Illness representations, mental health and quality of life in patients with advanced cancer

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Submitted

ABSTRACT

Objective

Quality of life (QoL) is an important yet complex outcome of care in patients with advanced cancer. QoL is associated with physical and psychosocial symptoms, and with patients' illness representations. Illness representations are modifiable cognitive constructs, developed to make sense of one's illness. Better understanding which factors contribute to patients' QoL and how is essential for delivering high quality care. We therefore investigated the mediating role of anxiety and depression in the association of illness representations with QoL.

Methods

Data from 377 patients with advanced cancer were used from PROFILES registry. Patients completed measures on illness representations (BIPQ), QoL (EORTC QLQ-C30) and symptoms of anxiety and depression (HADS). Causal mediation analyses were conducted to decompose the total effect of illness representations on QoL into a direct effect and an indirect effect.

Results

All illness representations but one ("Comprehensibility") were negatively associated with QoL ($p<0.05$); patients with more negative illness representations tended to have worse QoL. The effect was the strongest for patients who felt that their illness affected their life more severely (illness representation "Consequences"), patients who were more concerned about their illness ("Concern"), and patients who thought that their illness strongly affected them emotionally ("Emotions"). Anxiety mediated 41-87% and depression mediated 39-69% of the total effect of patients' illness representations on QoL.

Conclusions

Anxiety and depression mediate the association between illness representations and QoL. Modifying illness representations has the potential to reduce symptoms of anxiety and depression and thereby to improve QoL of patients with advanced cancer.

INTRODUCTION

Patients with advanced, incurable cancer experience impaired quality of life (QoL).[1] Their QoL is affected in a complex way by, among others, physical symptoms and psychological challenges,[2] such as the confrontation with the approaching death[3] and symptoms of anxiety and depression.[4,5] Whereas QoL is an important outcome of care, QoL is by definition multidimensional and subjective[2] and cannot be assessed by others, such as clinicians. Understanding which factors contribute to patients' QoL is therefore of utmost importance for the delivery of high quality care to patients with advanced cancer.[6]

The so-called self-regulation model conceptualizes illness representations as important and well-established determinants of QoL.[7,8] Illness representations are defined as cognitive constructs, developed by patients to make sense of and manage their illness experience.[9,10] Patients can adjust their illness representations after receiving new information, e.g. regarding the progression of the disease, from healthcare providers, the media, friends or family.[11,12] Illness representations can be in line with patients' actual medical situation, but they can also involve a distorted interpretation of medical facts.[11] A study among patients nearing death, including patients with advanced cancer, found a great variability in illness representations, indicating how differently patients perceive their illness.[13] Due to their modifiable nature, illness representations are a potential target for interventions aimed at improving patients' experiences of their illness and thereby their QoL.[8, 14, 15]

While the effects of illness representations on QoL have been described and are recognized,[8, 14, 15] there is little insight into the mechanisms underlying this relationship. Understanding these mechanisms can inform future interventions to improve patients' QoL. Previous research hypothesized a mediating role of anxiety and depression, since these are associated with both illness representations and QoL,[16, 17] and are particularly common in patients with advanced cancer.[18, 19] We therefore performed a study to clarify the relationship between illness representations and QoL, with symptoms of anxiety and depression as potential mediators, in patients with advanced cancer, accounting for interaction effects between the illness representations and the mediators.

MATERIALS AND METHODS

Participants and data collection

The data were derived from the 'Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship' (PROFILES) registry. This registry includes data to study the physical and psychosocial impact of cancer and its treatment. The rationale and design of PROFILES have been described elsewhere,[20] data and detailed information can be found at www.profilesregistry.nl. Ethical approval for the data collection was obtained from local certified Medical Ethics Committees of the Maxima Medical Centre Veldhoven, the Netherlands (colorectal cancer, approval number

0822), the certified Medical Ethics Committee of the Maxima Medical Centre, the Netherlands ((non)Hodgkin lymphoma) and deemed exempt from full review and approval by the Research Ethics Committee Maxima Medical Centre, Veldhoven, the Netherlands (thyroid cancer). Informed consent was obtained from all individual participants included in the study. We used data from adult patients diagnosed with stage IV (non)Hodgkin lymphoma, colorectal cancer, or thyroid cancer, without cognitive impairments (n=377).

Measures

Sociodemographic and clinical characteristics

The PROFILES registry includes the patient sociodemographic characteristics gender, age at the time of survey and at the time of diagnosis (≤40 or >40 years), and time passed since the diagnosis (<2 or ≥2 years). The socioeconomic status was assessed using an indicator developed by Statistics Netherlands, based on the postal code of the residential address of the patient.[21] The registry includes the clinical characteristic tumor subtype. Patients completed the Self-administered Comorbidity Questionnaire.[22]

Illness representations

The Brief Illness Perception Questionnaire (BIPQ)[23] is frequently used in cancer populations[24] and has good psychometric properties.[25] The BIPQ consists of eight items, each addressing a specific illness representation that is scored on a ten-point scale:[23]

Consequences:	“How much does your illness affect your life?” *(0-“No affect at all” to 10-“Severely affects my life”)*
Timeline:	“How long do you think your illness will continue?” *(0-“A very short time” to 10-“Forever”)*
Personal control:	“How much control do you feel you have over your illness”? *(0-“Absolutely no control” to 10-“Extreme amount of control”)*
Treatment control:	“How much do you think your treatment can help your illness?” *(0- “Not at all” to 10-“Extremely helpful”)*
Identity:	“How much symptoms do you experience from your illness?” *(0-“No symptoms at all” to 10-“Many severe symptoms”)*
Concerns:	“How concerned are you about your illness?” *(0-“Not at all concerned” to 10-“Extremely concerned”)*
Emotions:	“How much does your illness affect you emotionally?” *(0-“Not at all affected emotionally” to 10-“Extremely affected emotionally”)*
Comprehensibility:	“How well do you understand your illness?” *(0-“Don’t understand at all” to 10-“Understand very clearly”)*

For the statistical analyses, we recoded the responses of three items (personal control, treatment control, and comprehensibility) to be in the same direction as the other items. Higher scores imply more negative illness representations (e.g. experiencing more symptoms due to the illness or being more concerned about the illness).

Health-related quality of life

The European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30; version 3.0) is an often used, validated 30-item self-reported questionnaire that contains five functional scales, three symptom scales, and six single items.[26] We calculated the recently developed QLQ-C30 summary score (range 0-100).[27] A higher score indicates better QoL.

Symptoms of anxiety and depression

The Hospital Anxiety and Depression Scale (HADS) is a widely used self-reported questionnaire that measures levels of anxiety (HADS-A: seven items) and depression (HADS-D: seven items) of patients during the past week.[28] The HADS has shown good psychometric properties in various samples and settings.[29] The items are scored on a four-point Likert-scale (range total score for each subscale 0-21). A score of 8 or higher on the subscales (HADS-A and HADS-D) indicates mild to severe symptoms of anxiety or depression.[29]

Statistical analyses

Pearson correlation analyses were used to examine bivariate associations of illness representations, with anxiety and depression and QoL. From the original PROFILES registry, we selected the 377 patients who were diagnosed with advanced cancer. We conducted the mediation analyses with complete cases. Missing data varied from 0% for gender to 28% for comorbid conditions (Table 1 and 2). Among the 377 patients in the total sample, 216 (57%) to 224 (59%), depending on the exposure, provided full information on the exposure, mediator, outcome variables, and confounders.

The aim of this study was to estimate how much of the observed associations of illness representations (exposure variables) with QoL (outcome variable) could be explained by anxiety or depression (mediators, Figure 1a and b). The analyses were controlled for patient characteristics that, based on literature[30] and a priori assumptions, were suspected to have an impact on illness representations and QoL: tumor subtype, gender, age at time of diagnosis (≤40 or >40 years), time passed since diagnosis (<2 or ≥2 years), socioeconomic status (low, medium, high, living in care institutions), and the number of comorbidities (none, 1, ≥2). We found interaction effects between half of the illness representations and anxiety and depression on QoL. In the presence of interaction effects between exposure and mediator, traditional mediation methods such as the commonly used Baron and Kenny method, will generate invalid mediation effects.[31, 32] We therefore used a novel approach as described by Valeri and VanderWeele (2013), which allows for exposure-mediator interactions.[32] Using the counterfactual framework, the Valeri and VanderWeele method is able to decompose the estimated total effect of an exposure on an outcome into a natural direct effect (i.e. the effect of illness representations on QoL that occurs without mediation) and a natural indirect effect (i.e. the effect of illness representations on QoL that is mediated by symptoms of anxiety and depression). The percentage of the estimated total effect mediated was calculated by dividing the natural indirect effect by the total effect.

In the mediation analyses, the illness representation scores were standardized and natural direct and natural indirect effects were calculated by comparing the mean level of an illness representation score to the mean + 1 standard deviation [SD]. The estimated total effect thus expresses the change in QoL if an illness representation score increases from the mean to the mean + 1 SD. The natural direct effect expresses the change in QoL if an illness representation score increases from the mean to the mean + 1 SD, while the mediator, anxiety or depression, is kept at the level it would have at the mean level of the illness representation. The natural indirect effect expresses the change in QoL if an illness representation score is kept stable at mean + 1 SD, while the mediator score changes from the level it would take at the mean level of the illness representation to the level it would take at the mean + 1 SD level of the illness representation.

Analyses were performed using SPSS version 21. The mediation analyses were performed using Stata version 13 with the package 'Paramed'. *P*-values <0.05 were considered to indicate statistically significant associations. 95% confidence intervals were automatically generated by the package 'Paramed' (based on the delta method) around the estimated total effect, natural direct effect and natural indirect effect.

RESULTS

Patient sample

The majority of patients in our sample (n=377) were male (60%), older than 40 years at diagnosis (92%), and diagnosed with cancer two or more years prior to participation in the study (80%, Table 1). Two or more comorbid conditions were reported by 36% of patients.

Table 1. Sociodemographic and clinical characteristics (n=377)

	No. (%)
Gender	
Male	227 (60.2)
Female	150 (39.8)
Age at time of survey	
≤ 40 years	16 (4.6)
> 40 years	334 (95.4)
Tumor subtype	
Non-Hodgkin lymphoma	52 (13.8)
Hodgkin lymphoma	192 (50.9)
Colorectal cancer	114 (30.2)
Thyroid cancer	19 (5.0)
Age at time of diagnosis	
≤ 40 years	29 (8.3)
> 40 years	322 (91.7)

Table 1. Sociodemographic and clinical characteristics (n=377) (continued)

	No. (%)
Years since diagnosis	
< 2 years	77 (20.5)
≥ 2 years	299 (79.5)
Comorbid conditions	
0	95 (35.2)
1	78 (28.9)
≥2	97 (35.9)
Socioeconomic status	
Low	86 (25.1)
Middle	131 (38.2)
High	123 (35.9)
Living in a care institution	3 (0.9)

Missings: Age at survey n=27, Age at diagnosis n=26, Years since diagnosis n=1, Comorbidity n=107, Socioeconomic status n=34

The mean summary score of the QLQ-C30 was 83.1 (SD 15.7, Table 2). Mean scores on the BIPQ are presented in Table 2. Mild to severe symptoms of anxiety were reported by 26% of patients and 25% of patients reported mild to severe symptoms of depression. All but one ("Comprehensibility") of the illness representations were negatively and significantly associated with QoL ($p<0.05$), indicating that negative illness representations were associated with worse QoL (Table 2).

Table 2. Quality of life, illness representations, anxiety and depression: Summary scores and correlations

	Mean (SD)	Pearson Correlation Coefficients
Quality of life (EORTC QLQ-C30)		
Quality of life	83.11 (15.70)	1.00
Illness representations (BIPQ)		
Consequences	4.97 (2.64)	-.49 *
Timeline	6.94 (3.41)	-.17 **
Personal control	5.82 (3.13)	-.21 **
Treatment control	3.77 (2.61)	-.34 **
Identity	4.47 (2.70)	-.55 **
Concerns	4.97 (2.76)	-.17 **
Emotions	4.21 (2.59)	-.46 **
Comprehensibility	3.89 (2.71)	-.05
Anxiety and Depression (HADS)		
Anxiety	5.10 (4.07)	-.63 **
Depression	4.86 (3.98)	-.68 **

Missings: Quality of life n=8, Consequences n=62, Timeline n=54, Personal control n=46, Treatment n=51, Identity n=45, Concerns n=41, Emotions n=43, Comprehensibility n=40, Anxiety n=10, Depression n=11

Abbreviations: SD, standard deviation; EORTC, European Organisation for Research and Treatment, QLQ-C30, Quality of Life Questionnaire Core 30; BIPQ, Brief Illness Perception Questionnaire; HADS, Hospital Anxiety and Depression Scale

* $p<0.05$, ** $p<0.01$

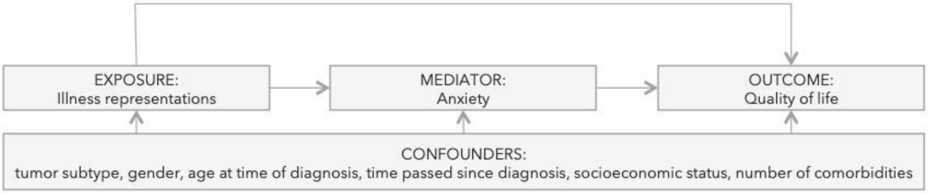

Figure 1a. Mediation model depicting the association of illness representations with quality of life, mediated by anxiety.

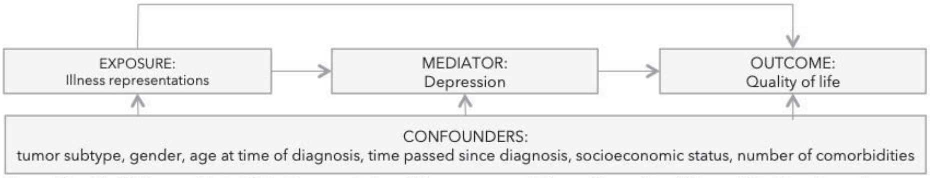

Figure 1b. Mediation model depicting the association of illness representations with quality of life, mediated by depression.

Mediation analyses

Anxiety as a mediator of the association of illness representations with quality of life

Having more negative illness representations was associated with more symptoms of anxiety and having more symptoms of anxiety was associated with worse QoL. The estimated total effect of the different illness representations on QoL was partly mediated by anxiety (Table 3). The total effect on QoL was largest for the illness representations “Consequences” (perceived effects and outcome of the illness on a patient’s life), “Identity” (experience of symptoms due to the illness), “Concerns” (extent to which the patient is concerned about the illness) and “Emotions” (emotional impact of the illness). 41% to 87% of the total effect of illness representations was mediated by anxiety: The mediating effect of anxiety was strongest for the illness representation “Emotions”. The total effect of the illness representation “Timeline” (how long the patient believes that the illness will last) on QoL, which was limited, was to a relatively large extent (84%) mediated by anxiety.

Depression as a mediator of the association of illness representations with quality of life

Having more negative illness representations was associated with more symptoms of depression, which, in turn, was associated with worse QoL. Depression mediated 39% to 69% of the effect of illness representations on QoL (Table 4). The mediating effects of depression were strongest for the illness representations “Emotions”, “Concerns”, and “Consequences”. The limited total effect of the illness representation “Timeline” on QoL was to relatively large extent (69%) mediated by depression. In general, the mediating effects of depression were somewhat weaker than the mediating effects of anxiety.

Table 3. Illness representations and quality of life: Natural direct effect and indirect effect mediated by anxiety

	Total effect			Natural direct effect			Natural indirect effect			Percentage of the total effect that was mediated
	Estimate	95%CI	*p*	Estimate	95%CI	*p*	Estimate	95%CI	*p*	%
Illness representations										
(1) Consequences (n=216)	-8.65	-1.74, -6.57	.000	-4.60	-6.44, -2.76	.000	-4.05	-5.52, -2.59	.000	47%
(2) Timeline (n=216)	-1.80	-3.87, .27	.088	-.28	-2.01, 1.44	.747	-1.52	-2.66, -.37	.009	84%
(3) Personal control (n=223)	-3.12	-5.18, -1.05	.003	-1.04	-2.73, .65	.228	-2.08	-3.32, -.83	.001	67%
(4) Treatment control (n=219)	-5.48	-7.53, -3.43	.000	-2.91	-4.63, -1.2	.001	-2.56	-3.89, -1.24	.000	47%
(5) Identity (n=220)	-7.81	-9.71, -5.92	.000	-4.61	-6.32, -2.89	.000	-3.21	-4.48, -1.94	.000	41%
(6) Concerns (n=223)	-7.03	-9.1, -4.96	.000	-1.95	-4, .09	.062	-5.08	-6.73, -3.44	.000	72%
(7) Emotions (n=224)	-6.43	-8.29, -4.57	.000	-.86	-3.09, 1.36	.446	-5.57	-7.34, -3.79	.000	87%
(8) Comprehensibility† (n=222)	-.37	-2.32, 1.58	.708	.80	-.85, 2.44	.344	-1.17	-2.3, -.04	.042	

† Comprehensibility affects quality of life via opposing direct and indirect effects. This makes calculating the mediated effect impossible.

Table 4. Illness representations and quality of life: Natural direct effect and indirect effect mediated by depression

	Total effect			Natural direct effect			Natural indirect effect			Percentage of the total effect that was mediated
	Estimate	95%CI	*p*	Estimate	95%CI	*p*	Estimate	95%CI	*p*	%
Illness representations										
(1) Consequences (n=216)	-8.02	-1.01, -6.04	.000	-4.19	-5.95, -2.43	.000	-3.83	-5.25, -2.41	.000	48%
(2) Timeline (n=216)	-2.08	-4.16, .01	.051	-.64	-2.29, 1.01	.447	-1.44	-2.71, -.16	.028	69%
(3) Personal control (n=223)	-2.98	-4.98, -.98	.003	-1.27	-2.86, .33	.119	-1.71	-2.97, -.46	.007	57%
(4) Treatment control (n=219)	-5.45	-7.48, -3.41	.000	-2.68	-4.35, -1.01	.002	-2.77	-4.14, -1.39	.000	51%
(5) Identity (n=220)	-7.70	-9.59, -5.81	.000	-4.71	-6.31, -3.11	.000	-2.99	-4.28, -1.71	.000	39%
(6) Concerns (n=223)	-6.81	-8.8, -4.81	.000	-2.88	-4.63, -1.13	.001	-3.93	-5.36, -2.49	.000	58%
(7) Emotions (n=224)	-6.72	-8.62, -4.83	.000	-2.79	-4.48, -1.1	.001	-3.94	-5.33, -2.54	.000	59%
(8) Comprehensibility† (n=222)	-.35	-2.28, 1.58	.723	.97	-.63, 2.56	.235	-1.32	-2.49, -.14	.028	

† Comprehensibility effects quality of life via opposing direct and indirect effects. This makes calculating the mediated effect impossible.

DISCUSSION

This study explored the mediating role of anxiety and depression in the association of illness representations with QoL in a large sample of patients with advanced cancer. We were able to confirm prior findings that having more negative illness representations (e.g. experiencing more symptoms due to the illness, being more concerned about the illness) is associated with worse QoL. Our study adds that this association is substantially mediated by symptoms of anxiety or depression.

It is not surprising that the total effect of the illness representation "Emotions" (emotional impact of the illness) on QoL was the largest and was to a relatively large extent mediated by symptoms of anxiety and depression, considering that this item measures the emotional impact of the illness on the patient. In accordance with previous research among patients treated for breast cancer,[33] we found that patients who feel that their illness affects their life more severly ("Consequences") and who experience many symptoms from their illness ("Identity") have a considerable worse QoL. Our findings add that nearly half of that association was mediated by symptoms of anxiety or depression. Patients scoring high on "Identity" tend to attribute commonly occurring symptoms (such as a headache) to their illness, even if no such association exists.[34] This applies in particular to patients with advanced cancer who have to deal with uncertainty about the extent to which their limited life expectancy and who tend to interpret symptoms as signs of potential progression of their illness.[35, 36] Over-interpretation of symptoms can thus lead to symptoms of anxiety and depression, which in turn impairs QoL.

Patients had the highest average score on the illness representation "Timeline", meaning that they believed that their illness would last "forever". Previous research has shown that "Timeline" scores were skewed towards the upper extreme in patients with advanced cancer, which suggests awareness of the incurable nature of their illness.[13] "Timeline" scores were only to a limited extent associated with QoL. This association however was to a large extent mediated by symptoms of anxiety and depression, meaning that being aware of the limited life expectancy does not have a strong direct effect on QoL itself, but mainly impacts QoL negatively through the strong experience of symptoms of anxiety and depression.

Addressing illness representations is a promising approach when supporting patients with symptoms of anxiety or depression, and can thus be a way of improving the QoL of patient with advanced cancer. Since the prevalence of symptoms of anxiety and depression is higher in patients with advanced cancer than in colorectal cancer survivors, and even higher in comparison to the normative population,[37] patients are in clear need of support. Our findings emphasize the importance of raising awareness for patients' illness representations,[38] especially since previous research found that healthcare providers' understanding of the illness representations of their patients was relatively poor,[39] also with regard to important topics such as prognosis.[40] The recent consensus guideline of the American Society of Clinical Oncology on patient-clinician communication highlights the importance of (improved) health care communication and its positive impact on many objective and subjective health outcomes.[38] Our results suggest that illness representations can play an important role in patient-clinician communication and in meeting patients' information needs.[30] Additionally, previous research indicated the usefulness of targeting illness representations as a way to improve health outcomes.[41] Patients who were recovering from a myocardial infarction found a brief intervention on altering illness representations to be effective in improving functional outcomes.[41] Further research on how to adapt negative illness representations of patients with advanced cancer is needed.

The main strengths of this study lie in the use of a relatively large dataset of patients with advanced cancer, a unique and vulnerable group of patients that is rarely investigated, and the use of recently developed mediation analysis techniques that allow for the decomposition of total effects into natural direct and indirect effects, while accounting for exposure-mediator interactions.

Some limitations need to be considered when interpreting the findings. Although previous research and theoretical models suggest a strong temporal sequence, with illness representations preceding symptoms of anxiety and depression,[17] this study cannot draw causal conclusions due to its cross-sectional study design. Second, to interpret the observed direct and indirect effects, one needs to assume that there are no unmeasured confounders of the exposure-mediator relationship, the mediator-outcome relationship and the exposure-outcome relationship.[32] Although we did adjust for several potential confounders, we cannot exclude the possibility that unmeasured confounders may have impacted the results. Third, we performed a complete case analysis on the subset of patients with full information on the exposure, mediator, outcome variables and confounders. While this method is widely applied to treat missing data, it may lead to biased results if the data are not missing completely at random.[42]

In conclusion, our study indicates that negative illness representations are associated with worse QoL in patients with advanced cancer. Symptoms of anxiety and depression substantially mediate this association. Further prospective research is needed to confirm these findings. QoL and symptoms of anxiety and depression in patients with advanced cancer may be improved by addressing illness representations during medical consultations.

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