

ORIGINAL ARTICLE

Development of a disease-specific health-related quality of life (HRQoL) questionnaire intended to be used in conjunction with the general European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ) in renal cell carcinoma patients

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ABSTRACT

Background. Studying health-related quality of life (HRQoL) following cancer treatment has become part of a growing number of standardized treatment protocols. The European Organization for Research and Treatment of Cancer (EORTC) has developed HRQoL questionnaires aimed at cancer patients. A disease-specific part is not available for renal cell carcinoma (RCC) patients, and the present aim was to develop an EORTC-compatible RCC-specific HRQoL questionnaire.

Material and methods. In total 413 RCC patients were treated with radical or partial nephrectomies in Western Norway during the period from 1997 to 2010. Three hundred and nine patients with histologically proven cancer were still alive at the inclusion time point and 185 RCC patients (71% response rate) returned the questionnaires. We determined HRQoL by the EORTC-QLQ C30 questionnaire. We also asked 13 candidates questions aimed at constituting a disease-specific part. Furthermore, we tested parts of personality by the Eysenck Personality Inventory and coping by the COPE questionnaire. Given tumor treatment, TNM stage, alcohol consumption level and smoking levels were also determined from the hospital records.

Results. A factor analysis showed that five factors were formed: one general symptomatic, one general functional, one with disease-specific questions (flank pain, blood in the urine, flank edema, urinary tract infection), one about sexuality and one about weight loss or gain. Ten RCC-specific HRQoL questions were derived from a factor analysis, including four questions related particularly to pain, mobility and social functioning, also representing a short version of the EORTC C30. The psychometric properties and the relation to other psychological and clinical variables were further determined to be satisfactory.

Conclusions. The suggested disease-specific EORTC-QLQ-style RCC10 version adds important information about the HRQoL of RCC patients, providing additional apparent value to the general questionnaire and personality variables, as well as being psychometrically satisfactory. The questionnaire has a potential as a "stand alone" HRQoL questionnaire among RCC patients.

Renal cell carcinoma (RCC) represents 2% of all new cancer cases in Norway. After prostate and bladder cancer, it is the third most common urological cancer. RCC affects men 1½-times more often than

women, and it occurs mostly in the sixth and seventh decades [1]. RCC is a general term for many different histological subtypes. The causes of kidney cancer are not well enough understood, though some

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risk factors, such as smoking, obesity and advanced kidney disease, are known. RCC is primarily treated by surgery only, and the only groups offered active surveillance for localized RCC are older and comorbid patients with limited life expectancy [2]. The cure rate is between two thirds and three quarters of diagnosed patients.

To study health-related quality of life (HRQoL) outcomes, is suggested when studying new cancer treatments [3]. Patient-reported outcome measures (PROMs) are further recommended to be an integrated part of the treatment, care and rehabilitation of cancer patients [4]. PROMs may also provide prognostic information supplementary to standard clinical parameters [5], with many approaches available in order to obtain HRQoL data. The European Organization for Research and Treatment of Cancer (EORTC) has developed general Quality of Life Ouestionnaires (EORTC-OLO) [6] aimed at cancer patients that have gone into widespread use [7]. These questionnaires are designed with one general part aimed at all cancer patients, and one part aimed at the specific cancer disease.

In general, HRQoL issues with regard to RCC patients have been poorly explored and understood. The published studies of this topic were judged in 2012 to be flawed by being "inconsistently defined, measured or reported" [8]. One reason for this is that no generally accepted disease-specific RCC HRQoL questionnaire exists, as only symptom burden indexes exist [9]. A disease-specific questionnaire for RCC patients within the EORTC QoL system would help fill a gap, and the present aim was to develop such a questionnaire.

We have previously reported on what determines HRQoL in presumably curatively treated RCC patients [10] using the EORTC core questionnaire (QLQ-C30) version 3.0 [6]. The results showed, e.g. that choice of surgical approach is important for RCC patients' HRQoL outcomes [10]. Open transabdominal, and in particular flank approaches to RCC tumor resection, were followed by reduced HRQoL scores compared with a general cohort of Norwegian citizens. However, former laparoscopically treated RCC patients had HRQoL scores at the population level [10]. That surgical approaches seemingly causing lowered HRQoL per se warrant further studies with a disease-specific QoL questionnaire.

Psychological characteristics, such as coping style [11] and personality [12], have been shown to be important when measuring HRQoL in RCC patients [10], as well as in relation to other urological cancers [13]. Our previous investigations have shown that EORTC C30 sum scores were negatively associated with the personality trait of neuroticism [common variance (CV): 19–36%], while the avoidant choice

of coping inversely also accounted for 9–18% of the total HRQoL variance. Indeed, all the QoL indexes except one were significantly correlated to neuroticism and avoidance coping. Moreover, present comorbidities were uniquely associated with a lowered HRQoL [10]. Such variables would be of interest to study in correlation to RCC diagnosis-specific QoL questionnaires with the aim of obtaining low associations, thus strengthening the specificity of such a questionnaire.

We have aimed to develop an EORTC-compatible, RCC-specific HRQoL questionnaire, and tested the proposed questionnaire in a broader setting.

Material and methods

Patient study sample

In total 413 RCC patients were treated with a radical or partial nephrectomy in Western Norway during the period from 1997 to 2010. Patients with a histologically proven RCC still alive on 1 February 2011were recruited from the nephrectomy database at the Haukeland University Hospital, serving Hordaland County in Western Norway. A total of 309 were still alive at the inclusion time of which 49 patients were excluded from the study due to reasons such as cognitive impairment, severe other disease or other malignant diseases. After exclusions, 260 patients vounger than 85 years and still alive were invited to answer the mailed questionnaires. If the patients did not return the first mailed questionnaire, a second invitation was sent. After two rounds of invitations, a total of 185 patients (a 71% response rate) had returned the questionnaires.

Clinical, demographic and disease characteristics were retrieved from the database (Table I) and has been presented in detail in previously published studies [14,10]. Table I demonstrates that there were no significant differences between responders and non-responders. Furthermore, as expected, patients already dead before the study were significantly older, had significantly more advanced RCC and had significantly more additional comorbidities.

Only patients treated by surgery are included in this study. In general, patients with localized RCC not offered operation, are of very old age, have several comorbidities and have limited life expectancy [15]. Such impairments would most likely significantly affect the outcome of HRQoL questionnaire scores. We therefore decided against the inclusion of this group of RCC patients in this study. Furthermore, even in primary metastatic RCC (mRCC), approximately 50% will undergo kidney surgery [16]. After initial treatment (tumor surgery and metastasectomy), some few of these will achieve long-term

Table I. Comparison of the characteristics of 185 RCC patients included in the OoL-study (responders), 74 not included (non-responders) and 104 patients dead at the time point of inclusion.

| | Alive – responders ^a $(n = 185)$ | Alive-non-responders $(n = 74)$ | p-Value ^b | Dead (n = 104) | p-Value ^c |
|---|---|---------------------------------|----------------------|-------------------|----------------------|
| Age at surgery (years) | 60.7 ± 0.8 | 58.9 ± 1.6 | p=0.263 | 65.9 ± 1.2 | p<0.001 |
| Primary tumor size (cm) | 5.0 ± 0.2 | 4.9 ± 0.3 | p = 0.704 | 7.8 ± 0.4 | p < 0.001 |
| Time from RCC surgery to QoL- questionnaire (years) | 4.7 ± 0.3 | 3.9 ± 0.4 | p = 0.092 | n.a. | n.a. |
| Male gender | 69% | 58% | p = 0.149 | 66% | p = 1.000 |
| BMI at operation (kg/(height in m²) | 26.6 ± 0.3 | 27.4 ± 0.6 | p = 0.258 | 25.3 ± 0.3 | p = 0.004 |
| Symptomatic detection | 39% | 36% | p = 0.778 | 70% | p < 0.001 |
| Type of surgery | | | p = 0.690 | | p < 0.001 |
| Radical nephrectomy | 62% | 66% | | 94% | |
| Partial nephrectomy | 38% | 34% | | 6% | |
| Preoperative ASA score | | | p = 0.956 | | p < 0.001 |
| I and II | 84% | 82% | • | 60% | • |
| III and IV | 16% | 18% | | 40% | |
| Preoperative ECOG Performance status | | | p = 0.507 | | p<0.001 |
| 0 | 90% | 88% | • | 49% | • |
| ≥1 | 10% | 12% | | 51% | |
| Preoperative Charlson comorbidity index | | | p = 0.780 | | p = 0.077 |
| 0–1 | 63% | 68% | | 49% | |
| ≥ 2 | 37% | 32% | | 51% | |

BMI, body mass index; QoL, quality of life; SEM, standard error of the mean.

survival without signs of disease and without any further treatment. These patients are included in the study. Primary mRCC patients not offered nephrectomy, usually have a very short life expectancy [16], and hence, this latter group is excluded.

Written informed consent was obtained from all patients. Both the general and the HRQoL database were approved by the Norwegian Social Science Data Services and the Regional Committee for Medical and Health Research Ethics in Western Norway (78/05 and 2010/2569).

Health-related quality of life inventory

General HRQoL was determined by employing the EORTC-QLQ C30, version 3.0 [6]. The answers were given according to a four-point Likert format (i.e. "not at all", "a bit", "quite a lot" and "all the time"), with the exception of questions about general health and general quality of life, which were given according to a seven-point Likert format. The indexes were scored according to the EORTC guidelines. The C30 functional scales and the global scale were transformed so that 100% indicated the best function and 0% the least function of the individual HROoL index, whereas the C30 symptom scales were transformed so that 0% indicated the least- and 100% the most symptoms.

RCC disease-specific questionnaire

Our disease-specific candidate questions (cq) were based upon the results of a few studies [17], and on urologists and urology nurses' experiences concerning common complaints from treated RCC patients. A review of other disease-specific parts of the EORTC QoL family questionnaires was also done, although the questions were not to semantically overlap.

We devised a list of 13 candidate RCC-specific HRQoL questions (Table II). The answers were reported according to an EORTC-OLO identical fourpoint Likert format (i.e. "not at all", "a bit", "quite a lot" and "all the time"), and the scores were transformed in the same manner as with symptom questions from the EORTC C30 QLQ questionnaire.

 $^{^{}a}$ 186 responded, but one returned out a blank form; b between responders and non-responders; c between patients alive (n = 259) and dead (n = 104) at time of inclusion. Data shown as mean \pm SEM or %, respectively.

Table II. Candidate questions, number of responders and suggested final questionnaire with factor analysis^a of EORTC QLQ-style RCC disease specific HRQoL questions with EORTC C30 general health/QoLsum score included.

| | | No. of responders | | ted final onnaire | Rotated component matrix ^a Component | | | | |
|----|--|-------------------|-------|----------------------|--|------|------|------|------|
| | Candidate RCC questions (cq) | by item | RCC6b | RCC10 | 1 | 2 | 3 | 4 | 5 |
| 1 | Have you had pain in the flank? | 184 | X | X | 0.46 | | 0.49 | | |
| 2 | Have you had pain elsewhere? | 185 | | X | 0.74 | 0.41 | | | |
| 3 | Have you used pain-killing medication? | 184 | | X | 0.81 | | | | |
| 4 | Have you had blood in your urine? | 184 | X | X | | | 0.79 | | |
| 5 | Have you had swelling in the flank? | 183 | X | X | 0.41 | | 0.38 | | |
| 6 | Have you had urinary tract infection(s)? | 184 | X | X | | | 0.80 | | |
| 7 | Have you felt ill? | 184 | | | 0.70 | | | | |
| 8 | Have you been less sexually interested? | 177 | X | X | | | | 0.93 | |
| 9 | Have you had less sexual pleasure? | 176 | | | | 0.42 | | 0.62 | |
| 10 | Have you gained weight? | 178 | | | | | | | 0.79 |
| 11 | Have you lost weight? | 181 | X | X | | 0.41 | | | 0.71 |
| 12 | Have you had trouble moving around? | 183 | | X | | 0.79 | | | |
| 13 | Have you had trouble with social interaction with friends or family? | 183 | | X | | 0.78 | | | |
| | EORTC C30 general health/QoL sum score | 185 | | | -0.69 | 0.54 | | | |

^aResult from principal component factor analysis (rotated Warimax solution). Kaiser-Meyer-Olkin measure of sampling adequacy: 0.763. Barlett's test of Sphericity: Chi-square = 713; D.F.: 91, p<0.001; ^bCore questionnaire with asking only about information not principally found in the EORTC C30 scores; ^cBarlett's test of Sphericity: $\chi^2 = 713$; D.F.: 91, p<0.001; ^dCore questionnaire with asking only about information not principally found in the EORTC C30 scores.

Eysenck Personality Inventory and COPE questionnaire

In addition, personality was tested by the Eysenck Personality Inventory [18] and choice of coping by the COPE questionnaire [11].

Statistical analysis

The statistical program package SPSS was employed (Ver. 22.0; SPSS Inc. Chicago, IL, USA). The choice of final questions to be included has been based on factor analyses [principal component analysis (PCA)], in which the original variables are transformed into a smaller set of linear combinations, with most of the variance in the original variables being kept [19]. The rotation method "Warimax with Kaiser Normalization" [19] was also employed. Factor analyses examine patterns of the responses from all respondents and identify

groups (factors) of the questions associated with response patterns. All questions belonging to one such group (factor/component) will have a high factor loading for this factor. A factor analysis reflects question response patterns, and may help reduce the number of questions in a questionnaire while still keeping most of the variance present. We included either the one or two questions in the final questionnaire most closely related to each formed factor, or questions clearly asking about unique features of the RCC HRQoL.

Results

Factor analysis including RCC candidate questions

A correlation matrix (Table III) and a factor analysis (Table II) including the RCC HRQoL 13 candidate questions (cq) and EORTC C-30 sum scores derived from the EORTC general QoL (C-30) questionnaire

Table III. Correlation matrix between RCC candidate questions.

| | RCCcq1 | RCCcq2 | RCCcq3 | RCCcq4 | RCCcq5 | RCCcq6 | RCCcq7 | RCCcq8 | RCCcq9 | RCCcq10 | RCCcq11 | RCCcq12 |
|---------|-------------------|------------|-------------------|------------|------------|-------------------|------------|-------------------|------------|-------------|------------|-------------------|
| RCCcq2 | 0.37 ^c | | | | | | | | | | | |
| RCCcq3 | 0.28^{b} | 0.60^{b} | | | | | | | | | | |
| RCCcq4 | 0.29^{c} | 0.20^{b} | 0.19^{b} | | | | | | | | | |
| RCCcq5 | 0.28^{c} | 0.24^{c} | 0.24^{c} | 0.27^{c} | | | | | | | | |
| RCCcq6 | 0.26^{c} | 0.19^{b} | 0.20^{b} | 0.46^{c} | 0.20^{b} | | | | | | | |
| RCCcq7 | 0.39 ^c | 0.48^{c} | 0.45^{c} | 0.25^{c} | 0.29^{c} | 0.32^{c} | | | | | | |
| RCCcq8 | 0.01 | 0.10 | 0.21^{b} | 0.03 | 0.01 | 0.04 | 0.22^{b} | | | | | |
| RCCcq9 | 0.20^{b} | 0.40^{c} | 0.31 ^c | 0.21^{b} | 0.14 | 0.14 | 0.25^{c} | 0.41^{c} | | | | |
| RCCcq10 | 0.23^{b} | 0.16^{a} | 0.14 | 0.22^{b} | 0.18^{a} | 0.13 | 0.08 | 0.04 | 0.20^{b} | | | |
| RCCcq11 | 0.10 | 0.21^{b} | 0.11 | 0.03 | -0.03 | 0.31 ^c | 0.24^{c} | 0.01 | 0.19^{a} | -0.21^{b} | | |
| RCCcq12 | 0.17^{a} | 0.48^{c} | 0.23^{b} | -0.05 | 0.13 | 0.14 | 0.30^{c} | 0.31 ^c | 0.37^{c} | 0.22^{b} | 0.27^{c} | |
| RCCcq13 | 0.11 | 0.41^{c} | 0.25^{c} | 0.17^{a} | 0.13 | 0.17^{a} | 0.36^{c} | 0.05 | 0.35^{c} | 0.19^{a} | 0.19^{b} | 0.51 ^c |

Table IV. Pearson's correlations matrix between responses from the proposed EORTC OLO-style RCC6 disease-specific core questionnaire and EORTC QLQ C30 sum scores.

| | | RCC candidate question number | | | | | | | | |
|--|---------------------------|---|---------------------------|---|--|---|--|--|--|--|
| | 1 | 4 | 5 | 6 | 8 | 11 | | | | |
| Sum gen. Health/QoL Sum C30 functional Sum C30 symptom | -0.34° -0.31° 0.45° | -0.21 ^b -0.27 ^c 0.22 ^b | -0.27° -0.25° 0.22b | -0.22 ^b -0.25 ^c 0.31 ^c | -0.21 ^b -0.25 ^c 0.10 | -0.21 ^b -0.21 ^b 0.26 ^c | | | | |

 $^{^{}a}p < 0.05; ^{b}p < 0.01; ^{c}p < 0.001.$

showed that five factors (components) were formed with the following main content (Table II):

- 1) Factor I was formed from RCC cq1-3, RCC cq5 and cq7 mostly concerning "pain" and "if felt ill" together with the EORTC QLQ C-30 sum score.
- 2) Factor II was mainly formed from RCC candidate questions about moving around (cq12) and interaction with family (cq13) along with the EORTC C-30 sum score.
- 3) Factor III loaded to four RCC-specific symptom candidate questions: one about flank pain (cq1), one about flank swelling (cq5), one about blood in the urine (cq4) and one about urinary tract infection (cq6).
- 4) Factor IV loaded to two questions about sexual functioning (cq8-9).
- 5) Factor V loaded to two questions about weight gain (cq10) or loss (cq11).

We suggest a core RCC6 questionnaire with six questions derived from factors III-V and a more complete RCC10 version with 10 questions including most information present from the original questions (Table II).

The RCC6 questions correlated only relatively moderate to each other as expected from the factor analysis (Table III). Sum scores from the general quality of life (C30) indexes (general health/QoL, general functional, general symptoms) were all significantly correlated to the disease-specific RCC6 question responses, but with relatively week correlations (Table IV).

RCC6 correlation with personality/choice of coping variables

The personality traits neuroticism and lie score, as well as levels of avoidant choice and problem focused coping all significantly correlated to the RCC6 questions, but mainly at a low level. None of the RCC6 questions correlated to emotional coping. The strength of the correlation to choice of coping was in general lower than to the EORTC QLQ30 responses (Table V).

RCC6 correlation with co-morbidity and tumor variables

We have studied various general- and tumor-disease related variables correlation to the RCC6 responses (Table VI). Only marginally significant correlation strengths accounting for maximum 4.5% were determined.

Table V. Pearson's correlations between reported Eysenck personality neuroticism & lie, choice of coping versus EORTC QLQ-style RCC6 disease-specific core questions and EORTC QLQ C30 sum scores.

| | Eyseno | ck | COPE | | | | | |
|----------------------|-------------------|-------------|------------------------|------------------|---------------------------|--|--|--|
| | Neuroticism | Lie | Problem focused coping | Emotional coping | Avoidant choice of coping | | | |
| RCC cq 1 | 0.38 ^c | -0.04 | 0.17 ^a | 0.12 | 0.25° | | | |
| RCC cq 4 | 0.16^{a} | -0.09 | 0.11 | -0.02 | 0.12 | | | |
| RCC cq 5 | 0.11 | 0.07 | 0.04 | -0.03 | 0.06 | | | |
| RCC cq 6 | 0.11 | -0.04 | 0.14 | -0.05 | 0.31 ^b | | | |
| RCC cq 8 | 0.08 | -0.03 | 0.08 | 0.13 | 0.01 | | | |
| RCC cq 11 | 0.05 | 0.06 | 0.07 | -0.03 | 0.17^{a} | | | |
| Sum gen0. Health/QoL | -0.43^{c} | 0.11 | -0.24^{b} | -0.13 | -0.30^{c} | | | |
| Sum C30 functional | -0.48^{c} | 0.19^{a} | -0.26^{c} | -0.13 | -0.38^{c} | | | |
| Sum C30 symptom | 0.60 ^c | -0.22^{b} | 0.26° | 0.17^{a} | 0.42^{c} | | | |

 $^{^{}a}p < 0.05$; $^{b}p < 0.01$; $^{c}p < 0.001$. cq, candidate question.

Table VI. Pearson's correlations between clinical characteristics, present co-morbidities versus EORTC OLO-style RCC6 disease-specific core questions.

| | Recurrent tumor or with primary metastasis | Age at primary surgery | BMI | Hypertension | Diabetes | Incidental tumor | Tumor size |
|----------|--|------------------------|------|--------------|------------|---------------------|-------------------|
| RCC cq1 | 0.00 | -0.06 | 0.05 | -0.03 | 0.13 | -0.06 | -0.07 |
| RCC cq4 | -0.07 | -0.11 | 0.12 | -0.08 | -0.09 | -0.15^{a} | -0.13 |
| RCC cq5 | -0.05 | 0.03 | 0.07 | -0.08 | 0.04 | 0.05 | -0.15^{a} |
| RCC cq6 | -0.07 | -0.05 | 0.08 | 0.04 | 0.11 | -0.07 | 0.02 |
| RCC cq8 | -0.01 | 0.10 | 0.02 | 0.13 | 0.06 | 0.00 | 0.15 ^a |
| RCC cq11 | 0.01 | 0.11 | 0.14 | 0.19^{a} | 0.21^{b} | 0.00 | 0.12 |

 $^{^{}a}p < 0.05$; $^{b}p < 0.01$. cq, candidate question.

RCC6 versus surgical access

Flank pain and swelling of the flank (Figure 1) were reported to be higher in flank treated patients than among patients treated with other surgical approaches as studied by ANOVA analyses supplemented with post hoc analyses. Using these responses as covariates studying different general HRQoL between the treatment groups, removed the statistically significant EORTC C-30 HRQoL sum scores dependent on treatment as previously published [10].

Discussion

An EORTC QLQ-like RCC-specific HRQoL questionnaire with 10 questions is suggested. The questionnaire has been tested in a broad setting and satisfactory properties have been determined.

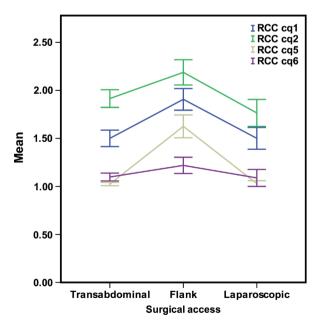


Figure 1. EORTC QLQ-style RCC-specific question mean ± standard error of the mean (SEM) response dependent on surgical access. RCC candidate questions (cq) 1 (p < 0.01), 2 (p < 0.05) and 5 (p < 0.001) were scored differently dependent on surgical access as analyzed by ANOVA analyses with flank-treated patients scoring higher than the other groups (RCC cq1 & 5) as measured by Bonferroni post hoc analyses.

Some limitations of the questionnaire should be acknowledged. The number of candidate questions included could have been higher, possibly providing a more thorough questionnaire. We aimed, however, the suggested questionnaire to include a limited number of questions therefore being user-friendly. The present cohort could have included more patients. Better quality of answers would also be anticipated if employed method was structured interviews. However, the study is from a consecutive cohort of patients including all patients diagnosed with RCC in a specific region during a specific time period. A higher percentage of the intended included patients could also have been included. We have, however, shown that the clinical characteristics of the responders and non-responders were the same. Furthermore, this questionnaire is intended for use in a surgically treated group of patients. We recognize this as a limitation. However, the waste majority of RCC patients are surgically treated. Furthermore, those not surgically treated, are significant clinically impaired and have short life time expectancy. All this makes them unsuitable for a study like this.

Four candidate questions about symptoms related to the urinary tract, flank pain, blood in the urine, flank edema and urinary tract infections were asked, with these questions being answered as one unique factor. We suggest incorporating all these questions into the final disease-specific questionnaire, as all these relate to important aspects of known RCCrelated symptoms [17,20]. Two candidate questions about sexuality were answered as one unique block, and the question with the highest load was included in the proposed questionnaire, as the importance of sexuality issues is underlined in a study showing a worsened sexual functioning in RCC patients compared to a general population [17]. The questions about weight loss or gain were also answered as one unique block. We propose to include the question about weight loss in the final questionnaire as this information may be of clinically interest. The six above-given questions then form a proposed RCC6 core questionnaire.

Our proposed RCC10 questionnaire includes questions loading to the factor analysis blocks, which also loaded to the EORTC C30 sum scores. From Block I, we included the candidate questions: "Have you had pain elsewhere?" and "Have you used painkilling medication?", while from Block II we included: "Have you had trouble moving around?" and "Have you had trouble with social interaction with friends or family?" The responses to the RCC10 HRQoL questionnaire will thus serve as a disease-specific questionnaire, and in addition capture substantial parts of the information from the answers of the general EORTC C30 OLO questionnaire. The proposed RCC10 questionnaire may serve as an easy to complete "stand alone" questionnaire that can be used in clinical screening of RCC patients.

The correlations between the various RCC10 questions were as expected, especially significant in relation to correlations between questions belonging to the same block. The correlations overall did not account for a large common variance. Therefore, each question may be accepted as questions giving unique information.

We also studied the association between the RCC6 core questionnaire and personality, as the personality trait neuroticism is particularly closely associated to general HRQoL in RCC patients [10]. The results showed some associations, but less than regarding general HRQoL. This adds to the specificity, and hence validity, of the proposed questionnaire because any overlap between personality and disease-specific HRQoL indexes should be avoided. Moreover, the choice of coping may also be directly tied to HROoL scores without any apparent association to the actual disease [10]. In the present investigation, the correlation between the reported level of coping and the response pattern of the suggested RCC6 core questionnaire is lower than to the general HRQoL sum scores. This also adds to the specificity and validity of the proposed diseasespecific questionnaire.

The reliability of our proposed questionnaire has not presently been tested over time, although HROoL responses are remarkably stable over time [21]. For example, this is illustrated by Husson et al. [22], who in a group of 306 thyroid cancer survivors found that the issues of the patients did not change across the cancer continuum, as only the severity of the issues changed over time. The RCC questionnaires have neither been tested specifically during recurrent treatment or in patients undergoing treatment, and further investigations are needed to address these areas.

We have previously published that flank-treated patients reported significantly lower HRQoL than RCC patients treated otherwise [10]. This is also supported when studying outcomes after live kidney donation, showing that persistent pain was reported in 21% in one study [23] and chronic pain in 35% in another study [24]. Flank pain and swelling were reported to be higher among flank-treated RCC patients than among other RCC patients. Furthermore, using these responses as covariates when studying different general HRQoL between the treatment groups removed the statistically significant HRQoL score dependent on treatment. This strengthens our previously published hypothesis [10] that the lowered HRQoL of flank-treated RCC patients compared to other RCC patients is secondary to surgical approach.

Among head and neck cancer patients, Osthus et al. [25] have shown that HRQoL scores predicted subsequent survival independently of established, generally used clinical prognostic factors [25]. The current proposed RCC10 questionnaire has the potential to be used in RCC patients for this purpose.

A next step of development of the proposed RCC-specific HRQoL questionnaire will involve administration to a large international group of RCC survivors. Translational procedures and adaption to different cultures will have to be addressed, and the psychometric properties of the questionnaire should also be studied further.

Conclusions

A disease-specific, EORTC-like questionnaire concerning RCC patients is proposed, seemingly adding important information about the HRQoL of the RCC patients. The questionnaire also has potential as a stand-alone HROoL questionnaire that can be clinically used among surgically treated RCC patients. Further testing of the proposed questionnaire is needed.

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