

Depressive symptoms and performance status are associated with (Health-Related) Quality of Life in patients with advanced-stage lung cancer: an observational multi-center cohort study

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Submitted in BMC Cancer

ABSTRACT

Background: Identification of variables associated with (Health-Related) Quality of Life ((HR)QoL) offers opportunities to enhance patient care during chemotherapy. The aim was to examine the association of sociodemographic variables, personality traits, and depressive symptoms with (HR)QoL in patients with advanced-stage lung cancer at the start of chemotherapy.

Methods: Patients (n=151) completed the State-Trait Anxiety Inventory (trait anxiety subscale), the Neuroticism-Extraversion-Openness-Five Factor Inventory (NEO-FFI), the Center for Epidemiologic Studies Depression (CES-D), the World Health Organization Quality of Life-BREF (WHOQOL-BREF), and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30). Simple linear regression analyses were performed to select (HR)QoL associated factors ($P \leq 0.10$) followed by multiple linear regression analyses using backwards stepwise selection.

Results: In the multiple regression analyses, CES-D score ($\beta = -0.63$ to -0.22 ; P-values < 0.03) was most often associated with the WHOQOL-BREF domains and general facet, whereas CES-D score ($\beta = -0.67$ to -0.40 ; P-values < 0.001) and Eastern Cooperative Oncology Group (ECOG) performance status ($\beta = -0.30$ to -0.19 ; P-values < 0.03) were most often associated with the scales of the EORTC QLQ-C30.

Conclusions: Higher scores on depressive symptoms and ECOG performance status are related to lower (HR)QoL in patients with advanced-stage non-small cell lung cancer. Supportive care interventions aimed at improvement of depressive symptoms and performance score may facilitate an increase of (HR)QoL during treatment.

INTRODUCTION

Patients with advanced-stage lung cancer have a poor prognosis [1]. A five year survival of 6% was reported in patients with stage four non-small cell lung cancer according to the datasets of the International Association for the Study of Lung Cancer staging project [1]. In addition, treatment is in most patients with advanced disease lung cancer associated with substantial adverse events which can directly influence Health-Related Quality of Life (HRQoL) and Quality of Life (QoL). Therefore, treatment goals should not be solely focused on survival benefits, but also consider the effect on patients' (HR)QoL.

Earlier, several factors have been associated with (HR)QoL in patients with lung cancer (i.e., age, performance status, gender, education, and having a spouse [2-4]). In addition, in patients with cancer, depressive symptoms are negatively related with HRQoL [5,6]. However, HRQoL measures only patients' feelings related to their health, while QoL also reflect additional concepts, such as the environment and spirituality [7]. Therefore, investigating the association between depressive symptoms and QoL provides further information about the relation between depressive symptoms and a patient's well-being.

Personality has been associated with depressive symptoms in chronic illnesses [8,9] and reduced emotional (HR)QoL in heart failure patients [10]. In breast cancer, high scores on certain personality traits (i.e., trait anxiety and neuroticism) were associated with lower overall QoL scores over time [11]. Considering these results, the assessment of the association of personality traits with (HR)QoL at the start of treatment in patients with lung cancer may help identify patients who are prone to low levels of (HR)QoL. Especially in these patients with low levels of (HR)QoL at the start of treatment further deterioration should be prevented. However, studies that have investigated the relation between these variables (i.e., personality, sociodemographic, clinical and psychological factors (e.g., depressive symptoms) and (HR)QoL) in patients with lung cancer are not reported. This is unfortunate especially since lung cancer patients are at risk to have lower scores on functioning and well-being given their disease, treatment-related adverse events, and life expectancy [12].

Therefore, knowledge of which factors are associated with (HR)QoL may be worthwhile, because these factors (e.g., depressive symptoms, anxiety) may require additional care in individual patients or provide starting points for the development of interventions. Contemplating on these considerations, we aimed to evaluate the association between depressive symptoms and personality traits and established their importance among known variables associated with HRQoL (i.e., age, performance status, gender, education, and having a spouse [2-4]) in patients with advanced-stage cancer who are prone to a deterioration in (HR)QoL resulting from cancer and treatment-related adverse events and poor prognosis. We analysed to which extent depressive symptoms and personality solely and in combination with these known variables are associated with (HR)QoL in patients with advanced-stage lung cancer at the start of treatment.

METHODS

Study population

PERSONAL is a prospective observational multi-center cohort study of patients with stage IIIB or IV non-squamous non-small cell lung cancer and unresectable mesothelioma receiving pemetrexed. Patients were recruited from October 2012 to November 2014 from three teaching hospitals (Erasmus University Medical Center, Amphia Hospital and Sint Franciscus Gasthuis hospital) and a regional hospital (Bravis hospital). Patients were enrolled if they met the following criteria: they were aged eighteen years or older, had a cytological or histological confirmed diagnosis of stage IIIB or IV non-squamous non-small cell lung cancer or unresectable malignant pleural mesothelioma, and started treatment with pemetrexed in combination with cisplatin or carboplatin as either first line or with pemetrexed monotherapy as second line. Patients were excluded if they were not able to read Dutch or could not complete the questionnaires because of a physical or mental condition. Informed consent was obtained from all individual participants included in the study. All procedures were in accordance with the ethical standards of the institutional review board of the Erasmus University Medical Center in Rotterdam, The Netherlands (approval number MEC-2012-232) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Study measures

The World Health Organization Quality of Life-BREF questionnaire (WHOQOL-BREF) is a cross-cultural and generic QoL instrument [13]. The WHOQOL-BREF comprises 24 items divided over four domains plus two general facet items describing overall QoL and general health. Items are scored on a Likert-scale from one (worst response) to five (best response). The domains represent physical health (seven items), psychological health (six items), social relationships (three items) and environment (eight items). WHOQOL-BREF domains are scored on a 4-20 scale and the general facet on a 2-10 scale with higher scores indicating better QoL [13,14]. The WHOQOL-BREF has satisfactory psychometric properties in patients with lung cancer [15], chronic diseases and other cancer types [13], except for the social relationships domain (i.e., relatively low Cronbach's alpha).

The European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire- Core 30 (EORTC-QLQ-C30) is a cancer specific HRQoL instrument [16]. It consists of 30 items and incorporates a global Health Status/QoL scale, five functional scales and several items assessing symptoms or problems. The functional scales represent physical functioning (five items), cognitive functioning (two items), emotional functioning (four items), role functioning (two items), and social functioning (two items). EORTC QLQ-C30 domains are scored on a 0-100 scale, with higher scores on the functional scales being

indicative of better HRQoL, whereas higher scores on the symptom scales represent worse symptoms [16]. The EORTC has demonstrated acceptable psychometric properties [17].

The State-Trait Anxiety Inventory (STAI) questionnaire assesses state and trait anxiety [18]. We used the 10-item STAI trait anxiety subscale (short version), which was developed in women suspected with breast cancer and breast cancer survivors [19]. Trait anxiety refers to the tendency to respond to threatening situations with increased anxiety intensity [11]. It is considered to be a personality factor. Items are scored on a four-point scale ranging from 1 (almost never) to 4 (almost always). A score of ≥ 22 is indicative for high trait anxiety [19]. The original Dutch translation of the STAI [18,20] and the 10-item subscale itself [19] have good psychometric properties.

The Center for Epidemiologic Studies Depression Scale (CES-D) is a 20-item questionnaire which evaluates depressive symptoms [21]. We used the 16-item version of the CES-D, in which the four positively formulated items of the original CES-D are removed [22,23] since they lacked validity and did not correspond well with the definition of depressive symptoms. Items are scored on a four-point scale with scores ranging from zero (rarely) to three (mostly). The CES-D has good psychometric properties [22,24].

The 60-item Neuroticism-Extraversion-Openness-Five Factor Inventory questionnaire (NEO-FFI) assesses personality based on the Five Factor Model [25-27]. It describes neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness. Neuroticism measures emotional stability, while extraversion assesses the level to which orientation, energy and attention are focused on the outside world instead of the inner world. Openness reflects to an open attitude regarding experiences, beliefs and people, whereas agreeableness relates to orientation in other people's experiences, goals and interests. Conscientiousness refers to the conscience as a guiding and reflective instrument for behavior [11]. Items are scored on a five-point scale with scores ranging from one (totally disagree) to five (totally agree). The NEO-FFI has good psychometric properties [28].

All questionnaires were completed after diagnosis and just before or at the first day of the first cycle of chemotherapy. In addition, we collected sociodemographic information (i.e., age, gender, educational level, ethnicity, employment, marital status, smoking status) and clinical information (i.e., history, cancer stage, disease response and the Eastern Cooperative Oncology Group (ECOG) performance status).

Statistics

Patient characteristics between patients who completed the questionnaires and those who did not were compared with Fisher's exact test and the independent T-test.

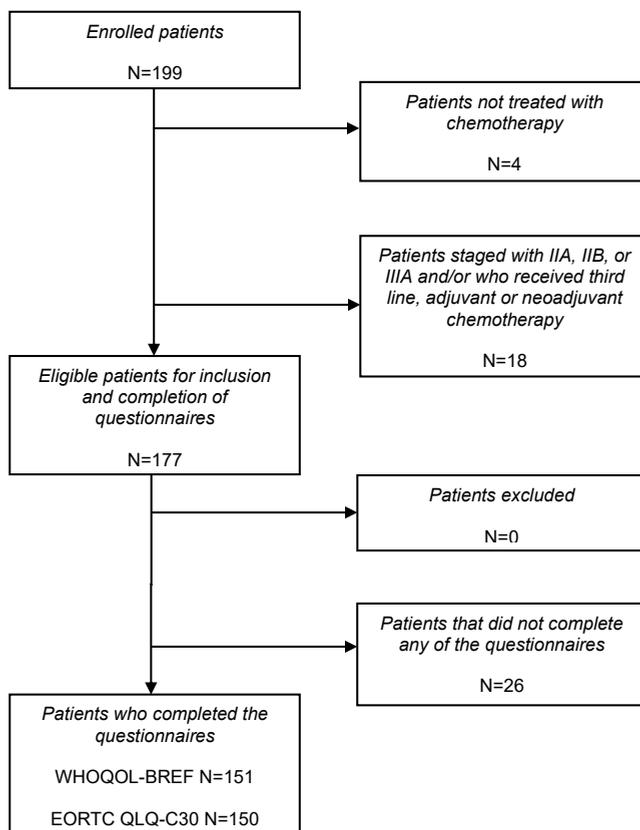
Given the sample size of 151 patients, simple linear regression analyses were performed as a minimal sample size of $50 + 8m$ (in which m is the number of predictors) is recommended [29]. Analyses were conducted for sociodemographic variables (i.e., age, gender,

ethnicity, education, employment, and partner status), ECOG performance status, CES-D score, STAI Trait subscale score, and NEO-FFI subscale scores to identify possible factors associated with the WHOQOL-BREF domains and EORTC QLQ-C30 scales. To prevent non-identification of important variables by using a more strict alpha of ≤ 0.05 , variables with an alpha of ≤ 0.10 were selected as possible predictors [30,31].

With the variables associated with the WHOQOL-BREF domains and EORTC QLQ-C30 scales according to the simple linear regression analyses, multiple linear regression analyses were performed. Subsequently, in a new model for each (HR)QoL scale/domain, age and gender were added if not identified as a possible factor in the simple regression analysis since these variables have been associated with HRQoL [4].

An alpha of ≤ 0.05 was used to identify significant factors in the multiple linear regression analyses. All analyses were performed using IBM SPSS Statistics for Windows version 21.0.

Fig. 1 Selection of patients



Abbreviations: N, number of patients; WHOQOL-BREF, World Health Organization Quality of Life-BREF questionnaire; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30

RESULTS

Patient characteristics

Figure 1 demonstrates the selection of patient. In total, 151 patients were used for analyses with the WHOQOL-BREF and 150 patients for analyses with the EORTC QLQ-C30. Table 1 summarizes the patient characteristics of the included patients and the patients who did not complete any of the questionnaires. These patients did not differ from the 151 included patients according to the age, sex, ethnicity, tumour type, and line of therapy, except for performance status. The proportion of patients with a performance status of two or higher was larger in the patients that were not available for the analyses than the included patients. WHOQOL-BREF domain scores, EORTC QLQ-C30 scale score, personality scale scores and CES-D scores are summarized in Table 2.

Linear regression analyses

Results of the simple linear regression analyses for each of the (HR)QoL domains/scales are demonstrated in the Supplementary Materials. Table 3 demonstrates the multiple linear regression analyses for the WHOQOL-BREF domains and general facet. CES-D score was negatively associated with the general facet and with all WHOQOL-BREF domains, except social relationships. For the EORTC QLQ-C30 scale scores, CES-D score was negatively associated with the functioning scales and the global Health Status/QoL score (Table 4). Moreover, for both WHOQOL-BREF and EORTC QLQ-C30 domains/scales, except for environment, the association with CES-D score was the strongest. ECOG performance status was negatively associated with the physical, role, and social functioning scale scores of the EORTC QLQ-C30 and with the physical health domain of the WHOQOL-BREF. For the NEO-FFI personality traits, only a positive association between the conscientiousness scale and the physical health domain of the WHOQOL-BREF was observed. Trait anxiety was negatively associated with environment (WHOQOL-BREF) and positively with role functioning (EORTC QLQ-C30). For the WHOQOL-BREF explained variances ranged from 0.20 to 0.55 and for the EORTC QLQ-C30 from 0.36 to 0.66.

DISCUSSION

Due to cancer diagnosis and treatment-related side effects advanced-stage lung cancer patients are at risk to experience lower (HR)QoL compared with the general population. Physicians are aware of this [32] and try to optimize (HR)QoL. To our knowledge, this prospective multi-centre observational study is the first to report the association of personality and depressive symptoms with (HR)QoL in patients with advanced-stage lung cancer. Considering that HRQoL reflects merely to those components of QoL that are influenced

Table 1. Characteristics of study population

Characteristic	Patients who completed questionnaires (N=151)	Patients who did not complete any questionnaire (N=26)	P _a
Age, years _b			
Mean (SD)	63.3 (9.1)	63.7 (8.7)	0.85
Min, max	37, 83	47, 80	
Gender			
Male	82 (54.3)	12 (46.2)	0.53
Ethnicity			
White / Caucasian	142 (94.0)	25 (96.2)	1.00
Other	9 (6.0)	1 (3.8)	
Education _c			
Low	113 (74.8)		
High	32 (21.2)		
Unknown	1 (0.7)	26 (100.0)	
Employment _b			
Yes	38 (25.2)	1 (3.8)	
No	112 (74.2)		
Unknown	1 (0.7)	25 (96.2)	
Partner status _b			
Partner	122 (80.8)	1 (3.8)	
No partner	28 (18.5)		
Unknown	1 (0.7)	25 (96.2)	
Cancer stage _b			
Locally advanced (IIIB)	19 (12.6)	2 (7.7)	
Metastatic (IV)	124 (82.1)	23 (88.5)	
Other	8 (5.3)	1 (3.8)	
Type of tumor _b			
Adenocarcinoma	136 (90.1)	24 (92.3)	1.00
Large cell carcinoma, mesothelioma, other	15 (9.9)	2 (7.7)	
Line of therapy			
First	140 (92.7)	22 (84.6)	0.24
Second	11 (7.3)	4 (15.4)	
ECOG performance status _b			
Grade 0 or 1	135 (89.4)	18 (69.2)	0.02
Grade 2 or higher	14 (9.3)	7 (26.9)	
Unknown	2 (1.3)	1 (3.8)	

Values are given in numbers (percentages) unless stated otherwise.

_aP-values reflect differences between patients who completed any questionnaire and those who did not.

_bMeasured at the start of treatment with chemotherapy

_cLow education: persons whose highest level of education is primary education, lower general education or lower vocational education. High education: persons whose highest level of education is higher general education, higher vocational education or university.

Abbreviations: N, number of patients; SD, standard deviation; ECOG, Eastern Cooperative Oncology Group (ECOG)

Table 2. WHOQOL-BREF, EORT QLQ-C30, NEO-FFI, CES-D, and STAI trait scale/domain scores

Questionnaire	Scale/domain	N	Median	Mean (SD)	Min, max (IQR)
WHOQOL-BREF					
	Physical health	145	13.1	12.9 (3.1)	4.0, 20.0 (4.6)
	Psychological health	145	14.7	14.5 (2.4)	9.3, 20.0 (3.3)
	Social relationships	145	16.0	16.3 (2.5)	8.0, 20.0 (3.3)
	Environment	145	16.0	15.9 (2.2)	10.0, 20.0 (3.0)
	General facet	142	6.0	5.8 (1.7)	2.0, 10.0 (2.0)
EORTC QLQ-C30					
	Physical functioning	150	66.7	68.1 (24.1)	6.7, 100.0 (33.3)
	Cognitive functioning	142	83.3	80.3 (23.1)	0.0, 100.0 (33.3)
	Emotional functioning	142	75.0	67.3 (24.0)	0.0, 100.0 (33.3)
	Role functioning	149	66.7	55.1 (32.8)	0.0, 100.0 (50.0)
	Social functioning	142	83.3	71.5 (27.0)	0.0, 100.0 (50.0)
	Global Health Status/QoL	142	58.3	54.8 (25.5)	0.0, 100.0 (41.7)
NEO-FFI					
	Neuroticism	137	28.0	28.1 (7.4)	12.0, 53.0 (8.5)
	Extraversion	133	40.0	40.4 (6.6)	22.0, 56.0 (9.5)
	Openness	134	34.0	34.3 (5.9)	20.0, 50.0 (7.3)
	Agreeableness	139	43.0	42.8 (5.0)	29.0, 54.0 (6.0)
	Conscientiousness	134	47.0	47.1 (5.7)	34.0, 60.0 (9.3)
CES-D					
	Depressive symptoms	148	6.2	8.5 (7.6)	0.0, 36.3 (10.5)
STAI					
	Trait anxiety	147	17.0	17.7 (5.3)	10.0, 34.0 (8.0)

Abbreviations: WHOQOL-BREF, World Health Organization Quality of Life-BREF questionnaire; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; NEO-FFI, Neuroticism-Extraversion-Openness-Five Factor Inventory; CES-D, Center for Epidemiologic Studies Depression Scale; STAI, State-Trait Anxiety Inventory; N, number of patients; SD, standard deviation; IQR, inter quartile range.

by treatment and disease [33], we choose to include a QoL measure (i.e., WHOQOL-BREF) as well since this offers additional information describing patients' feelings about their well-being. We observed that higher levels of depressive symptoms were associated with decreased (HR)QoL except for social relationships. Given the associations with both HRQoL and QoL, the fact that depressive symptoms are common [1, 2] and that adequate (HR)QoL management is mandatory in patients with a poor prognosis, our results emphasize the importance of physicians' awareness for depressive symptoms in patients with advanced-stage lung cancer. Moreover, they could stimulate early referral to a psychologist.

In the present study, NEO-FFI personality traits were not associated with (HR)QoL, except for conscientiousness. Trait anxiety was associated with only two (HR)QoL scales/

Table 3. Results of the multivariable regression analyses for the WHOQOL-BREF ($p < 0.05$)

Independent variables	N	B	SE	β	P-value	95% CI for B	R ²
General facet							
Age	117	-0.041	0.015	-0.232	0.006	-0.070, -0.012	0.402
CES-D		-0.133	0.021	-0.625	<0.001	-0.175, -0.091	
Physical health							
ECOG: 0 to 1 versus 2 or higher	117	-2.747	0.751	-0.262	<0.001	-4.234, -1.259	0.517
CES-D		-0.221	0.035	-0.542	<0.001	-0.291, -0.151	
NEO-FFI conscientiousness		0.111	0.045	0.201	0.016	0.021, 0.200	
Psychological health							
CES-D	117	-0.163	0.025	-0.534	<0.001	-0.213, -0.113	0.554
Social relationships							
Gender	119	1.107	0.467	0.222	0.020	0.181, 2.032	0.204
Partner status: no partner versus having a partner		1.428	0.588	0.216	0.017	0.262, 2.594	
Environment							
CES-D	116	-0.063	0.028	-0.224	0.026	-0.118, -0.008	0.375
STAI Trait		-0.163	0.049	-0.392	0.001	-0.259, -0.066	

Abbreviations: WHOQOL-BREF, World Health Organization Quality of Life-BREF questionnaire; N, number of patients; B, unstandardized beta; SE, standard error; β , standardized beta, CI, confidence interval; R², explained variance; CES-D, Center for Epidemiologic Studies Depression Scale; ECOG, Eastern Cooperative Oncology Group; NEO-FFI, Neuroticism-Extraversion-Openness-Five Factor Inventory questionnaire; STAI, State Trait Anxiety Inventory

domains, namely role functioning and environment. Considering that CES-D score was associated with almost all (HR)QoL scales/domains, we hypothesized whether the absent effect of personality on (HR)QoL was influenced by CES-D score. Therefore, new analyses were performed without CES-D score. For the WHOQOL-BREF, trait anxiety was associated with not only the environment domain, but also with physical and psychological health. Instead of an association with role functioning, trait anxiety was associated with the EORTC QLQ-C30 scales emotional functioning, cognitive functioning and social functioning. These results emphasize the importance of trait anxiety, especially in the absence of depressive symptoms. Given that neuroticism has been linked with depressive symptoms in patients with lung cancer [34], we expected that the effect of neuroticism was masked by CES-D score. However, after removal of CES-D score from the models, neuroticism was only associated with role functioning and psychological Health. Furthermore, none of the other NEO-FFI personality traits were associated with (HR)QoL. Therefore, the effect of personality (i.e., except for trait anxiety) on (HR)QoL may be less important in patients with lung cancer.

We observed some unexpected results during the multiple regression analyses. First, the direction of the beta of the STAI trait scale in the analysis with role functioning as dependent variable was positive rather than the expected opposite. To analyse whether

Table 4. Results of the multivariable regression analyses for the EORTC QLQ-C30 ($p < 0.05$)

Independent variables	N	B	SE	β	P-value	95% CI for B	R ²
General Health Status/Quality of Life							
Employment: yes versus no job	116	10.405	4.358	0.183	0.019	1.764, 19.045	0.417
CES-D		-2.062	0.314	-0.627	<0.001	-2.684, -1.439	
Physical functioning							
Employment: no versus having a job	117	10.684	3.885	0.204	0.007	2.981, 18.386	0.453
ECOG: 0 to 1 versus 2 or higher		-23.586	5.958	-0.304	<0.001	-35.398, -11.775	
CES-D		-1.357	0.284	-0.449	<0.001	-1.921, -0.793	
Role functioning							
ECOG: 0 to 1 versus 2 or higher	120	-30.890	7.975	-0.299	<0.001	-46.692, -15.088	0.414
CES-D		-2.197	0.384	-0.542	<0.001	-2.957, -1.437	
STAI Trait		1.840	0.687	0.295	0.009	0.479, 3.201	
Emotional functioning							
CES-D	117	-2.044	0.222	-0.668	<0.001	-2.483, -1.604	0.655
Cognitive functioning							
Educational level: low versus high	129	9.344	4.060	0.170	0.023	1.307, 17.382	0.359
CES-D		-1.572	0.274	-0.536	<0.001	-2.114, -1.030	
Social functioning							
Partner status: no partner versus having a partner	116	-12.786	5.817	-0.174	0.030	-24.318, -1.253	0.370
ECOG: 0 to 1 versus 2 or higher		-16.748	7.367	-0.188	0.025	-31.354, -2.141	
CES-D		-1.394	0.348	-0.401	<0.001	-2.085, -0.704	
Age _a	116	0.561	0.261	0.197	0.034	0.042, 1.079	0.400

^aAfter adding Age afterwards to the multiple regression model

Abbreviations: EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; N, number of patients; B, unstandardized beta; SE, standard error; β , standardized beta, CI, confidence interval; R², explained variance; CES-D, Center for Epidemiologic Studies Depression Scale; ECOG, Eastern Cooperative Oncology Group; STAI, State Trait Anxiety Inventory

this finding was due to multi-collinearity, we correlated the STAI trait scale with the other variables that were associated with role functioning (i.e., CES-D score and ECOG performance status). We observed a strong and positive correlation with CES-D score. This could indicate that the effect of trait anxiety is explained by CES-D score. Moreover, the alternative explanation, i.e., the positive direction of the beta is a true observation, seems rather unlikely. Second, we observed an unexpected negative direction of the beta of partner status in the analysis with social functioning as dependent variable. However, as only weak correlations were observed between partner status and ECOG performance status, CES-D score and age, indications for multi-collinearity were not found. Therefore, the direction of this beta may be a true observation, or just the effect of another variable that was not included in the analysis (i.e., a confounder). If partner status would be highly

correlated with this confounding variable, this could switch the direction of the beta in the expected direction. Other reasons for the observed unexpected results may be that they are merely due to chance (i.e., especially when there is a small sample size) or are the consequence of selection bias [35].

Some limitations of this study have to be addressed. First, because of the cross-sectional nature of our data, we cannot conclude whether depressive symptoms are a cause of decreased (HR)QoL or a consequence, or whether both depressive symptoms and (HR)QoL are caused by a third variable. Therefore, ideally, our findings should be cross validated in another study as the observed results may merely describe idiosyncrasies of the data at hand. Second, the relatively small number of patients may have influenced our results. This could have resulted in the non-identification of variables associated with (HR)QoL. This study has some strengths too. We are the first to investigate the association between sociodemographic variables, clinical variables, depressive symptoms, and personality traits with both HRQoL and QoL. Moreover, although our sample size was relatively small, we describe results of a prospective study with a homogeneous patient population that is comparable with patients seen in daily practice.

CONCLUSIONS

In conclusion, our results demonstrated that physicians are recommended to have high awareness for patients with depressive symptoms and those with an ECOG performance status of 2 or higher at the start of treatment as they may have low levels of (HR)QoL. Screening for the presence of these two factors before treatment is initiated may be worthwhile. The application of interventions designed to prevent a deterioration of (HR)QoL is recommended to be facilitated in these patients.

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SUPPLEMENTARY MATERIALS

Results of the simple linear regression analyses for the WHOQOL-BREF

General facet							
Independent variables	N	B	SE	β	P-value	95% CI for B	R ²
Age	142	-0.031	0.015	-0.168	0.046	-0.061, -0.001	0.028
Gender _a	142	-0.037	0.287	-0.011	0.897	-0.604, 0.530	0.000
Marital status: no partner versus having a partner _b	142	-0.340	0.369	-0.078	0.359	-1.069, 0.390	0.006
Educational level: low versus high _c	137	0.092	0.340	0.023	0.788	-0.581, 0.765	0.001
Ethnicity: Caucasian versus other ethnicity _d	142	-0.885	0.583	-0.127	0.131	-2.037, 0.267	0.016
Employment: yes versus having no job _e	142	0.840	0.318	0.218	0.009	0.211, 1.470	0.047
ECOG: 0 to 1 versus 2 or higher _f	140	-1.246	0.471	-0.220	0.009	-2.177, -0.315	0.048
CES-D	140	-0.118	0.016	-0.534	<0.001	-0.149, -0.087	0.285
STAI Trait	139	-0.075	0.026	-0.236	0.005	-0.128, -0.023	0.056
NEO-FFI neuroticism	135	-0.035	0.019	-0.153	0.076	-0.073, 0.004	0.024
NEO-FFI extraversion	130	0.049	0.022	0.196	0.025	0.006, 0.092	0.039
NEO-FFI openness	131	0.014	0.025	0.049	0.579	-0.036, 0.063	0.002
NEO-FFI agreeableness	136	0.017	0.029	0.051	0.555	-0.040, 0.073	0.003
NEO-FFI conscientiousness	131	0.050	0.025	0.172	0.049	0.000, 0.100	0.030
Physical health							
Independent variables	N	B	SE	β	P-value	95% CI for B	R ²
Age	145	0.014	0.028	0.042	0.614	-0.042, 0.071	0.002
Gender _a	145	-0.757	0.518	-0.121	0.146	-1.780, 0.266	0.008
Marital status: no partner versus having a partner _b	145	-0.805	0.664	-0.101	0.228	-2.118, 0.509	0.010
Educational level: low versus high _c	140	0.220	0.634	0.029	0.730	-1.034, 1.473	0.001
Ethnicity: Caucasian versus other ethnicity _d	145	-0.292	1.077	-0.023	0.787	-2.421, 1.837	0.001
Employment: yes versus having no job _e	145	1.446	0.584	0.203	0.014	0.292, 2.600	0.041
ECOG: 0 to 1 versus 2 or higher _f	143	-3.167	0.845	-0.301	<0.001	-4.837, -1.498	0.091
CES-D	143	-0.234	0.028	-0.575	<0.001	-0.289, -0.179	0.331
STAI Trait	142	-0.211	0.047	-0.356	<0.001	-0.303, -0.118	0.127
NEO-FFI neuroticism	137	-0.124	0.035	-0.296	<0.001	-0.193, -0.056	0.087
NEO-FFI extraversion	133	0.099	0.040	0.210	0.015	0.019, 0.178	0.044
NEO-FFI openness	134	-0.071	0.046	-0.132	0.128	-0.163, 0.021	0.017
NEO-FFI agreeableness	139	0.112	0.053	0.177	0.037	0.007, 0.216	0.031
NEO-FFI conscientiousness	134	0.162	0.046	0.291	0.001	0.070, 0.254	0.084
Psychological health							
Independent variables	N	B	SE	β	P-value	95% CI for B	R ²
Age	145	0.008	0.022	0.032	0.704	-0.035, 0.051	0.001

Gender _a	145	-0.357	0.397	-0.075	0.370	-1.142, 0.427	0.006
Marital status: no partner versus having a partner _b	145	0.236	0.510	0.039	0.644	-0.771, 1.243	0.002
Educational level: low versus high _c	140	0.481	0.473	0.086	0.310	-0.453, 1.416	0.007
Ethnicity: Caucasian versus other ethnicity _d	145	-1.011	0.818	-0.103	0.219	-2.629, 0.606	0.011
Employment: yes versus having no job _e	145	0.521	0.453	0.096	0.252	-0.375, 1.417	0.009
ECOG: 0 to 1 versus 2 or higher _f	143	-1.582	0.663	-0.197	0.018	-2.892, -0.272	0.039
CES-D	143	-0.201	0.020	-0.653	<0.001	-0.240, -0.162	0.427
STAI Trait	142	-0.233	0.032	-0.518	<0.001	-0.297, -0.168	0.268
NEO-FFI neuroticism	137	-0.158	0.024	-0.494	<0.001	-0.205, -0.110	0.244
NEO-FFI extraversion	133	0.101	0.030	0.278	0.001	0.041, 0.161	0.078
NEO-FFI openness	134	0.001	0.035	0.002	0.983	-0.069, 0.070	0.000
NEO-FFI agreeableness	139	0.076	0.039	0.163	0.056	-0.002, 0.154	0.027
NEO-FFI conscientiousness	134	0.129	0.034	0.314	<0.001	0.062, 0.197	0.098

Social relationships

Independent variables	N	B	SE	β	P-value	95% CI for B	R ²
Age	145	0.20	0.023	0.074	0.377	-0.025, 0.066	0.005
Gender _a	145	0.938	0.417	0.185	0.026	0.115, 1.762	0.034
Marital status: no partner versus having a partner _b	145	1.105	0.535	0.170	0.041	0.047, 2.162	0.029
Educational level: low versus high _c	140	0.658	0.500	0.111	0.190	-0.330, 1.646	0.012
Ethnicity: Caucasian versus other ethnicity _d	145	0.511	0.875	0.049	0.560	-1.219, 2.240	0.002
Employment: yes versus having no job _e	145	-0.106	0.485	-0.018	0.828	-1.064, 0.852	0.000
ECOG: 0 to 1 versus 2 or higher _f	143	-1.786	0.697	-0.211	0.011	-3.163, -0.409	0.045
CES-D	143	-0.056	0.027	-0.168	0.044	-0.110, -0.001	0.028
STAI Trait	142	-0.108	0.040	-0.225	0.007	-0.186, -0.030	0.051
NEO-FFI neuroticism	137	-0.078	0.028	-0.230	0.007	-0.133, -0.022	0.053
NEO-FFI extraversion	133	0.080	0.032	0.216	0.012	0.018, 0.143	0.047
NEO-FFI openness	134	0.016	0.036	0.039	0.658	-0.056, 0.088	0.001
NEO-FFI agreeableness	139	0.068	0.042	0.139	0.103	-0.014, 0.150	0.019
NEO-FFI conscientiousness	134	0.104	0.037	0.238	0.006	0.031, 0.177	0.057

Environment

Independent variables	N	B	SE	β	P-value	95% CI for B	R ²
Age	145	0.017	0.020	0.069	0.409	-0.023, 0.057	0.005
Gender _a	145	0.340	0.369	0.077	0.358	-0.390, 1.071	0.006
Marital status: no partner versus having a partner _b	145	0.450	0.473	0.079	0.343	-0.485, 1.385	0.006
Educational level: low versus high _c	140	0.903	0.445	0.170	0.044	0.023, 1.783	0.029
Ethnicity: Caucasian versus other ethnicity _d	145	0.092	0.766	0.010	0.905	-1.422, 1.605	0.000
Employment: yes versus having no job _e	145	0.381	0.423	0.075	0.369	-0.455, 1.216	0.006
ECOG: 0 to 1 versus 2 or higher _f	143	-0.918	0.624	-0.123	0.143	-2.152, 0.315	0.015
CES-D	143	-0.134	0.022	-0.465	<0.001	-0.177, -0.092	0.216

STAI Trait	142	-0.221	0.030	-0.522	<0.001	-0.281, -0.161	0.273
NEO-FFI neuroticism	137	-0.116	0.024	-0.389	<0.001	-0.162, -0.069	0.152
NEO-FFI extraversion	133	0.069	0.028	0.209	0.016	0.013, 0.125	0.044
NEO-FFI openness	134	-0.022	0.033	-0.059	0.500	-0.088, 0.043	0.003
NEO-FFI agreeableness	139	0.086	0.036	0.198	0.020	0.014, 0.158	0.039
NEO-FFI conscientiousness	134	0.115	0.033	0.295	0.001	0.051, 0.180	0.087

*P-values of $p \leq 0.10$

^aMale is reference

^bNo partner is reference

^cLow educational level is reference

^dOther ethnicity is reference

^eNo job is reference

^f0 to 1 is reference

CES-D score, STAI trait score and NEO-FFI scale scores represent continuous variables

Abbreviations: N, number of patients; B, unstandardized beta; SE, standard error; β , standardized beta; CI, confidence interval; R^2 , explained variance; WHOQOL-BREF, World Health Organization Quality of Life-BREF questionnaire; ECOG, Eastern Cooperative Oncology Group; CES-D, Center for Epidemiologic Studies Depression Scale; STAI, State Trait Anxiety Inventory; NEO-FFI, Neuroticism-Extraversion-Openness Five-Factor Inventory

Results of the simple linear regression analyses for the EORTC QLQ-C30

Independent variables	n	Global Health Status/QoL					
		B	SE	β	P-value	95% CI for B	R ²
Age	142	-0.144	0.235	-0.052	0.540	-0.608, 0.320	0.003
Gender _a	142	-5.815	4.275	-0.114	0.176	-14.267, 2.638	0.013
Marital status: no partner versus having a partner _b	142	-2.813	5.545	-0.043	0.613	-13.775, 8.149	0.002
Educational level: low versus high _c	137	-2.837	5.135	-0.047	0.582	-12.994, 7.319	0.002
Ethnicity: Caucasian versus other ethnicity _d	142	-5.799	8.796	-0.056	0.511	-23.189, 11.590	0.003
Employment: yes versus having no job _e	142	14.893	4.725	0.257	0.002	5.551, 24.234	0.066
ECOG: 0 to 1 versus 2 or higher _f	140	-17.063	7.104	-0.200	0.018	-31.111, -3.016	0.040
CES-D	142	-1.940	0.225	-0.589	<0.001	-2.385, -1.495	0.346
STAI Trait	139	-1.246	0.396	-0.260	0.002	-2.029, -0.463	0.067
NEO-FFI neuroticism	134	-0.938	0.292	-0.269	0.002	-1.516, -0.360	0.072
NEO-FFI extraversion	130	0.687	0.333	0.179	0.041	0.028, 1.347	0.032
NEO-FFI openness	132	-0.196	0.377	-0.045	0.605	-0.942, 0.551	0.002
NEO-FFI agreeableness	136	0.757	0.423	0.153	0.076	-0.079, 1.594	0.023
NEO-FFI conscientiousness	131	1.084	0.383	0.242	0.005	0.327, 1.841	0.059

Independent variables	n	Physical functioning					
		B	SE	β	P-value	95% CI for B	R ²
Age	150	-0.006	0.218	-0.002	0.978	-0.436, 0.424	0.000
Gender _a	150	-10.493	3.869	-0.218	0.007	-18.138, -2.847	0.047
Marital status: no partner versus having a partner _b	150	-4.692	5.050	-0.076	0.354	-14.671, 5.288	0.006
Educational level: low versus high _c	145	-0.347	4.858	-0.006	0.943	-9.950, 9.257	0.000
Ethnicity: Caucasian versus other ethnicity _d	150	-0.063	8.309	-0.001	0.994	-16.484, 16.357	0.000
Employment: yes versus having no job _e	150	13.603	4.397	0.246	0.002	4.913, 22.293	0.061
ECOG: 0 to 1 versus 2 or higher _f	148	-25.686	6.490	-0.311	<0.001	-38.512, -12.860	0.097
CES-D	148	-1.516	0.228	-0.482	<0.001	-1.967, -1.065	0.232
STAI Trait	147	-0.961	0.374	-0.209	0.011	-1.701, -0.222	0.044
NEO-FFI neuroticism	137	-0.511	0.266	-0.163	0.057	-1.036, 0.015	0.027
NEO-FFI extraversion	133	0.647	0.310	0.179	0.039	0.034, 1.259	0.032
NEO-FFI openness	134	-0.456	0.346	-0.114	0.189	-1.140, 0.228	0.013
NEO-FFI agreeableness	139	0.682	0.397	0.145	0.088	-0.103, 1.467	0.021
NEO-FFI conscientiousness	134	1.015	0.352	0.243	0.005	0.318, 1.712	0.059

Independent variables	n	Role functioning					
		B	SE	β	P-value	95% CI for B	R ²
Age	149	0.162	0.297	0.045	0.585	-0.424, 0.748	0.002
Gender _a	149	-12.170	5.322	-0.185	0.024	-22.688, -1.653	0.034

Marital status: no partner versus having a partner _b	149	-3.193	6.900	-0.038	0.644	-16.829, 10.444	0.001
Educational level: low versus high _c	144	-0.595	6.592	-0.008	0.928	-13.626, 12.436	0.000
Ethnicity: Caucasian versus other ethnicity _d	149	-2.407	11.322	-0.018	0.832	-24.782, 19.967	0.000
Employment: yes versus having no job _e	149	10.167	6.132	0.135	0.099	-1.951, 22.285	0.018
ECOG: 0 to 1 versus 2 or higher _f	147	-35.526	8.769	-0.319	<0.001	-52.858, -18.194	0.102
CES-D	148	-2.263	0.304	-0.525	<0.001	-2.863, -1.663	0.276
STAI Trait	146	-0.938	0.511	-0.151	0.069	-1.949, 0.072	0.023
NEO-FFI neuroticism	136	-0.940	0.365	-0.217	0.011	-1.662, -0.218	0.047
NEO-FFI extraversion	132	0.664	0.421	0.137	0.117	-0.169, 1.498	0.019
NEO-FFI openness	134	-0.852	0.473	-0.155	0.074	-1.788, 0.084	0.024
NEO-FFI agreeableness	138	0.864	0.546	0.135	0.116	-0.215, 1.944	0.018
NEO-FFI conscientiousness	133	1.067	0.488	0.187	0.031	0.101, 2.033	0.035

Independent variables	n	Emotional functioning					
		B	SE	β	P-value	95% CI for B	R ²
Age	142	-0.193	0.221	-0.074	0.382	-0.630, 0.243	0.005
Gender _a	142	-1.883	4.049	-0.039	0.643	-9.888, 6.122	0.002
Marital status: no partner versus having a partner _b	142	-8.175	5.180	-0.132	0.117	-18.416, 2.066	0.017
Educational level: low versus high _c	137	2.582	4.858	0.046	0.596	-7.027, 12.190	0.002
Ethnicity: Caucasian versus other ethnicity _d	142	-3.328	8.290	-0.034	0.689	-19.718, 13.062	0.001
Employment: yes versus having no job _e	142	6.517	4.571	0.120	0.156	-2.521, 15.554	0.014
ECOG: 0 to 1 versus 2 or higher _f	140	-10.053	6.678	-0.127	0.135	-23.257, 3.152	0.016
CES-D	142	-2.438	0.162	-0.786	<0.001	-2.759, -2.117	0.617
STAI Trait	139	-2.713	0.312	-0.597	<0.001	-3.330, -2.096	0.356
NEO-FFI neuroticism	134	-1.727	0.244	-0.525	<0.001	-2.208, -1.245	0.276
NEO-FFI extraversion	130	0.725	0.309	0.203	0.020	0.114, 1.335	0.041
NEO-FFI openness	132	0.240	0.360	0.058	0.507	-0.474, 0.953	0.003
NEO-FFI agreeableness	136	1.136	0.397	0.240	0.005	0.351, 1.921	0.058
NEO-FFI conscientiousness	131	0.769	0.369	0.181	0.039	0.039, 1.499	0.033

Independent variables	n	Cognitive functioning					
		B	SE	β	P-value	95% CI for B	R ²
Age	142	0.145	0.213	0.058	0.496	-0.275, 0.566	0.003
Gender _a	142	-7.509	3.851	-0.163	0.053	-15.124, 0.105	0.026
Marital status: no partner versus having a partner _b	142	-0.597	5.033	-0.010	0.906	-10.548, 9.355	0.000
Educational level: low versus high _c	137	11.602	4.554	0.214	0.012	2.596, 20.608	0.046
Ethnicity: Caucasian versus other ethnicity _d	142	0.696	7.990	0.007	0.931	-15.100, 16.493	0.000
Employment: yes versus having no job _e	142	7.782	4.386	0.148	0.078	-0.890, 16.454	0.022

ECOG: 0 to 1 versus 2 or higher _f	140	0.926	6.565	0.012	0.888	-12.054, 13.906	0.000
CES-D	142	-1.720	0.207	-0.575	<0.001	-2.128, -1.311	0.331
STAI Trait	139	-1.495	0.352	-0.341	<0.001	-2.192, -0.799	0.116
NEO-FFI neuroticism	134	-0.867	0.263	-0.276	0.001	-1.387, -0.347	0.076
NEO-FFI extraversion	130	0.057	0.312	0.016	0.856	-0.561, 0.675	0.000
NEO-FFI openness	132	-0.076	0.341	-0.020	0.824	-0.750, 0.598	0.000
NEO-FFI agreeableness	136	0.647	0.395	0.140	0.104	-0.134, 1.427	0.020
NEO-FFI conscientiousness	131	0.530	0.350	0.132	0.132	-0.162, 1.223	0.017

Independent variables	n	B	SE	Social functioning			
				β	P-value	95% CI for B	R ²
Age	142	0.353	0.248	0.120	0.156	-0.136, 0.843	0.014
Gender _a	142	-5.688	4.541	-0.105	0.212	-14.665, 3.289	0.011
Marital status: no partner versus having a partner _b	142	-11.373	5.809	-0.163	0.052	-22.858, 0.113	0.027
Educational level: low versus high _c	137	1.558	5.487	0.024	0.777	-9.294, 12.409	0.001
Ethnicity: Caucasian versus other ethnicity _d	142	-8.702	9.318	-0.079	0.352	-27.124, 9.720	0.006
Employment: yes versus having no job _e	142	11.158	5.102	0.182	0.030	1.072, 21.245	0.033
ECOG: 0 to 1 versus 2 or higher _f	140	-19.841	7.506	-0.220	0.009	-34.684, -4.999	0.048
CES-D	142	-1.765	0.255	-0.505	<0.001	-2.269, -1.260	0.255
STAI Trait	139	-1.435	0.421	-0.280	0.001	-2.267, -0.604	0.078
NEO-FFI neuroticism	134	-0.835	0.306	-0.231	0.007	-1.440, -0.230	0.053
NEO-FFI extraversion	130	0.798	0.355	0.195	0.026	0.096, 1.500	0.038
NEO-FFI openness	132	-0.305	0.400	-0.067	0.447	-1.098, 0.487	0.004
NEO-FFI agreeableness	136	0.789	0.457	0.148	0.086	-0.114, 1.692	0.022
NEO-FFI conscientiousness	131	1.371	0.396	0.292	0.001	0.588, 2.155	0.085

P-values of ≤ 0.10 are in bold

_aMale is reference

_bNo partner is reference

_cLow educational level is reference

_dOther ethnicity is reference

_eNo job is reference

_f0 to 1 is reference

CES-D, STAI trait, and NEO-FFI scale scores represent continuous variables

Abbreviations: n, number of patients; B, unstandardized beta; SE, standard error; β , standardized beta; CI, confidence interval; R², explained variance; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; ECOG, Eastern Cooperative Oncology Group; CES-D, Center for Epidemiologic Studies Depression Scale; STAI, State Trait Anxiety Inventory; NEO-FFI, Neuroticism-Extraversion-Openness Five-Factor Inventory