

APPLICATION STUDY OF THE EQ-5D-5L IN ONCOLOGY: LINKING SELF-REPORTED QUALITY OF LIFE OF PATIENTS WITH METASTATIC COLORECTAL CANCER TO CLINICAL DATA FROM A GERMAN TUMOR REGISTRY

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BACKGROUND

- In Germany, colon cancer is the second most frequent cancer among women and the third most frequent cancer among men. Approximately one out of eight cancers in Germany affects the bowel and more than 6% of the population are diagnosed with colorectal carcinoma during their lifetime.¹
- Colorectal cancer patients suffer from a high psychological and physical burden of disease and have a reduced quality of life due to various problems in social functioning and disease-specific symptoms.^{2,3}
- The EuroQoL five-dimension questionnaire with five answer levels (EQ-5D-5L) is widely used and well-accepted in oncology to generate health-related quality of life (hrQoL) weights.⁴
- The five dimensions include mobility, self-care, usual activity, pain/discomfort, and anxiety/depression and each of these dimensions is to be evaluated by five levels ranging from no problems to extreme problems.⁵
- In addition, the EQ-5D-5L includes a visual analogue scale (VAS), a continuous response scale ranging from 0 (worst possible health state) to 100 (best possible health state), to record patients' self-rated health on the day of the interview.⁵
- Clinical registries routinely collecting clinical data present an opportunity to link hrQoL with data about disease status.

OBJECTIVE

- First aim of this study was to perform a cross-sectional assessment of hrQoL data and to calculate EQ-5D-5L utilities of patients recruited into the German Tumor Registry Colorectal Cancer.
- Second aim was to explore the relationship between disease-specific health states and hrQoL by linking clinical data of the German Tumor Registry Colorectal Cancer to self-reported hrQoL measures from the EQ-5D-5L.

METHODS

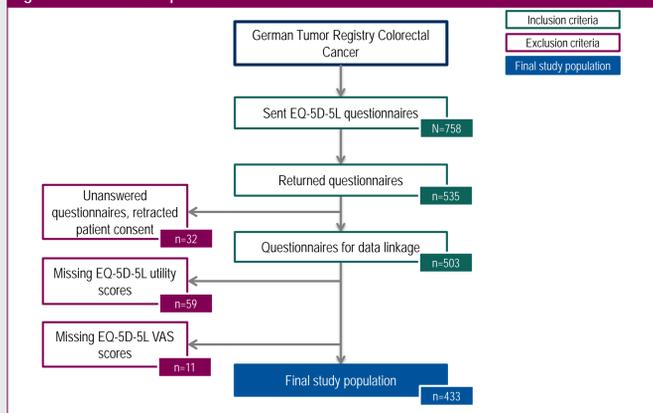
- The study sample included patients with metastatic colorectal cancer who had been recruited since March 2014 into the German Tumor Registry Colorectal Cancer.
- Criteria for being eligible for the registry were: histologically confirmed advanced or metastatic colorectal cancer, informed consent before or up to four weeks after start of palliative first-line chemotherapy, being at least 18 years of age, and willingness to participate in the patient-reported outcomes survey.
- The EQ-5D-5L questionnaire was applied to measure the hrQoL. Utility scores were calculated using a Germany-specific value set leading to scores from -0.661 to 1. VAS scores were recorded directly from the scale.⁶
- The questionnaire was administered once per patient as a paper version between November 2016 and May 2017. At the time of questioning, patients were at the beginning or at later stages of palliative treatment (0 to 24 months after first-line palliative therapy).
- The EQ-5D-5L utility scores were linked to pseudonymized clinical data from the registry.
- Potentially relevant tumor history and metastases, disease or treatment-related symptoms (pain, nausea and vomiting), and fatigue scores derived from the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire administered at the same time as the EQ-5D-5L) as well as treatment status and comorbidities were defined by literature review and by medical experts.

RESULTS

PATIENT SELECTION

- In total, N=758 questionnaires were sent to the patients and n=535 questionnaires were returned. After exclusion of unanswered questionnaires and questionnaires with retracted patient consents, data linkage of EQ-5D-5L data and clinical registry data was performed for n=503 patients.
- During data preparation, n=59 patients were excluded due to missing EQ-5D-5L utility scores and n=11 patients due to missing VAS scores.
- In total, n=433 patients were included in the final data analysis (Figure 1).

Figure 1. Flowchart of patient selection



PATIENT CHARACTERISTICS

DEMOGRAPHICS

- At the time of EQ-5D-5L questioning, the patients were on average 66.3 years (±9.5 years) old.
- The majority of patients (n=265, 61.2%) were male.

TUMOR HISTORY AND METASTASES

- The primary tumor was located in the colon in 56.4% and in the rectum in 43.4% of cases.
- At the time of the initial diagnosis, 19.9% of the patients were diagnosed with an inoperable primary tumor.
- At the time of last documentation before EQ-5D-5L questioning, 61.4% of patients had liver metastases, 23.8% had lung metastases, 14.6% had peritoneal metastases, and 3.0% had bone metastases.
- In 83.8% of patients, metastases were located at one or more localizations.

DISEASE OR TREATMENT-RELATED SYMPTOMS

- At the time of EQ-5D-5L questioning, the fatigue score calculated from the EORTC QLQ-C30 reached an average of 47.2, indicating a noticeable burden with regard to an achievable score range of 0 (lowest burden) to 100 (highest burden).
- The pain score was 26.6 and the nausea and vomiting score was 12.7 on average.

TREATMENT STATUS

- At the time of EQ-5D-5L questioning, the majority of patients was in first-line palliative therapy (55.2%), 23.3% were at break after first-line, 15.5% were in second-line or at break after second-line, and 5.1% in third-line or later.
- Antibodies that were given in addition to chemotherapy were VEGF-inhibitors (49.7%) and EGFR-inhibitors (26.1%), 22.6% of patients received no additional antibody treatment.

- About one-fifth of the patients (21.0%) had experienced at least one progression prior to questioning.

COMORBIDITIES

- At the time of inclusion in the registry, 61.7% had at least one of the reported comorbidities.
- The most frequent comorbidity among the patients was hypertension (41.3%), followed by diabetes (14.6%) and thyroid disease (9.0%) (Table 1).

Table 1. Descriptive statistics of patient characteristics

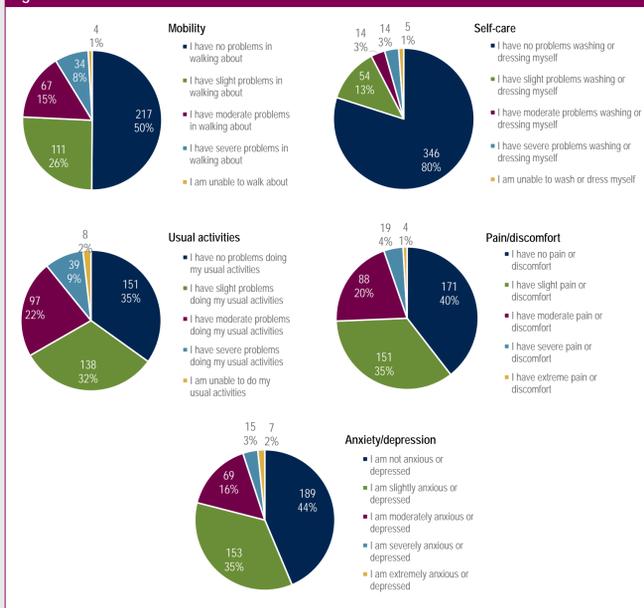
Variable	Definition	%, mean (standard deviation)
Demographic characteristics		
Age	Years	66.33 (±9.50)
Gender	Male	38.80%
	Female	61.20%
Tumor history and metastases		
Localization of tumor	Colon	56.35%
	Rectum	43.42%
Inoperable primary tumor		19.86%
Liver metastases		61.43%
Lung metastases		23.79%
Peritoneal metastases		14.55%
Bone metastases		3.00%
Number of metastatic localizations	0	10.85%
	1	51.27%
	2	24.94%
	≥3	7.62%
	Disease or treatment-related symptoms	
EORTC QLQ-C30	Fatigue	47.24 (±26.56)
	Pain	26.62 (±30.42)
	Nausea and Vomiting	12.71 (±20.28)
Treatment status		
Palliative treatment line	First-line	55.19%
	Break after first-line	23.33%
	Second-line or break afterwards	15.48%
	Third-line or later	5.08%
Antibodies	EGFR-inhibitor	26.10%
	VEGF-inhibitor	49.65%
Number of progressions experienced prior to questioning	0	75.29%
	≥1	24.71%
Comorbidities	Hypertension	41.34%
	Diabetes without impairment of organs	14.55%
	Thyroid disease	9.01%
	Coronary heart disease	8.31%
	Tumor other than colorectal, lymphoma or leukemia	7.85%
	Chronic gastric or bowel disease	6.70%
	Adiposity	6.47%
	Chronic pulmonary disease	5.77%
Anemia	4.39%	
Heart failure	4.16%	
Moderate or severe kidney disease	3.46%	

*Note: Missing values are not shown and therefore the single characteristics of each variable may not sum up to 100%.

DESCRIPTIVE ANALYSIS OF EQ-5D-5L UTILITY SCORES

- For most patients (n=332, 76.7%), the EQ-5D-5L questionnaire was sent out within the first 12 months after first-line palliative treatment initiation. The remaining patients (n=101, 23.3%) received the questionnaire up until 24 months after first-line palliative treatment initiation.
- The mean time until hrQoL questioning for all interviewed patients was 8.2 months after first-line palliative treatment initiation.
- The overall mean EQ-5D-5L utility score for patients with metastatic colorectal cancer was calculated to be 0.816 (±0.228).
- The detailed analysis of the five EQ-5D-5L dimensions showed that the majority of patients did not have any problems with self-care, whereas approximately two-thirds of the patients reported slight, moderate, or severe problems in performing usual activities or were even unable to perform them (Figure 2).

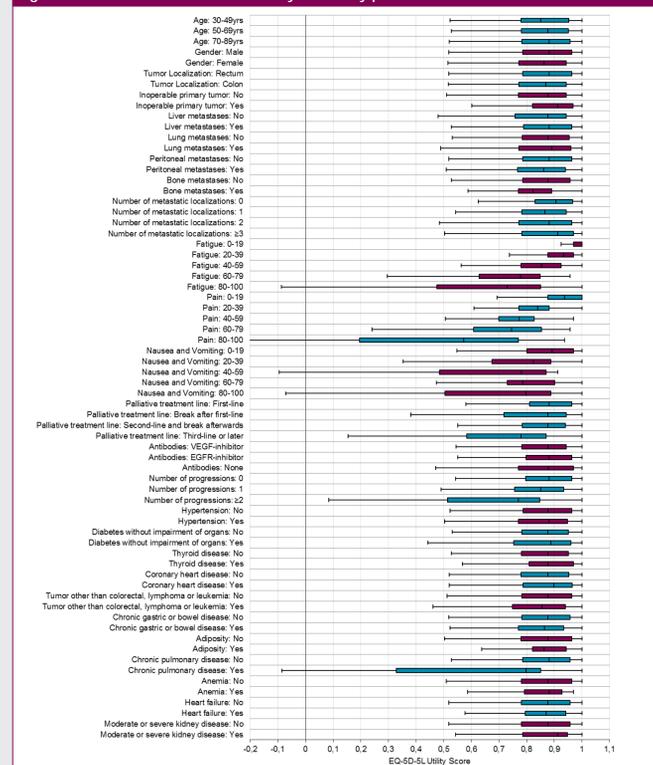
Figure 2. Level distribution in each EQ-5D-5L dimension



DESCRIPTIVE ANALYSIS OF HRQoL STRATIFIED BY PATIENT CHARACTERISTICS

- Figure 3 illustrates the distribution of the EQ-5D-5L utility scores by patient characteristics.
- Regarding the demographic characteristics, the distribution was very similar showing no difference in terms of age and gender.
- The categories of tumor history and metastases demonstrated a consistent distribution of hrQoL as well.
- Looking at the disease and treatment-related symptoms derived from the EORTC QLQ-C30, especially a high burden of fatigue and pain indicated a reduction in hrQoL.
- Patients in third or later palliative treatment lines had a remarkably lower hrQoL compared to patients in previous treatment lines.
- Patients with two or more progressions in previous treatment lines had a decreased hrQoL when compared to only one or no progression.
- For the noted comorbidities, patients with chronic pulmonary disease showed the lowest hrQoL.

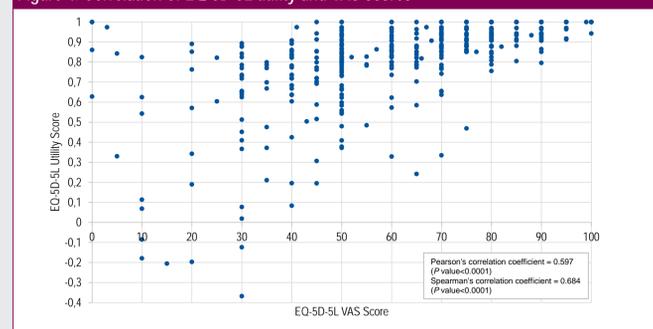
Figure 3. Distribution of EQ-5D-5L utility scores by patient characteristics



CORRELATION BETWEEN EQ-5D-5L UTILITY AND VAS SCORES

- The overall mean EQ-5D-5L VAS score for patients with metastatic colorectal cancer was 62.1 (±22.2).
- Compared to this observed mean EQ-5D-5L VAS score in patients with metastatic colorectal cancer, the EQ-5D-5L utility score was comparatively high (62.1 vs. 0.816).
- The correlation between the EQ-5D-5L utility and the VAS score was statistically significant (P<0.0001) but also indicated a broader distribution of the VAS score (Figure 4).

Figure 4. Correlation of EQ-5D-5L utility and VAS scores



CONCLUSIONS

- This study linking clinical registry data to hrQoL data showed a new opportunity for a cross-sectional study design.
- The evaluation of the EQ-5D-5L VAS score in metastatic colorectal cancer patients observed a reduced hrQoL compared to the general population (mean VAS 62.1 vs. 85.2).⁷
- On the contrary, the average EQ-5D-5L utility score was higher than expected compared to the general population in Germany (0.816 vs. 0.92).⁸
- The descriptive analyses showed that only a few of the investigated disease-specific health states were more common in patients with a decreased hrQoL, namely the symptoms fatigue and pain, palliative treatment line, number of progressions, and chronic pulmonary disease.
- A possible reason for the relatively high and stable EQ-5D-5L utility scores might be that seriously-ill patients have accepted their fate (coping) and recognize their disease, treatment, and comorbidities as part of their daily life. This behavior was also observed among cystic fibrosis patients.⁹
- Another explanation for the findings from the utility score could be that the investigated comorbidities are under control and not relevant when compared to the cancer diagnosis.
- Furthermore, delicate nuances that affect the hrQoL of palliative cancer patients might not be detectable with a generic instrument such as the EQ-5D-5L utility score. The VAS score might be more informative since it is not restricted to the five dimensions.

LIMITATIONS

- All analyses were descriptive and causal relations about hrQoL and its potentially affecting factors could not be drawn.
- Another limitation of the study was that the patient characteristics were documented at different points in time prior to questioning leading to possible unobserved changes at the time of EQ-5D-5L questioning.

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