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Lack of Correlation between Anxiety Parameters and Oestrogen Receptor Status in Early Breast Cancer

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Correlation between anxiety parameters and oestrogen receptor levels (ER) were investigated in 89 patients with primary breast cancer. Patients were divided into two groups, ER poor (< 0.05 fmol/μg DNA) and ER rich (> 0.05 fmol/μg DNA). No differences were found between anxiety levels, determined by a modified Hospital Anxiety and Depression (HAD) scale, in the two groups. This report does not support the findings from other studies, claiming an association between psychological parameters and oestrogen receptor status, which is believed to be a prognostic predictor.
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INTRODUCTION

FOR MANY YEARS it has been suggested that psychosocial factors have an impact on the course of breast cancer disease. Some studies [1, 2] have presented evidence that psychosocial profiles could be predictive with respect to survival in patients with breast cancer whereas others have failed to show such a correlation [3, 4].

Factors which are well established in predicting survival in operable breast cancer patients are tumour size [5] and number of involved axillary lymph nodes [5]. Other factors of less significant prognostic value are histological grading [6], and the presence of oestrogen receptors (ER) in tumour cells [7].

In a recent report, Razavi *et al.* found a correlation between psychosocial factors and tumour levels of ER [2]. ER-negative patients had significantly higher scores with respect to self-reported anxiety and global distress.

The aim of this study was to investigate whether or not a correlation could be found between ER status and anxiety parameters thereby confirming the observation made by Razavi *et al.* [2].

PATIENTS AND METHODS

A total of 94 patients with operable stage II–III breast cancer were invited to participate in the psychosocial screening procedure. The invitation was made after primary surgery including axillary dissection, when the results of the histopathological examination were available. The entry criteria required that patients were less than 65 years of age with either node-positive disease or a tumour diameter (measured on the surgical specimen) exceeding 30 mm. The histological staging of the tumour, however, was not considered. Of the 94 eligible patients, 2 refused to participate and for a further 2 oestrogen receptor status was unknown. 1 patient was excluded because the clinical records were unavailable.

Receptor assays

ER was measured by an enzyme immuno assay [8]. This technique is in excellent agreement with previously validated biochemical assays [8]. Tumours with an ER level below 0.05 fmol/μg DNA were classified as ER-poor in contrast to those with higher values which were classified as ER-rich. The ER-rich group included 66 patients and the ER-poor group included 23 patients.

Rating of anxiety

The rating of anxiety was performed before the second postoperative visit. At this time no information had been given about the ER status of the tumour, nor the options for adjuvant therapy. The patients were asked to complete a self report scale including a Hospital Anxiety and Depression (HAD) scale [9] with the assistance of a trained research nurse. The HAD scale was modified in the following manner: The two weakest items in the scale were deleted to increase the internal consistency, determined by calculating correlations between each item and the total anxiety score [10]. The anxiety scale was made up of five different statements with five response categories: never, seldom, sometimes, often and always, coded from 0–4 depending on whether the statement was negative or positive. The HAD scale has been translated into several languages and its cross-cultural use has been supported by the original authors. The Swedish version was developed by Sullivan and proved valid in patients with spinal cord injuries [11].

Data analysis

Data from medical records were collected regarding age of the patient, tumour size, lymph node involvement, menopausal status and oestrogen receptor status. Differences between means were tested by Student's *t*-test and differences in distributions between the groups were tested with χ^2 test. Our ambition was to perform a multiple logistic regression analysis if the bivariate analysis χ^2 and *t*-test had given several significant factors. Analyses were performed to see if correlations could be found

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Table 1. Patients' characteristics in ER-poor and ER-rich groups

	ER-poor	ER-rich	P value
Number of patients	23	66	
Age	51 ± 7*	52 ± 3*	0.365
Tumour size (mm)	27.2 ± 19*	25.5 ± 17*	0.685
Positive axillary nodes	56.5%	65.2%	0.626
Postmenopausal	43.5%	45.5%	1.0

* Values are expressed as mean ±S.D.

between total anxiety score and ER status and each anxiety statement separately in correlation to ER status.

This study was approved by the ethics committee of the Karolinska Institute.

RESULTS

Patient characteristics of the two patient groups are given in Table 1 and anxiety parameters are given in Table 2. There was no difference with respect to clinical characteristics between the two groups, nor did the anxiety rating differ between the two groups. Even though we analysed every statement separately we could not find any correlation between ER status and anxiety levels (Table 2).

DISCUSSION

In contrast to the results by Razavi *et al.* [2] we were not able to find any correlation between ER status and anxiety levels among patients with primary breast cancer. Anxiety scales used in our studies differed from those used by Razavi *et al.* [2]. To our knowledge, no studies have been performed comparing the HAD scales and the SCL 90 scale used in Razavi *et al*'s. study.

The HAD scale used in this study is considered a reliable and reproducible instrument, screening for clinically significant anxiety in patients with somatic disorders [9]. Zigmond and Snaith [9] have reported that the number of items composing the scales could vary between 4 and 10 without changing the performance of the scales. The scale has also been shown to be a valid measure of the severity of the disorder [9]. The method used for ER assay in the study by Razavi *et al.* [2] is not the same as the one we used. Thus, differences in assay methods may partly explain the lack of agreement. On the other hand, an excellent correlation between the enzyme immunoassay and the radioligand technique used by Razavi *et al.* [2] has been shown by others [8]. However, Razavi *et al.* [2] did not define which tumours were classified as ER-rich and ER-poor. Obviously, this limits the possibility of making a direct comparison between the studies. We considered an ER level of less than 0.05 fmol/μg DNA as ER-poor, since clinical experience has showed that patients with these low levels seldom respond to adjuvant endocrine therapy [12].

Table 2. Anxiety parameters in ER-poor and ER-rich patients

	ER-poor* $n = 23$	ER-rich* $n = 66$	P value	95% confidence interval for the mean differences (ER-poor–ER-rich)
Total anxiety score	7.9 ± 3.9	7.6 ± 3.6	0.769	− 1.6 ; 2.2
Nervousness	2.0 ± 1.1	1.9 ± 0.9	0.579	− 0.4 ; 0.6
Worry	2.0 ± 0.9	2.1 ± 0.9	0.484	− 0.5 ; 0.3
Difficulty to calm down	1.4 ± 0.8	1.2 ± 0.7	0.408	− 0.2 ; 0.6
Restless	1.5 ± 1.3	1.5 ± 1.1	0.975	− 0.6 ; 0.6
Panic	1.0 ± 1.0	0.9 ± 0.9	0.649	− 0.4 ; 0.6

* Values are expressed as mean ±S.D.

The study population in the report by Razavi *et al.* comprised a subset of 93 out of a total of 210 eligible patients who consented to participate. Although the study group that Razavi *et al.* used was younger than the group who did not want to participate (but otherwise medically comparable) it is not known if the 93 patients out of the 210 were psychologically different from the whole group [2]. Despite the fact that the patients in our study were selected as to clinical stage (tumour diameter > 30 mm or node positive) they were comparable with the patients reported by Razavi *et al.* with respect to population size, age, size of the primary tumour and menopausal status.

Finally, the patients reported in the work by Razavi *et al.* [2] had received various treatments including chemotherapy and/or surgery before the assessment was performed. Thus, the timing of this evaluation might vary considerably between patients in Razavi *et al.* group. In our study all patients were interviewed 4–6 weeks after surgery.

In conclusion, our study of primary breast cancer patients has not shown any correlation between anxiety parameters, as rated with a modified HAD scale and ER status.

1. Greer S, Morris T, Pettingale KW. Psychological response to breast cancer. *Lancet* 1979, **i**, 785–787.
2. Razavi D, Farvacques C, Delvaux N, *et al.* Psychosocial correlates of estrogen and progesteron receptors in breast cancer. *Lancet* 1990, **335**, 931–933.
3. Jamison RN, Burrish TG, Wallston KA. Psychogenic factors predicting survival in breast cancer patients. *J Clin Oncol* 1987, **5**, 762–772.
4. Cassileth BR, Lusk EJ, Miller DS, Brown LL, Miller C. Psychosocial correlates of survival in advanced malignant disease. *N Engl J Med* 1985, **312**, 1551–1555.
5. Say C, Donegan VL. Invasive carcinoma of the breast: prognostic significance of tumour size and involved axillary lymph nodes. *Cancer* 1974, **34**, 468–471.
6. Tough ICK, Carter DC, Frazer J, Bruce J. Histological grading of breast cancer. *Br J Cancer* 1969, **23**, 294–301.
7. Fisher B, Wickerham L, Brown A, *et al.* Breast cancer estrogen and progesteron values : their distribution, degree of concordance and relation to number of positive axillary nodes. *J Clin Oncol* 1983, **1**, 349–358.
8. Leclercq G, Bojar H, Goussard J, *et al.* Abbott monoclonal enzyme immuno assay measurement of estrogen receptors in human breast cancer. A European multicenter study. *Cancer Res* 1986, **46**, 4233–4236.
9. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psych Scand* 1983, **67**, 361–370.
10. Berglund G, Bolund C, Fornander T, Rutqvist LE, Sjödén P-O. Late effects of adjuvant chemotherapy and postoperative radiotherapy on quality of life among breast cancer patients. *Eur J Cancer* 1991, **27**, 1075–1081.
11. Lundqvist C, Sjösteen A, Blomstrand C, Lind B, Sullivan M. Spinal cord injuries. Clinical function and emotional status. *Spine* 1991, **16**, 78–83.
12. Rutqvist LE, Cedermark B, Glas U, *et al.* The Stockholm trial on adjuvant tamoxifen in early breast cancer. Correlation between estrogen receptor level and treatment effect. *Breast Cancer Res Treat* 1987, **10**, 255–266.

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