Health-related quality of life in long-term esophageal cancer survivors after potentially curative treatment

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Objective: Clinical outcomes have been investigated extensively in studies of esophageal cancer treatment. Less is known about long-term health-related quality of life outcomes. The aim of this study was to assess a range of health-related quality of life outcomes in patients with esophageal cancer treated with potentially curative intent at least 1 year earlier.

Methods: Between January 1995 and December 2007, 163 consecutive patients with cancer of the esophagus underwent a potentially curative treatment. All patients with a minimal follow-up of 1 year and without tumor recurrence were eligible. Questionnaires included the European Organization for Research and Treatment of Cancer core questionnaire (QLQ-C30), the European Organization for Research and Treatment of Cancer esophageal cancer-specific questionnaire (QLQ-OES18), and additional questions concerning survivorship issues.

Results: Thirty-seven patients met the inclusion criteria, of whom 36 completed the questionnaires. Twenty-one patients had received neoadjuvant therapy followed by surgery, 9 patients had undergone surgery only, and 6 patients had chemoradiation only. Median survival was 54 (range, 16–162) months. In general, patients reported better health-related quality of life than a reference sample of patients with esophageal cancer, but somewhat compromised health-related quality of life compared with a reference sample of individuals from the general population. Although some symptoms continued to persist, patients' overall evaluation on their treatment, employment status and finances, body weight and image, and survivorship issues was positive.

Conclusions: Patients who survive 1 year or more after potentially curative treatment for esophageal cancer can lead satisfactory lives. The results of this study can be used when informing patients with esophageal cancer about the long-term effects of treatment. (*J Thorac Cardiovasc Surg* 2010;140:777-83)

In patients with resectable esophageal cancer, surgery is recommended to cure the disease, and when that is not possible, to relieve symptoms and to prolong life. Length of (disease-free) survival is the most important clinical outcome parameter. Esophageal resection can also have serious negative effects on health-related quality of life (HRQoL), although after an initial postoperative decline, HRQoL often returns to baseline levels within 1 year after surgery.^{1–5} In the long-term, no significant differences have been observed in HRQoL as a function of type of surgery (ie, transhiatal vs transthoracic resection).⁶

Long-term survival for esophageal cancer treatment should be interpreted together with long-term results of

HRQoL outcomes. Most tumor recurrences after treatment with curative intent occur during the first year. Thereafter, patients have a relatively good life expectancy.³ Still, specific symptoms and functional problems related to esophageal cancer and its treatment may be persistent.⁷ Whether patients' HRQoL is comparable to baseline reference values for patients with esophageal cancer and to those for the general population is unknown.

The primary aim of the current study was to investigate the long-term HRQoL of patients with esophageal cancer curatively treated with neoadjuvant therapy followed by surgery, surgery only, or chemoradiation only. Results were compared with reference HRQoL values of a heterogeneous sample of patients with esophageal cancer in various stages of disease and of a sample of individuals from the general population.

PATIENTS AND METHODS

Patients

Between January 1995 and December 2007, 163 consecutive patients with cancer of the esophagus underwent a potentially curative treatment at The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital. Thirty-seven patients with a minimal follow-up of 1 year and without tumor recurrence were eligible for this study. In April 2009, they were contacted by a research physician (ECS) and asked for informed consent. One patient could not be reached because he had emigrated. The remaining 36 patients agreed to participate in the study.

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Abbreviations and Acronym

EORTC = European Organization for Research and Treatment of Cancer

HRQoL = health-related quality of life

Sociodemographic and Clinical Data

Information on patients' age at the time of the study, gender, tumor location and histology, clinical stage according to TNM classification, type of treatment, and length of follow-up was obtained from the medical records.

Health-Related Quality of Life

HRQoL was assessed with several self-report questionnaires. These included the European Organization for Research and Treatment of Cancer (EORTC) core questionnaire (QLQ-C30) and the EORTC esophageal cancer-specific module (QLQ-OES18).⁸⁻¹⁰ The QLQ-C30 contains 5 functional scales (physical, role, cognitive, emotional, and social), 3 symptom scales (fatigue, pain, and nausea/vomiting), a global health/quality-of-life scale, and 6 single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). The QLQ-OES18 contains 4 symptom scales (dysphagia, eating, reflux, and pain) and 6 single items (trouble swallowing saliva, choking, dry mouth, taste, cough, and speech). All scale and single items scores range from 0 to 100. A high score for a functional scale represents a higher ("better") level of functioning, whereas a high score for a symptom scale or item represents a higher ("worse") level of symptoms. A visual analog scale was also used to assess current overall HRQoL, with higher scores representing better HRQoL (range, 0–100).

Additional study-specific questions assessed patients' ratings of the treatment with chemo(radio)therapy or surgery (12 items), body weight (4 items), body image (4 items), employment status and finances (6 items), and survivorship issues (eight items).

Statistical Analysis

HRQoL data are presented as mean values with standard deviations. Both the QLQ-C30 and the QLQ-OES18 scores were compared with baseline HRQoL data from a large, heterogeneous sample ($N = 1031$) of patients with esophageal cancer in all stages of disease, including recurrent or metastatic disease.¹¹ The patients' QLQ-C30 scores were also compared with reference values derived from a general population sample of 7802 individuals.¹¹ No adjustments could be made for differences in sociodemographic or clinical characteristics because we did not have access to the original data for these comparison groups.

Student *t* tests were used to compare mean scores. Because of multiple testing, $P \leq .01$ was considered statistically significant. A Levene test was performed on all mean comparisons to ensure variance equality. Statistical analyses were conducted using the Statistical Package for the Social Sciences version 15.0 (SPSS Inc, Chicago, Ill) and R (a free software environment for statistical computing and graphics).¹²

RESULTS

Characteristics of the study sample, the reference group of patients with esophageal cancer, and the general population sample are summarized in Table 1. Twenty-one study patients underwent neoadjuvant therapy followed by surgery, 9 patients underwent surgery only, and 6 patients underwent chemoradiation only. The majority of the patients had a tumor located in the distal esophagus or at the esophagogastric junction (78%), and histology was mostly adenocarcinoma (61%). Median survival was 54 (interquartile range, 36–124) months.

Health-Related Quality of Life

QLQ-C30 mean scores and standard deviations for the study sample, the patient reference group, and the general population reference group are presented in Table 2. When compared with the patient reference group, the patient sample reported significantly better overall global health/quality of life ($P < .001$), better emotional functioning ($P = .01$), less pain ($P = .005$), and less constipation ($P < .001$), but more diarrhea ($P < .001$). Except for cognitive functioning, diarrhea, and financial difficulties, the patient sample scored consistently better than the patient reference group for the remaining function and symptom scales/items, although differences did not reach statistical significance.

The patient sample scored significantly lower than the general population reference group on physical functioning ($P = .01$), fatigue ($P = .01$), nausea/vomiting ($P < .001$), appetite loss ($P < .001$), and diarrhea ($P < .001$). A marginally statistically significant difference ($P < .05$) was observed for cognitive functioning.

Table 3 displays the mean scores and standard deviations on the QLQ-OES18 for the patient sample and the patient reference group. The patient sample reported significantly fewer problems with dysphagia ($P < .001$), pain ($P < .001$), and taste ($P < .001$) than the patient reference group. Nevertheless, it should be noted that half of our patient sample ($n = 18$) still reported dysphagia.

Table 4 shows the 10 most frequently reported symptoms. The most frequent symptom was early satiety ($n = 29$; 81%), and this symptom was even more prevalent ($n = 28/30$; 93%) when excluding the patients who did not undergo surgery.

The mean score on the EORTC QLQ-C30 global health/quality of life scale was $77 (\pm 19)$. This was similar to the score obtained from the visual analog scale HRQoL scale (76 ± 18).

When comparing patients with stage I or II ($n = 16$) and patients with stage III or IV ($n = 20$), there were no statistically significant differences in HRQoL (data not shown).

Patient Ratings of the Treatment With Chemo(radio)therapy or Surgery

A majority of patients reported they were well informed about the treatment they had undergone (Table 5). Treatment with chemo(radio)therapy was less severe than expected for 70% of evaluable patients, whereas the operation was less severe than expected for 86% of evaluable patients.

Body Weight and Body Image

Patients reported having lost a mean of $9.6 (\pm 10)$ kg (11%) compared with their body weight 1 year before treatment. Compared with their weight at the end of treatment, patients noted a small mean weight gain of $0.7 (\pm 8.0)$ kg (3%).

In regard to patients' body image, a majority (78%) of patients did not feel unattractive, but 18 patients (50%)

TABLE 1. Patient and tumor characteristics for 36 long-term survivors after potentially curative treatment for esophageal cancer, a reference group of 1031 patients with esophageal cancer, and a sample of 7802 individuals from the general population

Characteristic	Patient sample		Reference group of patients with esophageal cancer		General population reference group	
Total no. of patients	36	(100%)	1031	(100%)	7802	(100%)
Age at time of survey (y)						
<40	—	—	9	(1%)	2283	(29%)
40–49	3	(8%)	101	(10%)	1457	(19%)
50–59	9	(25%)	237	(23%)	1593	(20%)
60–69	8	(22%)	346	(34%)	1414	(18%)
70–79	13	(36%)	270	(26%)	741	(10%)
80+	3	(8%)	68	(7%)	182	(2%)
Not known	—	—	—	—	132	(2%)
Gender						
Male	23	(64%)	772	(75%)	4046	(52%)
Female	13	(36%)	248	(24%)	3749	(48%)
Not known	—	—	11	(1%)	7	(0%)
Clinical stage according to TNM classification						
Stage I	4	(11%)	118	(11%)	NA	
Stage IIA	11	(31%)				
Stage IIB	1	(3%)				
Stage III	12	(33%)	47	(5%)		
Stage IVA	8	(22%)				
Stage IVB	—	—				
Recurrent/metastatic	—	—	347	(34%)		
Not known	—	—	519	(50%)		

TNM, Tumor node metastasis; NA, not applicable.

TABLE 2. Mean quality-of-life scores (QLQ-C30) for 36 long-term survivors after potentially curative treatment for esophageal cancer compared with reference values for patients with esophageal cancer and the general population

	Patient sample (n = 36)		Reference group of patients with esophageal cancer (n = 1031)		P value	99% CI	General population reference group (n = 7802)		P value	99% CI
	Score	SD	Score	SD			Score	SD		
QLQ-C30										
Global health score	77	19	56	24	<.001	10.6 to 31.4	71	22	.1	–3.5 to 15.5
Functional scales										
Physical functioning	83	15	77	24	.14	–4.4 to 16.4	90	16	.01	–13.9 to –0.1
Role functioning	78	24	69	36	.14	–6.6 to 24.6	85	25	.09	–17.8 to 3.8
Emotional functioning	81	20	71	24	.01	–0.4 to 20.4	76	23	.19	–4.9 to 14.9
Cognitive functioning	79	22	83	22	.28	–13.6 to 5.6	86	20	.04	–15.6 to 1.6
Social functioning	81	23	76	28	.29	–7.2 to 17.2	88	23	.07	–16.9 to 2.9
Symptom scales/items										
Fatigue	35	27	37	27	.66	–13.8 to 9.8	24	24	.01	0.7 to 21.3
Nausea/vomiting	15	24	17	23	.61	–12.1 to 8.1	4	12	<.001	5.8 to 16.2
Pain	14	25	27	27	.005	–24.8 to –1.2	21	28	.13	–19.0 to 5.0
Dyspnea	16	25	19	27	.51	–14.8 to 8.8	12	23	.30	–5.9 to 13.9
Insomnia	19	28	30	33	.05	–25.4 to 3.4	21	30	.69	–14.9 to 10.9
Appetite loss	29	39	34	37	.43	–21.2 to 11.2	7	18	<.001	14.2 to 29.8
Constipation	6	15	26	31	<.001	–33.4 to –6.6	7	18	.74	–8.7 to 6.7
Diarrhea	21	32	7	19	<.001	5.5 to 22.5	7	18	<.001	6.2 to 21.8
Financial difficulties	17	29	15	28	.67	–10.2 to 14.2	10	23	.07	–2.9 to 16.9

QLQ-C30, Quality of Life core questionnaire; CI, confidence interval; SD, standard deviation. A high score for a functional scale represented a high (“better”) level of functioning, whereas a high score for a symptom scale or item represented a high (“worse”) degree of symptoms. Statistically significant results are in bold.

TABLE 3. Mean quality-of-life scores (QLQ-OES18) for 36 long-term survivors after potentially curative treatment for esophageal cancer compared with reference values for patients with esophageal cancer

Compared with Reference Values for patients with esophageal cancer						
	Patient sample (n = 36)		Reference group of patients with esophageal cancer (n = 1031)			
	Score	SD	Score	SD	P value	99% CI
QLQ-OES18						
Symptom scales/items						
Dysphagia	26	34	42	28	<.001	−28.3 to −3.7
Eating	38	30	43	29	.31	−17.7 to 7.7
Reflux	21	28	17	25	.35	−7.0 to 15.0
Pain	9	16	27	24	<.001	−28.4 to −7.6
Trouble swallowing saliva	10	26	23	33	.02	−27.3 to 1.3
Choking	19	22	18	29	.84	−11.6 to 13.6
Dry mouth	19	30	28	34	.12	−23.8 to 5.8
Taste	9	22	31	37	<.001	−38.0 to −6.0
Cough	17	23	20	29	.54	−15.6 to 9.6
Speech	6	16	12	25	.15	−16.8 to 4.8

QLQ-OES18, Esophageal site-specific questionnaire; CI, confidence interval; SD, standard deviation. A high score represented a high (“worse”) degree of symptoms. Statistically significant results are in bold.

felt that their appearance was affected by their treatment (Table 6). There were 2 patients who avoided people because of their physical appearance.

Employment Status and Finances

Before their treatment, 19 patients were retired, 16 patients had a job (14 in paid employment and 2 as volunteers), and 1 patient was unemployed. At the time of the survey, 3 additional patients had retired, and 3 patients had been unable to continue working. The remaining 10 patients resumed working, although half of them at a reduced level.

Eleven patients (31%) still had additional expenses related to their disease or its treatment, ranging from 60 to 155 Euros per month. Costs included expenses for medica-

tion, special food, complementary therapy, home care, and adjustments in the house. One patient had experienced trouble obtaining life insurance.

Perceived Health and Future Perspective

Patients’ current self-reported health status was compared with 3 different time periods (Table 7). Seventeen patients (47%) reported that their current health status was the same as before their diagnosis. Twenty-three patients (64%) rated their current health status as much better than 8 to 12 weeks after completion of the treatment.

Twenty-seven patients (75%) believed that they had been cured of their disease, and 67% believed they had a life expectancy similar to that of peers from the general population. Nevertheless, 19 patients (53%) worried that the disease might recur (“sometimes” to “always”).

TABLE 4. The ten most frequently reported symptoms

Symptom	Study sample				Mean score (1–4)
	Not at all (1)	A little (2)	Quite a bit (3)	Very much (4)	
Early satiety	7	9	8	12	2.7
Trouble with eating	14	13	3	6	2.0
Trouble with eating in front of other people	15	9	9	3	2.0
Trouble with enjoying meals	21	6	3	6	1.8
Acid indigestion/heartburn	23	5	4	4	1.7
Trouble with acid/bile in your mouth	23	6	6	1	1.6
Dry mouth	23	7	4	2	1.6
Choking when swallowing	18	15	3	–	1.6
Trouble with drinking liquids	25	6	3	2	1.5
Trouble with coughing	22	10	4	–	1.5

Temporal Analysis

With regard to time, no statistically significant differences in QLQ-C30 and QLQ-OES18 scores were observed between patients with a follow-up of less than 5 years (n = 21; median survival 37 [interquartile range 27–50] months) and patients with a follow-up of 5 years or more (n = 15; median survival 133 [interquartile range, 100–150] months) (data not shown).

DISCUSSION

The present study evaluated the HRQoL of long-term survivors after potentially curative treatment for esophageal cancer. The results indicate that (1) these patients reported better HRQoL than a large reference group of patients with esophageal cancer, but worse compared with a reference sample from the general population; (2) a variety of symptoms continued to persist in the majority of patients; (3)

TABLE 5. Patient ratings of the treatment with chemo(radio)therapy or surgery

Statement	Strongly agree	Agree	I do not know	Disagree	Strongly disagree
Chemo(radio)therapy (n = 27)*					
	No. of patients (percentage)				
I received sufficient information on possible side effects.	20 (74%)	7 (26%)	—	—	—
I was able to ask enough questions regarding the treatment.	26 (96%)	1 (4%)	—	—	—
The treatment was less severe than expected.	10 (37%)	9 (33%)	3 (11%)	4 (15%)	1 (4%)
The travel time to the hospital was a burden.	4 (15%)	6 (22%)	1 (4%)	6 (22%)	10 (37%)
I was well supported by my doctor during the treatment.	23 (85%)	4 (15%)	—	—	—
The recovery phase did not disappoint me.	10 (37%)	8 (30%)	3 (11%)	6 (22%)	—
The period after the treatment was a difficult time.	6 (22%)	13 (48%)	1 (4%)	5 (19%)	2 (7%)
Surgery (n = 30)†					
I received sufficient information on possible complications.	22 (73%)	4 (13%)	1 (3%)	2 (7%)	1 (3%)
I was able to ask enough questions regarding the operation.	24 (80%)	4 (13%)	—	—	2 (7%)
The operation was less severe than expected.	19 (63%)	7 (23%)	3 (10%)	1 (3%)	—
The recovery phase did not disappoint me.	11 (37%)	8 (27%)	1 (3%)	9 (30%)	1 (3%)
The period after the operation was a difficult time.	10 (33%)	13 (43%)	1 (3%)	4 (3%)	2 (7%)

*Alone or followed by surgery. †Alone or preceded by chemo(radio)therapy.

treatment-related experiences were generally rated favorably by patients compared with what they expected; (4) treatment had not seriously affected patients' body weight or body image; and (5) the majority of patients believed that they had been cured of their disease and had a life expectancy similar to that of peers from the general population.

Patients in the present study had survived a potentially life-threatening cancer. They had experienced an intense treatment period, but they had recovered. They probably knew the odds of surviving esophageal cancer, but now they were long-term survivors. The fact that our patient sample reported significantly better HRQoL than the reference patient group can be explained, at least in part, by the fact that the reference group was composed of patients with all stages of disease before the start of their treatment. If we had been able to use a more homogeneous reference group resembling more closely the current patient sample in terms of stage of disease and prognosis, the differences that we observed in HRQoL might have been minimized. In fact, except for diarrhea and financial difficulties, all scores in the symptom scales were better in our study sample than in the patient reference group. After surgery, patients could have developed post-vagotomy diarrhea, whereas patients from the reference patient group with recurrent or metastatic disease could have more symptoms of constipation caused by analgesic use. Despite the lack of information on exact stage distribution and treatment modalities in the reference patient group, these EORTC data on HRQoL are the best

available reference values derived from a large group of patients with esophageal cancer.

Most of the HRQoL scores of the patient sample were worse than those of the general population reference group. These differences, although likely reflecting residual problems due to the disease and its treatment, may also be due, in part, to the fact that our patient sample was older than the general population sample (eg, 67% were aged ≥ 60 years compared with 30% in the general population) (Table 1). This could also explain why the difference in physical functioning between the treatment group and the general population reference group was statistically significant, and not in the other functional scales.

Early satiety during a meal was the most frequently reported symptom (81%). This finding is in line with previous studies that have reported this symptom in 65% to 75% of patients with esophageal cancer.^{3,13} After esophageal resection, early satiety may occur as the result of an increasing pressure in the gastric tube and a diminished gastric reservoir. In the current study, 93% of surgically treated patients reported early satiety.

Most patients reported being well informed about the treatment that was given. Not surprisingly, the majority of patients experienced the period after treatment as difficult. In retrospect, both chemo(radio)therapy and surgery were rated as being well tolerated. It can be expected that scores would have been worse during or shortly after treatment. Seventy percent of patients, treated with chemo(radio)therapy, indicated that

TABLE 6. Body image ratings

Item	Not at all	A little	Quite a bit	Very much
	No. of patients (percentage)			
I felt unattractive in the past week.	28 (78%)	7 (19%)	—	1 (3%)
I found it difficult to see myself naked in the past week.	26 (72%)	7 (19%)	1 (3%)	2 (6%)
My physical appearance is affected by the treatment.	18 (50%)	14 (39%)	3 (8%)	1 (3%)
I avoided people because of my physical appearance.	34 (94%)	2 (6%)	—	—

TABLE 7. Perceived health and future perspective

	No. of patients and percentage					
	Much better	A little better	The same	A little worse	Much worse	
Current health compared with that before the diagnosis	4 (11%)	2 (6%)	17 (47%)	10 (28%)	3 (8%)	
Current health compared with that before the start of treatment	11 (31%)	4 (11%)	13 (36%)	7 (19%)	1 (3%)	
Current health compared with that 8–12 wks after the treatment	23 (64%)	5 (14%)	6 (17%)	1 (3%)	1 (3%)	
	Completely true	Mostly true	I do not know	Mostly false	Completely false	
I am cured of my disease.	27 (75%)	5 (14%)	4 (11%)	–	–	
I have the same life expectancy as other people.	24 (67%)	7 (19%)	4 (11%)	–	1 (3%)	
I live day to day.	5 (14%)	7 (19%)	4 (11%)	11 (31%)	9 (25%)	
I make future plans.	12 (33%)	14 (39%)	3 (8%)	5 (14%)	2 (6%)	
	Always	Mostly	Often	Sometimes	Rarely	Never
I fear that my disease will return.	2 (6%)	1 (3%)	4 (11%)	12 (33%)	11 (31%)	6 (17%)

the treatment was less severe than expected. The considerable, transient, negative effects that chemoradiation can have on most aspects of HRQoL during and shortly after treatment may explain this result, even though in our study it was scored at least 1 year after treatment.^{14–16}

The retired portion of the general population is increasing, and its demographic composition is changing. Many patients with esophageal cancer belong to this part of the population. Unfortunately, only half of the patients who were employed before treatment could resume their work, and those who did return to work often did so at a reduced level. Similar results have been reported by de Boer and colleagues.³

Older adults tend to express less positive attitudes toward their bodies than younger adults.¹⁷ Given that the median age of our sample at study entry was 66 years, it is actually somewhat surprising that the majority of patients reported being satisfied with their physical appearance. It may be that these patients placed less emphasis on body image than on other issues of greater importance to them after a potentially life-threatening illness.

Patients' views on cure and life expectancy seemed to be somewhat contradictory. On the one hand, the majority of patients believed that they had been cured. Yet, more than half of the patients worried that their disease might recur. Although this may suggest that the phrasing of the questions was not sufficiently clear, it may also reflect a genuine ambivalence among patients about their long-term prognosis. This finding deserves further investigation.

Surprisingly, a comparison between 2 groups with different follow-up times showed no statistically significant differences. It seems that for long-term esophageal cancer survivors, the exact duration of their survival does not influence quality of life scores.

The strengths of this study include the high response rate and the use of primarily standardized, validated questionnaires. The high response rate reduced the risk of selection bias and the use of validated, multidimensional questionnaires protected against information bias.

Study Limitations

Several limitations of the study should also be noted. The sample size was small, precluding the possibility of examining the extent to which HRQoL varies as a function of type of treatment. Also, the cross-sectional study design did not allow us to investigate directly changes in HRQoL over time, although we were able to pose some retrospective questions in this regard. In the case of the general population, there were differences in age and gender distribution, for which we did not correct. HRQoL is much more than physical symptoms. To overcome this limitation, we have added additional questions (eg, questions on survivorship issues). Finally, we did not have sufficient clinical information on the 2 reference groups to perform risk adjustments of the results. Despite these shortcomings, the study population is a unique group of patients with esophageal cancer who survived at least 1 year after potentially curative treatment. Multicenter studies are needed. It is extremely difficult to accrue large samples of long-term esophageal cancer survivors from a single center, because the overall 5-year survival is still low. The role of definitive chemoradiation is increasing in the treatment of this disease.^{18,19} If chemoradiation, with or without surgery, results in similar survival to surgery alone, then HRQoL issues may play an increasingly important role in treatment decision-making.

CONCLUSIONS

Our results indicate that some aspects of HRQoL are impaired in disease-free patients treated for esophageal cancer. However, in general, they can lead satisfactory lives. This information can be used to help inform patients during the pretreatment period about the long-term effects of treatment.

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