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

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BACKGROUND

In Germany, colorectal cancer (CRC) is the second most frequent cancer among women and the third most frequent cancer among men. During their lifetime, one out of 18 men and one out of 15 men is diagnosed with colorectal cancer. Overall, approximately one out of eight cancers affects the bowel.1 Affected 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.

The EuroQol five-dimensional questionnaire with five answer levels (EQ-5D-5L) is widely used and recommended as one of the gold-standard quality of life (QoL) weights and corresponding health states.2,3

However, for patients with advanced or metastatic CRC, there are no data available reporting the influence of certain comorbidities or health states on the EQ-5D.

OBJECTIVE

The aim of this study was to explore the relationship between demographic and clinical characteristics and EQ-5L among patients with advanced or metastatic CRC by linking clinical data of a German CRC registry to self-reported EQ-5L measures from the EQ-5D.

METHODS

The study sample included patients with advanced or metastatic CRC who had been recruited into the German Tumor Registry Colorectal Cancer since March 2014.

Data collection and methodology of the registry have been described previously.4

Inclusion criteria for the registry were age ≥18 years, histologically confirmed CRC, and signed informed consent from more than four weeks after the start of systemic/antineoplastic treatment for non-metastatic or first-line treatment for metastatic/irresectable disease.

Registered patients who had declared willingness to participate in patient-reported outcomes (PRO) surveys routinely received a PRO questionnaire including the Quality of Life Core Set (QOLS) version 2.07 of the European Organization for Research and Treatment of Cancer (EORTC QLC-C30). For this study, the EQ-5D was added.

The EQ-5D-5L was delivered once per patient by postal mail as part of the next round of PRO questionnaire delivery between November 2015 and May 2017. At the time of questioning, patients were at the beginning or at later stages of palliative treatment (T 0 to 24 months on palliative therapy).

Data from the EQ-5D-5L and EORTC QLC-C30 was linked to pseudonymized clinical registry data from the German tumor registry.

Patient, clinical, and treatment characteristics with the potential to influence HRQoL were defined by literature review and by medical expert consensus. Utility scores from the EQ-5D-5L were calculated using a Germany-specific value-based scoring from -0.581 (worst possible health state) to 1 (best possible health state).4,5

Scores from the EORTC QLC-C30 were calculated following the scoring manual published by the EORTC.6 In four cases from 0 to 100, with a higher score indicating a better level of functioning (functional scale) and a higher QoL (global health status/QoL scale), but a worse level of symptoms (symptom scale).7

A t-test regression analysis was performed to explore the impact of clinical, patient, and treatment characteristics on the EQ-5D-5L utility score. Marginal effects were then calculated at the sample mean.

Ordinary least squares (OLS) regression analyses were conducted to explore the impact of patient, clinical, and treatment characteristics on the EQ-5D-5L VAS score as well as the EORTC-QOL global health status/QoL score.

Significant impacts on the quality of the sample were determined at a level of significance at p<0.05.

RESULTS

PATIENT SELECTION

The PRO questionnaire was sent to N=758 patients with advanced or metastatic CRC in Germany between April 2015 and May 2017. More than two thirds of the patients returned the questionnaire (n=535 patients). Patients who had been treated before or had received or retained a blank or incomplete EQ-5D-5L questionnaire. The final study population consisted of n=433 advanced metastatic CRC patients for whom both an EQ-5D-5L utility as well as an EQ-5D-5L VAS score could be computed.

PATIENT CHARACTERISTICS

At the time of the PRO questioning, the patients were on average 68.3 years old (±10.5 years old).

The majority of patients (n=265, 61.2%) were male.

CLINICAL CHARACTERISTICS

Tumor History and metastasis

More than half of the primary tumors were in the colon (56.4%), whereas 43.3% were located in the rectum. Primary tumors were classified as inoperable in 19.9% of the patients.

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

Most of the patients (83.8%) had one or more metastases when filling in the PRO questionnaire with 81.4% of patients having liver metastases, 23.8% lung metastases, 14.5% peritoneal metastases, and 3.5% bone metastases.

Comorbidity

In the time of induction in the registry, 57.1% of patients had at least one of the pre-defined comorbidities including for example cardiovascular and metabolic diseases.

The most frequent comorbidity among the patients was hypertension (41.3%), followed by diabetes mellitus (37.0%) and chronic obstructive pulmonary disease (27.3%).

TREATMENT CHARACTERISTICS

Treatment status

More than half of the patients were in first-line palliative therapy (55.3%) when filling in the PRO questionnaire. 23.3% were at break after first-line therapy, 15.3% were in second-line or at break after second-line therapy, and 5.1% in first-line therapy.

The most current chemotherapy at the time of questioning was based on irinotecan (44.8%), oxaliplatin (27.4%) or bevacizumab (10.4%) of the patients were treated with fluoropyrimidine monotherapy. 43.9% of patients, 38.1% received ESFR-graf, and 22.6% of patients did not receive any monotherapic antibodies.

Disease or treatment-related symptoms

The EORTC QLC-C30 fatigue scale of the interviewed patients with advanced or metastatic CRC was calculated to be 47.2 at the time of questioning.

The EORTC QLC-C30 pain score was 26.0 and the EORTC QLC-C30 nausea and vomiting score was 12.7 at the time of questioning.

Overall, our hrQoL findings were in line with the findings of the previous study of Marventano et al.8

Table 1: Summary of the patient, clinical, and treatment characteristics of the included patients with advanced or metastatic CRC (n=433)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definition</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>years</td>
<td>68.3 (10.5)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>265 (61.2%)</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>hypertension</td>
<td>41.3%</td>
</tr>
<tr>
<td></td>
<td>diabetes mellitus</td>
<td>37.0%</td>
</tr>
<tr>
<td></td>
<td>chronic obstructive pulmonary disease</td>
<td>27.3%</td>
</tr>
<tr>
<td>Treatment status</td>
<td>first-line palliative therapy</td>
<td>55.3%</td>
</tr>
<tr>
<td></td>
<td>second-line or at break after second-line therapy</td>
<td>15.3%</td>
</tr>
<tr>
<td></td>
<td>in first-line therapy</td>
<td>5.1%</td>
</tr>
</tbody>
</table>

Table 2: Results from tobit and OLS regression analysis of the relationship between EQ-5D-5L utility score, EQ-5D VAS score, EORTC-QOL global health status/QoL score, and patient, clinical and treatment characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definition</th>
<th>Coefficient (SE)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQ-5D-5L utility score</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>EQ-5D VAS score</td>
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<td></td>
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<tr>
<td>EORTC-QOL global health status/QoL score</td>
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</table>

CONCLUSIONS

This study linking clinical registry data to HRQoL data illustrated a feasible approach for a cross-sectional study design.

The regression analyses revealed that none of the patient demographic and only few of the clinical and treatment characteristics, especially fatigue and pain, had a significant impact on the EQ-5D of patients with CRC.

Our findings are in line with a review by Marventano and colleagues which showed that gender was not a significant determinant of CRC patients' HRQoL. Furthermore, the review revealed that results on age were controversial and that symptoms induced by cancer or its treatment such as fatigue had a significant negative impact on HRQoL. On the contrary, the review depicted that disease had a significant effect on HRQoL, which was not confirmed in our study.

One explanation for the few significant determinants of HRQoL might be that serious diseases had an impact on the patients' life and treatment.

Another reason could be that the investigated comorbidities are under control and not relevant when compared to the symptoms associated with the cancer and its treatment.

Furthermore, data on patients with severely reduced HRQoL might be under-represented in our study because these patients are less likely to return the questionnaires.

LIMITATIONS

The patient characteristics were documented at different points in time prior to the PRO questioning leading to potential bias in the self-reporting.

Moreover, confounding by unmeasured variables cannot be ruled out.

REFERENCES


