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Mastectomy or Conservation for Early Breast Cancer: Psychological Morbidity

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A consecutive series of 197 women under 70 years of age with operable breast cancer, randomised to treatment by a conservation technique in comparison to mastectomy, were assessed using structured interviews. The prevalence of cases of anxiety and depression was high before treatment commenced, there were fewer cases in the conservation group but no significant difference at 3 or 12 months in the number of new cases, social adjustment, or capacity to return to work. Attitudes to treatment showed significant differences between the groups, more women in the conservation group were able to wear their usual clothes and most women rated the cosmetic result highly. Patients were more likely to stop sexual intercouse completely after mastectomy. An effective conservation technique should be an attractive treatment choice available to selected women with early breast cancer.
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INTRODUCTION

IN SELECTED PATIENTS with operable breast cancer, conservation treatment is a safe alternative to mastectomy in terms of local control and overall survival [1–3]. High levels of depression, anxiety and distress have been reported following mastectomy [4–6]. The view arose that breast conservation might protect women from this psychiatric morbidity. When our work began only one study had been published comparing the psychological effects of breast conserving treatment with mastectomy, and this had design faults including potentially biased recruitment, testing postsurgical factors over a wide time range, and using a poor measure of general psychological adjustment [7]. Since then, further studies have been published and have been critically reviewed by Kiebert *et al.* [8] and Hall and Fallowfield [9]. One reported only 38 patients responding to a non-validated postal questionnaire [10]. A better designed study, but with only 21 patients treated by breast conservation, did not find these patients to be less anxious or depressed [11]. A further study of 39 patients, again using a postal questionnaire, reported body image to be more severely impaired after mastectomy, fear of recurrence of the cancer to be unrelated to treatment type, and no significant difference between the groups with respect to "psychological complaints" [12]. A larger study, using a more satisfactory measure of psychiatric symptomatology, found 38% of women with states of anxiety or depression among the breast conservation group, compared with 33% in the mastectomy group [13]. However, this study had a retrospective design, pooled results with a wide time range, and did not analyse the relationship between morbidity and treatment variables. Hence, it is difficult to draw clear conclusions from these studies. In particular, it remains unclear whether psychiatric morbidity is affected by the type of treatment.

We have investigated the relationships between primary treatment and psychiatric morbidity in patients with early (stage I or II) breast cancer entered into a prospective randomised study comparing breast conservation with mastectomy. The main hypothesis we have tested is that conservation of the breast with a good cosmetic result leads to less psychosocial morbidity.

PATIENTS AND METHODS

Initial sample

The patients were a consecutive series admitted to the Breast Unit, Guy's Hospital, who fulfilled the entry criteria for the EORTC multicentre trial 10801 [14]. Ethical approval was given to this study, which was begun in the early 1980s, by the Guy's Hospital ethical committee. Patients were randomised to treatment by either modified radical mastectomy or breast conservation comprising tumorectomy, axillary clearance, iridium implant, and subsequent external beam radiotherapy [15]. Eligibility criteria included a single invasive breast carcinoma 4 cm diameter or less in patients less than 70 years. All patients aged less than 65 years who had axillary nodal metastases (found at axillary clearance) were further randomised to receive 12 cycles of adjuvant therapy (CMF) or no further treatment (control).

A pretreatment psychosocial assessment was completed before a biopsy confirmed diagnosis had been made. This was completed by 332 patients; additionally, 8 refused to take part in the psychosocial study, 7 refused the pretreatment assessment having initially agreed, 2 patients refused the treatment offered and another, a schizophrenic patient, was too mentally ill to be included. Subsequently, 197 were found to have a malignant tumour fulfilling the eligibility criteria, of whom 97 were treated by modified radical mastectomy and 100 by breast conservation. The remaining 135 women had benign tumours.

Psychosocial assessments

Patients were interviewed before treatment by a psychiatrist using the structured interviews of the Present State Examination

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[16] and the Social Adjustment Scale [17]. The latter is an observer rated structured interview which gives scores for role areas of work, social and leisure, extended family, marital, parental, family unit and economic. These scores can be analysed in three different ways: by deriving role area scores, qualitative scores (performance, interpersonal behaviours, friction, feelings and satisfactions) or by factor analysis.

All interviews were tape recorded, all three psychiatrists were trained in the use of the structured interviews and one (M.L.) acted as a referee for any rating difficulties.

Final sample

It was hoped to re-interview all patients at 3 and 12 months using the pretreatment measures and a structured interview to assess their attitudes to breast surgery, pain and side effects from treatment.

However, of the 197 women in the study, 14 (7%) refused to be interviewed at 3 months (10 treated by breast conservation, 4 treated by modified mastectomy) and one mastectomy patient had experienced a recurrence. At re-interview 12 months post-operatively, 24 (12%) refused to be interviewed (15 treated by breast conservation and 9 treated by mastectomy), a further 12 had experienced recurrences (6 in each group). The general practitioners and the physician conducting the follow-up were contacted to determine evidence of psychological morbidity in these women.

Analysis

The symptoms recorded in the interviews using the Present State examination were analysed using the CATEGO computer programme. The programme sorts symptoms into syndromes and thereby into an eight level "index of definition" (ID). Surveys [18] have shown high agreement between the global clinical judgement of "not a case" vs. "a case" and the ID level 1–4 vs. 5–8. Patients with an ID of 5 or more have thus been regarded as being psychiatric "cases".

Tables were analysed using the χ^2-test. For 2×2 tables, if the total number of observations was less than 20 or 20–40 with at least one expectation less than 5 the Fisher's exact test was used, otherwise Yates continuity correction to the standard χ^2 was used. For larger tables with *a priori* logical trend across groups, the more sensitive χ^2-test for linear trend was used.

RESULTS

Baseline variables

The two groups were comparable in variables which might be expected to affect morbidity, including age, parity, menopausal status, staging, receipt of adjuvant therapy, marital status, education, occupational status and religious conviction. With regard to social class, there was a greater proportion of conservation patients in social class 1, but this was offset as a group by a lower proportion in social class 3N. The proportion of patients in social classes 1, 2 and 3N combined, compared with classes 3M, 4 and 5 combined, was comparable between the two groups.

Psychiatric morbidity

The cases resulting from the CATEGO ANALYSIS of the PSE are shown in Table 1. Pre-operatively, 29% of patients treated by mastectomy and 21% of patients treated by conservation had either anxiety or depression which warranted treatment (caseness). Considering the high levels of caseness pre-operatively, new cases of depression or anxiety were defined where patients had been neither depressed nor anxious before treatment. At 3 months there was less anxiety/depression overall among the breast conservation group (14 vs. 21%) but this difference was not statistically significant. By 12 months 8% of the conservation group were cases compared to 11% of the mastectomy group ($\chi^2 = 0.14$; d.f. = 1; $P = 0.71$).

In terms of new cases at 3 months, there were six (6.8%) of depression or anxiety in patients treated by conservation and 10 (11.2%) in the mastectomy group (Fisher's exact test $P = 0.5$). At 12 months there were four new cases in each group (Fisher's exact test $P = 0.4$). Of the 9 women in the mastectomy group refusing interview at 1 year, 4 were reported to show some symptoms of anxiety or depression and 3 of them had been treated by their family doctor and one referred to a psychiatrist. In the conservation group, 4 of the 15 women refusing interview had some symptoms of anxiety or depression and 3 had been treated by their family doctor.

Postoperative pain predisposed to caseness. At 3 months, 81% of cases and 60% of non-cases had experienced some pain, this being severe in 31 and 11%, respectively. When cases/non-cases were analysed with regard to no/moderate/severe pain, the χ^2 for linear trend was 6.8, d.f. = 1, $P = 0.01$; after 12 months the same comparison gives χ^2 for linear trend 10.8, d.f. = 1, $P = 0.001$.

There were 32% of cases within the group given CMF compared with 13% in the control group but the difference was not statistically significant at either 3 or 12 months.

Age interacted with caseness in an interesting way; pretreatment there were more cases in the youngest age group (< 40 years) with a decreasing level with age (χ^2 linear trend = 9.81, d.f. = 1, $P = 0.003$). However, after treatment, at both 3 and 12 months there were more cases in the 41–55 year age group. The presence of a partner did not affect the likelihood of being a case.

Social adjustment

There were no significant differences between the groups by role score or qualitative category at 3 and 12 months. Factor analysis produced six elements interpreted as representing work performance, interpersonal friction, inhibited communication, submissive dependency, family attachment and anxious rumination. Comparisons of the factors at 3 and 12 months postoperatively showed no significant differences between the groups.

Most women in paid employment returned to work by 12 months. In the mastectomy group 38 (81%) returned to their original employment compared with 31 (71%) in the conservation group ($\chi^2 = 1.38$, d.f. = 1, $P = 0.25$).

Sexual adjustment

There were no significant differences between the groups comparing the median of the summed scores for diminished sexual intercourse, sexual problems and disinterest in sex for those women in a permanent relationship who had engaged in intercourse in the previous 2 months (Mann–Whitney test $P = 0.9$ at 3 months and 12 months).

At 3 months approximately one third of the women with partners, in both groups, had not engaged in intercourse in the previous 2 months. At 12 months mastectomy patients were more likely to have stopped sexual intercourse completely (22 mastectomy vs. 10 conservation; $\chi^2 = 4.03$, d.f. = 1, $P = 0.04$).

Attitudes to treatment

The attitudes of the patients to the surgical scars are shown in Table 2 which shows that patients treated by mastectomy had

Table 1. Cases of anxiety and depression in 97 women treated by mastectomy and 100 women treated by breast conservation, pre-operatively and 3 months and 12 months postoperatively

	Pre-operative*				3 months postoperative†				12 months postoperative‡			
	Mastectomy		Conservation		Mastectomy		Conservation		Mastectomy		Conservation	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Case depression	8	8.2	6	6	8	8.2	5	5.0	2	2.1	4	4.0
Case anxiety	20	20.6	15	15	13	13.4	9	9.0	9	9.3	4	4.0
Non-case	69	71.1	79	79	66	68.0	72	72.0	70	72.2	69	69.0
Refused interview	0	0.0	0	0.0	4	4.1	10	10.0	9	9.3	15	15.0
Missing data	0	0.0	0	0.0	5	5.2	4	4.0	1	1.0	2	2.0
Recurrence or 2nd primary	—		—		1	1.0	0	0.0	6	6.2	6	6.0
Total	97		100		97		100		97		100	

*Comparison between mastectomy and control groups for case vs.non-case depression and anxiety pre-operatively: $\chi^2 = 1.24$,d.f. = 1, $P = 0.27$.

†Comparison between mastectomy and control groups for case vs. non-case depression and anxiety at 3 months: $\chi^2 = 1.21$, d.f. = 1, $P = 0.27$.

‡Comparison between mastectomy and control groups for case vs. non-case depression and anxiety at 1 year: $\chi^2 = 0.14$, d.f. = 1, $P = 0.71$.

Table 2. Patients' reactions to surgical scars

	3 months postoperative*				12 months postoperative†			
	Mastectomy		Conservation		Mastectomy		Conservation	
Mean score	No.	%	No.	%	No.	%	No.	%
No distress	48	49.5	74	74.0	50	51.5	71	71.0
Some distress	26	26.8	9	9.0	21	21.6	3	3.0
Moderate and severe distress	12	12.4	1	1.0	9	9.3	1	1.0
Refused interview	4	4.1	10	10.0	9	9.3	15	15.0
Missing data	6	6.2	6	6.0	2	2.1	4	4.0
Recurrence or 2nd primary	1	1.0	0	0.0	6	6.2	6	6.0
Total	97		100		97		100	

*Comparison between mastectomy and conservation groups for no/some/moderate and severe upset at 3 months: χ^2 linear trend = 22.5, d.f. = 1, $P = < < 0.001$.

†Comparison between mastectomy and conservation groups for no/some/moderate and severe upset at 12 months: χ^2 linear trend = 20.6, d.f. = 1, $P = < < 0.001$.

significantly more distress. After 3 months 19% of the mastectomy cases were unable to wear their usual clothes compared with 9% of the conservation group ($P = 0.06$). Similarly, at 12 months more were unable to wear their usual clothes (33 vs. 14%, $P = 0.004$).

The emotional reactions to change in breast contour are shown in Table 3, with significantly more mastectomy patients moderately or severely upset.

Cosmetic outcome was rated by both patient and doctors. At 3 months the opinions were in agreement in 52% of cases. In 23 (27%) the doctor's opinion was higher and in 18 (21%) the patients' opinion was higher. There was concordance in 49% of cases at 12 months with the doctor's opinion being higher in 11 (15%) and the patients' opinion higher in 27 (36%).

DISCUSSION

Our study confirms a high prevalence of psychiatric morbidity in women presenting with a breast lump. Cases identified had a symptom level compatible with diagnoses of anxiety neurosis or depressive neurosis of a severity expected to be found in out-patient or in-patient psychiatric clinics.

Both anxiety and depression diminished with time as noted in other studies [19]. It has to be questioned whether the fewer cases found at follow-up related to the patients refusing re-interview. Our survey of GPs and the physician assessing their physical well-being provided no evidence that the morbidity in the refuser group would have affected between group comparisons. Nearly twice as many women in the conservation group refused follow-up interview. This probably resulted from more hospital attendances for postoperative radiotherapy, and some women simply expressed the view that they were "fed up" with hospital appointments, examinations and interviews.

Total cases of depression and anxiety were fewer in the conservation group but the difference was not significant at 3 or 12 months. There was no significant difference in the number of new cases of depression and anxiety subsequent to treatment. Pain and adjuvant therapy were clinical variables contributing to caseness. Younger women were more likely to be cases

Table 3. Patients' reactions to breast loss (mastectomy) or contour change (conservation)

	3 months postoperative*				12 months postoperative†			
	Mastectomy		Conservation		Mastectomy		Conservation	
Mean score	No.	%	No.	%	No.	%	No.	%
No distress	38	39.2	74	74.0	39	40.2	67	67.0
Some distress	31	32.0	11	11.0	31	32.0	8	8.0
Moderate and severe distress	18	18.6	0	0.0	10	10.3	0	0.0
Refused interview	4	4.1	10	10.0	9	9.3	15	15.0
Missing data	5	5.2	5	5.0	2	2.1	4	4.0
Recurrency or 2nd primary	1	1.0	0	0.0	6	6.2	6	6.0
Total	97		100		97		100	

*Comparison between mastectomy and conservation groups for no/some/moderate and severe upset at 3 months: χ^2 linear trend = 38.6, d.f. = 1, $P = < < 0.001$.
†Comparison between mstectomy and conservation groups for no/some/moderate and severe upset at 12 months: χ^2 linear trend = 29.9, d.f. = 1, $P = < < 0.001$.

pretreatment and middle-aged women post-treatment. No evidence was found to support the view that the presence of a partner reduced the chance of being a case.

There was no significant difference between the groups in respect of social adjustment and capacity to return to work, although it is possible that the instrument was not sensitive enough. However, most women lived within supportive social networks which might have reduced any potentially adverse effect of the treatment on social functioning. A significant difference was found in psychosexual adjustment in that mastectomy patients were more likely to have stopped intercourse completely by 12 months.

Patients treated by mastectomy were significantly more distressed by the scars resulting from the operation and were more upset by the loss of a breast in comparison to the conservation patients' distress concerning change in contour of their conserved breast. Additionally, more of the conservation group were able to wear the same clothes as they did before treatment and almost all were happy that the breast had been conserved.

The study is open to the criticism that informed consent was not sought before patients were entered into the clinical trial. The trial was given ethical approval at its commencement; a time when informed consent was not widely sought. Attitudes of patients and doctors have changed over the past 10 years and the difficult and sensitive ethical issues given further debate [20].

This study has not shown a significant difference in cases of anxiety and depression between the treatment groups although there were fewer cases in the conservation group, these findings being in line with other recent studies (see Kiebert *et al.* [8]). It is likely, therefore, that morbidity relates to stressors common to both groups, particularly that of having cancer. Fallowfield [21] found that, for most women, fear of cancer was their primary fear rather than losing a breast. However, distress concerning the operation, difficulty wearing usual clothes and sexual dysfunction after mastectomy suggests that an effective conservation technique should be an attractive choice to selected women requiring treatment for early breast cancer. Shorter courses of radiotherapy might improve patients' tolerance of the conservation treatment. Clinicians treating women with breast cancer must be vigilant for symptoms of anxiety and depression, both before and after treatment, and particularly in patients experiencing pain or receiving adjuvant therapy.

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Comparison of Three Protracted Antiemetic Regimens for the Control of Delayed Emesis in Cisplatin-treated Patients

Isabel Moreno, Rafael Rosell, Albert Abad, Agusti Barnadas, Joan Carles, Nuria Ribelles, Victoria Solano and Albert Font

Antiemetic activity of three protracted regimens for the control of cisplatin-evoked delayed emesis was explored. 63 patients were randomly assigned to receive one of three protracted antiemetic schedules over 4 days. Group C patients received dexamethasone 8 mg twice daily on days 2 and 3, then 4 mg twice daily on days 4 and 5; in group B, alizapride 2.5 mg/kg four times daily on days 2–5 plus dexamethasone as in group C was administered; and in group A, metoclopramide 0.5 mg/kg four times daily on days 2–5 plus dexamethasone was given at the same dose-schedule as in groups C and B. Complete protection from delayed vomiting was achieved in 44% of group C, 30% of B and 70% of group A ($P = 0.02$). Mild side-effects were noted in all three groups. A higher complete protection for delayed emesis was obtained in metoclopramide–dexamethasone-treated patients. Neither of the regimens used in the protection of delayed emesis controlled late nausea.
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INTRODUCTION

AN ACCEPTABLE CONTROL of acute cisplatin-induced emesis has been achieved with intermittent high-dose metoclopramide plus the addition of dexamethasone and diphenhydramine or lorazepam [1–3]. Less often are efforts marshalled to successfully develop protracted antiemetic trials to enhance the prevention of delayed emesis. The incidence of delayed emesis has been as low as 16–25% [1, 4], but later when patients received cisplatin doses of 120 mg/m^2 incidence was as high as 74% [5]. In our experience, in spite of complete protection (CP) of acute cisplatin-evoked emesis in half of the high-dose (3 mg/kg × 2) metoclopramide-treated patients, delayed emesis syndrome was witnessed in 65%. In this randomised trial when alizapride was given instead of metoclopramide with both dexamethasone and lorazepam, although less acute CP was recorded, the frequency of delayed emesis (68%) remained similar to the metoclopramide arm [6].

These findings prompted us to undertake the current trial in which three protracted antiemetic regimens are compared: metoclopramide–dexamethasone, alizapride–dexamethasone or single dexamethasone. The object of this trial, therefore, is to evaluate the control of delayed vomiting and nausea.

PATIENTS AND METHODS

From October 1987 to November 1988, 63 chemotherapy-naive patients were included in this trial. All patients with histologically-proven cancer were to receive cisplatin-based chemotherapy and those with a Karnofsky index equal to or greater than 60% were eligible. Each patient received cisplatin at doses between 60 and 120 mg/m^2 administered over 30 min intravenously on an in-patient basis on day one. They also received other chemotherapeutic agents in several of the following combinations: ifosfamide 3 g/m^2, mitomycin 8 mg/m^2, vindesine 3 mg/m^2, etoposide 170 mg/m^2, cyclophosphamide 600 mg/m^2 or 5-flurouracil (5-FU) 1000 mg/m^2. All patients were hospital in-patients during the 24 h before cisplatin administration. Each patient signed an informed consent.

This study was a randomised, single-blind, parallel group trial. All 63 patients were randomly allocated to receive an acute antiemesis regimen consisting of either MDL : intravenous metoclopramide (3 mg/kg × 2 doses) diluted in 250 ml of 0.9% sodium chloride given 30 min pre- and 90 min post-cisplatin. A

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