Optimism and Survival in Lung Carcinoma Patients

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BACKGROUND. It is popular belief that the psychologic response to a diagnosis of cancer influences survival in patients with cancer; however, research has produced contradictory results. In this prospective study, the authors investigated the relation between pretreatment levels of optimism and survival in patients with non-small cell lung carcinoma (NSCLC).

METHODS. Two hundred four patients who were participating in a randomized trial that compared accelerated and conventional radiotherapy with and without carboplatin chemotherapy were asked to complete two questionnaires assessing optimism. The first assessment was just prior to commencing treatment and the second assessment took place after completing treatment. Survival was measured from the date of randomization to the date of death. Surviving patients were followed until February 8, 2001.

RESULTS. The pretreatment questionnaire was completed by 179 patients, and 148 of those patients completed the posttreatment questionnaire. There was a small but significant reduction in optimism scores after treatment ($P = 0.005$). There was no association noted between pretreatment optimism and progression-free survival ($P = 0.52$, unadjusted; $P = 0.22$, adjusted for Eastern Cooperative Oncology Group performance status and patient age), nor was there an association noted between pretreatment optimism and overall survival ($P = 0.36$, unadjusted; $P = 0.19$, adjusted for disease stage).

CONCLUSIONS. There was no evidence that a high level of optimism prior to treatment enhanced survival in patients with NSCLC. Encouraging patients to "be positive" only may add to the burden of having cancer while providing little benefit, at least in patients with NSCLC. *Cancer* 2004;100:1276–82.
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KEYWORDS: lung carcinoma, survival, optimism, psychology.

Lung carcinoma is one of the most common cancers worldwide, and the incidence is rising as the prevalence of smoking increases.[1] To our knowledge, to date, the long-term results of currently available lung carcinoma treatments are poor. Even with best-practice treatment, the proportion of patients who remain alive 5 years after diagnosis is currently $< 15\%$.[2] However, the length of survival can vary substantially, even among patients with similar disease and demographic characteristics who receive similar treatment regimens. This has led to speculation that psychologic factors may play a role in the course of the disease.

It is popular belief that an individual's psychologic response to cancer, particularly optimism or "a positive attitude," influences survival. In an Australian study of audiotaped consultations, it was found that cancer patients often try to develop a positive attitude or fighting spirit in the belief that it will enhance their chances of survival.[3] Oncologists tended to encourage this strategy, which they perceive as potentially helpful to patients.[3] In the current study, we investigated

the relation between pretreatment levels of optimism and survival in patients with nonsmall cell lung carcinoma (NSCLC).

Potential Mechanisms

Salovey et al. proposed several potential mechanisms or pathways by which psychologic factors may influence survival.[4] First, there may be direct effects of an individual's psychologic state on their physiology, especially the immunologic and neuroendocrine systems. Other, perhaps more plausible mechanisms specify indirect pathways between psychologic state and survival. The individual's psychologic state may affect their health-related behavior. Positive mood states, such as optimism, may facilitate enhanced self-care activities, such as healthy eating, quitting smoking, moderate alcohol consumption, and exercise.[5] Moreover, optimists may obtain more information regarding their disease and treatment, which, in turn, may enhance their ability for self-care or may lead to better treatment decisions.[5]

Previous Research on Psychologic Factors and Survival

A systematic review of the influence of psychologic factors on survival in individuals with cancer has been published recently.[6] The bulk of research has focused on fighting spirit and helplessness/hopelessness, and most of these studies reported no significant associations with survival. A smaller number of studies investigated other psychologic responses to cancer, such as problem-focused or emotion-focused coping, denial, and fatalism. The evidence that these other types of psychologic responses influenced survival also was weak. Randomized controlled trials that tested the effects of group therapy on psychological coping and survival on cancer patients also have produced mixed results, with some showing a positive influence[7,8] and others showing no influence[9,10]; however, methodologic weaknesses well may account for the positive results.

To our knowledge, few studies published to date have investigated the role of optimism on survival in cancer patients despite the popular notion that "being positive" improves chances of survival. Scheier and Carver[5] have defined dispositional optimism as the global expectation that good things will be plentiful in the future and that bad things will be scarce. Those authors argue that optimistic individuals believe that their goals can be achieved in the face of adversity and will continue to try to attain the goal, whereas pessimistic individuals are more likely to give up. Hence, it may be expected that optimistic patients may pursue life-prolonging treatments more vigorously and may

be more vigilant about self-care activities such as diet, exercise, and managing treatment side effects.

To our knowledge the few studies published to date that have investigated the relation between optimism/pessimism and survival have produced significant results, but most displayed methodologic weaknesses. In a study of mixed cancer types,[11] no independent effects of optimism or pessimism on survival were found; however, there was a significant interaction effect between pessimism and age. However, pessimism scores may have reflected the extent or sites of metastases, which were not controlled for in the analyses. Another study reported that optimism prolonged survival in patients with metastatic melanoma.[12] Optimism in that study was represented by the patients' perceived aim of treatment, and the authors acknowledged that this item may have reflected what their oncologists had told them based on clinical signs. A study of patients with lung carcinoma reported a significant association between depressive coping and survival after controlling for confounders.[13] Depression and pessimism typically are correlated.[11] However, in that study, disease stage was controlled for but not metastatic site; hence, depressive coping scores may reflect patient knowledge of clinical signs. One study of breast carcinoma patients found no association between pessimism and survival after adjusting for confounders at 3 years, 5 years, and 10 years of follow-up.[14]

Objectives of the Study

The objective of the current study was to examine prospectively the association between optimism assessed prior to commencing treatment and survival among patients with NSCLC. Specifically, we expected that patients who had high optimism scores would have longer survival, both progression-free and overall, compared with patients who had low optimism scores. Because patients' levels of optimism may reflect how they perceive that they are responding to treatment, we also investigated whether optimism changed over time and with respect to type of treatment and response to that treatment.

MATERIALS AND METHODS
Setting and Patients

The study sample was comprised of patients with unresectable NSCLC who were enrolled in a multicenter Phase III study[15] using a 2×2 factorial design comparing accelerated with conventional fractionation radiotherapy both with and without concurrent chemotherapy. The four treatment arms were as follows: R6: standard radiotherapy for 6 weeks (60 grays [Gy] in 30 fractions at 5 per week); R3: accelerated radiotherapy

for 3 weeks (60 Gy in 30 fractions at 10 per week); R6C: standard radiotherapy plus chemotherapy (intravenous carboplatin at a dose of 70 mg/m² per day on Days 1–5 and Days 29–33 of radiotherapy); and R3C: accelerated radiotherapy plus chemotherapy (intravenous carboplatin at a dose of 70 mg/m² per day on Days 1–5 of radiotherapy). Patients were eligible if they had histologically or cytologically proven NSCLC that was inoperable, an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, disease confined to the primary site or regional lymph nodes, no pleural effusions, weight loss ≤ 10%, and no prior chemotherapy or radiotherapy. All patients were required to provide written informed consent, and the protocol was approved by all relevant ethics committees. Between April 3, 1989, and May 16, 1995, 204 eligible patients were randomized to 1 of the treatment arms.

Response Criteria

Response to treatment[16] was defined as a complete response (the disappearance of all known disease) or a partial response (reduction of at least 50% in tumor size). Nonresponse to treatment was defined as progressive disease (an increase ≥ 25% in tumor size) or stable disease (no change, a reduction < 50% in tumor size, or an increase < 25% in tumor size). Further details of the Phase III study were reported previously.[15] It showed no significant survival advantage for any of the treatment arms.

Measures

Each patient was asked to complete two Life Orientation Tests (LOT)[17]: one prior to the commencement of treatment and one at the first posttreatment assessment, which occurred 6 weeks after the completion of treatment and prior to disease progression. The LOT was comprised of 12 items: 4 items assessing an optimistic attitude, 4 items assessing a pessimistic attitude, and the remaining 4 filler items, which were not used. Representative items included: "In uncertain times, I usually expect the best," and "If something can go wrong for me, it will." A 5-point Likert response scale was used, which ranged from 1 (agree strongly) to 5 (disagree strongly). The scale has demonstrated reliability and validity.[17] The scores for the optimistic items were reversed. Then, the scores for the optimistic and pessimistic items were averaged to obtain a mean optimism score for each person. Basic demographic and medical information was recorded at the pretreatment assessment, including gender, age, ECOG performance status, weight loss in the last 3 months, overall TNM stage, and months between diagnosis and randomization.

Statistical Methods

A Student t test for paired data was used to determine whether there was a significant change in optimism score after treatment. The mean pretreatment scores and changes between pretreatment and posttreatment scores were compared using Student t tests or analyses of variance.

All patients were followed until February 8, 2001. For overall survival, all deaths were counted regardless of cause. For progression-free survival, disease progression at any site or death from any cause was counted as an event. Overall and progression-free survival from the date of randomization were estimated using the Kaplan–Meier product-limit method, and 95% confidence intervals for median survival were estimated using the Brookmeyer–Crowley method.

For the Kaplan–Meier survival curves, the pretreatment optimism scores were divided into three groups: low (scores < 3), medium (scores from 3 to < 4), and high (scores = 4–5). Multifactor analyses to estimate the effect of pretreatment optimism (as a continuous variable) on progression-free and overall survival were performed using Cox proportional hazards regression, adjusting for those prognostic factors with a P value < 0.1 in unifactor analyses. The prognostic factors considered were ECOG performance status, weight loss, histology, disease stage, hospital, and treatment arm. The P value for each factor was based on the change in the likelihood when that factor was omitted from the model. S-plus software[18] was used to obtain the survival curves, and SPSS software[19] was used for the Student t tests, analyses of variance, and Cox proportional hazards regression analyses.

RESULTS
Patient Characteristics

Of 204 randomized patients, 179 patients (88%) completed the LOT prior to treatment and 148 of those patients (83%) also completed the LOT after treatment. Table 1 shows mean pretreatment optimism scores by patient characteristics for the group who completed the pretreatment LOT. There were more males (78%) than females, the median age was 65 years (range, 40–79 years), 66% of patients had an ECOG performance status of 1, and 69% of patients reported no weight loss. Sixty-three percent of patients presented with squamous cell lung carcinoma, and 79% had TNM Stage III disease. Pretreatment optimism scores did not appear to differ significantly with age, gender, ECOG performance status, histology, weight loss, or disease stage. There was a significant difference in optimism scores between hospitals, with patients at one of the hospitals more optimistic than patients at other sites.

TABLE 1
Patient Characteristics and Mean Pretreatment Optimism Scores

Characteristic	No. of patients	Pretreatment mean ± SE	P value
All patients	179	3.61 ± 0.04	—
Hospital			
Peter MacCallum Cancer Centre	136	3.55 ± 0.05	0.003
Royal Adelaide Hospital	22	3.66 ± 0.10	
Queensland Radium Institute	13	4.13 ± 0.15	
Mater Misericordiae Hospital	8	3.72 ± 0.09	
Gender			
Male	140	3.58 ± 0.05	0.18
Female	39	3.72 ± 0.09	
ECOG performance status			
0	60	3.69 ± 0.07	0.19
1	119	3.57 ± 0.05	
Histology			
Squamous	112	3.62 ± 0.05	0.84
Nonsquamous	67	3.60 ± 0.07	
Weight loss			
None	123	3.64 ± 0.05	0.30
≤10%	56	3.55 ± 0.07	
Overall stage			
T1–T2N0 (Stage I)	31	3.54 ± 0.10	0.50
T1–T2N1 (Stage II)	7	3.51 ± 0.19	
T1–TN2, T3N0–N2 (Stage IIIA)[a]	89	3.59 ± 0.06	
T1–T4N3, T4N0–N3 (Stage IIIB)	52	3.70 ± 0.07	

SE: standard error; ECOG: Eastern Cooperative Oncology Group.

[a] Includes one patient with T?N2 stage disease.

Changes in Optimism over Time

The mean (± standard error) pretreatment optimism score for patients who completed both LOTs was 3.61 (± 0.05) and the mean posttreatment optimism score was 3.51 (± 0.04) (Table 2). Although it was small, this difference was statistically significant ($P = 0.005$). However, there was no significant difference between the 4 treatment arms with respect to changes in optimism scores after treatment ($P = 0.57$) or between patients who did and did not respond to treatment ($P = 0.87$).

Survival and Optimism

Of 179 patients who completed the pretreatment LOT, 171 patients (96%) had died by the close-out date. Of those eight patients who were alive, five patients remained progression free.

In the Cox unifactor regression analyses of progression-free survival, 2 prognostic factors were eligible for inclusion in the multifactor analysis: ECOG performance status ($P = 0.1$) and stage of disease ($P = 0.018$). However, there was no significant effect of optimism on progression-free survival with or without adjusting for disease stage or performance status ($P = 0.52$ with no adjustments; $P = 0.22$ adjusting for disease stage and performance status).

Disease stage ($P = 0.1$) was the only prognostic factor that was eligible for inclusion in the Cox multi-factor regression analyses of overall survival. Again, there was no significant effect of optimism on overall survival with or without adjusting for disease stage ($P = 0.36$ with no adjustment; $P = 0.19$ adjusting for stage). Figure 1 displays the Kaplan–Meier progression-free survival curves, and Figure 2 shows the overall survival curves for the three pretreatment optimism groups.

DISCUSSION

Optimism in patients did not appear to influence the length of overall or progression-free survival in this study. Indeed, there was not even evidence of a trend in this direction. These findings are consistent with one study[14] but stand in contrast to other previous research.[11–13] The likely reason for this difference is the methodologic strengths of this study. We used a reliable and valid measure of optimism that was administered to a reasonably large, inception cohort of patients with a single type of cancer, NSCLC. None of them had evidence of metastatic disease at that point. Potential confounders were adjusted for in the data analysis. The follow-up time frame was > 5 years.

Flaws in Previous Research

Many of the studies investigating this issue fail to provide an adequate answer to the question of whether psychological factors have an effect on survival because of significant flaws in the research design.[6] Some studies report findings based on very small samples, samples that are unrepresentative, or samples that are recruited late in the disease process, raising concerns regarding the robustness of findings. Many studies fail to control for potential confounders, such as type of cancer, stage of disease, performance status, patient age, or histologic grade, either statistically or by sampling. Probably the most serious of these is grouping different cancer types together within analyses, because different cancers have very different biologic profiles. For instance, it may be more plausible biologically for melanoma to be influenced by psychologic factors through the immune system than lung carcinoma because the immune system has been implicated in the pathogenesis of melanoma.[20,21] Some studies report results based on short follow-up. The influence of psychologic factors may become apparent only after a longer time. Alternatively, psychologic factors may produce initial survival benefits because of enhanced self-care, which may dissipate over a longer time. Finally, some studies have used inadequately defined or measured psychologic constructs.

TABLE 2
Changes in Optimism Scores after Treatment

		Mean ± SE		
Characteristic	No. of patients	Pretreatment	Posttreatment	Change
All patients	148	3.61 ± 0.05	3.51 ± 0.04	−0.11 ± 0.04
By treatment arm[a]				
R6	31	3.71 ± 0.12	3.68 ± 0.10	−0.03 ± 0.07
R3	33	3.67 ± 0.09	3.48 ± 0.09	−0.19 ± 0.07
R6C	41	3.58 ± 0.09	3.48 ± 0.07	−0.10 ± 0.07
R3C	43	3.53 ± 0.08	3.42 ± 0.08	−0.11 ± 0.09
By response to treatment				
Responder	99	3.59 ± 0.06	3.48 ± 0.06	−0.11 ± 0.05
Nonresponder	49	3.66 ± 0.08	3.56 ± 0.07	−0.10 ± 0.06

SE: standard error.

[a] R6: standard radiotherapy for 6 weeks (60 grays [Gy] in 30 fractions at 5 per week); R3: accelerated radiotherapy for 3 weeks (60 Gy in 30 fractions at 10 per week); R6C: standard radiotherapy plus chemotherapy (intravenous carboplatin given at a dose of 70 mg/m^2 per day on Days 1–5 and on Days 29–33 of radiotherapy); R3C: accelerated radiotherapy plus chemotherapy (intravenous carboplatin given at a dose of 70 mg/m^2 per day on Days 1–5 of radiotherapy).
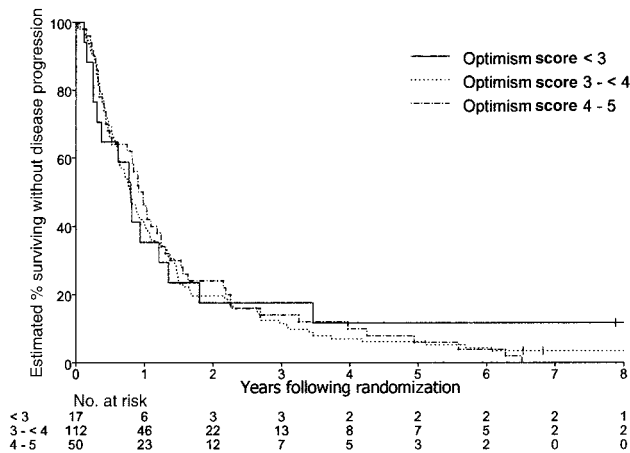

FIGURE 1. Progression-free survival in the three pretreatment optimism groups.

FIGURE 2. Overall survival in the three pretreatment optimism groups.

Changes in Optimism over Time

A small but significant drop in optimism scores was noted over time, but there was no significant difference in change in optimism levels between those who responded to treatment and those who did not respond, nor were there any differences related to the type of treatment received. Thus, there is no evidence that either treatment arm or lack of response to treatment was responsible for the decrease in optimism after treatment. It can be speculated that the most likely reasons for this drop in optimism were that, as patients experienced the toxicity of treatment or gained more information concerning their disease, and particularly the likelihood of long-term survival, they felt less optimistic about their future.
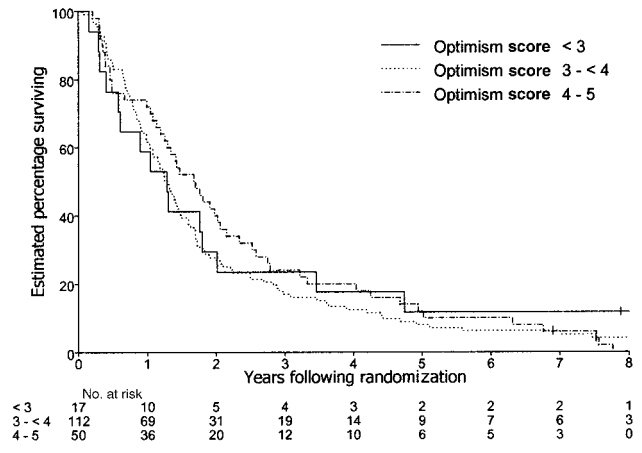
Fostering Appropriate Hope

We should question whether it is valuable to encourage optimism if it results in the patient concealing his or her distress in the misguided belief that this will afford survival benefits. If a patient feels generally pessimistic or is going through a period of pessimism, then it is important to acknowledge these feelings as valid and acceptable. A patient should not be encouraged to be optimistic if they are not feeling so inclined. Several researchers in the area have recognized that cancer patients feel social pressure to think or be positive about their disease.[22,23] There may even be an unintentional implication that patients ultimately are responsible for the outcome of their illness by not being sufficiently optimistic. However, optimism confers other significant benefits. It is associated strongly with lower levels of depression[11] and higher levels of subjective well being and quality of life.[24] Because optimism seems to be unrelated to sur-

vival from lung carcinoma, any benefits of encouraging optimism would need to relate to enhanced quality of life or reduced psychologic distress. However, whether psychologic interventions can change a patient's level of optimism will depend on the extent to which optimism is dispositional. This is not to say that positive hopes for the future should not be discussed. Indeed, it has been argued that physicians have an obligation to cultivate appropriate hope in patients as an integral part of care.[25] Patients with metastatic disease say that it is crucial that physicians are hopeful in their discussions about prognosis.[26] However, hope should be conveyed in an environment that supports the expression of fears and uncertainty for the future, so that the patient does not feel stymied emotionally. The most successful approaches are likely to be those that are tailored to the individual's natural dispositional outlook.

In his discussion of hope, Nunn[27] points out that hope is too often associated with unrealistic expectations. Hence, it is critical that the messages of hope that are provided to patients are appropriate. Links and Kramer[28] assert that, in the context of a poor prognosis such as lung carcinoma, legitimate hope may not be the same as that of a probable event. They argue that it is not necessarily inappropriate to hope for a cure, even if it is unlikely, but that messages of hope also should include more probable events related to quality-of-life issues, such as long periods of remission and remaining free from pain. However, fostering false optimism of a cure when a cure is not possible ultimately can be a source of regret,[29] because it may hinder patients and family making sensible treatment decisions and lifestyle decisions to make the best use of the remaining time together.

Limitations

There were some potentially confounding demographic variables that were not collected in the current study, such as marital status and education level. However, to our knowledge, there is no conclusive evidence that these factors affect survival in patients with lung cancer. Nevertheless, in hindsight, it would have been useful to collect this information. In addition, patients who consented to this study understood that they had localized disease and were being offered radical treatment with a small but definite prospect of extension of survival. Hence, they may have been more optimistic than the overall population of lung carcinoma patients.

Conclusions

There was no evidence that optimism was related to survival in patients with lung carcinoma. Hence, en-

couraging patients to be positive may represent just an additional burden. Instead, it is important to focus on fostering appropriate hopes for the future in an emotionally supportive environment so that patients and their family can make sensible treatment decisions and, if time is short, can make the most of the remaining time together.

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