ACTA ONCOLOGICA, 2017
VOL. 56, NO. 2, 198–204
http://dx.doi.org/10.1080/0284186X.2016.1266088

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ORIGINAL ARTICLE

Health-related quality of life and anxiety and depression in patients diagnosed with cholangiocarcinoma: a prospective cohort study

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ABSTRACT

Background: Cholangiocarcinoma (CCA) is a rare cancer associated with a poor prognosis. Psychosocial challenges may negatively affect daily functioning and health-related quality of life (HRQOL). The primary aim was to evaluate HRQOL, and to assess anxiety and depression in these patients.

Material and methods: From 93 eligible patients diagnosed with CCA, 76 were included in a prospective cohort over a period of 15 months. Patients answered the European Organization for Research and Treatment of Cancer QLQ C30 (EORTC QLQ C30) and Hospital Anxiety and Depression Scale (HADS) questionnaires at baseline, one, three and six months after initial treatment; defined as radical operation, explorative laparotomy, chemotherapy or drainage of the bile ducts. Scores were compared between the radically operated patients ($n = 25$) and palliative patients ($n = 51$; 12 of these had explorative laparotomy), using repeated measures ANOVA and unpaired ANOVA.

Results: The groups were similar in demographic characteristics, except for fewer radically operated men ($p = 0.015$). There was no significant change over time in HRQOL in total or between groups. At baseline nausea and vomiting scores were higher in the palliative group ($p = 0.035$), and at one month follow-up, the radical group had higher pain scores ($p = 0.009$). The majority reported normal/mild anxiety and depression throughout the study; there were no differences between the groups.

Conclusions: It was not possible to measure any differences between the groups, regarding HRQOL, anxiety or depression, despite the fact that one of the groups had the prospect of total cure. In clinical settings, observed mean changes in HRQOL scores are generally small; probably due to psychological adaptation by patients to changing health status over time.

ARTICLE HISTORY
Received 12 August 2016
Accepted 21 November 2016

Cholangiocarcinoma (CCA) is a rare cancer arising from the epithelium of the bile ducts. Depending on location, CCA is intrahepatic CCA (IH-CCA) or extrahepatic (EH-CCA) [1,2]. EH-CCA is either central (Klatskin tumors) involving the bile ducts to a varying extent immediately outside the liver or situated distally in the common bile duct. Central CCA is the most common (80–90%) and 90% of central CCAs are adenocarcinomas. They may be indistinguishable from cancer in the gallbladder, which has a more dismal prognosis. Risk factors for CCA include primary sclerosing cholangitis, parasitic infections, intrahepatic bile stones (Asia), toxins and chronic viral hepatitis (B and C) [3].

Despite advances in surgical and palliative treatment, CCA remains associated with a dismal prognosis due to late manifestation of clinical signs and hence advanced stages of disease at the time of diagnosis [2,4]. The majority of patients (>65%) have non-resectable disease at diagnosis [4]. Surgical resection remains the mainstay curative treatment with the best chance of long-term survival [5].

Curative resection and chemotherapy is challenging for patients, mentally and physically, and a good preoperative performance status (PS) ≤ 2 and normal plasma bilirubin levels are prerequisite [6]. CCA diagnosed at an advanced stage and classified as non-resectable may be treated palliatively with stenting for biliary drainage and/or chemotherapy [2]. Curative and palliative treatment should be provided in referral centers by specialized multidisciplinary teams familiar with the complex symptoms and needs of this patient group [2].

Whether resectable or non-resectable, CCA patients are burdened by secondary symptoms of gastrointestinal obstruction such as jaundice, itching and nausea and they face potential harmful side effects of extensive surgical resection and chemotherapy [2], all of which may affect quality of life [7–10].

Symptoms and side effects experienced by patients may be underestimated or even missed by clinicians [11]. Patient-reported outcome (PRO) measures represent a patient-centred approach to assessing the patient experience, for example health-related quality of life (HRQOL), anxiety and depression, symptoms and functional status [11]. PROs are reliable and feasible for assessing quality of care and for enabling patients to bring experienced symptoms and side effects of treatment to the attention of clinicians [11].

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Few studies have prospectively investigated HRQOL and anxiety and depression in patients with CCA. Mihalache et al. (2010) [7] assessed HRQOL in a prospective cohort study of 91 Romanian patients with CCA, and found an improvement from baseline to six month post-diagnosis, however, at nine months post-diagnosis, HRQOL decreased [7]. Woradet et al. (2015) [8] likewise evaluated HRQOL prospectively from diagnosis and up to two months post-diagnosis in 99 Thai patients with CCA. They found that HRQOL increased from baseline up to two months follow-up. None of the studies assessed anxiety and depression.

The primary aim of our study was to prospectively examine HRQOL and anxiety and depression during the first six months after initial treatment in a cohort of Danish CCA patients receiving curative or palliative treatment. Secondary aims were to examine whether experienced HRQOL and anxiety and depression differed between patients who had undergone curative treatment and patients receiving palliative treatment.

Material and methods

Design and setting

This was a prospective observational cohort study reported according to the guidelines for reporting of observational cohort studies – the STROBE Statement [12].

The study was conducted at the referral centers of two university hospitals in the capital region of Denmark (Department of Surgical Gastroenterology and Transplantation, Rigshospitalet, Blegdamsvej and Department of Oncology, Herlev Gentofte Hospital). These hospitals collaborate in providing specialized treatment and care for patients with CCA in the region of Zealand and the capital region of Denmark (2.5 million inhabitants). Together, the centers treat the majority of CCA patients in Denmark.

Study population

Inclusion criteria were: $\geq$18 years, histological and clinical diagnosis of central or peripheral CCA or gall bladder cancer, no severe cognitive disability and sufficient Danish language proficiency. Inclusion took place in connection with multidisciplinar team conferences. Exclusion criteria were: uncertain histology. We consecutively included patients in the study from July 2013 to October 2014. Six months follow-up for all patients was completed in March 2015. Eligible patients were identified and recruited at the first outpatient visit at one of the two recruiting sites. The first and third author (KD, AM) approached eligible patients in connection with planned outpatient visits to obtain informed consent. Patients were instructed to self-report HRQOL, anxiety and depression at baseline, defined as the first outpatient visit after diagnosis, and at one, three and six months after index treatment defined as initial treatment received.

Measures

The primary outcome was HRQOL measured by the European Organization for Research and Treatment of Cancer (EORTC) QLQ C30 (generic) version 3.0 [13]. Secondary outcomes were anxiety and depression measured by the Hospital Anxiety and Depression Scale (HADS) [14].

To assess HRQOL we used the Danish version of the EORTC QLQ C30. It is a well validated generic instrument for measuring self-rated quality of life in cancer patients in clinical settings. We were unable to use the disease-specific questionnaire for patients with CCA and cancer of the gall bladder (EORTC QLQ BIL21), as it has not been translated into Danish [15]. At each follow-up, participants were asked to rate their physical, psychological and social wellbeing within the preceding week. The EORTC QLQ C30 consists of 30 items, the majority of which are rated on a four-point Lickert scale from 1 to 4 where 1 is 'not at all' and 4 is 'very much'. Higher scores on the EORTC QLQ C30 functioning and the global HRQOL scales indicate better functioning or better HRQOL. Higher scores on the symptom scales indicate a higher symptom burden. Raw scores and missing data were analyzed according to the scoring manual of the EORTC Quality of Life Group [16].

To assess anxiety and depression, we used the Danish version of HADS, which is a widely used self-reported generic measure for emotional distress in patients in clinical settings [14]. HADS includes two subscales, anxiety and depression, each with seven items rated on four-point Likert scale 'not at all (0)' to 'very often indeed [3]'. Responses are summed to provide separate scores for anxiety and depression. We used the recommended cutoff $\geq$8 (on each subscale) to distinguish between normal anxiety and depression and anxiety or depression disorder (mild, moderate or severe) [17].

Study procedure

We mailed the EORTC QLQ C30 and HADS questionnaire and accompanying stamped and addressed return envelopes to patients 10 days before scheduled follow-up. A reminder and a new set of questionnaires were sent by mail to non-responders after 14 days.

Data were entered into a database and cross-checked for discrepancies prior to analysis. We grouped participants into two groups: resectable patients receiving curative treatment defined as surgical resection and adjuvant chemotherapy (the radical group), and non-resectable patients receiving palliative treatment defined as stenting and/or chemotherapy (the palliative group) [2,7].

Data analysis

We analyzed data using descriptive statistics with means (parametric data) and standard deviations (SD), medians and ranges (non-parametric data), and numbers and percentages as appropriate.

We tested differences in EORTC QLQ C30 and HADS scores between the radical and palliative group using unpaired t-tests and changes within groups over time using repeated measures ANOVA. To explore the potential effect of missing data, we performed a comprehensive explorative analysis: principal component analysis with cluster analysis, paired

(repeated measures ANOVA), unpaired (ANOVA) and multiple comparisons of the means. Due to a small sample size, we did not adjust for baseline variables or possible confounders.

The alpha level was set at a two-tailed p-value <0.05. Analyses were performed using SPSS Software version 22 (SPSS, Chicago, IL, USA) and Microsoft Excel version 2010 (Microsoft, Redmond, WA, USA).

Ethics

The Central Science Ethics Committee in the capital region of Denmark evaluated the study protocol and deemed further formal approval unnecessary (H-4-2013-FSP). The study was approved by the Danish Data Protection Agency (2007-58-0015) and performed in compliance with the Declaration of Helsinki.

Results

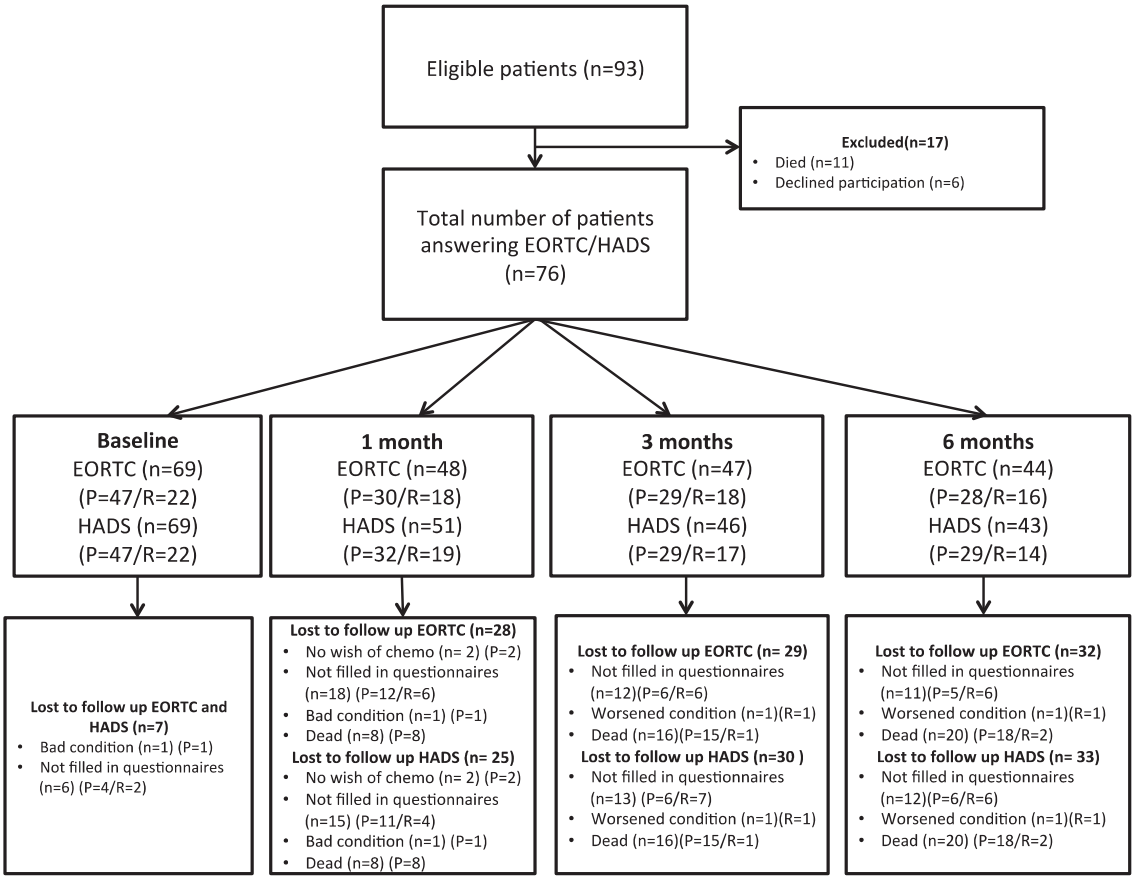
Characteristics of participants

In total, 93 consecutive, eligible patients were identified. Of these, 76 were included in the study (Figure 1). The main reasons for not participating were rapid disease progression and death. Twenty-nine patients were recruited from the Department of Oncology, Herlev Hospital. Patient characteristics are illustrated in Table 1. The palliative group was larger than the radical group, with 51 versus 25 patients, respectively. There were significantly fewer men in the radical group ($p = 0.015$). The mean number of days of follow-up in the

Table 1. Descriptive demographic characteristics among 76 Danish patients diagnosed with cholangiocarcinoma.

Variable	Palliative group (n = 51)	Radical group (n = 25)	p-Value
Age (years)	64.8 (10.5)[a]	60.6 (13.3)[a]	0.177[d]
Male	32 (62.7)[b]	8 (32)[b]	0.015[e]
Time of follow-up (days)	228.7 (142.8)[c]	340.8 (122.4)[c]	0.001[d]
Marital status			–
Living alone	16 (31.4)[b]	7 (28)[b]	0.309[f]
Unknown	4 (7.8)[b]	0[b]	–
Occupation			
Working	14 (27.5)[b]	13 (52)[b]	0.061[f]
Unknown	4 (7.8)[b]	0 (0)[b]	
Performance score	0 (0–3)[c]	0 (0–2)[c]	0.161[f]
Unknown	5 (9.8)[b]	0 (0)[b]	–
Living in the capital region	35 (68.6)[b]	14 (56)[b]	0.315[e]
Smoker	14 (27.5)[b]	7 (28)[b]	0.998[f]
Unknown	4 (7.8)[b]	2 (8)[b]	–

[a]Values are mean ± SD;
[b]Values are n (%);
[c]Values are median (range);
[d]Independent t-test;
[e]Fishers Exact test;
[f]Pearson's χ^2.



Abbreviations
P= Palliative patients
R= Radical patients

Figure 1. Recruitment and follow-up of patients in the study.

Table 2. Distribution in health-related quality of life (HRQOL QLQ C30) from baseline to six months follow-up among patients diagnosed with cholangiocarcinoma over time.

EORTC QLQ C30	Baseline (n = 69)				1 month (n = 48)				3 months (n = 47)				6 months (n = 44)			
Variable	Total	Palliative	Radical	p-Value	Total	Palliative	Radical	p-Value	Total	Palliative	Radical	p-Value	Total	Palliative	Radical	p-Value
Global health status																
Global health status/QoL	54.4 ± 25.9	52.9 ± 28	57.3 ± 21.4	0.564	53 ± 25	56.9 ± 26.5	46.8 ± 21.8	0.161	61.9 ± 23.2	61.8 ± 24.3	62 ± 22	0.877	63.4 ± 20.7	62.5 ± 20.6	65.1 ± 21.6	0.666
Functional scales[a]																
Physical functioning	69.9 ± 25.4	67.1 ± 24	75.4 ± 27.6	0.103	67.6 ± 23	71.3 ± 17.9	61.4 ± 29.2	0.280	68.9 ± 23.6	70.5 ± 20.9	66.2 ± 27.9	0.774	73.9 ± 22.4	75.2 ± 17.9	71.7 ± 29.1	0.883
Role functioning	57.7 ± 37	55.1 ± 37	63 ± 37.3	0.353	59.2 ± 33.7	60 ± 34.1	57.8 ± 33.9	0.787	60 ± 35.4	58.9 ± 36.7	61.8 ± 34.2	0.858	64.8 ± 30.8	64.3 ± 29.7	65.6 ± 33.6	0.960
Emotional functioning	70.1 ± 24.5	73.1 ± 22.8	64.3 ± 27.1	0.198	74.1 ± 27.7	79.2 ± 23.5	65.6 ± 32.5	0.137	75.5 ± 26.4	75 ± 25.7	76.4 ± 28.3	0.689	75.1 ± 22.7	74.8 ± 22.2	75.5 ± 24.2	0.757
Cognitive functioning	79.7 ± 23.5	81.2 ± 19.8	76.8 ± 30	0.957	79.9 ± 25.7	80.6 ± 22.4	78.7 ± 31.2	0.716	78 ± 24.1	78.2 ± 24	77.8 ± 24.9	0.954	86.7 ± 17.5	86.9 ± 15.4	86.5 ± 20.4	0.650
Social functioning	80.2 ± 25.3	80.8 ± 24.6	79 ± 27.2	0.706	74.3 ± 32.2	76.7 ± 29.3	70.4 ± 37.3	0.750	75.2 ± 29.7	75.3 ± 27.7	75 ± 33.5	0.678	70.8 ± 28.6	70.8 ± 25.1	70.8 ± 34.7	0.633
Symptoms scales/items[b]																
Fatigue	46.6 ± 28.6	47.7 ± 29.4	44 ± 27.4	0.512	47.5 ± 22.4	46.7 ± 20.7	48.8 ± 25.6	0.914	45.6 ± 25.5	44.8 ± 22.7	46.9 ± 30.1	0.782	41.7 ± 23.1	41.7 ± 19.7	41.7 ± 28.3	0.970
Nausea and vomiting	17.9 ± 24	22.5 ± 26.6	8.7 ± 14.1	0.039[c]	17.7 ± 19.6	16.7 ± 19.6	19.4 ± 20	0.597	11.3 ± 19.4	7.5 ± 11.4	17.6 ± 27.1	0.213	13.6 ± 16.6	14.3 ± 16.8	12.5 ± 16.7	0.672
Pain	29.7 ± 31.6	33 ± 33.6	23.2 ± 26.5	0.262	26.4 ± 28.7	19.4 ± 28.4	38 ± 26.1	0.009[c]	24.8 ± 25.5	24.1 ± 26.9	25.9 ± 23.7	0.698	22 ± 22.7	25.6 ± 25.5	15.6 ± 15.5	0.249
Dyspnea	18.8 ± 27.1	22.5 ± 28.2	11.6 ± 23.8	0.067	13.9 ± 18	13.3 ± 16.6	14.8 ± 20.5	0.940	18.1 ± 26	16.7 ± 21.3	20.4 ± 32.6	0.897	19.7 ± 24.2	21.4 ± 22.6	16.7 ± 27.2	0.326
Insomnia	28.9 ± 33	31.9 ± 35	22.7 ± 28	0.383	32.6 ± 35.4	28.9 ± 34.7	38.9 ± 36.6	0.343	28.3 ± 33.7	25.3 ± 32.9	33.3 ± 35.4	0.403	31.8 ± 32	29.8 ± 29.2	35.4 ± 37.5	0.766
Appetite loss	42.3 ± 38.3	44 ± 37	36.9 ± 41.5	0.433	41.7 ± 37.4	40 ± 37.5	44.4 ± 37.9	0.674	28.4 ± 34	31 ± 33.3	24.1 ± 35.8	0.380	28 ± 34.4	31 ± 35.1	22.9 ± 33.8	0.355
Constipation	14.9 ± 28.6	17.8 ± 29.8	9.1 ± 25.6	0.149	20.6 ± 29.1	23 ± 31	16.7 ± 26.2	0.478	22 ± 32.9	23 ± 31	20.4 ± 36.4	0.450	11.4 ± 23.8	9.5 ± 23.8	14.6 ± 24.2	0.334
Diarrhea	16.2 ± 28.5	16.3 ± 27.2	15.9 ± 31.6	0.656	9.7 ± 20.6	8.9 ± 17.4	11.1 ± 25.6	0.977	9.2 ± 21.6	10.3 ± 23.7	7.4 ± 18.3	0.725	7.6 ± 21.4	14.3 ± 21.1	8.9 ± 26.6	0.163
Financial difficulties	11.1 ± 25.4	14.5 ± 29.5	4.4 ± 11.5	0.227	4.9 ± 16.8	5.6 ± 19.7	3.7 ± 10.8	0.936	9.2 ± 23.8	10.3 ± 25.4	7.4 ± 21.6	0.596	7.6 ± 21.4	8.3 ± 25.1	6.3 ± 13.4	0.581

p-Values between palliative versus radical surgery (Mann Whitney U-test).
[a]Higher scores indicates a higher level of functioning and QoL;
[b]Higher scores indicate a higher degree of symptoms;
[c]Significant difference.

total population was 267.01 (145.24); in the radical group 342.48 (122.64) days and in the palliative group 230.02 (142.06) days.

Health-related quality of life

We did not identify any significant overall change from baseline to follow-up in HRQOL in the total sample, within the groups over time or between groups at follow-up (Table 2). In total, 25 patients were lost to six months follow-up; of these 19 patients were palliative (see Figure 1). At baseline, the palliative group reported higher scores of nausea and vomiting ($p = 0.035$) than the radical group. At one month follow-up, the radical group reported significantly higher pain scores ($p = 0.009$) than the palliative group; these subsequently decreased at six months follow-up.

Otherwise, the groups were comparable in global health status and largely showed similar non-significant fluctuations in functioning and symptom domains over time. Global health status decreased at one month in the radical group, but subsequently increased to the same level in both groups. Role and emotional functioning, insomnia and diarrhea were comparable and stable from baseline to six months in both groups. Cognitive functioning followed the same improving trend in both groups from three to six months. The radical group had lower social functioning scores at one month; from three to six months both groups decreased in social functioning. At baseline, the palliative group reported more dyspnea; however, both groups scored similarly from one to six months. Loss of appetite and fatigue decreased slightly in both groups from baseline to six months. The palliative group reported more financial difficulties at baseline, but these were at the same level as the radical group at one month.

Anxiety and depression

The majority of patients in both groups reported normal or mild cases of anxiety and depression throughout the study (Table 3). In total 26 patients were lost to six months follow-up; of these 18 were palliative (see Figure 1). We found no significant differences between groups or within groups in mean scores for anxiety and depression at any follow-up times.

At baseline, more patients in the radical group compared to the palliative group reported anxiety; 31.8% versus 8.5% reported moderate anxiety and, correspondingly, 9.1% versus 4.3% reported severe anxiety.

Discussion

The aim of this study was to examine HRQOL, anxiety and depression during the first six months after initial treatment in a cohort of Danish CCA patients and compare these parameters between patients treated with curative or palliative intent.

Similar to the findings of previous studies, less than one third of included patients were resectable at diagnosis,

Table 3. Distribution in self-reported HADS (anxiety and depression scale) among patients diagnosed with cholangiocarcinoma over time.

	Baseline				1 month				3 months				6 months			
n (%)	T (n = 69)	P (n = 47)	R (n = 22)	p-Value[a]	T (n = 51)	P (n = 32)	R (n = 19)	p-Value[a]	T (n = 46)	P (n = 29)	R (n = 17)	p-Value[a]	T (n = 43)	P (n = 29)	R (n = 14)	p-Value[a]
Anxiety																
Normal cases	38 (55.1)	26 (55.3)	12 (54.5)		31 (60.8)	21 (65.6)	10 (52.6)		32 (69.6)	20 (69)	12 (70.6)		30 (69.8)	22 (75.9)	8 (57.1)	
Mild cases	16 (23.2)	15 (31.9)	1 (4.5)		12 (23.5)	8 (25)	4 (21.1)		11 (23.9)	6 (20.7)	5 (29.4)		7 (16.3)	3 (10.3)	4 (28.6)	
Moderate cases	11 (15.9)	4 (8.5)	7 (31.8)		6 (11.8)	2 (6.3)	4 (21.1)		1 (2.2)	1 (3.4)			5 (11.6)	3 (10.3)	2 (14.3)	
Severe cases	4 (5.8)	2 (4.3)	2 (9.1)		2 (3.9)	1 (3.1)	1 (5.3)		2 (4.3)	2 (6.9)			1 (2.3)	1 (3.4)		
Anxiety mean ± SD		6.6 (4.2)	7.7 (4.9)	0.360		5.5 (4.3)	7.4 (5.2)	0.183		5.3 (4.4)	4.5 (3.7)	0.516		5.4 (4.1)	6.7 (3.7)	0.293
Depression																
Normal cases	56 (81.2)	39 (83)	17 (77.3)		39 (76.5)	25 (78.1)	14 (73.7)		37 (80.4)	24 (82.8)	13 (76.5)		33 (76.7)	22 (75.9)	11 (78.6)	
Mild cases	10 (14.5)	6 (12.8)	4 (18.2)		6 (11.8)	3 (9.4)	3 (15.8)		5 (10.9)	2 (6.9)	3 (17.6)		6 (14)	4 (13.8)	2 (14.3)	
Moderate cases	2 (2.9)	2 (4.3)			5 (9.8)	4 (12.5)	1 (5.3)		2 (4.3)	1 (3.4)	1 (5.9)		2 (4.7)	1 (3.4)	1 (7.1)	
Severe cases	1 (1.4)		1 (4.5)		1 (2)		1 (5.3)		2 (4.3)	2 (6.9)			2 (4.7)	2 (6.9)		
Depression mean ± SD		4.6 (3.2)	4.8 (4)	0.840		4.4 (3.9)	5.5 (5.3)	0.426		3.9 (4.9)	3.9 (4.1)	0.994		4.6 (4.8)	3.9 (3.5)	0.613

T: total sample; P: Palliative Group; R: Radical Group.
[a]Unpaired t-test.

emphasizing the difficulty of early diagnosis of CCA [2,7]. The groups were comparable with the exception that there were significantly fewer men in the radical group. This is in line with previous research showing that men react to symptoms and seek medical attention even later than women [18].

Quality of life

HRQOL was stable and even improved slightly over time in both groups, with both radical and palliative patients reporting overall comparable levels of HRQOL. This was interesting given that radical patients faced the prospect of total cure. The mean global health status score in the total sample was 54.4 ± 25.9 at baseline and 63 ± 20.7 at six months' follow-up. King et al. [19] argue that a mean score of 70 in global HRQOL is a relatively high score whereas a mean score of 55 is a relatively low score. In our study, we found an increase of nine in global HRQOL in the total sample. According to Cocks et al. (2012), this represents a medium size improvement [20]. Although not statistically significant, this improvement might partly indicate that patient-reported symptoms and functioning in both radical and palliative patients were relevantly addressed by treatment and care. It might also reflect that patients recalibrate their expectations and values concerning key aspects of HRQOL, the so-called response shift [21].

The palliative group reported significantly more nausea and vomiting at baseline compared to the radical group, probably as a result of more advanced disease, for example high plasma levels of bilirubin causing nausea. Careful attention to these symptoms in non-resectable patients is therefore important as a performance score $\leq$2 and normal bilirubin levels are required to receive palliative chemotherapy and surgery [6]. Radical patients reported significantly higher pain scores at one month follow-up probably due to the extensive surgery. An evaluation of the current standard post-operative analgesic regime seems relevant and more precise preoperative information may also modulate the expectations and coping of patients. Pain scores in the palliative population increased slightly from one to six months follow-up; indicating that routine re-evaluation of current pain treatment at every outpatient visit is mandatory.

The lack of any difference in mean global health scores between the groups may to some extent reflect that both groups reported substantial symptom burdens. This might indicate that the symptoms associated with CCA, whether resectable or non-resectable, have consequential impact on HRQOL, perhaps more so than being terminally ill or facing the prospect of cure.

Anxiety and depression

The larger percentage of radical patients reporting moderate to severe anxiety at baseline may reflect the anxiety of not knowing whether or not their surgery would be curative. This opposed to those palliative patients who knew with certainty that curative treatment was not an option.

Supportive care targeting patients who are waiting to know their treatment options might alleviate some of this

anxiety [22,23]. The higher prevalence of moderate to severe anxiety in radical patients at baseline might also reflect that clinicians, at this point in the treatment trajectory, prioritize information about and initiation of curative therapy, while they prioritize the emotional and existential needs of palliative patients. Furthermore, the prospect of extensive curative resection and adjuvant chemotherapy with harmful side effects potentially constitutes a serious trauma.

Strengths and limitation

A strength of the study is that all participants were diagnosed by histology and clinical examination, ensuring that that only patients with CCA were included. Although the sample size was small, it is comparable to other studies within this patient population [8]. These factors add to the generalizability of the results. Another strength of the study is the prospective design that only few studies have used in this patient population [7–9].

As CCA is relatively rare in Denmark, the study has inherent limitations. The small sample size limits statistical power. We also chose not to adjust for potential confounding factors due to the relatively small sample size and increasing loss to follow-up over time.

Increasing loss to follow-up during the study reflects the challenges associated with conducting prospective studies in patients with a short life expectancy. It is likely that the patients who dropped out of the study were sicker than those who completed the study. Our results are therefore possibly biased towards higher HRQOL scores and less anxiety and depression, especially in the palliative group. This might obscure any potential differences between the groups. Finally, using a generic cancer questionnaire rather than a cancer diagnosis-specific questionnaire (EORTC QLQ BIL21) and the generic HADS might have impaired sensitivity and precision to detect subtle changes over time and differences between the radical and palliative groups [20].

Conclusion

It was not possible to measure any significant differences from baseline to follow-up within groups or at follow-up between the groups in quality of life, anxiety and depression when using the EORTC and HADS measures despite the fact that one of the groups had the prospect of total cure. In clinical settings, observed mean changes in HRQOL scores are generally small; probably due to psychological adaptation by patients to changing health status over time. Relevant treatment and care combined with psychological adaptation among patients to changing health status over time may explain the lack of difference between the groups. The similar HRQOL scores between the groups may also simply mirror the substantial burden of symptoms associated with CCA and undergoing radical or palliative treatment.

Acknowledgments

We would like to thank all the participants who so generously took their time to answer the questionnaires. Furthermore, we would like to thank Lars Maaløe who assisted with statistical analysis of data.

Disclosure statement

The authors report no conflicts of interest.

Funding

We would like to thank Flemming Topsøe for funding and making this study possible.

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