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Screening for Anxiety and Depression in Cancer Patients: the Effects of Disease and Treatment

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The General Health Questionnaire 28 (GHQ 28), Hospital Anxiety and Depression Scale (HADS), and Rotterdam Symptom Checklist (RSCL) seemed promising in their ability to detect anxiety and depression in cancer patients. To compare their screening performance, 513 patients were recruited from four cancer centres, and visited at home by a trained interviewer. Paired combinations of questionnaires (GHQ 28 + HADS, GHQ 28 + RSCL or RSCL + HADS) were used, and then the Psychiatric Assessment Schedule was administered to enable a psychiatric diagnosis to be made using DSM III diagnostic criteria. A receiver operating characteristics curve was drawn by plotting the true positive rate (sensitivity) against the false positive rate (1 −specificity) for each possible score on each questionnaire. In the overall sample, the HADS and RSCL performed well comparably. The HADS did best in those free of disease and when the disease was judged to be stable. Only the RSCL performed well in those with progressive disease. Both the HADS and RSCL were effective in those on treatment. The GHQ was superior to the RSCL in those off treatment. The choice of questionnaire and threshold score should take disease and treatment status into account, but all three questionnaires have a definite role in screening out anxiety and depression.
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INTRODUCTION

PATIENTS DIAGNOSED and treated for cancer have an increased risk of developing an anxiety state and/or depressive illness [1, 2]. Unfortunately, only 20–50% of patients so affected are identified and treated appropriately [3]. Patients are reluctant to disclose their mood disorder while doctors and nurses are loathe to enquire about it.

Training specialist cancer nurses in the relevant assessment skills so that they could monitor patients undergoing mastectomy much improved the recognition and psychiatric referral of those who developed an affective disorder [4], although there were disadvantages. The nurse had to restrict his or her attention to one diagnostic group, and to assess all patients including many who were coping well. More economic ways of detecting affective disorders are needed if all cancer patients are to be screened, and specialist nurses are to have more time for therapeutic interventions.

Self-rating questionnaires are cheap and convenient. They could be used in clinics and hospital wards to identify patients likely to have an affective disorder. The specialist nurse could then assess such patients to check if they warranted help. For this to be feasible, it would have to be shown that the questionnaires could detect the affected patients accurately, even when they had active disease and were still on treatment.

Three questionnaires appeared promising in this screening role. The General Health Questionnaire 28 (GHQ 28) has been validated in patients with other physical illness [5–7]. The Hospital Anxiety and Depression Scale (HADS) was developed specifically for physically ill patients [8]. The Rotterdam Symptom Check List (RSCL) was developed for patients with cancer [9].

Therefore, we carried out a study to compare the ability of these three questionnaires to screen out those cancer patients who developed an anxiety state or depressive illness, and to determine the effect of disease status and treatment on their performance.

PATIENTS AND METHODS

Sample

Patients were recruited from outpatient clinics or day wards in the Christie and Withington Hospitals (Manchester), the Royal Marsden Hospital (Sutton, Surrey) and the Queen Elizabeth Hospital (Birmingham). Patients were consecutive re-attenders waiting to see a doctor. Each patient was informed about the study by a research assistant, and invited to participate. Those who consented were visited at home within a few days by a trained interviewer.

Assessment

Each patient was first asked to complete two questionnaires. Three paired combinations were used (GHQ 28 + RSCL, RSCL + HADS and HADS + GHQ 28). Each questionnaire within a combination was presented first or second an equal number of times to allow for order effects. Within each centre, combinations were given in a predetermined randomised order.

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The interviewer next administered the Psychiatric Assessment Schedule [10]. The interviews were tape recorded to permit later rating and checks of inter-rate reliability. The Diagnostic and Statistical Manual III of the American Psychiatric Association was used to decide if a patient had a generalised anxiety disorder or major depressive illness.

Training

Interviewers were trained by videotape demonstration, practice and feedback of performance during a 2-day workshop. They continued to practice over the next 3 months, and were given feedback on the basis of their tape recordings and ratings. Finally, a 2-day workshop was held to consolidate their skills.

Clinical assessment

The relevant clinician was asked to assign each patient to one of three disease groups: disease free, stable (less than 25% increase in the last month) and progressive disease (progressed 25% or more in the last month). The clinician also indicated if the patient was receiving active treatment or no treatment.

Analysis

Sensitivity represents the proportion of true cases [true cases/(true cases plus false positives)] correctly identified. Specificity is the proportion of true normals [true normals/(false positives plus true normals)] identified correctly. The positive predictive value gives the proportion of high scorers who are cases [true cases correctly identified/(false positives plus true cases correctly identified)]. The receiver operating characteristic curves [11] were obtained by plotting sensitivity and (1 − specificity) for each possible score on each questionnaire. The greater the area under the curve, the better the performance of the questionnaire.

RESULTS

Sample

546 patients were invited to participate but 21 (4%) refused. 11 (2%) were lost through tape-recorder failure. The disease status of 1 patient could not be determined. 231 (45%) men and 282 women (55%) participated. Their median age was 50–59 years (range 16–86). Most patients had cancer of the breast (93, 18%), lung or bronchus cancer (159, 31%), Hodgkin's disease or lymphoma (103, 20%). 267 (52%) patients were interviewed within the first year of diagnosis, while 503 (98%) were seen within 5 years.

More patients had stable (192, 37%) than progressive disease (159, 31%). 161 patients (31%) were considered disease-free, while 291 (57%) were on chemotherapy or radiotherapy.

Reliability

Four tapes were assessed by all four interviewers. Average agreement on all items was 90%.

Prevalence

86 (17%) patients were found to be suffering from a generalised anxiety disorder or major depressive illness as assessed by the Psychiatric Assessment Schedule. Affective disorders were related both to the disease (disease-free 20, 12%; stable 31, 16%; progressive 35, 22%) and treatment status (off treatment 31, 14%; on treatment 55, 19%).

Overall performance

Questionnaires had to achieve a sensitivity of 80% and a specificity of 70% for the areas under the curve to be compared. The results are summarised in Tables 1 and 2.

The HADS performed best in the whole sample (area 0.88). At a score of over 14, it had a sensitivity of 80%, specificity of 76% and a positive predictive value of 41%. Thus, 2/5 patients scoring over 14 would be true cases. The RSCL (area 0.83) performed almost as well (at a threshold of over 7, sensitivity 83%, specificity 71%, and positive predictive value 37%). The GHQ failed to meet the minimal criteria (sensitivity 72%, specificity 71%) at an optimal threshold score of over 7.

Effect of disease status

The HADS (area 0.95) best identified those patients who had an affective disorder despite being free of cancer. At a threshold of over 19, sensitivity was 92%, specificity 95% and the positive predictive value 72%. Hence, nearly 3/4 high scorers were cases.

The GHQ (area 0.89) performed just below the required level for sensitivity (75%) at a score of over 8, but had a high specificity

Table 1. Screening performance by disease status

Overall sample	Number completeted	Area under the curve	Confidence intervals	Optimal score	Sensitivity (%)	Specificity (%)	Positive predictive value (%)
HADS	284	0.88	(0.83–0.93)	> 14	80	76	41
RSCL	266	0.83	(0.77–0.89)	> 7	83	71	37
Disease-free							
HADS	88	0.95	(0.90–0.99)	> 19	92	95	72
GHQ	95	0.89	(0.85–0.93)	> 8	75	92	69
RSCL	81	0.84	(0.74–0.93)	> 7	80	74	30
Stable disease							
HADS	113	0.89	(0.82–0.96)	> 15	83	78	42
RSCL	102	0.86	(0.78–0.95)	> 7	84	74	34
Progressive disease							
RSCL	83	0.77	(0.66–0.88)	> 9	83	71	45

Table 2. Screening performance by treatment status

	Number completed	Area under the curve	Confidence intervals	Optimal score	Sensitivity (%)	Specificity (%)	Positive predictive value (%)
On treatment							
RSCL	146	0.84	(0.77–0.91)	> 7	83	72	41
HADS	165	0.90	(0.84–0.95)	> 15	85	77	47
Off treatment							
GHQ	133	0.85	(0.77–0.92)	> 7	88	79	41
RSCL	146	0.81	(0.73–0.90)	> 7	82	70	31

(92%) and positive predictive value (69%). The RSCL (area 0.84) performed least well in terms of the positive predictive value of 30% in those scoring over 7.

Stable disease

The HADS (area 0.89) was the most effective questionnaire in those with stable disease. At a threshold of over 15, it had a sensitivity of 83%, a specificity of 78% and a positive predictive value of 42%. The RSCL (area 0.86) did almost as well (sensitivity 84%, specificity 74%, positive predictive value 34%).

Progressive disease

Only the RSCL (area 0.77) achieved the required sensitivity and specificity in this group. At a score of over 9, sensitivity was 83%, specificity 71%, with a positive predictive value of 45%.

Effect of treatment

The HADS (area 0.90) worked best in patients on active treatment. At a score of over 15, the sensitivity was 85%, specificity 77% and positive predictive value 47%. The RSCL (area 0.84) was slightly less effective (sensitivity 83%, specificity 72%, positive predictive value 41%). The GHQ did not meet the required criteria (sensitivity 73%, specificity 60%).

In patients off treatment, the GHQ (area 0.85) was superior. At a score of over 7, sensitivity was 88%, specificity 79% and positive predictive value 41%. The RSCL failed to meet the criteria (sensitivity 79%, specificity 72%), while the HADS just fulfilled them (sensitivity 82%, specificity 70%, positive predictive value 31%).

DISCUSSION

The prevalence rate of 17% of patients with cancer having a major depressive illness and/or generalised anxiety disorder is lower than the psychiatric morbidity reported by Derogatis and colleagues [1]. However, we excluded adjustment disorders from our analyses because we wished to focus on major mental illness which should respond to psychiatric interventions. Adjustment disorders accounted for most of their morbidity. The fact that nearly 1 in 5 cancer patients within a heterogeneous sample suffer from an affective disorder justifies the case for screening.

As Derogatis and coworkers [1] found, the prevalence of affective disorders increased with disease status and treatment.

Both the HADS and RSCL performed well in the overall sample, confirming the findings of Razavi and coworkers [12], and de Haes *et al.* [13], respectively. Thus, clinicians or nurses could use them to screen out 'probable cases'. High scorers could then be assessed by a specialist nurse who could initiate therapy, refer the patient for a psychiatric opinion or liaise with the general practitioner. A controlled trial in which half the high scorers were referred to a specialist nurse and half were given routine cancer care would determine the value of screening for affective disorders.

The performance of the three questionnaires varied by disease and treatment status. The RSCL performed most consistently in those with disease or on treatment. It was the only questionnaire to be effective in patients with progressive disease. However, the threshold scores had to be adjusted by disease status for case-finding to be optimal.

As expected, the HADS did well in all groups, except those with progressive disease. Adjustments in threshold scores according to disease and treatment status were necessary for optimal case-finding. The better performance of the HADS in patients receiving radiotherapy or chemotherapy suggests that the absence of somatic items prevents adverse side-effects from contaminating the result. Yet, the exclusion of somatic items did not prevent its screening performance weakening in those with progressive disease.

The GHQ 28 performed reasonably well in those who were off treatment. However, it failed to fulfil the minimum criteria in the other groups. Increasing the threshold score was not as effective here as a strategy as it was in a study of affective disorders in patients with multiple sclerosis [6].

Overall, the HADS and the RSCL were the more effective questionnaires at detecting major depressive illness and generalised anxiety disorders in a wide spectrum of cancer patients. As an earlier study of patients with advanced breast cancer found [14], they may screen out different individuals with affective disorders. This possibility, together with the effects of psychiatric diagnostic systems on screening performance, are considered in a comparison paper. Meanwhile, the use of either or both of these questionnaires by clinicians or specialist nurses should do much to improve the recognition and treatment of affective disorders in patients with cancer.

1. Derogatis LR, Morrow GR, Fetting J, *et al.* The prevalence of psychiatric disorders among cancer patients. *J Am Med Assoc* 1983, **249**, 751–757.
2. Maguire P. Psychological morbidity associated with cancer and cancer treatment. *Clin Oncol* 1985, **4**, 559–575.
3. Maguire P. Barriers to psychological care of the dying. *Br Med J* 1985, **291**, 1711–1713.
4. Maguire GP, Tait A, Brooke M, Thomas C, Sellwood RA. Effect of counselling on the psychiatric morbidity associated with mastectomy. *Br Med J* 1980, **281**, 1454–1456.

5. Gold I, Haughey L, Baraff LJ. Psychiatric screening in the emergency department: validation of the General Health Questionnaire. *Am J Emergency Med* 1985, **3**, 419–422.
6. Bridges KW, Goldberg DP. The validation of the GHQ-28 and use of the MMSE in neurological inpatients. *Br J Psychiatry* 1986, **148**, 548–553.
7. Morris PLP, Goldberg RJ. Validity of the 28-item General Health Questionnaire in hospitalised gastro-intestinal patients. *Psychosomatics* 1986, **30**, 290–295.
8. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiat Scand* 1983, **67**, 361–370.
9. de Haes JCJM, Pruyn JFA, van Knippenberg FCE. Klachtenlijst voor kankerpatienten, erste ervaringen. *Ned Tijdschr Psychol* 1983, **38**, 403–422.
10. Dean C, Surtees PG, Sashideran SP. Comparison of research diagnostic systems in an Edinburgh Community sample. *Br J Psychiatry* 1983, **142**, 247–256.
11. Hanley JA, McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. *Radiology* 1983, **148**, 839–842.
12. Razavi D, Delvaux N, Farvacques C, Rabaye E. Screening for adjustment disorder and major depressive illness in cancer inpatients. *Br J Psychiatry* 1990, **156**, 79–83.
13. de Haes JCJM, van Knippenberg FCE, Neijt JP. Measuring psychological and physical distress in cancer patients: structure and application of the Rotterdam Symptom Checklist. *Br J Cancer* 1990, **62**, 1034–1038.
14. Hopwood P, Howell AH, Maguire P. Screening for psychiatric morbidity in patients with advanced breast cancer: validation of two self-report qustionnaires. *Br J Cancer* 1991, **64**, 353–356.

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Non-palpable Lesions of the Breast Detected by Mammography — Review of 1182 Consecutive Histologically Confirmed Cases

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We report on 1182 consecutive histologically confirmed non-palpable breast lesions detected by mammography (infiltrating carcinoma 427, *in situ* carcinoma 121, benign 634). The proportion of cancer cases varied according to age (< 50 years = 33%; 50–59 years = 46%; > 59 years = 63%), mammographic pattern (regular opacities = 8%, parenchymal distortions = 20%, isolated calcifications = 42%, irregular opacities = 62%, stellate opacities = 73%), and calendar period (1970–1985 = 29%, 1986–1989 = 56%; 1990–1992 = 69%). A sharp decrease of the benign/maligant biopsy ratio was evident after routine fine-needle aspiration cytology (sonography-guided or stereotaxic) was introduced in 1986. The independent significant association of cancer frequency to age, calendar period and mamographic pattern was confirmed by multivariate analysis. A signifcant trend over time in favour of conservative surgery was also observed for cancer cases (1970–1979 = 6%, 1980–1985 = 41%, 1986–1992 = 83%). Among invasive cancers, node involvement was observed in 11.5% of cases, being associated with tumour size (pT1a = 0%, pT1b = 7%, pT1c = 13%, pT2a = 33%). Five-, ten- and fifteen-year overall survivals of invasive cancers were 98.1, 95.7 and 87.3%, respectively.
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INTRODUCTION

SUSPICIOUS NON-PALPABLE lesions of the breast are increasingly detected due to the widespread use of mammography, performed either for screening or clinical purpose [1, 2]. Unfortunately, mammography is not very specific, and the detection of subclinical cancer results in a relatively high number of unnecessary biopsies for benign lesions [1, 3]. The use of stereotactic or sonography-guided cytology has greatly improved the accuracy of preoperative diagnosis, and the benign/malignant biopsy ratio has been reduced considerably [3–6].

Non-palpable breast cancer may be managed by conservative surgery in the majority of cases, and has a very favourable prognosis in terms of survival [2, 7]. Although length biased sampling, lead time bias and overdiagnosis must be taken into account, preclinical detection is possibly the major benefit of mammographic screening, which has been shown to significantly reduce breast cancer mortality [8].