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Associations between Psychosocial Findings and Quality of Life One Year after Primary Treatment for Common Types of Cancer: A Multicenter Observational Study on Patient-Reported Outcomes

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Abstract

Background: Cancer patients suffer from a significant number of psychosocial challenges related to disease or straining treatments. As more are surviving cancer and its treatment, we aimed to explore associations between psychosocial topics, selected physical and treatment-related variables with health-related Quality of Life (QOL) one year after initial diagnosis and curative treatment of common types of cancer. The main goal was to identify factors that are relevant to patients' QOL and generate hypotheses to address modifiable factors by focused interventions.

Methods: In this prospective observational study, we used standardized, validated questionnaires to assess psychosocial topics pre- and 1-year post-cancer treatment and to investigate their impact on global QOL (EORTC QLQ-C30): Anxiety and depression, hope, social support, religion and spirituality, coping, resilience and a selected number of clinical parameters and symptoms. Uni- and multi-variate analyses for risk prediction were performed.

Results: This study included 297 patients (median age 66 years (± 11.9)) of whom 170 could be reached for follow-up. The most frequent diagnosis was gastro-intestinal cancer (n=121; 40.7%). While median global QOL was stable after one year across the entire patient population, there were clinically significant changes in values of single items (e.g. fatigue, physical and role functioning). A general deterioration of QOL was observed in 55/170 (35%) patients and 39/170 (25%) experienced a decline of more than 10 points. Multimodal treatment including chemotherapy was the single parameter that bore a high risk for poor subjective outcomes (p=0.0001). Further, multivariate analyses revealed that those who experienced a change in one of three parameters (i.e. anxiety, resilience or functionality) during the year of observation were at highest risk to experience a decrease in QOL.

Conclusion: Baseline psychosocial and clinical assessment data do not sufficiently predict for poor outcome while an adverse change in anxiety, resilience or functionality seems to endanger QOL. Patients whose treatment concepts include chemotherapy are at highest risk for reduced QOL. We suggest prospective randomized interventional studies with focused support beyond standard aftercare to improve the quality of survivorship. This will reveal important information on how to plan support, education, and counselling for a growing group of cancer survivors.

Trial registration: DRKS-ID: DRKS00010674. Registered on 05.07.2016.

Keywords: Psychosocial factors; Cancer patients; Curative treatment; Patient-reported outcomes

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Abbreviations

AP: Appetite Loss; CO: Constipation; DI: Diarrhoea; DY: Dyspnea; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire C30; EF: Emotional Functioning; FA: Fatigue; FI: Financial difficulties; FKV: Freiburg Fragebogenzur Krankheits Verarbeitung; GI: Gastro-Intestinal; HADS-A : Hospital Anxiety and Depression Scale-Anxiety; HADS-D: Hospital Anxiety and Depression Scale-Depression; HHI-D: The Herth Hope Index; MOS: Medical Outcomes Study; NV: Nausea and Vomiting; PA: Pain; PF: Physical Functioning; PSI: Physical Symptom Index; RF: Role Functioning; RS-11: Resilience Skale 11 Questions; SD: Standard Deviation; SF: Social Functioning; SL: Insomnia; SpREUK: Spirituality and Coping Questionnaire; TNM: Tumor-Node-Metastasis Classification of Malignant Tumors; UICC: Union for International Cancer Control

Background

More than 60,000 patients are diagnosed in Germany per year with each of the major tumor entities: Colon, breast and prostate cancer [1]. For an increasing number of patients, we can nowadays offer curative treatment, which can nonetheless be stressful and demanding. Generally, the largest group of cancer patients have their tumors removed surgically (45%). Of all cancer patients, about one third has radiotherapy and another third has chemotherapy as part of their treatment protocol [2].

Beyond survival, most cancer treatment guidelines incorporate symptom control and functionality as endpoints that can best be measured by Patient-Reported Outcomes (PROs) [3]. Nowadays, survivors live with cancer or adverse consequences of its treatment for extended periods. This highlights the importance of focusing on longer-term healthcare outcomes as well as the factors that may have an influence on them [4]. With more cancer patients living longer, a growing population of survivors and their needs will have to be considered in the future.

The diagnosis of cancer influences a patient's health-related Quality of Life (QOL) and functioning in many ways. QOL is affected even years after diagnosis, as suggested in some publications, regardless of treatments [5,6]. It has been shown that throughout the illness trajectory, patients experience physical symptoms related to the disease and treatment under which QOL declines [7]. The impact of cancer obviously does not end after the completion of its primary treatment [5]. We wished to explore how patients fare in the first post-interventional year and which factors might influence their well-being and ability to function. The aim of the present study was to assess the prognostic impact of baseline measurements of a broad selection of psychosocial questionnaires as well as disease and treatment related variables on QOL twelve months after surgery, chemo and/or radiotherapy.

Methods

This project was designed as a prospective observational study. Our study cohort included consecutive patients at six participating clinics in Germany from 2018 to 2020 meeting the following inclusion criteria: Patients with initial diagnosis of malignancies, scheduled for elective surgery or anti-tumor treatment with curative intent, life expectancy >1 year, and written informed consent. The aim was to define predictive variables for QOL at twelve months out of a set of questionnaires and variables that are specified below.

Instruments and data acquisition

Sociodemographic data were self-reported, whereas clinical information was retrieved from clinical records. Trained nurses handed out and supported the completion of paper copy questionnaires at two time points: Baseline (closest visit to initial treatment) and twelve months (within regular out-patient follow-up appointments, by phone or mail). To assess QOL, we used the EORTC QLQ-C30 version 3.0 [8]. The questionnaire contains one subscale for global quality of life, five functioning subscales, and nine symptom subscales, with all subscales linearly converted to a 0 to 100 scale. High scores in symptom scales indicates more symptoms while a high score in functioning (and global QOL) means better functioning. A 10-point change is generally considered to represent a significant clinical change [9]. Patients were asked to complete a selection of questionnaires to document various psychosocial dimensions pre- and one-year post-cancer treatment (Table 1).

Statistical analyses

The primary endpoint was global QOL after 12 months. The primary objective of our study was to define predictive instruments for global QOL in curatively treated cancer patients. Thus, sample size calculations were based on the primary objective to assess the impact of baseline variables on global QOL on a scale from 0 to 100, Standard Deviation (SD)=18. The trial was designed to detect differences in factors with a power of 80% at a two-sided significance level of 5%, when comparing two groups according to a relevant prognostic factor occurring in the population in a ratio of 20:80 and considering possible correlations among predictors. Anticipating a dropout rate of 33%, we calculated a sample size of 300 patients, resulting in 190 evaluable data sets.

Data were analyzed using R 4.1.2. Descriptive statistics were applied: Patient demographics are presented as mean and standard deviations and medians with frequencies and proportions (%), as appropriate. The next step consisted of univariate linear regression models to identify potentially predictive factors for global QOL, the primary endpoint. A two-sided p value of <0.05 was considered statistically significant. The statistically significant variables were then used in two multivariate regression models. In the first model, variables in t=1 were used as regressors; in the second model, the change in variables from t=1 to t=2 was used.

For the description of changes in results of the EORTC QLQ C30 questionnaire, a difference of more than 10 points has been suggested as indicative for a clinical as opposed to sole statistically significant relevance [10].

Results

There were 297 patients that participated in baseline assessments. All patients were contacted again personally and 170 patients were available for follow-up assessments after 12 months. The dropout rate was within the anticipated range.

Patients with gastrointestinal cancer (n=121; 40.7%) formed the largest cohort, followed by breast cancer (n=82; 27.6%). Primary cancer treatments were performed with comparable frequency to what can be found in the literature [2]: the majority of patients had surgery to remove their tumor (55.9%), followed by chemo- and radiation-therapy with 24.9% and 25%, respectively. The percentages do not sum to 100%, as some patients underwent more than one type of treatment. Further patient baseline characteristics are depicted in

Table 1: variables and respective questionnaires.

	Variable	Questionnaire	Reference	No.
Psycho-Social dimension	Quality of life	EORTC QLQ-C30	Osoba, Aaronson et al. 1997	[22]
	Anxiety and depression	HADS-D	Thombs, Benedetti et al. 2016	[23]
	Hope	The Herth Hope Index (HHI-D)	Geiser, Zajackowski et al. 2015	[24]
	Social support	MOS	Sherbourne and Stewart 1991	[25]
	Religion and spirituality	SpREUK	Bussing, Matthiessen et al. 2005	[26]
	Coping	Freiburg Fragebogen zur Krankheitsverarbeitung (FKV)	Muthny 1989	[27]
	Resilience	RS-11	Schuhmacher, Leppert et al. 2005	[28]
Patient-specific dimension	Physical Symptoms	PSI	Spector, Jex 1998	[29]
	Performance status	Karnofsy Index	Karnofsky and Burchenal 1950	[30]
	Comorbidities	Charlson Index	Charlson, Carrozzino et al. 2022	[31]
Disease-specific dimension	Tumor entity			
	Stage		TNM Classification UICC	[32]
Treatment-specific dimension	Surgery			
		Post-operative complications	Clavien, Barkun et al. 2009	[33]
	Chemotherapy			
	Antihormonal treatment			
	Radiation therapy			

Table 2: Patient baseline characteristics.

Variable		
Median age, years [± Std Dev]		66 (± 11.92)
Charlson Comorbidity Index [Mean [SD]]		1.39 (± 2.07)
Karnofsky Index [Mean [SD]]		76.24 (± 38.37)
Variable		**N of patients (%)**
Female		169 (66.3)
Male		86 (33.7)
Primary location of tumor	GI	121 (40.7)
	Urogenital	21 (7.1)
	Breast	82 (27.6)
	Hematologic	5 (1.7)
	Other	23 (7.7)
Stage [UICC]	I	55 (18.5)
	II	37 (12.4)
	III	36 (12.1)
	IV	8 (2.7) e.g. intra-operative finding
	Other	6 (2.0) e.g. lymphoma
Treatment [multiple treatments per patient possible]	Surgery	165 (55.9)
	Chemotherapy	74 (24.9)
	Anti hormonal treatment	46 (15.5)
	Radiation therapy	75 (25.25)

Table 2.

While median global QOL was stable after one year across the entire patient population (Table 3), a deterioration of QOL was observed in 55/170 (35%) patients and 39/170 (25%) patients experienced a decrease of more than 10 points, a cut-off value considered as clinically meaningful. With respect to the trajectory of QOL dimensions, two functional scales deteriorated most in patients over the course of time, physical functioning (T1: 84.5 *vs.* T2: 75.5) and role functioning (T1: 79.7 *vs.* T2: 71.3), while the symptom fatigue increased relevantly from T1: 27 to T2: 37.8.

The comparison of baseline characteristics of 55 patients with a decline in global QOL *vs.* the entire patient population suggests some variations according to cancer type and stage. In the subgroup with decreased QOL, we saw a relative increase in the number of patients

Table 3: Assessment variables EORTC QLQ-C30 at T1 and T2 [n=170].

	T 1	Mean	SD	Median	T2	Mean	SD	Median
Global health status/QoL	QL	63.78	23.12	66.67		65.93	21.63	66.67
Functional Scales								
Physical Functioning	PF	84.55	19.57	93.33		75.03	22.49	80.00
Role Functioning	RF	79.71	27.99	100.00		71.33	27.46	66.67
Emotional Functioning	EF	61.54	26.16	66.67		67.84	25.79	75.00
Cognitive Functioning	CF	86.69	21.28	100.00		78.93	24.55	83.33
Social Functioning	SF	78.99	26.19	83.33		72.15	29.63	83.33
Mean		78.64	18.84	85.00		73.4	20.28	77.33
Symptom Scales								
Fatigue	FA	27.05	26.87	22.22		37.79	26.18	33.33
Nausea and vomiting	NV	3.58	12.25	0.00		4.29	11.05	0.00
Pain	PA	18.59	26.97	0.00		25.21	29.6	16.67
Dyspnoea	DY	18.7	26.93	0.00		22.76	28.78	0.00
Insomnia	SL	30.69	31.97	33.33		36.86	33.8	33.33
Appetite loss	AP	14.02	27.13	0.00		10.37	20.75	0.00
Constipation	CO	9.64	23.22	0.00		12.58	24.21	0.00
Diarrhoea	DI	18.01	28.38	0.00		20.5	29.83	0.00
Financial difficulties	FI	12.03	26.12	0.00		15.82	26.79	0.00
Mean		16.63	14.32	12.96		20.13	15.06	18.52

Table 4: a): Multivariate analysis. b) Multivariate analysis using change in variables (T1 *vs.* T2) as regressors.

a) Multivariate analysis	**Estimate**	**std. error**	**t-statistic**	**p-value**
EORTC QLQ-C30 Global QOL	0.3014	0.1989	1.5153	0.1377
EORTC QLQ-C30 Mean functional score	0.2413	0.3039	0.794	0.432
EORTC QLQ-C30 Mean symptom score	0.0968	0.3596	0.2691	0.7892
HADS A Score	-1.4664	1.1775	-1.2454	0.2204
HADS D Score	0.3486	1.0197	0.3419	0.7343
MOS Score	6.5857	6.6334	0.9928	0.3269
PSI Score	-1.1028	1.1292	-0.9767	0.3348
FKV mean Score	9.0758	5.3774	1.6878	0.0994
Clavien Dindo Index	-3.0455	2.1667	-1.4056	0.1678
Surgery	-10.3603	15.1354	-0.6845	0.4977
Chemotherapy	-26.1526	5.7744	-4.5291	0.0001
b) Multivariate regression models using the change in variables [T1 *vs.* T2] as regressors				
EORTC QLQ-C30 Global QOL	0.6212	0.1077	5.7666	0
Delta EORTC QLQ-C30 Mean functional score	0.4147	0.1867	2.2208	0.0331
Delta EORTC QLQ-C30 Mean symptom score	-0.3623	0.268	-1.352	0.1853
Delta HADS A Score	1.5866	0.577	2.7496	0.0095
Delta HADS D Score	-0.6394	0.7184	-0.89	0.3797
Delta MOS Score	4.1286	5.4519	0.7573	0.4541
Delta SpREUK mean Score	0.1484	0.1631	0.9098	0.3693
Delta PSI Score	0.5472	0.5353	1.0223	0.3139
Delta FKV mean Score	-5.5688	4.0661	-1.3696	0.1798
Delta RS Score	-0.3477	0.135	-2.5753	0.0145
Clavien Dindo Index	-0.0298	1.7115	-0.0174	0.9862
Surgery	22.7373	10.1335	2.2438	0.0315
Chemotherapy	-11.7437	5.1434	-2.2832	0.0288

with urogenital cancer (data available at the authors).

With respect to uni- and multi-variate analyses, the following factor reached statistical significance: Primary cancer treatment including chemotherapy was a statistically significant prognostic factor for reduced global QOL (p=0.0001) (Table 4a). None of the other psychosocial, religious, coping questionnaires or symptom scores reached significance (univariate analyses available at the authors).

When using changes in variables (T1 *vs.* T2) as regressors, a change in EORTC functional scores (summed up to a mean score) implied an impact on global QOL at T2 (p=0.0331). Furthermore, a decrease in the scoring value of resilience at T2 was predictive for poorer outcome (p=0.0145), as was an increase in anxiety (p=0.0095) (Table 4b).

Discussion

In our non-interventional study on the trajectory of QOL and risk factors for a decline in patient-reported outcomes within one year after primary cancer treatment, it was reassuring to realize that QOL was maintained in the majority of patients. Data on QOL are nearly identical to a very recently publishes work on outcome quality after colorectal cancer resection in German Certified Colorectal Cancer Centers [11]. Nevertheless, every fourth patient experienced a clinically relevant decline in global QOL after primary cancer treatment. We noticed a non-significant variability in QOL according to cancer type and treatment. Certain types of cancer such as urogenital malignancies were slightly more common within the group of patients that experienced a decline in QOL.

In uni- and multivariate analyses, having chemotherapy as monotherapy or part of the primary treatment regime was the strongest adverse risk factor for poorer QOL. In our patient cohort, chemotherapy was part of a multimodal treatment approach in the majority of cases (66/74), suggesting an added toxicity and protracted treatment duration. As chemotherapy was associated with adverse patient-reported outcomes, this underlines the importance of collecting data on QOL when evaluating that treatment option, in addition to standard measures such as survival in clinical research. Unfortunately, our data do not answer the question as to which negative aspects of treatment (e.g. side effects such as neuropathy, need for isolation, fatigue, or treatment duration etc.) resulted in the relevant decrease in global QOL. Still, results underline that those who had been treated with chemotherapy may require protracted special attention, i.e. "survivorship programs with focused oncological aftercare and interventions" which unfortunately is not yet the standard in Germany.

A change in functionality (as opposed to changes in symptom load) proved to be a risk factor for poor QOL after primary treatment is completed. This is in accordance with a large Australian study in which more than 20% of long-term (> 2 years) cancer survivors had severe physical functioning limitations. Similarly, there was an elevated prevalence of poor QOL apparent. Although physical functioning and QOL were reduced overall for cancer survivors, worse outcomes were observed with increasing recency of diagnosis, more advanced stage, and treatment within the last month. The prevalence of psychological distress also increased markedly with increasing limitations to physical functioning [12]. Other previous studies in breast cancer patients support these findings and strengthen the evidence of increased distress/reduced QOL with reduced physical functioning [13,14]. Our results emphasize the need to offer support to affected survivors early in the course of recovery to maintain functionality, e.g. by offering tailored physical or occupational therapy. In this context, Kim et al. [15] were able to demonstrate that a 12-week home-based exercise program improved physical activity, QOL, fatigue, and psychological health in colorectal cancer patients.

Searching for further factors that influence patients' quality of survival after cancer diagnosis, it has been shown before that optimistic coping strategies/illness acceptance resulted in significantly better QOL [16]. Accordingly, in our patient population, an increase in anxiety constituted a risk factor for global QOL. In an effort to ease anxiety and other mental health disorders, distress and impairments ought to be assessed and psychological support should be offered post-interventionally.

Resilience seems to play a major role in determining mental health in the somatically ill [17]. Resilience is regarded as the result of adaption to stressors and increasingly understood as a dynamic process that can be trained [18]. There have been suggestions for successful psychological interventions to promote resilience in cancer patients. Resilience-enhancing measures that were provided in the period immediately after the diagnosis of cancer and in parallel with somatic treatment had the greatest positive effect on resilience [19].

In our study, the repeat use of quickly and widely available questionnaires for QOL (EORTC QLQ-C30), Hospital Anxiety and Depression Scale (HADS) and Resilience (RS) were stronger in predicting adverse outcomes than all other questionnaires or patient parameters. We propose to use these in regular intervals during oncological aftercare or within survivorship programs to identify and treat patients at high risk for adverse outcomes.

There are limitations to this analysis: Obviously, we had a variety of different tumor entities and treatment approaches. We accounted for this from the beginning, as it was our intent to highlight real-world cancer patient scenarios in German hospitals. In a next step, the focus may be narrowed down to subgroups of patients.

Presumably, chemotherapy came closer to the time of the follow-up survey than other treatment options. In future trials, surveys should be repeated at later time points to further clarify this assumption and chemotherapy's longer-lasting effects on QOL.

With our selection of questionnaires, we wanted to cover broad fields of psychosocial interactions. Certainly, we can only obtain partial insight and might have missed important variables like socio-economic status, which has very recently been shown to be strongly associated with 12-month postoperative PRO results in colorectal cancer patients [11].

Despite efforts to reach out to all patients, there was a large amount of missing data. Missing data are a common problem in studies using patient-reported outcomes, bearing the danger of a potential bias as sicker patients may be less likely to complete QOL questionnaires [20]. This is taken into account when discussing the data and we report all data collected on the one hand and base the statistical results on valid pre- and post-tests on the other hand.

Conclusion

Findings suggest that a relevant number of patients experience a clinically significant decrease of QOL within the first year of cancer treatment. Multimodal treatment including chemotherapy implied the highest single risk for poor subjective outcomes. Furthermore,

multivariate analyses revealed that those who report a change in one of three parameters (i.e. anxiety, resilience or functionality (EORTC QLQ-C30)) during the year of observation were at highest risk to experience a decrease in QOL. As has been shown in other studies, the first year seems to be a vulnerable period within the individual cancer trajectory [21]. Our data suggest the need to focus on physical functioning as well as social and psychological support to maintain resilience and ease anxiety. Adverse changes are key drivers of reduced QOL. Ideally, assessment of patient-reported outcomes and tailored interventions should be part of routine clinical assessments at key time points such as start and completion of treatment and guideline-compliant care of cancer survivors. However, this has not been adopted into the routine clinical practice in Germany. Prospective studies should evaluate the effectiveness of proposed interventions on survivorship outcomes.

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