
Emotional functioning	8	0.76
Body image	4	0.69
Fear of recurrence	2	0.65
Social support	6	0.94
Physical functioning	6	0.79
Leisure activities	2	0.79
Treatment preference	1	–

on a cross-sectional view of the data and did not consider the QOL of patients at baseline, immediately after surgery or after a longer period of time.

Nevertheless, the results of the study are in line with earlier research [2–4]. Even though the patient population in this trial is over 70 years, for patients undergoing tumour excision their judgement regarding body image is perhaps less negative than in those treated by mastectomy. Moreover, there appears to be an advantage for these patients in terms of arm function since they were not subjected to axillary surgery.

The majority of patients appeared to be satisfied with their treatment with 62 and 72% of patients in the mastectomy and tumorectomy arms, respectively, reporting that if a friend or daughter became ill with the same breast disease, they would definitely recommend

the same medical treatment that they received. We have seen in other studies that, in general, patients tend to favour the treatment they have undergone [19]. Preferring another treatment option over one's own might lead to regret or cognitive dissonance: it would imply that one should live with the idea of having undergone a less than optimal therapy. In addition, whatever treatment patients receive, they have to adjust to their situation and therefore may become less critical about its nature. In the light of these mechanisms, the fact that more patients seem to favour tumour excision may be meaningful even though not significant in a statistical sense.

The fact that no negative implications of conservative treatment were found, suggests that such treatment should, if medically appropriate, be made available to both older and younger women. Patients tend to depend

Table 3

Characteristics at entry of patients with completed on-study forms as compared to patients not included in the QOL study

Feature	Patients in QOL study		Patients not in QOL study	
	Mastectomy ( <i>N</i> = 65)	Local excision + tamoxifen ( <i>N</i> = 71)	Mastectomy ( <i>N</i> = 51)	Local excision + tamoxifen ( <i>N</i> = 44)
	<i>N</i> (%)	<i>N</i> (%)	<i>N</i> (%)	<i>N</i> (%)
Age (years)				
70–74	18 (28)	9 (13)	13 (25)	11 (25)
75–79	26 (40)	34 (48)	25 (49)	22 (50)
≥ 80	21 (32)	28 (39)	13 (25)	11 (25)
WHO Performance Status				
0	56 (86)	60 (85)	43 (84)	41 (93)
1	8 (12)	8 (11)	6 (12)	3 (7)
2	0 (0)	3 (4)	1 (2)	0 (0)
3	1 (2)	0 (0)	0 (0)	0 (0)
Unknown	0 (0)	0 (0)	1 (2)	0 (0)
Tumour site				
Right	29 (45)	39 (55)	29 (57)	23 (52)
Left	36 (55)	32 (45)	22 (43)	21 (48)
Tumour localisation				
Upper outer	29 (45)	34 (48)	26 (51)	21 (48)
Upper inner	12 (18)	19 (27)	8 (16)	10 (23)
Lower outer	10 (15)	10 (14)	3 (6)	6 (14)
Lower inner	1 (2)	2 (3)	4 (8)	3 (7)
Central	13 (20)	6 (8)	10 (20)	4 (9)
Tumour size (UICC)				
T1	12 (18)	12 (17)	13 (25)	8 (18)
T2	51 (78)	54 (76)	33 (65)	27 (61)
T3	1 (2)	5 (7)	5 (10)	9 (20)
T4	1 (2)	0 (0)	0 (0)	0 (0)
Axillary nodes (UICC)				
N0	45 (69)	54 (76)	30 (59)	25 (57)
N1a	6 (9)	8 (11)	7 (14)	6 (14)
N1b	13 (20)	9 (13)	14 (27)	9 (20)
N2	0 (0)	0 (0)	0 (0)	1 (2)
Nx	1 (2)	0 (0)	0 (0)	3 (7)
Other concomitant diseases				
No	46 (71)	41 (58)	28 (53)	27 (61)
Yes	19 (29)	30 (42)	24 (47)	17 (39)

WHO, World Health Organization; UICC, International Union Against Cancer; QOL, quality of life.

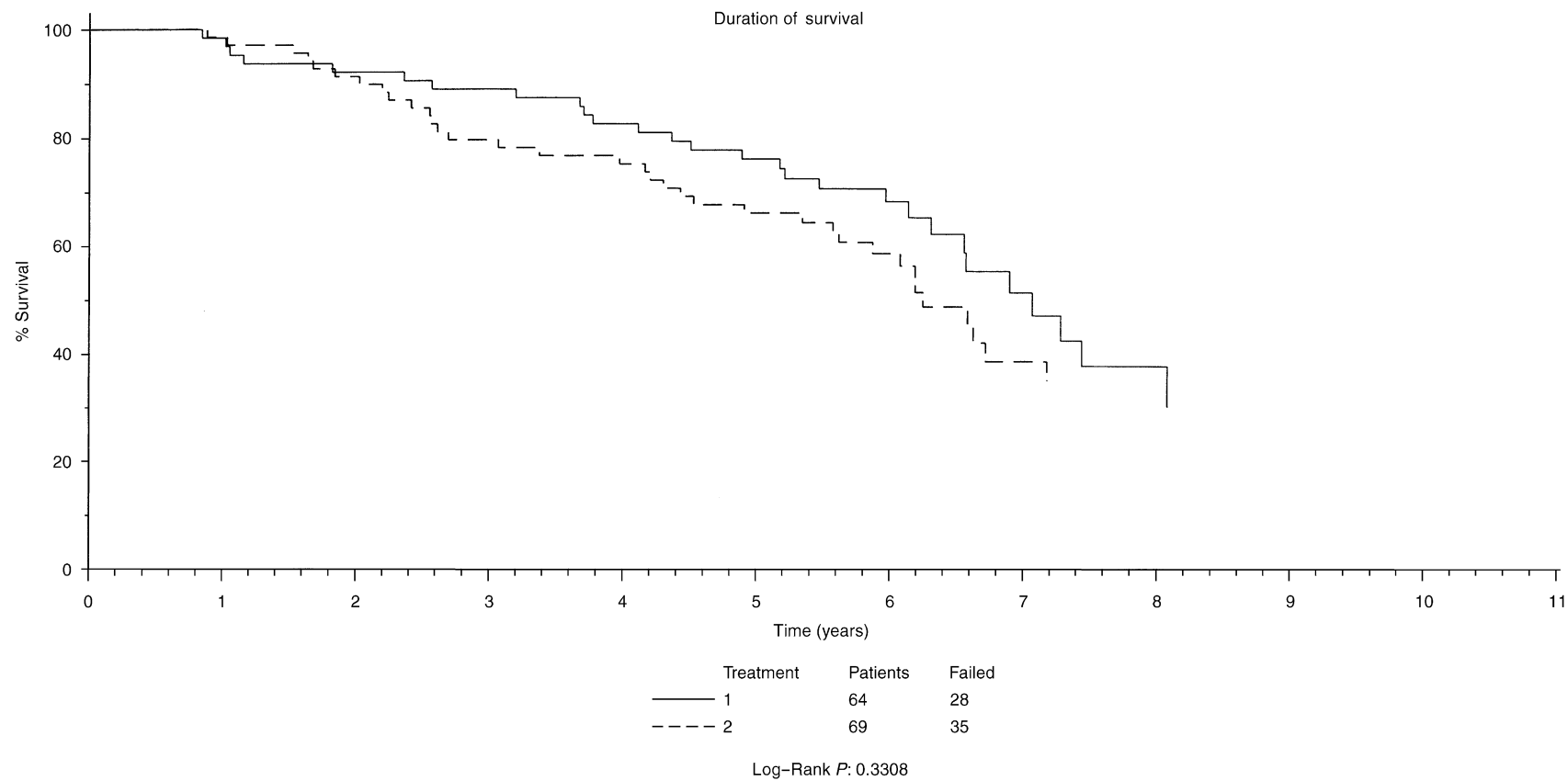


Fig. 1. Survival of patients involved in the QOL assessment after mastectomy (treatment 1) versus tumorectomy plus tamoxifen (treatment 2).

Table 4

Quality of life scores by treatment arm

	Mastectomy <i>N</i> = 65 <i>N</i> (%)	Local excision + tamoxifen <i>N</i> = 71 <i>N</i> (%)	Proportion treated by mastectomy	<i>P</i> value
Arm problems				
0–25	0 (0)	3 (4)	0.00	0.04
26–50	5 (8)	4 (6)	0.56	
51–70	10 (15)	3 (4)	0.77	
71–90	15 (23)	10 (14)	0.60	
91–100	35 (54)	51 (72)	0.41	
Fatigue and malaise				
0–25	0 (0)	5 (7)	0.00	0.98
26–50	7 (11)	7 (10)	0.50	
51–70	20 (31)	15 (21)	0.57	
71–90	27 (42)	35 (49)	0.44	
91–100	11 (17)	8 (11)	0.58	
Unknown	0 (0)	1 (1)		
Emotional functioning				
0–25	0 (0)	1 (1)	0.00	0.85
26–50	5 (8)	5 (7)	0.50	
51–70	10 (15)	10 (14)	0.50	
71–90	28 (43)	29 (41)	0.49	
91–100	22 (34)	26 (37)	0.46	
Body image				
0–25	0 (0)	1 (1)	0.00	0.06
26–50	3 (5)	1 (1)	0.75	
51–70	4 (6)	4 (6)	0.50	
71–90	14 (22)	6 (8)	0.70	
91–100	44 (68)	57 (80)	0.44	
Unknown	0 (0)	2 (3)		
Fear of recurrence				
0–25	0 (0)	3 (4)	0.00	0.55
26–50	11 (17)	5 (7)	0.69	
51–70	10 (15)	22 (31)	0.31	
71–90	16 (25)	12 (17)	0.57	
91–100	27 (42)	27 (38)	0.50	
Unknown	1 (2)	2 (3)		
Social support				
0–25	8 (12)	3 (4)	0.73	0.89
26–50	10 (15)	14 (20)	0.42	
51–70	10 (15)	11 (15)	0.48	
71–90	12 (18)	18 (25)	0.40	
91–100	23 (35)	20 (28)	0.53	
Unknown	2 (3)	4 (6)		
Physical functioning				
0–25	2 (3)	6 (8)	0.25	0.84
26–50	10 (15)	7 (10)	0.59	
51–70	9 (14)	8 (11)	0.53	
71–90	13 (20)	14 (20)	0.48	
91–100	31 (48)	36 (51)	0.46	
Leisure time activities				
0	11 (17)	11 (15)	0.50	0.65
50	8 (12)	8 (11)	0.50	
100	46 (71)	52 (73)	0.47	
Treatment preference				
0	1 (2)	0 (0)	1.00	0.19
33	1 (2)	0 (0)	1.00	
67	17 (26)	13 (18)	0.57	
100	40 (62)	51 (72)	0.44	
Unknown	6 (9)	7 (10)		

on their surgeons when choosing between surgical options [3,20]. If given such choice, even patients over 70 years of age seem to prefer conservative treatment in most cases [21]. The results of this study suggest that surgeons should propose tumorectomy and tamoxifen to older breast cancer patients as a reasonable alternative to mastectomy in a more systematic manner than is currently the case.

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