ORIGINAL ARTICLE

Coping, Distress, and Survival Among Patients With Lung Cancer

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Background: This study addresses the question of whether coping and emotional state are predictors of survival among patients with lung cancer. The hypotheses were (1) active coping is linked with longer survival time and (2) depressive coping, emotional distress, and depression are linked with shorter survival.

Methods: The study was based on a sample of 103 patients who were investigated after their diagnosis and before the beginning of primary treatment. The psychological variables were assessed by means of self-reports and interviewer ratings. After follow-up of 7 to 8 years, 92 patients had died; survival data were censored for the remaining 11 patients. The prediction of the survival time was performed by the Cox regression, while adjusting for biomedical risk factors (tumor stage, histological classification, and Karnofsky performance status).

Results: The self-reported depressive coping ($P = .007$) and the interviewer-rated emotional distress ($P = .04$) were significantly associated with shorter survival, independent of the influence of the biomedical prognostic factors.

Conclusions: Both coping and emotional distress had a statistically independent effect on survival among patients with lung cancer. However, the naturalistic design of the study does not allow for any causal interpretation. Thus, the nature of this relationship warrants further investigation.

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THE QUESTION as to whether psychological factors influence survival among patients with cancer has stimulated considerable research. Previous research with breast cancer patients demonstrates that coping attitudes, such as a fighting spirit and denial, were predictive of longer survival, as compared with hopelessness and fatalism.[1-4] Many subsequent investigations, however, yielded conflicting findings and had methodological limitations.

The findings on the predictive power of active coping could partially be replicated in predictor[5,6] and intervention studies,[7] while the results regarding denial proved inconsistent.[6,8-11] However, other studies[11-16] produced evidence of a relationship between emotional distress and shorter survival. Yet even these results were inconclusive, because some researchers found that the expression of distress predicted a better outcome.[7,17,18] Moreover, other studies[19-25] did not detect any associations between psychological factors and survival. Consequently, the question of the impact of psychological variables on the course of cancer is still under discussion.[26-34]

There are few studies that address the relationship between the psychological factors and the course of the disease among patients with lung cancer. The prognosis of lung cancer is rather unfavorable. The 1-year survival rate is 37%, and the 5-year survival rate is 5% to10%. Survival times may reflect tumor stage, performance status, and histological classification.[35-45] Patients with non–small cell tumors are usually treated surgically, but only 30% of these patients can be operated on with a curative intention. If resection is not possible, the tumor can be irradiated. Small cell tumors have an especially high rate of malignancy. The median survival time of a limited disease is 12 to 15 months and of an extensive disease, 6 to 9 months. Chemotherapy is the usual treatment, because small cell tumors tend to spread at an early stage. Radiation is given as an additional or palliative treatment.[46,47]

Because of the high rate of malignancy and rapid progression of lung cancer, it seems rather unlikely at first glance that psychological factors could play a significant role.[48] One study of patients with nonmetastatic non–small cell carcinomas did not detect any links between interviewer assessments of familial coping pat-

SUBJECTS AND METHODS

SAMPLE SELECTION

Only patients with lung cancer who were newly diagnosed and who had not yet begun their primary treatment were included in the sample. The sampling procedure aimed at a sample size of 50 patients with small cell carcinoma and 50 patients with non–small cell carcinoma. One hundred fifty-two newly diagnosed lung cancer patients, who had been admitted to a large tumor center (Thorax Clinic Heidelberg-Rohrbach, Heidelberg, Germany), and whose condition had been explained to them, were asked to participate in the study. Participants gave written informed consent. One hundred twenty patients agreed to participate. The relatively high refusal rate stems largely from implementation problems in the surgical wards, while the refusal rate in the internal wards was as low as 10%. The subsample that refused to participate contained more patients with non–small cell tumors who later received surgical treatment, and more women. It should be noted that the women, the surgically treated patients, and the patients with non–small cell tumors who did participate in the study did not differ significantly on the psychological variables when compared with the men, the nonsurgically treated patients, and the patients with small cell tumors. Another 17 patients had already been treated in other hospitals, which was only later revealed, and thus had to be excluded from the sample after being assessed psychologically. Consequently, the final sample consisted of 103 patients. The patients were recruited between June 1989 and December 1991. Follow-up assessments of survival times were performed in January 1998, which was 7 to 8 years after diagnosis. By this time, 92 patients had died.

ASSESSMENT

Coping methods and affective states were assessed by both self-reports and interviewer ratings, as is recommended.[6,15,31,53] Assessments were completed within 3 days after confirmation of diagnosis. However, some patients had already received diagnostic tests prior to their admission to the study hospital and thus may have gained an idea about their disease. The interviewer ratings were performed on the basis of the information obtained by a semistructured interview. The interview began with the request, "I would like you to tell me how it all began." Once the patients had described their history, the issue of emotional state was brought up with the questions, "Sometimes people feel depressed when they suffer from an illness like that. Do you know this sort of feeling yourself?" "Have you ever had feelings of anxiety during the course of your illness?" The basis for the interviewer ratings of coping was the question, "What helps you to come to terms with your situation?" The interviews were tape-recorded. The interviewers were advanced medical and psychology students who were familiar with the hospital ward setting, had received extensive training, and were supervised once a week. Details of the patients' medical records were unknown to the interviewers.

Coping was measured by the well-validated Freiburg Questionnaire of Coping With Illness,[23,54] which contains both a self-report format and an interviewer rating format. It consists of 35 short statements on coping behaviors (eg, "I am seeking information about illness and treatment") rated on a 5-point Likert scale with 1 indicating not at all and 5, very much. The interviewers rated the same 35 items. The *active, problem-focused coping* scale consisted of 5 items: seeking information about illness and treatment, undertaking problem-solving efforts, making plans of action and following them, intending to live more intensively, and deciding to fight against the illness (Cronbach α: self-report, 0.64; interviewer rating, 0.74; and interrater reliability, Spearman ρ, 0.65). *Depressive coping* was measured by 5 items: brooding, arguing with fate, pitying oneself, acting impatiently and taking it out on others, and withdrawing from other people (Cronbach α: self-report, 0.68; interviewer rating, 0.69; and interrater reliability, Spearman ρ, 0.78). The additive scales of the Freiburg Questionnaire of Coping With Illness were divided by the number of items, so that the scores ranged from 1 to 5.

To evaluate possible interviewer biases, we computed an analysis of variance for the different interviewers. One interviewer rated the active coping scale systematically higher ($P<.001$). However, this interviewer bias did

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terns and survival.[13] In 2 studies[49,50] with positive findings, severe methodological limitations were evident: well-established prognostic factors were not taken into account, psychological variables were assessed after the completion of treatment, and multiple variables were tested retrospectively. However, Kaasa et al[51] demonstrated that patients with inoperable non–small cell lung cancer had a longer survival if their psychological well-being was good. In a recent study[52] of newly diagnosed lung cancer patients, self-reported depression predicted shorter survival after controlling for biomedical prognostic factors such as stage of the disease and performance status. However, in this study, post hoc–selected single items of a standardized test (rather than the total scores of the entire test) were used as predictors in the multivariate model. Moreover, it remains unclear how the authors chose their multivariate model, which did not contain patients' physical performance. Neither the study by Kaasa et al[51] nor Buccheri[52] assessed coping styles. To summarize, evidence on the prognostic significance of both coping and affective state among patients with lung cancer is rather weak. Above all, there are only a few prospective studies that have been aimed at addressing this important and unresolved question.

We conducted a prospective study, with a 7- to 8-year follow-up, to determine whether both coping and emotional distress were predictors of survival among patients with lung cancer, while controlling for biomedical prognostic factors. Assessments were performed before patients began treatment. The hypotheses that guided the study were that active coping is linked with longer survival, and that depressive coping, emotional distress, and depression are linked with shorter survival.

RESULTS

DEMOGRAPHIC AND BIOMEDICAL DATA

The mean (SD) age of the participants was 59 (9) years (range, 32-84 years). Eight-three percent were men. Age

not seem to influence the results, because there were no significant differences of survival time among the patients judged by the different interviewers, and the effects were even reproduced when the 7 patients who were rated by the biased interviewer were excluded.

Emotional distress was measured by a newly developed scale consisting of the following 5 items: I am anxious, I am depressed, I am distressed by the disease, I am distressed by the diagnostic tests, and I am nervous. Respondents were asked to rate themselves on 5-point scales ranging from 1 (not at all) to 5 (very much). The sum scores of the scale were divided by the number of items, so that the scores had values between 1 and 5. The outside estimates given by the interviewers were performed using analogous statements (eg, the patient is anxious, etc). Cronbach α values were 0.82 (self-report) and 0.87 (interviewer rating). Interrater reliability (Spearman ρ) was 0.70. Validation data of this clinical scale have been presented elsewhere.[55,56]

The degree of *depression* was measured by means of the well-established Depression Scale D-S.[57,58] It was designed to assess the intensity of depressive, anxious, and irritable or dysphoric mood rather than the nosological entity of depression (sample items: I feel depressed and melancholic. Often I feel miserable. Recently I have been very anxious and nervous.). It can be used to evaluate both healthy persons and psychiatric patients. Each of the 16 items is rated on a 4-point scale from 0 to 3, yielding a total possible depression score ranging from 0 to 48.

Unfortunately, there is no validated German version of any internationally accepted instrument for the assessment of coping. As for depression, German versions of both the Beck Depression Inventory and the Hospital Anxiety and Depression Scale have become available in the meantime. However, these instruments were published in 1993 and 1995, respectively, after the assessments in our study had been completed.

The following *biomedical variables*, which were routinely collected by the study hospital, were taken into account: histological cell type, tumor stage, and Karnofsky performance status.[59] The Karnofsky performance status is a clinician's appraisal of the level of patient's functioning. In addition, the attending physicians made 3 ratings concerning (1) severity of the disease, (2) unfavorable prognosis, and (3) expected treatment success. These judgments were performed before the commencement of treatment. They were rated on 5-point scales, with 1 indicating not at all and 5, very much.

STATISTICAL PROCEDURES

The outcome variable was time from diagnosis to death. Survival times are often censored data. Here the term "censored" means that the total survival time is only known for patients who have already died. For patients who are still alive, the only available information is on the length of survival from the time of diagnosis to the last point of observation. In the present sample, 92 patients were deceased and 11 were censored. With these kind of data, the probabilities of survival can be computed with the method of Kaplan and Meier.[60] The statistical comparison of the probabilities was performed using the log-rank test. For the Kaplan-Meier analysis, the continuous variables were dichotomized at the median. We first tested the individual effects of the psychological and biomedical variables on survival. Then the Cox proportional hazards regression model[61-63] was used to determine the relationship between psychological variables and survival adjusted for multiple covariates. Biomedical and psychological variables that proved significant in the bivariate tests were simultaneously entered into the Cox regression. To examine whether the association between independent variables and survival is influenced by the levels of interrelated variables, we included the terms describing the interaction of independent variables. Furthermore, we ensured that the included variables satisfied the assumptions of the Cox model by modeling them as binary variables (median split). Stage was split in the following manner: stages I, II, IIIa vs IIIb, and IV. The testing for proportional hazards functions was done with empiric log-(-log)-plots and with the acceleration test of Breslow.[62] $P<.05$ was considered significant, and all P values reflect 2-tailed tests. The statistical analyses were performed using SPSS 8.0 for Windows (SPSS Inc, Chicago, Ill).

and sex composition corresponded with the data given in the literature.[46,47] Seventy-nine percent were married. For 84% of the patients, the highest level of education was middle school. The respondents were employed as unskilled workers (23%), skilled workers (22%), and middle-level salaried employees (40%). Of these, 33% had already retired by the time of investigation.

Histological classifications were as follows: small cell (n = 48), squamous cell (n = 30), adenocarcinoma (n = 17), large cell (n = 4), mixed (n = 4). One patient was stage I, 8 were stage II, 21 were stage IIIa, 30 were stage IIIb, and 43 were stage IV. As expected from the sampling criteria, patients with small cell carcinoma and those with advanced-stage disease were overrepresented. This fact is reflected in the frequencies of treatments: the majority of patients received chemotherapy (n = 15), radiotherapy (n = 14), or both (n = 44). Thirty patients were treated surgically. Of the surgical patients, 14 received additional radiation, 2 received chemotherapy, and 2 received both. Histological classification, tumor stage, and type of treatment were interrelated. Only 1 patient with small cell tumor was given surgical treatment. Patients with non–small cell lung cancer were more frequently operated on when their tumors were in earlier stages. The respective figures were: stage I/II, 100%; stage IIIa, 73%; stage IIIb, 56%; and stage IV, 17%. The mean (SD) score on the Karnofsky performance scale was 82 (13) (median, 80).

INTERCORRELATIONS OF PSYCHOLOGICAL AND BIOMEDICAL VARIABLES

Table 1 shows that self-reports and interviewer ratings of a specific construct were correlated. Different indicators of depressive mood (depressive coping, emotional distress, and depression) were interrelated, whereas active coping was independent of these. There were no effects of age and tumor stage on psychological variables. The Karnofsky performance status was correlated with active coping, as judged by the interviewers, and, inversely, depression. Physician ratings were on the whole

Table 1. Means and Correlations of Psychological and Biomedical Variables (n = 103)*

				Intercorrelations of Psychological Variables						Correlations With Biomedical Variables					
													Physician Ratings†		
	No.	Mean	SD	2	3	4	5	6	7	Age	Stage	KPS	1	2	3
Active coping, IR	103	2.81	0.74	0.38‡	−0.04	0.05	−0.12	0.14	−0.07	0.05	−0.08	0.32‡	−0.01	−0.06	0.16
Active coping, SR	97	3.48	0.96		0.08	−0.10	−0.04	0.13	−0.03	−0.00	0.13	0.17	−0.01	−0.01	0.08
Depressive coping, IR	103	2.30	0.63			0.41‡	0.57‡	0.46‡	0.45‡	−0.05	0.04	0.08	0.07	0.17	−0.03
Depressive coping, SR	97	1.69	0.67				0.31‡	0.32‡	0.39‡	−0.02	0.04	−0.13	0.02	0.13	−0.24‡
Emotional distress, IR	103	2.95	0.90					0.58‡	0.36‡	−0.04	0.04	0.14	−0.00	0.13	−0.01
Emotional distress, SR	98	2.33	0.93						0.55‡	−0.02	0.05	0.10	0.04	0.23‡	−0.20
Depression, D-S	92	5.52	5.18							−0.04	0.11	−0.24‡	0.10	0.14	−0.16

*KPS indicates Karnofsky performance status; IR, interviewer rating; SR, self-report; and D-S, Depression Scale.
†Physician rating 1, severity; physician rating 2, unfavorable prognosis; and physician rating 3, expected treatment success.
‡Spearman correlation coefficients; significant at $P<.05$.

Table 2. Kaplan-Meier Analyses of Survival With Psychological Predictors (n = 103)*

Variable	Cutoff Points (Median Split)	No.	Median Survival, mo	P
Active coping, IR (n = 103)	≤2.6	53	7	.17
	>2.6	50	15	
Active coping, SR (n = 97)	≤3.6	49	11	.99
	>3.6	48	12	
Depressive coping, IR (n = 103)	≤2.2	56	12	.13
	>2.2	47	12	
Depressive coping, SR (n = 97)	≤1.6	58	14	.007
	>1.6	39	9	
Emotional distress, IR (n = 103)	≤3.0	56	15	.02
	>3.0	47	9	
Emotional distress, SR (n = 98)	≤2.2	50	14	.31
	>2.2	48	10	
Depression, SR (n = 92)	≤4	51	12	.19
	>4	41	10	

*IR indicates interviewer rating; SR, self-report. Comparison of survival distributions by log-rank test.

Table 3. Cox Proportional Hazards Regression on Survival (n = 93)

Variable	Regression Coefficient	SE	P
Tumor stage	−0.89	0.26	<.001
Karnofsky performance status	0.94	0.24	<.001
Depressive coping, self-report	−0.90	0.33	.007
Emotional distress, interviewer rating	−0.76	0.37	.04
Interaction of depressive coping, self-report, and emotional distress, interviewer rating	0.46	0.48	.34

fairly unrelated to psychological variables, yet highly interrelated: the severity rating was correlated with the unfavorable prognosis rating ($r = 0.57$, $P<.001$) and the treatment success rating ($r = -0.47$, $P<.001$), and these 2 ratings were also interrelated ($r = -0.68$, $P<.001$). No differences in psychological variables were noted between histological cell types.

KAPLAN-MEIER ANALYSES OF SURVIVAL PROBABILITIES

Table 2 shows the results of the Kaplan-Meier analysis of survival probabilities for the psychological scales that were dichotomized at the median. Median splits did not always result in equal frequencies within the subgroups, because the scale values representing the medians were occupied by more than 1 patient. Two of the 7 median split tests were significant. Patients with high values of self-reported depressive coping had significantly shorter survival than patients with low values. Emotionally distressed patients had shorter times of survival, when assessed by the interviewer ratings.

The biomedical predictors that were related with survival time were tumor stage ($P = .002$), Karnofsky performance status ($P<.001$), and histological cell type, ie, small cell vs non–small cell tumors ($P = .01$). In addition, physicians' ratings of the severity of the disease were predictive of shorter survival ($P = .02$), and a tendency was also revealed in their judgments of an unfavorable prognosis ($P = .07$). However, their estimates of expected treatment success ($P = .54$), age ($P = .72$), and sex ($P = .91$) were not significant predictors.

COX REGRESSION USING MULTIPLE COVARIATES

Psychological and biomedical variables that showed a significant effect on survival in the bivariate analyses were entered into the Cox proportional hazards regression model. Thus, included among the psychological variables were both the self-report of depressive coping and the interviewer rating of emotional distress. The effect of an interaction between these 2 variables was also examined. Of the biomedical variables, tumor stage and Karnofsky performance status were taken into account. **Table 3** shows that the tumor stage, the Karnofsky performance status, the self-report of depressive coping, and the interviewer rating of emotional distress were independent predictors of survival.

When cell type and its interaction with tumor stage were included in the multivariate model, the self-report of depressive coping ($P = .006$), the interviewer rating of

emotional distress ($P = .02$), and the Karnofsky performance status ($P < .001$) remained significant. However, both tumor stage and cell type were no longer significant as single variables, but their interaction proved to have an effect on survival ($P = .01$).

The physician rating of the severity of the disease was not entered into the Cox regression during the first step because to do so would have unduly restricted the model's statistical power (sample size, n = 78). However, when the physician rating was included in the model, it showed no independent effect on survival ($P = .44$). Yet the predictive effects of the tumor stage ($P = .02$), the Karnofsky performance status ($P = .001$), the self-report of depressive coping ($P = .04$), and the interviewer rating of emotional distress ($P = .04$) remained significant.

To test the suggestion that patients who showed depressive coping or were emotionally distressed might prematurely discontinue chemotherapy, we correlated the number of chemotherapy cycles that part of the patients later received with the coping measures, and found a significant negative correlation with the self-report of depressive coping ($r = -0.27$, $P = .04$), but not with the interviewer rating of emotional distress ($r = -0.14$, $P = .30$). However, when the number of cycles was included in the Cox model (n = 57), the interviewer rating of emotional distress remained significant ($P = .04$), while the number of cycles proved nonsignificant ($P = .63$). In this subgroup analysis, the self-report of depressive coping only revealed a trend ($P = .12$), as did both the tumor stage ($P = .12$) and the Karnofsky performance status ($P = .06$), probably reflecting reduced statistical power that comes from the smaller sample size.

COMMENT

In this study, both self-reported depressive coping and interviewer-rated emotional distress were independently associated with shorter survival among patients with lung cancer. Adjusting for biomedical risk factors, these effects remained significant.

There are several strengths to the study. The study was prospective and guided by hypotheses. It started before the commencement of treatment and thereby guaranteed that the psychological measures that were assessed at that time were not influenced by prior treatment. However, the possibility cannot be excluded that psychological variables were indicators of the course of the disease prior to the time of assessment. Since many patients had late-stage cancers, they possibly had some time to develop coping strategies and emotional distress before the assessments were performed. In addition, the physicians' opinions could have been conveyed to them and might have influenced their emotional state. Furthermore, we cannot rule out the possibility that the links we found were produced by some unknown intervening variables.[48] A major limitation in our study stems from the relatively small size and the selectivity of the sample, in which advanced stages and small cell tumors were overrepresented. Moreover, the study only reports cross-sectional data regarding psychological variables.

Our findings concur with those of other studies that suggest that both emotional distress and depressive coping predict shorter survival.[11-16,51] The link determined between the interviewer ratings and survival may reflect a crucial issue: the raters may have based their judgments on their perceptions of the physical state of the patient. However, the self-reports of depressive coping were predictive as well. The degree of distress may be influenced by such coping attitudes as denial or stoicism. The prognostic significance of both the tumor stage and the Karnofsky performance status was confirmed in our sample.[35-45]

Several models for the relationship between coping and the course of cancer can be conceptualized.[31,64,65] The course of the disease may have some impact on coping, either in a direct manner via psychologically active paraneoplastic hormones,[66,67] or in a more indirect manner through the emotional reaction of the patients to bodily symptoms. The physical damage is sometimes reflected better by psychological variables, which are closer to the patients' experience than the cruder biomedical staging classifications. Thus, several studies have shown quality of life to be an independent predictor of survival in patients with lung[49,51,68-72] and other cancers.[73-76]

Coping may influence the course of the disease, either in a direct manner via psychoneuroimmunological mechanisms (eg, active coping might increase and depressive coping decrease natural killer cell activity),[7,77-82] or in an indirect manner via compliance,[83] such as when patients who cope actively might receive a higher amount of chemotherapy whereas those who are depressed might discontinue such therapy earlier.[84]

To conclude, the present study revealed some evidence pointing to a relationship between coping, distress, and survival among patients with lung cancer, after controlling for biomedical risk factors.

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