Taylor & Francis healthsciences

Anxiety and Depressive Symptoms Measured by the Hospital Anxiety and Depression Scale as Predictors of Time to Recurrence in Localized Cutaneous Melanoma

Mia Bergenmar, Bo Nilsson, Johan Hansson and Yvonne Brandberg

From the Department of Oncology-Pathology, Karolinska Hospital and Institutet, Stockholm, Sweden

Correspondence to: Mia Bergenmar, Department of Oncology-Pathology, Karolinska Hospital, SE-171 76 Stockholm, Sweden. Tel: +46 8 5177 3193. Fax: +46 8 326 113. E-mail: mia.bergenmar@ks.se

Acta Oncologica Vol. 43, No. 2, pp. 161–168, 2004

The purpose of this study was to investigate anxiety and depression as predictors for recurrence-free survival in cutaneous melanoma, when corrected for known prognostic factors. The association between known prognostic factors and anxiety and depression were also studied. Consecutive patients (n = 437) completed the Hospital Anxiety and Depression Scale (HAD) approximately three months after diagnosis of melanoma. Neither anxiety, nor depression turned out to be prognostic factors for time to recurrence. A higher proportion of young patients, women, patients without ulcerated tumours, patients with tumours with low mitotic index and Clark's level II tumours scored ≥ 8 (possible clinical levels of anxiety) on the anxiety scale. Furthermore, on the depression scale, a higher proportion of young patients scored ≥ 8 (possible clinical level of depression). Using the HAD scale, a well-validated instrument for assessing anxiety and depression in patients with somatic diseases, our data did not show any associations between anxiety or depression and outcome in terms of recurrence in patients with localized disease.

Received 6 June 2003
Accepted 22 October 2003

Clinical and histopathological factors predicting outcome of patients with cutaneous malignant melanoma (CMM) have been investigated in a number of studies. In a large study of 13 581 cases of melanoma without evidence of nodal or distant metastases conducted in the US, the most important prognostic variables were tumour thickness and ulceration (1). Patient age, tumour site level of invasion and gender were other statistically significant prognostic factors. For patients with thin melanomas (≤ 1.00 mm), the level of invasion was more predictive of survival than tumour ulceration. In a Swedish population-based study, 936 CMM cases diagnosed in the South Swedish Health Care Region were included in an analysis of prognostic factors in invasive CMM (2). In addition to the variables identified by Balch et al. (2001) (1), nodular melanoma was associated with shorter survival in a univariate analysis, but not in a multivariate analysis.

Quality of life and other psychosocial factors have been investigated as prognostic factors for relapse and survival in various cancer types and stages of the diseases (3–15). Studies on psychosocial variables as prognostic factors for melanoma have also been performed in both early (3) and advanced disease (5, 8). In a study investigating psychosocial variables in relation to outcome among patients with early stage CMM, patients who perceived the aim of treatment to be cure, who made less use of avoidance as a coping strategy and who were more concerned about their disease were shown to have longer relapse-free survival after they were controlled for important clinical and pathological factors (3). Being concerned about the disease also significantly predicted longer survival. In another study including CMM patients with advanced disease participating in a chemotherapy trial, mood, appetite and overall quality of life were independent prognostic factors as well as liver metastases and performance status in the multivariate analysis (8). In a study of psychosocial factors and survival in metastatic melanoma, patients who perceived the aim of their treatment to be cure or long-term prolongation of life, who minimized the impact of cancer on their lives and who expressed greater anger about their illness survived longer (5), irrespective of other prognostic factors. In the univariate analysis, all quality of life variables (GLQ-8) were statistically significant prognostic factors, as well as the presence of liver, brain and visceral metastases, not receiving treatment, and being married or widowed. In a 6-year follow-up of a randomized study, Fawzy and co-workers demonstrated an increase in the length of survival among patients with melanoma who had participated in a psycho-

© Taylor & Francis 2004. ISSN 0284-186X
DOI: 10.1080/02841860310021518

educational group intervention (16). However, at the 10-year follow-up there was no significant difference for survival or recurrence between participants in the intervention group and those in the control group (17).

To our knowledge, there has been no other study of anxiety and depressive symptoms after diagnosis as prognostic factors for the outcome of CMM, although it is frequently believed, both among patients and healthcare professionals, that such parameters may influence the faith of patients. In a study of newly diagnosed lung cancer patients 'Depressive reactions' to diagnosis were found to be predictive of survival (4). Depressed patients survived for a significantly shorter time than non-depressed subjects. We therefore sought to investigate the possible influence of anxiety and depression on the outcome of patients with CMM.

In the present study, data on anxiety and depression measured by a standardized instrument were analysed as independent predictors for recurrence in cutaneous melanoma together with well-documented biological risk factors (gender, age at diagnosis, tumour thickness, ulceration, mitotic index, histogenetic type and Clark's level of invasion). The potential interactions of psychological and biological variables in the expression of, and subsequent course of cancer disease have been debated (18). In one of our earlier studies, women who later relapsed had lower scores on the anxiety subscale than those who did not (19). It was hypothesized that lack of worry was associated with delay in seeking medical advice for a suspicious lesion. Thus, a secondary aim was to investigate the association between anxiety and depression and the established prognostic factors mentioned above.

MATERIAL AND METHODS

Subjects

The total study population of 437 patients with CMM consisted of three samples of consecutive patients diagnosed with localized CMM without satellites. Patients aged 20–70 years at first diagnosis of invasive CMM were included in samples 1 and 2 while the upper age limit was ≤ 75 years in sample 3. Patients with another malignant diagnosis before the melanoma, apart from cutaneous squamous cell carcinoma in situ, basal cell cancer and carcinoma in situ of the cervix, were excluded.

Sample 1: 135 patients who participated in a study investigating psychological reactions in patients with malignant melanoma between March 1989 and March 1990 (19).

Sample 2: 203 patients who were included in a randomized study of an information programme diagnosed between October 1991 and April 1993 (20).

Sample 3: 99 patients diagnosed with cutaneous malignant melanoma with a tumour thickness >2.0 mm who participated in a study of the consequences on quality of life of two margins of wide excision diagnosed between April 1994 and December 1999.

Samples 1 and 2 represent long-term follow-up in comparison to sample 3. Patient characteristics are presented in Table 1.

Data collection

Clinical and histopathological parameters. Data were collected from the Stockholm–Gotland Regional Melanoma Registry. Since 1976, all patients in the Stockholm–Gotland Health Care Region (population in the year 2000, 1.8 million, representing 20% of the population of Sweden) with CMM including melanoma in situ and melanoma of unknown origin are prospectively registered. Clinical and histopathological parameters such as gender, age at diagnosis, tumour thickness according to Breslow, ulceration, mitotic index, histogenetic type, level of invasion according to Clark are included in the registry. Before data are registered, all histopathological slides are reviewed by pathologists specialized in CMM. Events such as local recurrence, regional lymph node metastases, disseminated disease and death are reported to the registry and recorded prospectively. Disease recurrence is diagnosed using fine-needle aspiration cytology, histopathology of excised tumours or diagnostic radiological imaging.

Data from clinical records were used in those cases where the patients resided outside the Stockholm–Gotland region at the time of diagnosis but underwent wide excision and follow-up in Stockholm.

The Hospital Anxiety and Depression scale. The Hospital Anxiety and Depression scale (HAD scale) was designed to assess symptoms of anxiety and depression in patients with somatic diseases (21), thus severely psychopathological symptoms and somatic symptoms of anxiety and depression are not included in the questionnaire. The HAD scale consists of 14 items, measuring anxiety and depression on two separate subscales, each consisting of 7 items. There are four response categories to each item (scored 0–3) with a maximum total for each subscale of 21. In a number of studies, the HAD scale has been shown to be reliable and valid in assessing anxiety and depression (22–24).

In a previous Swedish study of patients with cutaneous melanoma, Cronbach's alpha for the anxiety subscale was 0.85 and 0.81 for the depression subscale (25).

All patients completed the HAD scale before the medical examination at the first follow-up visit at the Department of Oncology, which usually occurred approximately three months after wide excision. The patients had been informed about the melanoma diagnosis before the visit to the Department of Oncology. Each of the studies was approved by the Ethics Committee of the Karolinska Hospital (89:26, 91:178) and Karolinska Institutet (93:170).

Table 1

Patient characteristics in the study population

	Total		Sample 1		Sample 2		Sample 3	
	n	%	n	%	n	%	n	%
Gender*								
Female	206	47	69	51	107	53	30	30
Male	231	53	66	49	96	47	69	70
Age at diagnosis								
< 45	158	36	53	39	79	39	26	26
45–64	182	42	56	41	92	45	34	34
> 64	97	22	26	19	32	16	39	39
Tumour thickness (mm)								
≤ 1.0	227	52	84	62	141	69	2	2
1.1–2.0	59	14	25	19	33	16	1	1
2.1–4.0	107	24	20	15	14	7	73	74
> 4	37	8	4	3	11	5	22	22
Unclassifiable	7	2	2	1	4	2	1	1
Ulceration								
Present	97	22	26	19	35	17	36	36
Absent	334	76	104	77	168	83	62	63
Unavailable	6	1	5	4	–	–	1	1
Mitotic index**								
Per HPF < 1	360	82	95	70	189	93	76	77
Per HPF ≥ 1	43	10	10	7	13	6	20	20
Unavailable	34	8	30	22	1	0	3	3
Histogenetic type								
SSM	303	69	104	77	165	81	34	34
NM	78	18	15	11	19	9	44	44
LMM	7	2	4	3	1	0	2	2
ALM	3	1	1	1	2	1	–	–
Unclassifiable	46	10	11	8	16	8	19	19
Clark's level of invasion								
II	171	39	71	53	100	49	0	–
III	144	33	44	33	66	32	34	34
IV	105	24	18	13	28	14	59	60
V	10	2	0	–	6	3	4	4
Unclassifiable	7	2	2	1	3	1	2	2
Anxiety								
Mean	4.4		4.5		4.6		3.8	
SD	4.0		3.9		3.9		4.2	
Depression								
Mean	2.2		2.2		2.3		2.2	
SD	2.7		2.6		2.8		2.8	
Dead by 25-06-2001***								
Malignant melanoma	56	73	23	74	16	57	17	94
Other reasons	21	27	8	26	12	43	1	6

Abbreviations: HPF = High Power Field; SSM = Superficial Spreading Melanoma; NM = Nodular Melanoma; LMM = Lentigo Maligna Melanoma; ALM = Acral Lentiginous Melanoma.
Significant differences between samples:
*df = 2, $\chi^2 = 14.6$, $p < 0.001$.
**df = 2, $\chi^2 = 14.3$, $p < 0.001$.
***df = 2, $\chi^2 = 7.7$, $p = 0.002$.

Statistical methods

In the initial univariate analyses the continuous variables age and tumour thickness were transformed into categories (age: < 45 years, 45–64 years, > 64 years; tumour thickness: ≤ 1 mm, 1.1–2.0 mm, 2.1–4.0 mm, > 4.0 mm). The scores for anxiety and depression were summarized for each of the two subscales with a maximum of 21. No values were imputed for missing data. The patients were divided between the 'no disorder' or 'clinical disorder' categories, according to whether they scored below or above the 'cut-off point' of ≥ 8, on both subscales, respectively, as recommended by Zigmond & Snaith (21).

χ^2-tests were employed to evaluate differences in categorical variables between the study samples and also between the two levels of anxiety and depression.

Analyses were performed with respect to time to recurrence using life tables. The log-rank statistic was used to test the impact of the different background factors univariately. In the multivariate analysis, the Cox regression was used.

RESULTS

The overall information concerning the study groups are presented in Table 1 and the median follow-up time with ranges are displayed in Table 2. The study population, consisting of 439 patients included in three different studies, represents a compliance rate of 89% (n = 135) and 83% (n = 245) in samples 1 and 2, respectively. Patients in the third sample are included in a study still open for inclusion.

Anxiety and depression as prognostic factors for time to recurrence

Using recurrence as an endpoint, neither anxiety nor depression turned out to be prognostic factors in the univariate analysis. As expected, gender, age, tumour thickness, ulceration, mitotic index, histogenetic type and Clark's level of invasion were associated with time to recurrence in the univariate analyses (Table 3). In the multivariate analysis, gender, age, tumour thickness, ulceration and Clark's level of invasion were statistically significant prognostic variables (Table 4). A total of 11 patients with recurrent disease had a score of 11 or above on the anxiety scale, and one of those patients also scored 11 or above on the depression scale.

Association between anxiety and clinical and histopathological prognostic factors

χ^2-tests were performed to investigate the association between the HAD-anxiety subscale scored in two categories (0–7: 'no clinical anxiety level' and ≥ 8: 'clinical anxiety level') and clinical and histopathological prognostic factors of outcome of malignant melanoma. The proportions of patients reporting levels of anxiety above the cut-off point according to the other prognostic variables are presented in Table 5. Gender, age, ulceration, high mitotic index and Clark's level of invasion showed statistically significant associations with anxiety. A statistically, significantly higher proportion of the women compared with the men reported 'clinical levels' of anxiety. A higher proportion of patients in the younger age groups scored in the 'clinical anxiety level' compared with older patients. Patients scoring in the 'clinical anxiety level' (≥ 8) usually had tumours with a low mitotic index and Clark's level II tumours but rarely had ulcerated tumours.

Depressive symptoms and clinical and histopathological prognostic factors

The proportions of patients reporting levels of depression above the cut-off point according to the other prognostic variables are presented in Table 6. A statistically significant association was found between the HAD-depression subscale and age and tumour thickness. Younger patients reported more depression compared with older patients. No associations were found between the HAD-depression subscale and the other variables tested.

DISCUSSION

In the present study, three samples of melanoma patients were included in an analysis of anxiety and depressive symptoms as prognostic factors of outcome of melanoma. We found no association between time to recurrence and anxiety or depression. On the other hand, as expected, gender, age, tumour thickness, ulceration, mitotic index, histogenetic type and Clark's level of invasion were predictive of recurrence-free survival.

The HAD scale is a widely used well-validated questionnaire for the assessment of anxiety and depression among patients with somatic illnesses. We chose the cut-off point of ≥ 8, thus taking the risk of including patients without clinical anxiety or depression. The implication of choosing a cut-off that could include 'false' positives is that anxiety and depression as prognostic variables might be missed. On the other hand, including only patients with a cut-off of ≥ 11 would reduce the number of patients in the 'clinical disorder' groups, and thus decrease the power of the statistics. In our study, there were no indications of an association between anxiety/depression and time to recurrence. Thus, the possibility of missing such an association by choosing the lower cut-off levels seems less probable.

Table 2

Median follow-up and range for separate patient categories in the study population

	n	Median follow-up (months)	Range (months)
Living and recurrence-free patients	331	111	19–174
Living patients with recurrence of CMM	28	21.5	6–108
Dead patients with recurrence of CMM	58	20	1–115
Dead patients without recurrence of CMM	19	56	9–135

Abbreviation: CMM = cutaneous malignant melanoma.

Table 3

Univariate life table analysis of time to recurrence. Tests between groups were carried out with the log-rank statistic (LR)

	N	n of recurrences	%	LR	p-value
Gender				15.2	< 0.001
Female	206	26	12.6		
Male	230	60	26.1		
Age at diagnosis				13.0	0.002
< 45	158	26	16.5		
45–64	194	33	17.0		
> 64	84	27	32.1		
Tumour thickness (mm)				99.7	< 0.001
≤ 1.0	226	10	4.4		
1.1–2.0	59	20	33.9		
2.1–4.0	107	33	30.8		
> 4	37	20	54.1		
Ulceration				41.2	< 0.001
Present	97	39	40.2		
Absent	333	46	13.8		
Mitotic index				21.5	< 0.001
Per HPF < 1	359	59	16.4		
Per HPF ≥ 1	42	17	40.5		
Histogenetic type				27.5	< 0.001
SSM	302	44	14.6		
NM	78	29	37.2		
Clark's level of invasion				89.8	< 0.001
II	170	5	3.0		
III	144	30	20.8		
IV	105	42	40.0		
V	10	6	60.0		
Anxiety				1.4	0.232
0–7	343	71	20.7		
≥ 8	92	14	15.2		
Depression				0.3	0.559
0–7	408	82	20.1		
≥ 8	26	4	15.4		

Abbreviations: HPF = High Power Field; SSM = Superficial Spreading Melanoma; NM = Nodular Melanoma.

A study in a random sample of the Swedish population showed a mean value of 4.6 (SD 3.8) for the anxiety subscale and a mean value of 4.0 (SD 3.5) for the depression subscale (26). Although, higher values could be expected among the patients with melanoma, the normative value for anxiety corresponds to the figures found in our study. Even more surprising is finding a lower value for depression in the patient group as compared to the normative data. When looking at the proportion of patients scoring above the cut-off point (≥ 8) the figures in the population data are 20% in comparison with 21% in our sample. The corresponding figures for the depression scale are15% in the population sample and 6% in this study. It should be borne in mind that the study sample patients in the normative study were 30–

Table 4

Cox multivariate regression analysis of time to recurrence. Relative hazards (RH) and 95% confidence interval (CI) for anxiety and depression

Factor	Wald	df	p-value	RH	CI
Gender	5.5	1	0.019		
Age	5.9	2	0.053		
Tumour thickness	8.4	3	0.038		
Ulceration	8.0	1	0.005		
Mitotic index	0.2	1	0.892		
Histogenetic type	0.3	1	0.602		
Clark's level of invasion	16.2	3	0.001		
Anxiety	0.5	1	0.471	1.35	0.60–3.02
Depression	2.3	1	0.128	0.37	0.10–1.33

For coding details, see Table 3.

Table 5

Proportion of patients reporting levels of anxiety under or above the cut-off point according to the other prognostic variables

	Anxiety ≤ 7 n (%)	Anxiety ≥ 8 n (%)	χ^2	df	p-value
Gender			12.0	1	< 0.001
Female	147 (72)	58 (28)			
Male	197 (85)	34 (15)			
Age at diagnosis			10.7	2	0.005
< 45	113 (72)	45 (28)			
45–64	146 (80)	36 (20)			
> 64	85 (89)	11 (11)			
Tumour thickness					NS
≤ 1	174 (77)	53 (23)			
1.1–2.0	45 (76)	14 (24)			
2.1–4.0	91 (86)	15 (14)			
> 4.0	28 (76)	9 (24)			
Ulceration			4.3	1	0.038
Present	83 (86)	13 (14)			
Absent	256 (77)	78 (23)			
Mitotic index			5.7	1	0.017
< 1/HPF	277 (77)	83 (23)			
≥ 1/HPF	39 (93)	3 (7)			
Histogenetic type					NS
SSM	237 (78)	65 (22)			
NM	64 (82)	14 (18)			
Clark's level			8.7	3	0.033
II	123 (72)	48 (28)			
III	116 (81)	28 (19)			
IV	90 (87)	14 (13)			
V	8 (80)	2 (20)			

Abbreviations: HPF = High Power Field; SSM = Superficial Spreading Melanoma; NM = Nodular Melanoma.

59 years of age and the response rate was 48%. Thus, this normative study may have recruited patients with emotional problems and those without this experience would perhaps be less likely to comply in such a study. Another explanation for the low levels of reported emotional problems in our studies samples is that they all the patients responded to the questionnaire within three month after surgery. They were told at the Department of Plastic and Reconstructive Surgery that their melanoma had been successfully removed.

During the study period, melanoma patients with localized melanoma were treated surgically and offered follow-up depending on tumour thickness. At the time of inclusion of the first two samples, all melanoma patients in the Stockholm–Gotland region were followed at the Department of Oncology, Karolinska Hospital. The patients in the third sample were followed at one or the other of the two departments of oncology in the Stockholm area (Karolinska Hospital and Huddinge University Hospital). During the three periods of data collection, consecutive patients were asked to participate and 89% of the patients in the first sample and 83% in the second sample were included. The patients in the third sample are included in a study that is not yet closed. The data in the Regional Melanoma Registry are regularly compared, twice a year, with those in the Swedish Cancer Registry. During the period 1976–1999, the average coverage rate was 98%. It was not possible to compare compliant with non-compliant subjects in our samples. The patients included in our study were similar with respect to clinical and histogenetic variables to those in the registry data, which indicates that our patients may be representative of the melanoma patients diagnosed in the Stockholm–Gotland region during the study period.

A lower proportion of men and older patients reported clinical levels of anxiety compared with women and younger patients. This is in concordance with findings in previous studies of melanoma patients (19, 20, 25). Age was the only clinical factor associated with depressive symptoms. The association between anxiety and low number of mitoses in the tumour cells is a surprising finding, which it is difficult to explain. We might speculate that tumours with a low mitotic index could have been present in the skin for a long period thereby increasing the likelihood that they would be observed by the patient and cause anxiety. Still, we regard this result as uncertain, since, although statistically significant, the conclusion is based on a very limited sample, where only 42 patients had a mitotic index ≥ 1/HPF. The association between a clinical level of anxiety and tumours with Clark's level of invasion II and absence of ulceration may be due to an association between anxiety and body

Table 6

Proportions of patients reporting levels of depression under or above the cut-off point according to the other prognostic variables

	Depression ≤ 7 n (%)	Depression ≥ 8 n (%)	χ^2	df	p-value
Gender					NS
Female	191 (93)	15 (7)			
Male	218 (95)	11 (5)			
Age at diagnosis			6.6	2	0.037
< 45	144 (91)	14 (9)			
45–64	169 (94)	11 (6)			
> 64	96 (99)	1 (1)			
Tumour thickness			10.4	3	0.015
≤ 1	217 (96)	10 (4)			
1.1–2.0	53 (90)	6 (10)			
2.1–4.0	101 (96)	4 (4)			
> 4.0	31 (84)	6 (16)			
Ulceration					NS
Present	88 (93)	7 (7)			
Absent	315 (94)	19 (6)			
Mitotic index					NS
< 1/HPF	336 (94)	23 (6)			
≥ 1/HPF	40 (95)	2 (5)			
Histogenetic type					NS
SSM	284 (94)	19 (6)			
NM	73 (95)	4 (5)			
Clark's level					NS
II	160 (94)	11 (6)			
III	136 (94)	8 (6)			
IV	97 (94)	6 (6)			
V	9 (90)	1 (10)			

Abbreviations: HPF = High Power Field; SSM = Superficial Spreading Melanoma; NM = Nodular Melanoma.

awareness, contributing to early detection. This could result in a greater proportion of patients with early melanomas among individuals with high anxiety scores. However, since we did not find a significant association between anxiety and thin tumours when measured according to Breslow, our data do not fully support a clear association between levels of anxiety and early diagnosis of melanoma. Further investigations of the hypothetical association between psychosocial parameters such as anxiety and time of diagnosis may lead to information that could be useful in the planning of preventive programmes.

Other studies have shown quality of life to be predictive of survival in cancer patients (7, 12, 27), including patients with melanoma (8). Quality of life assessment involves a number of areas, some of them relating to physical functioning and related symptoms. To our knowledge, there is no study reporting on emotional functioning, anxiety and depression as prognostic factors. It is possible that the quality of life variables predicting survival are those related to the patients' performance status, thus reflecting the severity of the disease. Emotional variables have been proposed to be important for the outcome of the disease in patients with localized melanoma through their influence on the immune system (28). The reason for choosing 'time to recurrence' as outcome variable is that a possible influence of anxiety or depression on the disease should be more readily detected in tumour recurrence rather than mortality. Our data, however, do not lend support to psychosocial intervention targeted to emotional problems in order to improve survival. Nevertheless, psychosocial interventions are important for those patients who need them to cope with their illness and related problems.

CONCLUSIONS

In this sample, neither anxiety nor depression was associated with time to recurrence in localized cutaneous melanoma. A higher proportion of patients with tumours with the following histopathological features, absence of ulceration, low mitotic index or Clark's level II, reported high levels of anxiety. A greater proportion of women and younger patients had high scores on the anxiety scale. In addition, younger patients were more likely to have high scores on the depression scale.

ACKNOWLEDGEMENTS

This study was supported by grants from Cancer Society in Stockholm, the King Gustaf V Jubilee Fund, and the Swedish Cancer Society.

REFERENCES

1. Balch CM, Soong S-J, Gershenwald JE, et al. Prognostic factors analysis of 17 600 melanoma patients: Validation of the American Joint Committee on Cancer Melanoma Staging System. J Clin Oncol 2001; 19: 3622–34.
2. Måsbäck A, Olsson H, Westerdahl J, Ingvar C, Jonsson N. Prognostic factors in invasive cutaneous malignant melanoma: a population based study and review. Melanoma Res 2001; 11: 435–45.
3. Brown JE, Butow PN, Culjak G, Coates AS, Dunn SM. Psychosocial predictors of outcome: time to relapse and survival in patients with early stage melanoma. Br J Cancer 2000; 83: 1148–53.
4. Bucceri G. Depressive reactions to lung cancer are common and often followed by a poor outcome. Eur Respir J 1998; 11: 173–8.
5. Butow PN, Coates AS, Dunn SM. Psychosocial predictors of survival in metastatic melanoma. J Clin Oncol 1999; 17: 2256–63.
6. Chang VT, Thaler HT, Polyak TA, Kornblith AB, Lepore JM, Portenoy RK. Quality of life and survival. Cancer 1998; 83: 173–9.
7. Coates A, Gebski V, Signorini D, et al. Prognostic value of quality-of-life scores during chemotherapy for advanced breast cancer. J Clin Oncol 1992; 10: 1833–8.
8. Coates A, Thomson D, McLeod GRM, et al. Prognostic value of quality of life scores in a trial of chemotherapy with or without interferon in patients with metastatic melanoma. Eur J Cancer 1993; 29A: 1732–4.
9. Coates A, Gebski V. On the receiving end. VI. Which dimensions of quality-of-life scores carry prognostic information? Cancer Treat Rev 1996; 22 (Suppl A): S63–7.
10. Coates A, Porzsolt F, Osoba D. Quality of life in oncology practice: prognostic value of EORTC QLQ-C30 scores in patients with advanced malignancy. Eur J Cancer 1997; 33: 1025–30.
11. Coates AS, Hürny C, Peterson HF, et al. Quality-of-life scores predict outcome in metastatic but not early breast cancer. J Clin Oncol 2000; 18: 3768–74.
12. Kaasa S, Mastekaasa A, Lund E. Prognostic factors for patients with inoperable non-small cell lung cancer, limited disease. Radiother Oncol 1989; 15: 235–42.
13. Seidman A, Portenoy R, Yao T-J, et al. Quality of life in phase II trials: a study of methodological and predictive value in patients with advanced breast cancer treated with paclitaxel plus granulocyte colony-stimulating factor. J Natl Cancer Inst 1995; 87: 1316–22.
14. Tamburini M, Brunelli C, Rosso S, Ventafridda V. Prognostic value of quality of life scores in terminal cancer patients. J Pain Symptom Manage 1996; 1: 32–41.
15. Wisløff F, Hjort M. Health-related quality of life assessed before and during chemotherapy predicts for survival in multiple myeloma. Br J Haematol 1997; 97: 29–37.
16. Fawzy FI, Fawzy NW, Hyun CS, et al. Malignant melanoma. Effects of an early structured psychiatric intervention, coping, and affective state on recurrence and survival 6 years later. Arch Gen Psychiatry 1993; 9: 681–9.
17. Fawzy FI, Canada AL, Fawzy NW. Malignant melanoma: effects of a brief structured psychiatric intervention on survival and recurrence at 10-year follow-up. Arch Gen Psychiatry 2003; 60: 100–3.
18. Dalton SO, Boesen EH, Ross L, Schapiro IR, Johansen C. Mind and cancer: do psychological factors cause cancer? Eur J Cancer 2002; 38: 1313–23.
19. Brandberg Y, Månsson-Brahme E, Ringborg U, Sjödén PO. Psychological reactions in patients with malignant melanoma. Eur J Cancer 1995; 31A: 157–62.
20. Brandberg Y, Bergenmar M, Bolund C, et al. Information to patients with malignant melanoma: a randomized group study. Patient Ed Couns 1994; 23: 97–105.
21. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression scale. Acta Psychiatr Scand 1983; 67: 361–70.
22. Herrmann C. International experiences with the Hospital Anxiety and Depression scale—a review of validation data and clinical results. J Psychosom Res 1997; 42: 17–41.
23. Herrmann C, Brand-Driehorst S, Kaminsky B, Leibing E, Staats H, Rüger U. Diagnostic groups and depressed moods as predictors of 22-month mortality in medical inpatients. Psychosom Med 1998; 60: 570–7.
24. Bjelland I, Dahl A, Tangen Haug T, Neckelmann D. The validity of the Hospital Anxiety and Depression scale: an updated literature review. J Psychosom Res 2002; 52: 69–77.
25. Brandberg Y, Bolund C, Sigurdardottir V, Sjödén PO, Sullivan M. Anxiety and depressive symptoms at different stages of malignant melanoma. Psycho-Oncology 1992; 1: 71–8.
26. Lisspers J, Nygren A, Söderman E. Hospital Anxiety and Depression scale (HAD): some psychometric data for a Swedish sample. Acta Psychiatr Scand 1997; 96: 281–6.
27. Maisey NR, Norman A, Watson M, Allen MJ, Hill ME, Cunningham D. Baseline quality of life predicts survival in patients with advanced colorectal cancer. Eur J Cancer 2002; 38: 1351–7.
28. Fawzy FI, Kemeny ME, Fawzy NW, et al. A structured psychiatric intervention for cancer patients. II. Changes over time in immunological measures. Arch Gen Psychiatry 1990; 8: 729–35.