Prognostic Understanding and Quality of Life in Patients With Advanced Lung Cancer: A Multicenter Study

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Abstract

Communication about the palliative setting remains difficult for many physicians. This seems a valid concern. Our study has shown that prognostic understanding will be associated with poorer emotional well-being and more pain but not with a worse mood. A poor mood has a detrimental effect on all aspects of quality of life. Our data suggest the need for psychological support, in addition to communication about the palliative setting.

Introduction: Communication about the palliative setting remains a barrier for many physicians because they are afraid to harm the patient by giving bad news. We sought to determine whether this a valid concern; the influence of prognostic understanding on patients' quality of life (QoL); and which factors influence this relationship. **Methods:** The present multicenter, cross-sectional study used a questionnaire to measure patients' prognostic understanding, QoL, mood, and coping strategy. **Results:** We surveyed 125 patients with advanced lung cancer. Prognostic understanding correlated significantly with emotional well-being ($r = -0.20$; $P = .01$) and pain ($r = 0.43$; $P = .00$) but not with anxiety ($r = 0.12$, $P = .12$) or depression ($r = 0.05$; $P = .29$). Patients with anxiety ($r = -0.23$; $P = .01$) and patients with depressive feelings ($r = -0.63$; $P = .00$) experienced poorer QoL. Four in 10 patients reported feelings of anxiety and/or depression. Positive reframing as a coping strategy was associated with a better QoL ($r = 0.25$; $P = .00$). **Conclusion:** Prognostic understanding was related to poorer emotional well-being and more pain but does not affect mood. Four in 10 patients reported feelings of anxiety and/or depression, which were associated with a poorer QoL. A holistic approach seems necessary when physicians communicate about the palliative setting.

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Introduction

Advanced lung cancer is associated with a poor prognosis and a median survival of ~10 months, which implies the use of palliative treatment from the diagnosis.[1] In the palliative setting, patients will choose quality of life (QoL) over prolongation of life through potentially toxic treatments.[2] QoL is a personal, multidimensional construct covering physical, psychological, spiritual, and social functioning. In such a care pathway, the patient is the only person who can decide which treatment option will be most suitable for optimizing their QoL. It is, therefore, important to inform patients

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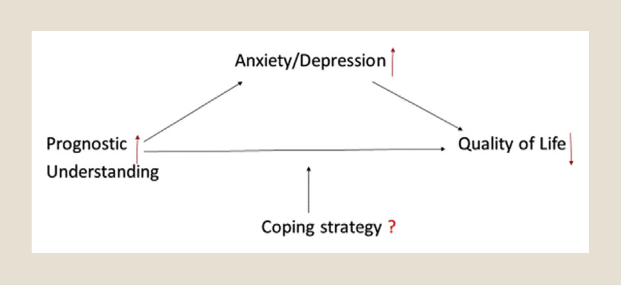
that the proposed treatment is unlikely to be curative to obtain prognostic understanding.[3] This allows for shared decision-making and leads to "the right therapy for the right patient at the right time," enabling personalized treatment.[4]

Patients' QoL is key in the treatment of patients with advanced lung cancer, and it is important to inform patients regarding the palliative intent of their treatment. It remains uncertain, however, whether patients' prognostic understanding influences QoL and whether their mood and the use of coping strategies play a role in this relationship. Some investigators have reported a possible detrimental effect of prognostic understanding on patients' QoL[5-7] and reported that prognostic understanding will lead to anxiety and/or depression, with lower QoL ensuing as a result. It has been suggested that adding psychological support to early palliative care, thus enhancing favorable coping strategies, would buffer this effect (Figure 1).

Figure 1 Relationship Between Prognostic Understanding, Mood, Coping and QoL



Methods

We conducted a multicenter cross-sectional study in 10 hospitals in Flanders, Belgium: Antwerp University Hospital, AZ Groeninge Kortrijk, ZNA Sint-Erasmus Borgerhout, AZ Monica Deurne, Sint-Jozef Kliniek Bornem and Willebroek, Ghent University Hospital, ZNA Middelheim Antwerp, Heilige Familie Reet, Ziekenhuis Oost Limburg, and Ziekenhuis Maas en Kempen, Maaseik. The ethical committee of all the hospitals approved the present study.

Patients with advanced lung cancer at any time in the disease trajectory were eligible for inclusion in the present study if they were aged >18 years and were able to read and write in Dutch. After the patients had provided written informed consent, the treating physician asked the patients to complete the questionnaires, either when visiting the outpatient clinic or during hospitalization. The following data were obtained: age, gender, marital status, religion, date of diagnosis, and World Health Organization performance status.[8]

Prognostic understanding was evaluated using the patients' responses to the statements "I can be cured" and "My treatment can cure me" on a 4-point Likert scale ranging from "very likely" to "not at all likely." Previous research has shown that prognostic understanding measured using this method is valid and reliable.[3] We also used the QLQ-C15-PAL, a shortened version of the European Organization for the Research and Treatment of Cancer QLQ-C30, a widely used instrument for measuring QoL in cancer research.[9] The QLQ-C15-PAL questionnaire contains 4 multi-item scales and 6 individual items that have been identified as important in the palliative population. All items are rated from 1 (not at all) to 4 (very much) in severity, except for the overall QoL scale, which is rated from 1 (very poor) to 7 (excellent). A high score on the symptom scale suggests increased distress, and a high score on the functional scale shows increased functional ability. Each scale was converted to a score ranging from 0 to 100.

Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS), which consists of 14 items: 7 items on the anxiety subscale (HADS Anxiety) and 7 on the depression subscale (HADS Depression). The HADS Anxiety scale focuses mainly on the symptoms of generalized anxiety disorder and the HADS Depression scale focuses on anhedonia, the main symptom of depression.[10] Each item is scored on a response scale with 4 alternatives, ranging from 0 to 3. After adjusting for 6 items that are reverse scored, all responses were summed to obtain the 2 subscales. The cutoff scores recommended by Zigmond and Snaith[11] are 8 to 10 for doubtful cases and ≥11 for definite cases. An optimal balance between sensitivity and specificity has been found using a cutoff score of 8 for both the HADS Anxiety and the HADS Depression scales.

The use of coping strategies was assessed using the brief COPE (Coping Orientation for Problem Experiences) questionnaire.[12] We incorporated 6 coping strategies that are considered highly relevant to patients with incurable cancer[7]: emotional support, positive reframing, active coping, acceptance, self-blame, and denial. The developer of the instrument has encouraged such selective and flexible use of the subscales. Participants select the degree to which they have used each type of coping (1, not at all; 2, a little bit; 3, a medium amount; and 4, a lot).

Statistical Analysis

All data were collected and encoded in an SPSS database (SPSS statistics, version 24; IBM Corp, Armonk, NY) by the principal investigator. A sum score was calculated for all scales, with the median, standard deviation, and Cronbach's α. The data were analyzed using descriptive statistics. Pearson's correlation coefficient or regression analysis and multiple hierarchical regression analysis were used to determine the relationships between the different parameters. The results were considered significant at $P = .05$. To determine whether the coping strategy had a moderating effect on the relationship between prognostic understanding and QoL, the interaction term between prognostic understanding and coping strategy was added to a multiple regression model.[13]

Results

The trial included 125 patients from 10 hospitals and the studio period was from May 1 to June 31, 2017. We asked a total of 128 patients to participate. Three patients were not willing to complete the questionnaire: 1 was too tired, 1 reported being tired of completing questionnaires, and 1 did not give a reason. The sociodemographic characteristics of all the patients are listed in Table 1.

The range, number of items, mean, standard deviation, and Cronbach's α of the prognostic understanding, mood, and coping strategy are listed in Table 2. The mean value for prognostic understanding was 2.9. Of the 125 patients, 47% were aware of the incurability of their lung cancer. Of these, 33% showed prognostic

Table 1 Demographic Characteristics

Variable	Value
Age, y	
Median	65
Range	41-85
Interval from diagnosis, mo	
Median	12
Range	1-88
Gender, n (%)	
Male	75 (60)
Female	50 (40)
WHO grade, n (%)	
0	23 (19)
1	47 (56)
2	35 (28)
3	18 (15)
Marital status	
Married	85 (69)
Unmarried	11 (9)
Divorced	18 (15)
Widow(er)	10 (8)
Religious	
Yes	65 (59)
No	45 (41)
Children	
Yes	113 (91)
No	11 (9)

Abbreviation: WHO = World Health Organization.

understanding, meaning that they were also aware that their treatment was not meant to cure them. The median interval from diagnosis was 12 months (range, 1-88 months). Prognostic understanding correlated significantly with the interval from diagnosis ($r = 0.34$; $P = .00$). Emotional well-being did not correlate significantly with the interval from diagnosis ($r = -0.16$; $P = .1$). The longer the interval from the diagnosis with lung cancer, the better the patients' prognostic understanding. However, the interval from the diagnosis did not correlate with the patients' emotional well-being.

In our study, 1 in 4 patients were experiencing anxiety or depression. Of our 125 patients, 20% and 26% had mild complaints related to anxiety or depression, 11% and 10% had moderate complaints, and 4% and 2% were severely anxious or severely depressed (Table 3). The range, number of items, mean, standard deviation, and Cronbach's α for the various dimensions of QoL are presented in Table 4. These dimensions are explored in more depth in the subsequent paragraphs in relation to the results presented in Table 5.

The correlations between prognostic understanding and the different aspects of QoL are presented in Table 5. Emotional well-being significantly and negatively correlated with prognostic understanding ($r = -0.20$; $P < .05$) and with pain ($r = -0.22$; $P < .05$). No other significant correlations were observed between prognostic understanding and the other aspects of QoL.

The correlations between mood and QoL are also listed in Table 5. Anxiety correlated significantly with general QoL ($r = -0.23$; $P < .05$), physical well-being ($r = -0.21$; $P < .05$), emotional well-being ($r = -0.44$; $P < .01$), pain ($r = 0.46$; $P < . 01$), dyspnea ($r = 0.21$; $P < .05$), insomnia ($r = 0.38$; $P < .01$), and constipation ($r = 0.21$; $P < .05$). Depression correlated significantly with general QoL ($r = -0.63$; $P < .01$), physical well-being ($r = -0.44$; $P < .01$), emotional well-being ($r = -0.73$; $P < .01$), pain ($r = 0.37$; $P < .01$), fatigue ($r = 0.49$; $P < .01$), dyspnea ($r = 0.44$; $P < .01$), insomnia ($r = 0.20$; $P < .01$), loss of appetite ($r = 0.45$; $P < .01$), nausea ($r = 0.29$; $P < .01$), and constipation ($r = 0.27$; $P < .01$).

The correlations between the use of coping strategies and QoL are also presented in Table 5. Positive reframing correlated significantly with general QoL ($r = -0.25$; $P < .01$), emotional well-being ($r = -0.33$; $P < .01$), pain ($r = -0.30$; $P < .01$), fatigue ($r = -0.22$; $P < .01$), loss of appetite ($r = -0.22$; $P < .01$), and nausea ($r = -0.24$; $P < .01$). Emotional coping correlated significantly with physical well-being ($r = -0.20$; $P < .05$). Self-blame correlated significantly with emotional well-being ($r = -0.19$; $P < .05$) and insomnia ($r = 0.19$; $P < .05$).

A 2-stage hierarchical multiple regression analysis was conducted to investigate whether the use of coping strategies moderates the relationship between prognostic understanding and emotional well-being. In the first step, the standardized scores of the sum scales for prognostic understanding, acceptance, active coping, emotional support, self-blame, positive reframing, and denial were

Table 2 Range, Number of Items, Mean, Standard Deviation, and Cronbach's α

Variable	Range	Items, n	Mean	SD	Cronbach's α
Prognostic understanding	1-4	2	2.9	1.01	0.92
Anxiety	0-21	7	6.5	4.1	0.81
Depression	0-18	7	6.4	3.6	0.72
Acceptance	0-4	2	3.0	0.75	0.69
Denial	0-4	2	1.8	0.89	0.78
Active coping	0-4	2	2.3	0.60	0.81
Emotional support	0-4	2	3.5	0.66	0.89
Positive reframing	0-4	2	2.5	0.84	0.69
Self-blame	0-4	2	1.7	0.85	0.79

Abbreviation: SD = standard deviation.

Table 3 Percentage of Patients With Normal, Mild, Moderate, and Severe Complaints

HADS Score	Anxiety, %	Depression, %
0-7 (normal)	65	62
8-10 (mild)	20	26
11-14 (moderate)	11	10
>14 (severe)	4	2

Abbreviation: HADS = Hospital Anxiety and Depression Scale.

incorporated as predictors, and the sum scale of emotional well-being was added as an independent variable. Model 1 showed statistically significant results [$F(6,105) = 4.0$; $P < .01$]. The variability was 23% ($R^2 = 0.23$). No significant correlation was found between prognostic understanding and emotional well-being ($P = .34$). Acceptance ($\beta = 0.21$; $P = .03$) and positive reframing were significantly related to emotional well-being. In the second step, the following interaction terms were added: prognostic understanding*acceptance, prognostic understanding*active coping, prognostic understanding*emotional support, prognostic understanding*self-blame, prognostic understanding*positive reframing, and prognostic understanding*denial. The results from model 2 were not significant [$F(12,99) = 1.5$; $P = .21$]. The variability was 28% ($R^2 = 0.28$). None of the interaction terms was found to be significant. The present study showed no statistically significant correlations between prognostic understanding and anxiety ($r = 0.12$; $P = .12$) or depression ($r = 0.05$; $P = .05$).

Discussion

To the best of our knowledge, the present study is the first European study to investigate the relationship between prognostic understanding and QoL in patients with advanced lung cancer. Our results showed that prognostic understanding was associated with poorer emotional well-being and more pain. We found no relationship between prognostic understanding and the other domains of QoL, nor with mood. In contrast, more anxious and/or depressive feelings were found to correlate with detrimental effects in the different domains of QoL. Patients who were using positive reframing as a coping strategy reported a better QoL.

A limited number of previous studies have explored the relationship between prognostic understanding and the QoL of patients with advanced cancer. Three monocentric studies on prognostic understanding and QoL were conducted by the same research group from Massachusetts General Hospital (MGH).[5-7] The investigators showed that prognostic awareness was related to worse overall QoL and mood. It is likely that their results differ from our results because of differences in the methodological approach. Two main differences have been discussed in the subsequent paragraphs.

First, the MGH investigators used the Functional Assessment of Cancer Therapy—General, version 4, questionnaire to measure QoL. This questionnaire consists of 27 questions and combines functional, physical, social, and emotional well-being. It is not clear whether some or all of the specific domains of QoL were related to prognostic understanding in these studies. In our study, prognostic understanding was evaluated using 2 items: "I can be cured" and "My treatment can cure me." The response options were given using a 4-point Likert scale, ranging from "very likely" to "not at all likely." Previous research has shown that prognostic understanding measured using this method is valid and reliable in our patient population.[3] Patients who have obtained prognostic understanding will choose QoL as goal of therapy significantly more often statistically than will patients who are not aware of the incurability of their disease.

Second, the MGH studies used different terms for defining prognostic understanding, resulting in different outcomes for QoL and mood. Of the MGH patients, 50% to 67% had prognostic understanding, depending on how it was defined.[7] This is a high proportion compared with that reported by other studies.[3,13,14] The use of the word "terminal" to define prognostic understanding resulted in patients reporting a poorer QoL and mood.[7] When prognostic understanding was defined as "knowing one cannot be cured," it did not correlate with poorer QoL or mood. Patients who indicated that their doctors' intention was not to cure them reported poorer QoL and more anxiety. In the present study, we did not use the term "terminal" because it refers to care at the end of life, in contrast to "palliative," which focuses on relieving pain rather than treating the condition. Thus, the definitions of prognostic understanding are key and can make comparisons difficult.

The results of the present study have confirmed the findings from earlier research conducted of patients with gastrointestinal cancer,[5]

Table 4 Range, Number of Items, Median, Standard Deviation, and Cronbach's α of the Different Dimensions of Quality of Life

Variable	Range	Items, n	Mean	SD	Cronbach's α
General quality of life	0-100	1	61.29	19.4	NA
Physical quality	0-100	3	78.6	22.34	0.70
Emotional well-being	0-100	2	72.4	24.87	0.73
Pain	0-100	2	26.37	30.06	0.87
Fatigue	0-100	2	24.6	27.44	0.77
Dyspnea	0-100	1	32.5	31.66	NA
Insomnia	0-100	1	33.3	34.93	NA
Loss of appetite	0-100	1	31.4	35.4	NA
Constipation	0-100	1	14.6	27.7	NA
Nausea	0-100	1	18.0	28.47	NA

Abbreviations: NA = not applicable; SD = standard deviation.

in which accurate prognostic understanding was associated with lower QoL. Prognostic understanding was assessed using the question "In your opinion, what is the chance that your cancer is curable?" The answers were given using a 7-point Likert scale, ranging from 0% ("no chance") to >90% ("extremely high"). Scores of 1 to 3 were considered to indicate prognostic understanding. Measured using this scale, prognostic understanding was related to worse overall QoL and worse social and emotional well-being. Mood did not correlate with prognostic understanding. This measurement of prognostic understanding was similar to that used in our study, with a similarity reflected in the results. Patients who have described themselves as "terminally ill" (indicating that they have prognostic understanding) have reported poorer QoL and mood.[5] In another study of patients with hematologic disease, prognostic understanding was measured differently.[6] One Chinese study of 137 patients with epidermal growth factor receptor-mutated lung cancer concluded that prognostic understanding will be associated with poorer QoL and more anxiety and depressive feelings.[14] Prognostic understanding was determined using an interview: patients were asked whether they could name their disease. If the patient did not know that they had lung cancer, no further questions were asked. If the patient was aware that they had lung cancer, they were asked if their cancer could be cured. The patients were then divided into 3 groups: fully aware, partially aware (if only the diagnosis was known), and unaware. In that study, 21% were found to be fully aware, 63% were anxious, and 72% had depressive symptoms.[15] More studies are needed to investigate the influence of prognostic understanding on QoL in a range of different patient populations.

An additional result of our study was that the patients had a high psychological symptom burden, with 40% experiencing anxiety or depressive feelings—the most important factors in QoL. This finding was consistent with those from previous studies.[16,17] The questionnaire used in our study also showed that a coping strategy, namely positive reframing, can positively influence QoL in this patient population. This, too, has been reported previously.[18]

The results from the present study have confirmed the general public's perception that prognostic understanding is responsible for lower QoL. Also, oncologists worry about damaging patients' emotional well-being, which might explain why many admit to withholding prognostic information.[19,20] This seems a valid concern, considering the data from our study. Communication with patients regarding the palliative setting remains challenging. Nevertheless, it is important to inform patients regarding the palliative intent of the treatment from the beginning, despite its effect on emotional well-being. The treating oncologist/pulmonologist should inform the patient of the bad news. This conversation should be rehearsed, announced, and held had in the presence of the patients' caregivers and family in a calm environment. In most cases when bad news is presented, a part of the message will not be received. It will require time and several visits. Providing care as treating physicians enables us to establish longitudinal relationships with the patients and their families to help patients understand their prognosis and make decisions about their care over time. In real life, treating oncologists have tended to focus on treatment and "forget" to talk about the prognosis.[21]

Table 5 Correlations Between Prognostic Understanding, Mood, Coping Strategy, and Quality of Life

Variable	Domain[a]									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Prognostic understanding	−0.07	−0.10	−0.20[b]	0.22[b]	0.16	0.05	0.03	0.04	0.11	−0.17
Anxiety	−0.23[b]	−0.21[b]	−0.73[c]	0.37[c]	0.11	0.21[b]	0.38[c]	0.12	0.11	0.21[b]
Depression	−0.63[c]	−0.44[c]	−0.44[c]	0.46[c]	0.49[c]	0.44[c]	0.20[c]	0.45[c]	0.29[c]	0.27[c]
Positive reframing	0.25[c]	0.09	0.33[c]	−0.30[c]	−0.22[c]	0.03	−0.13	−0.22[c]	−0.24[c]	−0.11
Active coping	0.06	0.11	−0.06	0.03	−0.15	0.04	0.16	−0.04	−0.15	−0.07
Acceptance	−0.00	−0.08	0.16	−0.13	0.02	0.06	−0.07	−0.00	−0.14	0.05
Emotional coping	−0.08	−0.20[b]	−0.05	−0.01	0.16	0.04	−0.09	0.90	0.08	0.10
Denial	0.04	−0.11	0.05	−0.01	−0.12	0.17	−0.10	−0.11	−0.07	−0.05
Self-blame	−0.02	0.01	−0.19[b]	0.07	−0.09	0.02	0.19[b]	−0.08	−0.13	−0.08

[a] Domain: 1, general quality of life; 2, physical well-being; 3, emotional well-being; 4, pain; 5, fatigue; 6, dyspnea; 7, insomnia; 8, loss of appetite; 9, nausea; and 10, constipation.

[b] $P < .05$.

[c] $P < .01$.

However, prognostic understanding is considered to be of vital importance for informed decision-making and advanced care planning at the end of life. The results of our former study have confirmed this finding. Patients with prognostic understanding were more aware of the primary goal of their palliative treatment. We have concluded that it is beneficial to inform such patients that treatment cannot cure them, because this will lead them toward other choices better suited for palliative treatment.[3] The question remains whether patients can be informed of the prognosis from the diagnosis onward without detrimental effects on their QoL. It seems that this is only possible if the necessary preconditions (ie, early palliative care with holistic support of the patient and family) have been met. The studies from Temel et al[2] and Bakitas et al[22] showed that informing patients from the diagnosis with an integrated holistic approach (early palliative care) will lead to a better Qol and, even, better survival, in combination with better prognostic understanding. Studies have found that the late implementation of palliative care cannot fully improve patients' QoL.[23,24] Also, the results from a real-world study have provided supporting evidence that earlier palliative care will be associated with a greater process of care quality score, predominantly driven by improvements in the domain of information and care planning.[25]

In the present study, we sought to emphasize the importance of informing patients of their palliative setting, provided that patients are provided psychological and holistic support, as seen in early palliative care. The key elements of early palliative care have been provided in a prospective study, suggesting that palliative care clinicians can help improve the QoL and mood outcomes in patients with incurable cancer in part by enhancing effective coping processes.[26] Our study also showed that positive reframing as a coping strategy has a positive effect on QoL. Further research is needed to confirm these promising results. Physicians must be educated on how to improve their patients' coping skills.

At present, it is not possible for all patients with advanced lung cancer to be treated and/or counseled on a regular basis by a psychologist in our hospital. We plan to measure anxiety and depressive feelings using the HADS questionnaire during first-line chemotherapy. Patients with higher scores than normal (4 of 10 in our study) will be referred for psychological evaluation. This workload seems achievable for the psychologist. Our team believes that informing patients about the palliative setting remains important despite its negative effects on well-being. A holistic approach with psychological support seems mandatory when treating patients with advanced lung cancer to overcome this deterioration of QoL. All team members must be expected to allow for some time for psychological support during visits.[27]

The present research had limitations related to cross-sectional investigations. First, the patients completed the questionnaires only once. If another time frame had been chosen, it might have provided other results. Because no comparisons were made over time, causality could not be evaluated. Second, only 3 patients were not willing to complete the questionnaires. This was a very low screening failure rate, indicating a possible bias, because only patients who were already communicating openly about their prognosis were asked to participate. In addition, we found no reference standard for measuring prognostic understanding, which has hindered research on this important topic.

Conclusion

Patients who possess prognostic understanding will have poorer emotional well-being and more pain. Prognostic understanding was not associated with more anxiety or depressive feelings. The QoL of patients with advanced lung cancer will be especially influenced by their mood. Approximately 40% of patients will be anxious or have depressive feelings. Patients with advanced lung cancer require psychological support, not only when proposing the palliative setting, but also to ameliorate their mood, perhaps through the teaching of more favorable coping strategies. The "positive reframing" coping strategy improved the QoL of patients with advanced lung cancer. In the future, we plan to conduct a prospective study to investigate whether favorable coping strategies can be taught and whether they have an effect on QoL.

Clinical Practice Points

- To the best of our knowledge, ours is the first European study to investigate the relationship between prognostic understanding and QoL in patients with advanced lung cancer.
- Our results have shown that prognostic understanding is associated with poorer emotional well-being and more pain but not with a worse mood.
- The QoL of patients with advanced lung cancer is especially influenced by their mood.
- Approximately 40% of patients will have anxious or have depressive feelings.
- Patients who were using positive reframing as a coping strategy reported a better QoL.
- Patients with advanced lung cancer require psychological support, not only when proposing the palliative setting, but also to ameliorate their mood, perhaps through the teaching of more favorable coping strategies.

Disclosure

The authors declare that they have no competing interests.

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