PERGAMON

European Journal of Cancer 37 (2001) 216–223

European Journal of Cancer

www.ejconline.com

Predicting mood disorders in breast cancer patients

G. Morasso [a,*], M. Costantini [b], P. Viterbori [b], F. Bonci [c], L. Del Mastro [d], M. Musso [a], O. Garrone [d], M. Venturini [d]

[a] *Department of Psychology, National Cancer Institute, L.go R.Benzi, 10, 16132 Genova, Italy*
[b] *Unit of Clinical Epidemiology and Trials, National Cancer Institute, Genova, Italy*
[c] *Department of Medical Oncology, Ospedale S.Chiara, via Roma, 67, 56127 Pisa, Italy*
[d] *Department of Medical Oncology I, National Cancer Institute, Genova, Italy*

Received 12 May 2000; received in revised form 12 September 2000; accepted 23 October 2000

Abstract

Prediction of delayed psychiatric disorders in breast cancer patients by using a screening procedure was investigated. Two questionnaires, the Psychological Distress Inventory and the Hospital Anxiety and Depression Scale, were administered before and during chemotherapy, and at the first follow-up visit. A psychiatric diagnosis was assigned to 50 of the 132 patients (38%) evaluated at follow-up. Including a set of clinical and demographic variables in a logistic regression, increasing age ($P = 0.001$) and psychiatric history ($P < 0.001$) were associated with psychiatric morbidity at follow-up. The accuracy of the two questionnaires in predicting delayed psychiatric disorders increased from the evaluation before chemotherapy to the evaluation during chemotherapy. The most accurate prediction was observed for the concurrent evaluation at follow-up. The accuracy of three predictive models developed for each evaluation point by including age, psychiatric history and psychological distress measured with each of the two questionnaires was not significantly better than that observed using only the questionnaires' scores as predictors.

Keywords: Breast cancer; Hospital Anxiety and Depression Scale; Psychological Distress Inventory; Prediction

1. Introduction

Psychological and psychiatric disturbance related to breast cancer have been previously reported [1,2]. In particular, the prevalence of depressive disorders in breast cancer patients ranges from 0 to 46% and that of anxiety from 1 to 49% depending on the time of evaluation [3]. Generally, psychological disturbance diminishes in the course of time and only few patients develop psychiatric problems, although the frequency of psychiatric disorders has been found to remain stable in the first year after surgery [4]. Many psychological intervention programmes have been shown to be beneficial in cancer patients [5,6]. Nevertheless, only a minority of patients is appropriately referred for psychosocial support [7]. For this reason, screening procedures have been described in order to promote the detection of cancer patients with psychological problems who could benefit from specific interventions [8,9]. Various self-report questionnaires such as the Hospital Anxiety and Depression Scale (HAD), the General Health Questionnaire, the Rotterdam Symptom Checklist and the Brief Symptom Inventory have been used for such purpose [10,11].

Another approach involves predicting those patients who are likely to develop affective disorders, so that interventions can be aimed at high-risk patients in order to reduce subsequent morbidity. Self-report questionnaires administered pre-operatively or immediately after diagnosis have been used for this purpose [12,13]. Alternatively, the use of a set of potential predictors of psychiatric morbidity such as patient characteristics, disease and treatment variables, factors relating to patient's environment has also been suggested [14].

The aim of this study was to investigate the possibility of predicting the occurrence of a psychiatric disorder during follow-up, by means of a screening procedure performed before or during the adjuvant chemotherapy in breast cancer patients. The study involved: (1) the

* Corresponding author. Tel.: +39-010-560-0643; fax: +39-010-353-4643.
E-mail address: morasso@hp380.ist.unige.it (G. Morasso).

0959-8049/01/$ - see front matter
PII: S0959-8049(00)00390-7

identification of a possible association between the patients' demographic and clinical characteristics obtained before chemotherapy, and the subsequent diagnosis of a psychiatric disorder at follow-up; (2) the assessment of the sensitivity and specificity of two self-report questionnaires administered before or during the chemotherapy in predicting the psychiatric disorder; and (3) the development of a model based on the data resulting from points 1 and 2, in order to provide a better estimate of the probability of subsequent psychiatric morbidity.

2. Patients and methods

All patients enrolled in the MIG-1 (Mammella Inter-Group) randomised trial between December 1994 and October 1996 by two centres (Genoa and Pisa) were asked to participate in this study. Written consent was only requested for the main randomised study (MIG-1). For this study, verbal consent was requested from patients. Patients who agreed were considered eligible. According to the MIG-1 protocol [15], stage I-III breast cancer patients (T1-4, N0-1, M0) aged less than 70 years, were randomised to receive standard adjuvant chemotherapy with six cycles of 5-fluorouracil, epirubicin and cyclophosphamide every 21 days, or the same chemotherapy every 14 days supported by granulocyte-colony stimulating factor. Patients with unifocal tumours, with a diameter less than 5 cm, were offered conservative therapy, and subsequent regional radiotherapy limited to the remaining breast. Patients with oestrogen receptor positive tumours received tamoxifen 20 mg/day concurrently or at the end of chemotherapy.

Potential predictors of psychiatric morbidity at the follow-up visit included patient-related factors (age, menopausal status, education, psychiatric history), disease and treatment-related variables (TNM, histology, oestrogen and progesterone receptors, type of surgery). Global psychological distress was evaluated by two self-report questionnaires validated as screening instruments (the Psychological Distress Inventory (PDI) and the HAD). These were administered before the start of the chemotherapy, 42 days after the first cycle, and at the first follow-up visit, when psychiatric morbidity was also evaluated. The PDI is a questionnaire conceived and validated in Italy [16] for use in cancer patients. It evaluates the general emotional condition of the patient and the psychological disorders related to illness adjustment. It consists of 13 items answerable on a five-point Likert scale. The global score ranges from 13 to 65 with higher scores reflecting greater distress. The HAD is a 14 item questionnaire developed to detect states of anxiety (seven items) and depression (seven items), and specifically designed for patients with physical illness [17]. Each item is answerable on a four-point Likert scale. The global score ranges between 0 and 42, with higher scores reflecting greater distress. The psychometric properties of the Italian version of the HAD have been tested and reported elsewhere [18]. Demographic and clinical data, including psychiatric history, were obtained from medical records. A psychiatric history was considered present if the presence of a psychiatric problem or the use of specific treatments for psychiatric disturbance was reported in the medical records.

Psychiatric morbidity was assessed at the first follow-up visit in the first year after the start of chemotherapy. Patients were interviewed by two clinical psychologists blind to the scores of the questionnaires previously administered, using a shortened version of the Structured Clinical Interview (SCID) [19]. The interview was aimed at identifying patients with a full psychiatric diagnosis according to the DSM-III-R criteria [20]. For the purpose of the present analysis, a patient was defined 'a psychiatric case', if the clinical interview led to a psychiatric diagnosis according to the DSM-III-R criteria. After the first four interviews, the procedures used by the two clinical psychologists to interview the patients and to evaluate their clinical symptoms were discussed at a consensus meeting with the main investigator.

3. Statistics

The association between demographic and clinical characteristics of the patients and the psychiatric morbidity diagnosed at the follow-up visit was studied using the standard Chi-square for heterogeneity test. The diagnostic accuracy of the questionnaires in identifying the psychiatric disorder diagnosed at the follow-up visit was evaluated by means of a ROC analysis. The ROC curve, expressing the relationship between sensitivity and specificity for each score of the questionnaire, represents an index of the accuracy of the test. The overall accuracy of the test was estimated by means of the area under the curve (AUC).

In multivariate analysis, the probability of identifying a psychiatric disorder at the follow-up visit was firstly modelled as a function of the demographic and clinical characteristics of the patients using a logistic regression analysis. Starting from the complete model, with all variables included, variables with a P value >0.15 were progressively deleted with a step-down procedure, based on a likelihood ratio test. For each questionnaire, three clinical prediction models were then developed, one for each evaluation, that incorporated the variables identified in the previous step. For each variable, the coefficients ($\pm$SEM) were computed as a measure of the strength of the association. The accuracy of each model in identifying the psychiatric disorder at the follow-up visit was evaluated by means of the ROC analysis, and the corresponding AUC reported.

4. Results

197 patients were randomised in the MIG-1 trial in the two centres participating to this study. 13 patients were excluded (12 refused and 1 because the patient was deaf and dumb), leaving 184 patients eligible for this study.

A clinical interview was administered to 132 patients (71.7%). The interview and both the questionnaires were available for 113 patients at baseline (61.4%), 105 patients during chemotherapy (57.1%), and 132 at the follow-up visit (71.7%). Practical and administrative problems account for approximately 80% of the missing data. After enrolment, only 1 patient (during chemotherapy) declined to fill in the questionnaires. Clinical and demographic characteristics of the 184 eligible patients, and the number and proportions of evaluated patients at the three points of evaluation are reported in Table 1.

50 patients (38%) of the 132 who had a clinical interview were assigned a current DSM-III-R psychiatric diagnosis. According to DSM-III-R criteria, 13 patients

Table 1
Characteristics of the 184 eligible breast cancer patients, and number (%) of patients evaluated before and during chemotherapy and at the follow-up visit

		Evaluated patients[a]		
	n	Before chemotherapy *n* (%)	During chemotherapy *n* (%)	Follow-up *n* (%)
Age (years)				
⩽ 50	74	44 (59.5)	44 (59.5)	49 (66.2)
51–60	62	37 (59.7)	34 (54.8)	46 (74.2)
>60	48	32 (66.7)	27 (56.3)	37 (77.1)
Menopausal status				
Pre menopausal	76	46 (60.5)	46 (60.5)	53 (69.7)
Post menopausal	108	67 (62.0)	59 (54.6)	79 (73.1)
Education (years)				
⩽5	69	49 (71.0)	46 (66.7)	56 (81.2)
6–8	52	26 (50.0)	21 (40.4)	32 (61.5)
>8	58	38 (65.5)	38 (65.5)	44 (75.9)
unknown	5			
Psychiatric history				
No	124	105 (84.7)	97 (78.2)	124 (100.0)
Yes	8	8 (100.0)	8 (100.0)	8 (100.0)
Unknown	52			
Pathological tumour size				
pT1	104	69 (66.3)	62 (59.6)	79 (76.0)
pT2-4	80	44 (55.0)	43 (53.8)	53 (66.3)
Pathological nodes				
pN0	80	59 (73.8)	52 (65.0)	62 (77.5)
pN1	104	54 (51.9)	53 (51.0)	70 (67.3)
Histology				
Ductal	152	96 (63.2)	91 (59.9)	112 (73.7)
Others	32	17 (53.1)	14 (43.8)	20 (62.5)
Oestrogen receptors				
Positive	68	47 (69.1)	44 (64.7)	54 (79.4)
Negative	111	65 (58.6)	60 (54.1)	75 (67.6)
Unknown	5			
Progesterone receptors				
Positive	103	67 (65.0)	60 (58.3)	76 (73.8)
Negative	72	44 (61.1)	43 (59.7)	51 (70.8)
Unknown	9			
Surgery				
Conservative	135	89 (65.9)	82 (60.7)	102 (75.6)
Radical	49	24 (49.0)	23 (46.9)	30 (61.2)
All patients	184	113 (61.4)	105 (57.1)	132 (71.7)

[a] Evaluated patients at each point are those who received a clinical interview and completed the two questionnaires available.

(9.8%) were diagnosed with Major Depressive Disorder. Adjustment disorders were classified as adjustment disorders with depressed mood (14 patients); with anxiety (8 patients); with mixed anxiety and depressed mood (6 patients); with mixed disturbance of emotions and conduct (3 patients); and unspecified (1 patient). Anxiety disorders were identified in 2 patients, dementia in 1 patient and a hypomanic episode in 2 patients.

The association between demographic and clinical variables and the presence of a psychiatric disorder at the follow-up visit are reported in Table 2. The proportion of psychiatric disorders significantly increased with increasing age ($P<0.001$), and was higher among post menopausal patients (46% versus 26%; $P=0.026$), and in patients with a history of psychiatric disorders (88% versus 35%; $P=0.003$). No significant difference in the proportion of mood disorders was observed for the other variables (Table 2) and between the two chemotherapy regimes ($P=0.225$; data not shown). When all variables were included in a logistic regression analysis only age ($P=0.001$) and psychiatric history ($P<0.001$) were retained in the model, using a P value of 0.15 as a cut-off.

Sensitivity, specificity and positive predictive value (PPV) of the PDI and the HAD, at the three points of evaluation are reported in Table 3. Before chemotherapy, the AUC for the PDI and the HAD were 73.9 and 68.6, respectively. The optimum threshold for the

Table 2
Distribution of the psychiatric disorders diagnosed at the follow-up visit in 132 breast cancer patients

		Psychiatric disorders at follow-up	
	n	*n* (%)	
Age (years)			
< 50	49	12 (24)	
51–60	46	15 (33)	
> 60	37	23 (62)	$P=0.001$
Menopausal status			
Premenopausal	53	14 (26)	
Postmenopausal	79	36 (46)	$P=0.026$
Education (years)			
⩽5	56	27 (48)	
6–8	32	9 (28)	
> 8	44	14 (32)	$P=0.104$
Psychiatric history			
No	124	43 (35)	
Yes	8	7 (88)	$P=0.003$
Pathological tumour size			
pT1	79	28 (35)	
pT2–4	53	22 (42)	$P=0.481$
Pathological nodes			
pN0	62	27 (44)	
pN1-2	70	23 (33)	$P=0.206$
Histology			
Ductal	112	42 (38)	
Others	20	8 (40)	$P=0.832$
Oestrogen receptors			
Positive	54	20 (37)	
Negative	75	29 (39)	$P=0.851$
Progesterone receptors			
Positive	76	33 (43)	
Negative	51	15 (29)	$P=0.110$
Surgery			
Conservative	102	40 (39)	
Radical	30	10 (33)	$P=0.559$
All patients	132	50 (38)	

Table 3
Ability of the two questionnaires (PDI and HAD) administered before, during and after chemotherapy in identifying a psychiatric disorder at the follow-up visit

	SENS	SPEC	PPV	AUC (95% CI)
Before chemotherapy ($n=113$)				
Psychological Distress Inventory				
27	73.8	66.2	56.4	
28	71.4	69.0	57.7	
29	64.3	73.2	58.7	73.9
30	54.8	74.6	56.1	(65–83)
Hospital Anxiety and Depression Scale				
9	81.0	47.9	47.9	
10	71.4	53.5	47.6	
11	71.4	60.6	51.7	68.6
12	66.7	62.0	50.9	(59–79)
During chemotherapy ($n=105$)				
Psychological Distress Inventory				
27	79.5	68.2	59.6	
28	79.5	69.7	60.8	
29	76.9	71.2	61.2	81.5
30	76.9	78.8	68.2	(73–90)
Hospital Anxiety and Depression Scale				
9	79.5	60.6	54.4	
10	74.4	72.7	61.7	
11	66.7	77.3	63.4	77.5
12	64.1	78.8	64.1	(68–86)
1st Follow-up visit ($n=132$)				
Psychological Distress Inventory				
27	84.0	78.0	70.0	
28	72.0	86.6	76.6	
29	68.0	90.2	81.0	91.1
30	64.0	93.9	86.5	(86–96)
Hospital Anxiety and Depression Scale				
9	84.0	70.7	63.6	
10	84.0	79.3	71.2	
11	70.0	87.8	77.8	88.7
12	70.0	91.5	83.3	(83–94)

SENS, sensitivity; SPEC, specificity; PPV, positive predictive value; AUC, area under the curve; CI, confidence intervals.

PDI was 28, corresponding to a PPV of 57.7, and to a sensitivity and specificity of 71.4 and 69.0, respectively. Using a cut-off of 11, the sensitivity and specificity of the HAD were 71.4 and 60.6, respectively, and the PPV was 51.7. During chemotherapy, the performance of the two questionnaires increased, with an AUC for the PDI and the HAD of 81.5 and 77.5, respectively. When the questionnaires were administered at the follow-up visit, concurrently with the evaluation of the psychiatric morbidity, the AUC for the PDI and the HAD was 91.1 and 88.7, respectively.

Six models were fitted to the data by including age, presence of psychiatric disorders and psychological distress measured, in turn, with the PDI and with the HAD, at baseline, during chemotherapy, and at the follow-up visit (Table 4). In all models, psychological distress, measured with either the PDI or the HAD, was significantly associated with the outcome. The contribution of the other two variables (age and psychiatric history) decreased from the evaluation before chemotherapy to the evaluation at the follow-up visit. The accuracy of the two multivariate models (with the PDI and with the HAD) was comparable before chemotherapy (AUC = 78.2 and 77.0, respectively), during chemotherapy (AUC = 81.6 and 80.4, respectively), and at the follow-up (AUC = 91.8 and 90.7, respectively).

The overall accuracy of the multivariate models, measured with the AUC, was only slightly better than that observed in the univariate approach before and during chemotherapy (Fig. 1a and b), and virtually the same at the follow-up visit (Fig. 1c).

Table 4
Ability of the three models (before, during and after chemotherapy) to identify a psychiatric disorder at the follow-up visit

	Multivariate analysis[a]			
	With the PDI		With the HAD	
	Coefficient ±SEM	*P* value	Coefficient ± SEM	*P* value
Before chemotherapy ($n=113$)				
Age	0.74±0.28	0.009	0.78±0.28	0.005
Psychiatric history	2.82±1.20	0.019	3.05±1.19	0.010
PDI	0.11±0.04	0.002	–	–
HAD	–	–	0.10±0.04	0.005
AUC (95%CI)	78.2 (69–87)		77.0 (68–86)	
During chemotherapy ($n=105$)				
Age	0.29±0.30	0.346	0.38±0.30	0.202
Psychiatric history	2.07±1.14	0.071	2.56±1.15	0.026
PDI	0.13±0.04	<0.001	–	–
HAD	–	–	0.12±0.03	< 0.001
AUC (95%CI)	81.6 (73–90)		80.4 (72–89)	
First follow-up visit ($n=132$)				
Age	0.31±0.36	0.379	0.50±0.34	0.142
Psychiatric history	1.48±1.33	0.268	3.09±1.30	0.017
PDI	0.31±0.06	<0.001	–	–
HAD	–	–	0.33±0.06	<0.001
AUC	91.8 (87–96)		90.7 (85–96)	

[a] Coefficients ± standard errors estimated from multiple logistic regression models including age, psychiatric history, and the psychological distress measured before, during chemotherapy, and at the first follow-up visit (with the Psychological Distress Inventory and with the Hospital Anxiety and Depression Scale).

SEM, standard error of the mean; PDI, Psychological Distress Inventory; HAD, Hospital Anxiety and Depression Scale; AUC, area under the curve.

5. Discussion

Screening strategies for detecting psychiatric disorders in cancer patients are usually aimed at identifying existing psychological morbidity. The effectiveness of such an approach has been assessed using many brief instruments, in a number of different populations [10,11,16].

In this study, the accuracy of the PDI and the HAD against a clinical interview at the first follow-up visit was high, and comparable with previous findings [11]. Although a specific threshold has not been proposed for the PDI, the overall accuracy is similar to that previously observed in a validation set [16]. For the HAD, using a cut-off of 11, sensitivity and specificity were 70 and 88%, respectively. In our study, no major difference was found in the accuracy of the two questionnaires when they were administered at the same time of the clinical interview, to detect concurrent psychiatric disorders.

The alternative strategy, which was explored in this study, aims to evaluate to what extent a psychiatric disorder at follow-up can be predicted by a brief questionnaire administered 3 to 6 months earlier. In this case, the accuracy of the PDI and the HAD was comparable at both evaluation points. The overall accuracy, measured by the AUC, of the PDI and HAD questionnaires decreased by 19 and 23%, respectively, when administered before chemotherapy, and by 10 and 13%, respectively, when administered during chemotherapy, as compared with the concurrent evaluation. At a threshold of 11, the sensitivity and specificity of the HAD were 71.4 and 60.6%, respectively, before chemotherapy, and 66.7 and 77.3%, respectively, during chemotherapy. The probability of having a psychiatric disorder among patients positive at the test (the PPV reported in Table 3) ranged from 48 to 59 before chemotherapy and from 54 to 68 during chemotherapy.

Although an association between initial psychological status and subsequent adaptation has been shown in many studies [21–23], only two other groups have explored the possibility of using a short questionnaire administered before treatment in order to predict subsequent psychiatric disorder [12,13]. Ramirez and colleagues [12] administered the HAD preoperatively

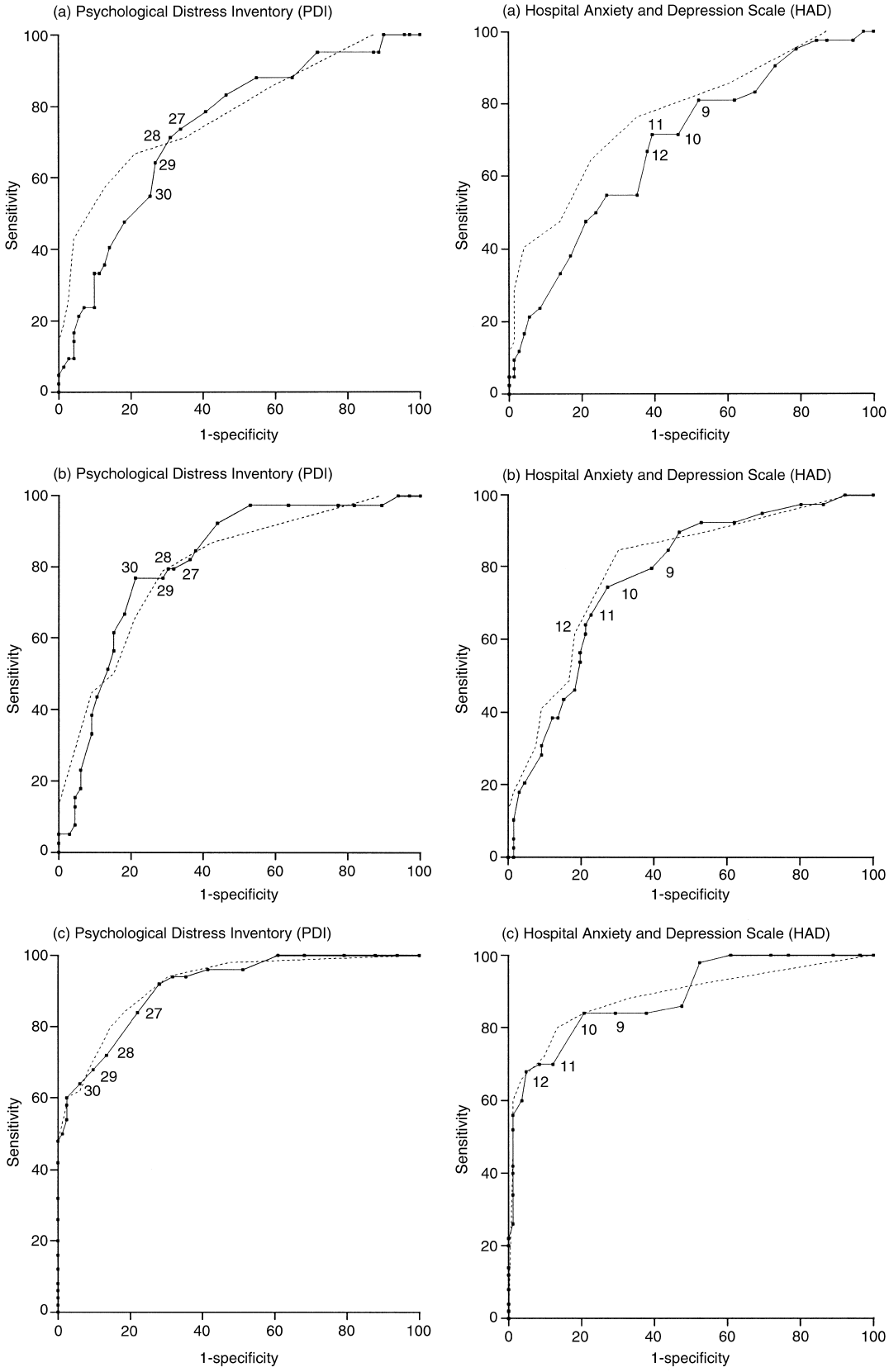

Fig. 1. Receiver operating characteristics (ROC) curves of the questionnaires administered (a) before chemotherapy; (b) during chemotherapy; and (c) concurrently with the clinical interview, and of the multivariate logistic models in detecting patients with psychiatric disorders at the follow-up: univariate analysis —; multivariate analysis - - - -. Note: the probability of identifying a psychiatric disorder at the follow-up was estimated in each multivariate logistic model by including the score of the questionnaire (either the PDI or the HAD), age and psychiatric history.

and found that, with a cut-off of 11, 70% of breast cancer patients at risk of having full or borderline mood disorders at some point in the year after diagnosis were correctly identified. Nordin and Glimelius [13] reported that the HAD with a cut-off of 8 in addition to a subscale of the Impact of Event Scale administered close to diagnosis could identify patients at risk of delayed anxiety and depression with a sensitivity of 75% and a specificity of 98%.

The use of a model including age and psychiatric history in addition to psychological distress measured with the two questionnaires did not increase the predictive accuracy significantly. The association between demographic and clinical variables and the presence of psychiatric disorders at follow-up visit was consistent with previous studies [2,12,14,21–31]. Unexpectedly, increasing age was predictive of mood disorders at the follow-up visit. Among cancer patients, some studies have shown no relationship between age and psychiatric morbidity [14], and, when an association has been demonstrated, older patients fare better [3,12]. The trend observed in this study — confirmed also when the definition of cases was limited to depression and anxiety — is difficult to explain. If confirmed in other studies, this discrepancy should be studied further with more analytical approaches. Factors such as tumour size, pathological nodes and histology were not found to predict subsequent psychological status as previously reported [22,24]. Also type of surgery did not have a predictive value. The relationship between total mastectomy and psychological distress has been well documented [25,26] and it has been suggested that breast-conservative surgery might have been associated with better illness adjustment [27]. Nevertheless, studies that compared the psychosocial outcome of mastectomy with conservative surgery have found little difference in terms of psychiatric morbidity [28,29]. No association has been found between psychological distress and hormone receptor status. Oestrogen receptor status has been suggested as a possible link between psychological factors and disease course in breast cancer. Razavi and colleagues [30] reported more psychological distress in patients with negative oestrogen receptors and suggested that this results could explain the relationship between psychological variables and survival. In contrast, Tjemsland and colleagues [31] did not find any association between a broad spectrum of psychological dimensions and oestrogen receptor status. Psychological variables, such as coping styles, and factors relating to patient's environment, such as social support, have been found to be associated with illness adjustment, besides demographic and clinical characteristics [14]. Though these variables were not taken into account in the present study, since they are not assessed in current clinical practice, further studies are needed to explore their role in predicting psychological disorders.

The prevalence of psychiatric disorders found in the present sample (38%) is difficult to compare with that of previous studies. Dean [26] found, for example, that 5% of women evaluated by a psychiatrist were clinically ill 12 months after surgery, while 18% had minor depressive disorders and 5% generalised anxiety disorders. Hall and colleagues [32] using the Present State Examination identified anxiety disorders and depressive illness, respectively, in 49.6 and 37.2% of women treated for early breast cancer and evaluated during the first three months after their initial surgery. The use of different diagnostic criteria may account for the difference in rates. For example, diagnosis of major depression in cancer patients differs depending on the diagnostic system used [33]. Furthermore, time of evaluation is another important factor since psychological disturbance changes in the course of time [3,12].

A comparison between a predictive and concurrent screening for psychiatric disorders must consider both the accuracy of the procedure and the benefit of the intervention. Unfortunately, little is known about the efficacy and the costs of an early psychosocial intervention in cancer patients. It is, therefore, difficult to make a comparison between a more accurate screening procedure which detects existing psychiatric morbidity and a less accurate procedure which predicts it. If the decrease in accuracy of a predictive approach were, for example, balanced by an increase in efficacy due to the earlier intervention, such a strategy might be considered.

Acknowledgements

This work was supported in part by P.F. CNR ACRO. The authors thank Dr Paolo Bruzzi, head of the Unit of Clinical Epidemiology and Trials (National Cancer Institute, Genova) for the statistical revision of this paper.

References

1. Kissane DW, Clarke DM, Ikin J, *et al*. Psychological morbidity and quality of life in Australian women with early-stage breast cancer: a cross-sectional survey. *Med J Aust* 1998, **169**, 192–196.
2. Green BL, Rowland JH, Krupnick JL, *et al*. Prevalence of post-traumatic stress disorder in women with breast cancer. *Psychosomatics* 1998, **39**, 102–111.
3. Van't Spijker A, Trijsburg RW, Duivenvoorden HJ. Psychological sequelae of cancer diagnosis: a meta-analytical review of 58 studies after 1980. *Psychosom Med* 1997, **59**, 280–293.
4. Omne-Ponten M, Holmberg L, Burns T, Adami HO, Bergstrom R. Determinants of the psychosocial outcome after operation for breast cancer: results of a prospective study following mastectomy and breast conservation. *Eur J Cancer* 1992, **20A**, 1062–1067.
5. Fawzy IF, Fawzy NV, Arndt LA, Pasnau RO. Critical review of psychosocial interventions in cancer care. *Arch Gen Psychiatry* 1995, **52**, 100–113.

6. Mejer TJ, Mark MM. Effects of psychosocial interventions with adult cancer patients: a meta-analysis of randomised experiments. *Health Psychol* 1995, **14**, 101–108.
7. Maguire P. The recognition and treatment of affective disorder in cancer patients. *Int Rev Appl Psychol* 1984, **33**, 479–491.
8. Razavi D, Delvaux N, Farvacques C, Robaye E. Screening for adjustment disorders and major depressive disorders in cancer patients. *Br J Psychiatry* 1990, **156**, 79–83.
9. Carroll BT, Kathol RG, Noyes R, Wald TJ, Clamon GH. Screening for depression and anxiety in cancer patients using the HADS. *Gen Hosp Psychiatry* 1993, **15**, 69–74.
10. Payne DK, Hoffman RG, Theodoulou M, Dosik M, Massie MJ. Screening for anxiety and depression in women with breast cancer. Psychiatry and medical oncology gear up for managed care. *Psychosomatics* 1999, **40**, 64–69.
11. Ibbotson T, Maguire P, Selby P, Priestman T, Wallace L. Screening for anxiety and depression in cancer patients: the effects of disease and treatment. *Eur J Cancer* 1994, **30A**, 37–40.
12. Ramirez AJ, Richards MA, Jarret SR, Fentiman IS. Can mood disorders in women with breast cancer be identified pre-operatively? *Br J Cancer* 1995, **72**, 1509–1512.
13. Nordin K, Glimelius B. Predicting delayed anxiety and depression in patients with gastrointestinal cancer. *Br J Cancer* 1999, **79**, 525–529.
14. Harrison J, Maguire P. Predictors of psychiatric morbidity in cancer patients. *Br J Psychiatry* 1994, **165**, 593–598.
15. Treatment of early breast cancer — MIG-1. A phase III multicentric randomised trial. National Cancer Institute's PDQ DATABASE, No. CNR-012307.
16. Morasso G, Costantini M, Baracco G, Borreani C, Capelli M. Assessing psychological distress in cancer patients. Validation of a self-administered questionnaire. *Oncology* 1996, **53**, 295–302.
17. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983, **67**, 361–370.
18. Costantini M, Musso M, Viterbori P, *et al*. Psychometric properties and clinical application of the Italian version of the Hospital Anxiety and Depression Scale. *Support Care Cancer* 1999, **7**, 121–127.
19. Spitzer RL, Williams JBW, Gibbon M, First MB. *Structured Clinical Interview for DSM-III-R*. Washington, DC, American Psychiatric Press, 1990.
20. American Psychiatric Association. *Statistical Manual of Mental Disorders*. 3rd edn. Washington, DC, American Psychiatric Press, 1987.
21. Ganz PA, Hirjik K, Myung-Shin S, *et al*. Predicting psychosocial risk in patients with breast cancer. *Med Care* 1993, **31**, 419–431.
22. Ell K, Nishimoto R, Morvay T, Mantell J, Hamovitch M. A longitudinal analysis of psychological adaptation among survivors of cancer. *Cancer* 1989, **63**, 406–413.
23. Hughes J. Emotional reactions to the diagnosis and treatment of early breast cancer. *J Psychosom Res* 1982, **26**, 277–283.
24. Taylor SE, Lichtman RR, Wood JV, *et al*. Illness-related and treatment-related factors in psychological adjustment to breast cancer. *Cancer* 1985, **55**, 2506–2513.
25. Maguire GP, Lee EG, Bevington DJ, *et al*. Psychiatric problems in the first year after mastectomy. *Br Med J* 1978, **1**, 963–965.
26. Dean C. Psychiatric morbidity following mastectomy: pre-operative predictors and types of illness. *J Psychosom Res* 1987, **31**, 385–392.
27. Mueller CB. Valid alternatives in the management of early breast cancer. *Adv Surg* 1987, **20**, 183–216.
28. Fallowfield LJ, Baum M, Maguire GP. Effects of breast conservation on psychological morbidity associated with diagnosis and treatment of early breast cancer. *Br Med J* 1986, **293**, 1331–1334.
29. Dorval M, Maunsell E, Deschenes L, Brisson J. Type of mastectomy and quality of life for long term breast carcinoma survivors. *Cancer* 1998, **83**, 2130–2138.
30. Razavi D, Farvaques C, Delvaux N, *et al*. Psychosocial correlates of hormone receptor status in breast cancer. *Lancet* 1990, **336**, 931–933.
31. Tjemsland L, Soreide JA, Malt UF. Psychosocial factors in women with operable breast cancer. An association to estrogen receptor status? *J Psychosom Res* 1995, **39**, 875–881.
32. Hall A, A'Hern R, Fallowfield L. Are we using appropriate self-report questionnaires for detecting anxiety and depression in women with early breast cancer? *Eur J Cancer* 1999, **35**, 79–85.
33. Kathol RG, Mutgi A, Williams J, Clamon G, Noyes R. Diagnosis of major depression in cancer patients according to four sets of criteria. *Am J Psychiatry* 1990, **147**, 1021–1024.