RESEARCH ARTICLE

Quality of Life for Patients with Esophageal/Gastric Cardia Precursor Lesions or Cancer: A One-year Prospective Study

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Abstract

Background: The current study examined health-related quality of life (QoL) for patients with esophageal/gastric cardia precursor lesions or cancer before and after treatment to facilitate improved prevention and treatment. Materials and Methods: Patients with different stages of esophageal/gastric cardia lesions completed two QoL questionnaires, EORTC QLQ-C30 and supplemental QLQ-OES 18, before primary treatment, and at 1, 6 and 12 months after treatment. Results: Fifty-nine patients with precursor lesions, 57 with early stage cancer, and 43 with advanced cancer responded to our survey. Patients with precursor lesions or early stage cancer reported better QoL overall than those with advanced cancer before treatment ($p<0.01$). Global QoL scores before treatment and at 1 month after treatment were 71±9 versus 69±9 ($p>0.01$), 71±8 versus 61±11 ($p<0.01$), 67 ± 11 versus 62 ± 9 ($p<0.01$) for three stages of lesions. At 6 months after treatment, some QoL measures recovered gradually in precursor lesion and early cancer patients, while some continuously deteriorated in advanced cancer patients. At 12 months, all QoL scores were comparable to baseline for patients with precursor lesions ($p>0.01$), while global QoL, social, pain, and insomnia scores for early stage and advanced cancer were inferior to corresponding baseline levels (difference between means>5, $p<0.01$). At this time point, compared with patients with early stage cancer, those with advanced cancer showed worse QoL with all function and most symptom measures ($p<0.01$). Conclusions: Patients with precursor lesions or early stage esophageal/gastric cardia cancer show better QoL than those with advanced cancer. This indicates that screening, early diagnosis and treatment may improve the QoL for esophageal/gastric cardia cancer patients. Target intervention and counseling should be given by health care providers during treatment and follow-up to facilitate QoL improvement.

Keywords: Esophageal cancer - gastric cardia cancer - quality of life - QLQ-C30 - QLQ-OES 18 - China

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Introduction

Esophageal cancer is a common malignancy. Its incidence and mortality, respectively, rank at eighth and sixth among all cancers, with 456,000 new cases and 400,000 deaths in 2012 worldwide (Ferlay et al., 2013). About half of these cases and of deaths occur in China, giving it the highest incidence and mortality rates in the world. Although the mortality of esophageal cancer has decreased over the last three decades, it remains the fourth leading cause of cancer deaths in China (Wei et al., 2011). There is also wide disparity in the burden of esophageal cancer. In some rural areas with limited health resources and under-developed economy, the mortality of esophageal cancer is three times higher than the average of the country (Chen, 2008). Esophageal cancer is considered as a major public health challenge in these high risk areas (Wei et al., 2011b; Wang et al., 2013).

To date, major risk factors for esophageal cancer are not well understood and specific primary prevention strategies are lacking; screening, early diagnosis and treatment are regarded as important methods for esophageal cancer prevention and control. Screening for esophageal cancer aims to detect the lesion at an early stage and alter its natural course before symptoms are observed (Tomizawa and Wang, 2009). The prognosis of patients with esophageal cancer is dismal, with overall 5-year survival rates of 10-30% even in developed countries (Rouvelas et al., 2005; Jemal et al., 2006). Most esophageal cancer cases are asymptomatic at an early stage, and once diagnosed, the condition may be locally advanced and unresectable. Since the survival of esophageal cancer is strongly correlated with the stage at diagnosis, the detection of early neoplasia and subsequent treatment can lead to an improved outcome, with the 5-year survival rate increasing over 85% (Wang et al.,

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2004). In such context, the Early Detection and Early Treatment of Esophageal Cancer (EDETEC) Program, funded by Chinese Central Financial Transfer Payment Program, has been conducted in several high-risk areas in China since 2005 (Wei et al., 2011a).

In clinical practice, survival and mortality rates are the main outcome measurements in most cancer research and practice, because of their obvious relevance and ease of calculation and interpretation (Scarpa et al., 2013). However, with the development of self-administered structured and validated instruments for the assessment of quality of life (QoL) for cancer patients, QoL research appears increasingly important (Darling, 2013). The QoL outcome not only reflects the influence of disease and treatment on patients' physical, psychological and social function and informs clinical decision, but also provides information for health economic evaluation to select suitable prevention strategies of esophageal cancer, such as early detection and treatment (Avery et al., 2007; Lagergren et al., 2007; Zeng and Liu, 2012). Although QoL assessments for patients with esophageal cancer have attracted attention in academia, most studies focus on QoL for patients receiving different treatment modalities (Reynolds et al., 2006; Zeng and Liu, 2012; Zapletal et al., 2014), and very few have explored QoL for patients with different clinical stages of esophageal cancer during treatment and follow-up.

There are two types of rating scales used to measure QoL among cancer patients: one is for general measures of QoL for patients with various cancers (such as EORTC QLQ-C30 and FACT-G), and the other for measuring disease-specific issues for patients with specific cancers (such as QLQ-OES18 and FACT-E for esophageal cancer patients and QLQ-LC13, FACT-L for lung cancer patients). For esophageal cancer patients, QLQ-C30 and QLQ-OES18 have shown good psychometric and clinical validity, and the combined use of the two rating scales can reflect patients' QoL accurately and objectively (Aaronson et al., 1993; Blazeby et al., 2003; Parameswaran et al., 2010).

This study was conducted using QLQ-C30 v3.0 and the esophageal cancer-specific module QLQ-OES18 to evaluate the QoL for patients with esophageal/gastric cardia cancer at different clinical stages and its change along the timeline of treatment in Linzhou, a high risk area in China. Gastric cardia cancer was not distinguished from esophageal cancer regarding diagnosis and treatment in clinical practice in many hospitals in China when the study was conducted. Thus our study did not deliberately focus only on esophageal precursor lesion and cancer, and gastric cardia cancer and precursor cases were also enrolled. We aimed to explore the relationship between early detection and QoL for esophageal/gastric cardia cancer patients and provide information to facilitate improved QoL in clinical practice.

Materials and Methods

Research subjects

The study enrolled patients with severe dysplasia or more of esophageal/gastric cardia mucosa at Linzhou Cancer Hospital through the EDETEC program or who were referred to the hospital after diagnosis between 2009 and 2010 and followed to 2011. All patients were aware of their disease condition and voluntarily participated in the survey. None of them were unable to understand the content of the questionnaires or had other previous or concurrent malignancies. Informed consent was obtained from all participants prior to survey. The study was approved by the Institutional Review Board of the Cancer Institute of Chinese Academy of Medical Sciences.

For the purpose of this study, participants were divided into three groups based on pathology diagnosis: the precursor lesion group, including severe dysplasia and carcinoma in situ; the early stage cancer group, including intramucosal carcinoma and submucosal carcinoma; and the advanced cancer group, i.e. invasive carcinoma. Patients were treated according to recommended clinical guidelines. For patients with precursor lesion, endoscopic mucosal resection (EMR) or argon plasma coagulation (APC) was selected; for those with early stage cancer, EMR or surgery was suggested; and for those with advanced cancer, common treatment modalities, including surgery, radiotherapy, chemotherapy, or a combination, were chosen depending on physical condition, disease severity and patients' requests for the treatment.

Questionnaire survey

All participants were surveyed with the Chinese versions of QLQ-C30 v3.0 and QLQ-OES18 before primary treatment, and at 1, 6 and 12 months after treatment (±2 weeks). Both questionnaires were developed by the European Organization for Research and Treatment of Cancer (EORTC) and well validated in Chinese population (Wan et al., 2005; Xu et al., 2007). The QLQ-C30 v3.0 has been used to assess QoL for patients with different cancers in international clinical trials (Aaronson et al., 1993; Farooqui et al., 2013). It includes 30 items in one global QoL scale, five function scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, nausea/vomiting, and pain), and six single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). The QLQ-OES 18 is a QLQ-C30 supplement that is designed to collect information on esophageal/gastric cardia cancer-specific symptoms and side effects. Its 18 questions are categorized into four symptom scales (dysphagia, eating difficulties, reflux, and esophageal pain) and six single items (trouble swallowing saliva, choking when swallowing, dry mouth, trouble with taste, trouble with coughing, and speech difficulties). There are four responses in each question of both questionnaires: "not at all", "a litter", "quite a bit", and "very much", except for the global QoL scale, which has seven responses ranging from "very poor" to "excellent". All responses are converted linearly into scores on a 0 to 100 scale according to the EORTC scoring manual (Fayers et al., 2001). High scores for global QoL and function scales represent better levels of overall QoL and function, while high scores for symptom scales/items indicate more or worse symptoms. A 5 to 10-point difference in mean scores between comparison groups or time points is considered

clinically significant (Osoba et al., 1998).

The patients were interviewed face to face in the first survey before primary treatment, and by phone at different time points after treatment. All interviewers were well-trained postgraduate students or health care workers. When the patients had difficulty in comprehending the meaning of items in questionnaires, neutral explanations were made by the interviewers to avoid biased responses. Demographic and clinical information was collected from their medical records and verified in the surveys.

Statistical analysis

IBM SPSS Statistics version 20.0 (Armonk, New York, United States) was used for statistical analysis. Demographic and clinical data were compared between different stage groups using Chi-square test or Student's t-test. QoL scores for each measure were expressed as mean±standard deviation (SD). Comparisons between groups were made using multivariate analysis of variance (MANOVA) at each time point (for each of the measures), adjusting for age and sex, to identify QoL differences between patients with different clinical stages. Comparisons between specific assessment points (within-clinical-stage group) were conducted using analysis of variance for repeated measures to assess QoL changes over time. $p<0.05$ was considered statistically significant for Chi-square test or Student's t-test, whereas for comparison of QoL scores, $p<0.01$ was a level of significance due to multiple testing.

Results

Characteristics of patients

A total of 166 patients participated in the survey before primary treatment, including 60 with precursor lesion, 58 with early stage cancer, and 48 with advanced cancer. During the 12 months after treatment, 59 with precursor lesion, 57 with early stage cancer, and 43 with advanced cancer (5 were died before the last survey) were successfully followed up. The patients who did not complete the survey at all four time points were excluded from subsequent data analysis.

The average age of all patients was 57.3±7.6 (mean±SD) years (range: 36-83). Patients with advanced cancer were older than those with precursor lesion and early stage cancer ($p<0.001$). 53 (89.8%) patients in the precursor lesion group, 42 (73.7%) in the early stage cancer group, and 7 (16.3%) in the advanced cancer group were identified through the screening (i.e. EDETEC) program ($p<0.001$). There were 59 (100%) with esophageal precursor lesion in the precursor lesion group; 31 (54.4%) with esophageal cancer and 26 (45.6%) with gastric cardia cancer in the early stage cancer group, and 40 (93.0%) and 3 (7.0%) respectively in the advanced cancer group ($p<0.001$). 57 (96.6%), 8 (14.0%), and no patients in three groups received EMR or APC, respectively; 2 (3.4%), 48 (84.2%), and 32 (74.4%) patients underwent surgery alone or a combination including surgery, respectively; and 0, 1 (1.8%), and 11 (25.6%) patients received radiotherapy and/or chemotherapy, respectively ($p<0.001$). Other baseline characteristics are listed in Table 1.

Comparisons of QoL scores for patients with different stages of esophageal/gastric cardia lesions

Before primary treatment, there were no significant differences in all measures of QoL between the precursor lesion and early stage cancer groups ($p>0.01$), and function scales were generally good in both groups (mean scores>90). Patients in the advanced cancer group reported worse cognitive and social functions, and more problems with insomnia, appetite loss, financial difficulties, eating, reflux, and choking compared with those in the other two groups (difference between means>10, $p<0.01$) (Table 2).

At 1 month after treatment, patients with early stage or advanced cancer had worse QoL in most function and symptom measures than those with precursor lesion (Table 2). QoL declined most in the early stage cancer group, which showed lower global QoL, physical, role, and social function scores, and higher fatigue, pain, dyspnea, and appetite loss scores compared with corresponding baseline values (difference between means>5, $p<0.01$). There was significant deterioration in fatigue, pain, and insomnia scores in the precursor lesion group, and in global QoL, social function, pain, and financial difficulties in the advanced cancer group (difference between means>5, $p<0.01$) (Table 3).

At 6 months after treatment, scores for fatigue, pain, appetite loss, and dry month domains in the precursor lesion group returned to baseline values ($p>0.01$) (Table 3). Compared with 1 month after treatment, physical, role, social, fatigue, pain, and dyspnea measures in the early stage cancer group showed significantly superior results (difference between means>5, $p<0.01$), while most domains in the advanced cancer group did not demonstrate

Table 1. Demographic and Clinical Characteristics of Patients in Different Stage Groups

	Precancerous (n=59)(%)	Early cancer (n=57)(%)	Advanced cancer (n=43)(%)	*p*-value
Age (mean ± SD), years	54.8 ± 7.0	57.0 ± 6.1	61.0 ± 8.7	<0.001
Gender				0.015
Male	31 (52.5)	43 (75.4)	22 (51.2)	
Female	28 (47.5)	14 (24.6)	21 (48.8)	
Education level				0.652
Illiterate/Primary school	33 (55.9)	38 (66.7)	24 (55.8)	
Junior high school	18 (30.5)	15 (26.3)	15 (34.9)	
Senior high school or equivalent	8 (13.6)	4 (7.0)	4 (9.3)	
Marital status				0.551
Married	55 (93.2)	55 (96.5)	39 (90.7)	
Divorced/Widowed	4 (6.8)	2 (3.5)	4 (9.3)	
Occupation				0.967
Farmer	56 (94.9)	55 (96.4)	40 (93.0)	
Worker	2 (3.4)	1 (1.8)	2 (4.7)	
Managerial personnel	1 (1.7)	1 (1.8)	1 (2.3)	
Screening				<0.001
Screening	53 (89.8)	42 (73.7)	7 (16.3)	
Non-screening	6 (10.2)	15 (26.3)	36 (83.7)	
Lesion location				<0.001
Esophagus	59 (100.0)	31 (54.4)	40 (93.0)	
Gastric cardia	0 (0)	26 (45.6)	3 (7.0)	
Treatment				<0.001
APC	4 (6.8)	0 (0)	0 (0)	
EMR	53 (89.8)	8 (14.0)	0 (0)	
Surgery alone or combined with surgery	2 (3.4)	48 (84.2)	32 (74.4)	
Radiotherapy and/or chemotherapy	0 (0)	1 (1.8)	11 (25.6)	

Table 2. Mean Scores (SD) for Selected QLQ-C30 and QLQ-OES18 Domains at Different Time Points for Different Stage Groups

	T1			T2			T3			T4		
	Precursor	Early stage	Advanced	Precursor	Early stage	Advanced	Precursor	Early stage	Advanced	Precursor	Early stage	Advanced
Global QoL	71 (9)	71 (8)	67 (11)	69 (9)	61 (11)**	62 (9)**	69 (9)	59 (11)***	60 (10)**	70 (9)	58 (11)***	60 (10)**
Function scales												
Physical	100 (1)	99 (4)	96 (8)*	99 (4)	89 (7)***	92 (9)**	99 (2)	96 (6)*	93 (8)**	100 (1)	97 (7)*	91 (9)**
Role	99 (4)	98 (9)	93 (14)**	99 (4)	92 (14)**	90 (16)**	100 (0)	97 (10)	91 (15)**	100 (0)	96 (10)	88 (16)***
Cognitive	98 (8)	93 (15)	75 (18)***	97 (8)	92 (15)	74 (17)***	97 (8)	92 (15)	74 (16)***	97 (8)	93 (15)	74 (17)***
Emotional	100 (2)	97 (8)	90 (11)***	100 (2)	96 (9)*	88 (12)***	100 (2)	96 (8)	87 (13)***	100 (2)	96 (8)	87 (13)***
Social	99 (4)	94 (16)	81 (21)***	99 (5)	80 (19)***	75 (20)***	99 (4)	90 (18)**	74 (20)***	99 (4)	89 (18)***	74 (20)***
Symptom domains												
Fatigue	0 (3)	2 (7)	10 (12)**	10 (8)	15 (10)**	14 (12)	1 (4)	7 (10)**	15 (11)***	0 (3)	6 (11)**	15 (11)***
Pain	1 (3)	3 (9)	8 (13)**	12 (13)	17 (12)	18 (14)**	1 (4)	9 (13)**	13 (14)***	1 (4)	10 (12)**	15 (13)***
Dyspnea	0 (0)	2 (8)	4 (11)*	1 (6)	13 (16)***	5 (12)	0 (0)	5 (12)*	7 (14)**	0 (0)	4 (11)*	7 (14)**
Insomnia	2 (7)	4 (10)	15 (21)***	12 (16)	7 (14)	15 (21)	6 (13)	14 (17)**	22 (20)***	3 (10)	11 (16)**	22 (20)***
Appetite loss	2 (8)	7 (14)	26 (14)***	6 (13)	16 (17)***	27 (13)***	5 (12)	15 (17)***	30 (10)***	5 (12)	18 (17)***	30 (10)***
Financial difficulties	0 (0)	5 (13)	15 (24)***	0 (0)	9 (20)**	20 (24)***	0 (0)	9 (17)**	23 (25)***	0 (0)	8 (17)**	24 (24)***
Dysphagia	4 (7)	8 (13)	16 (16)***	3 (6)	8 (14)	18 (17)***	3 (6)	6 (11)	21 (18)***	2 (4)	5 (10)	23 (19)***
Eating difficulties	0 (1)	4 (12)	15 (14)***	1 (3)	6 (12)**	16 (13)***	0 (1)	6 (13)**	18 (13)***	0 (1)	6 (13)**	18 (12)***
Reflux	3 (9)	8 (13)	23 (13)***	4 (10)	9 (13)	24 (12)***	3 (8)	14 (15)***	26 (10)***	2 (8)	18 (15)***	26 (11)***
Choking	3 (10)	9 (17)	31 (15)***	4 (11)	11 (18)**	33 (14)***	3 (9)	11 (17)**	31 (15)***	2 (8)	10 (17)**	29 (17)***
Dry mouth	1 (4)	2 (9)	8 (14)**	5 (12)	3 (10)	11 (17)	0 (0)	6 (13)**	9 (17)**	1 (6)	8 (14)**	12 (18)***

*T1 represents before primary treatment; T2, 1 month after treatment; T3, 6 months after treatment; and T4, 12 months after treatment. For global QoL and function scales, higher scores represent better levels of overall QoL and function; for symptom domains, higher scores represent more or worse symptoms. Compared with the precursor lesion group. *p<0.01 alone; **p<0.01 and difference between means>5; ***p<0.01 and difference between means>10

Table 3. Difference between Mean Scores (95% CI) for Selected QLQ-C30 and QLQ-OES18 Domains between Different Time Points for Different Stage Groups

	T2-T1			T3-T1			T4-T1		
	Precursor	Early stage	Advanced	Precursor	Early stage	Advanced	Precursor	Early stage	Advanced
Global QoL	-2 (-3.0)	-10 (-12.-7)**	-5 (-8.-3)**	-2 (-3.0)	-12 (-15.-9)***	-7 (-11.-5)**	-1 (-3.1)	-13 (-15.-10)***	-7 (-10.-4)**
Function scales									
Physical	-1 (-2.0)	-10 (-12.-8)***	-4 (-7.-2)*	-1 (-1.0)	-3 (-4.-1)*	-3 (-5.-2)*	0 (0.0)	-2 (-4.-1)	-5 (-7.-3)*
Role	0 (-2.2)	-6 (-9.-2)**	-3 (-6.-1)	1 (0.2)	-1 (-2.0)	-2 (-5.0)	1 (0.2)	-2 (-3.0)	-5 (-8.-2)**
Cognitive	-1 (-2.0)	-1 (-2.0)	-1 (-4.1)	-1 (-2.0)	-1 (-3.0)	-1 (-4.1)	-1 (-2.1)	0 (0.0)	-1 (-4.1)
Emotional	0 (-1.0)	-1 (-2.0)	-2 (-3.1)	0 (-1.0)	-1 (-1.0)	-3 (-4.-1)	0 (-1.0)	-1 (-1.0)	-3 (-4.0)
Social	0 (-1.0)	-14 (-19.-10)***	-6 (-10.-2)**	0 (0.0)	-4 (-8.-2)*	-7 (-11.-3)**	0 (0.0)	-5 (-9.-2)**	-7 (-12.-4)**
Symptom domains									
Fatigue	10 (7.11)**	13 (11.16)***	4 (2.7)*	1 (0.2)	5 (3.7)*	5 (2.7)*	0 (-1.1)	4 (2.6)*	5 (2.7)*
Pain	11 (8.14)***	14 (11.16)***	10 (7.13)***	0 (-1.1)	6 (3.9)**	5 (2.8)*	0 (-1.2)	7 (4.9)**	7 (4.10)**
Dyspnea	1 (0.3)	11 (8.16)***	1 (-1.4)	0 (0.0)	3 (1.5)	3 (0.6)	0 (0.0)	2 (0.4)	3 (0.6)
Insomnia	10 (6.14)***	3 (1.6)	0 (-4.4)	4 (1.7)*	10 (6.15)***	7 (2.12)**	1 (-1.5)	7 (4.11)**	7 (2.12)**
Appetite loss	4 (1.7)*	9 (5.13)**	1 (-3.4)	3 (1.5)	8 (5.12)**	4 (1.7)	3 (0.5)	11 (6.15)***	4 (1.7)
Financial difficulties	0 (0.0)	4 (0.9)	5 (2.9)**	0 (0.0)	4 (1.7)	8 (4.13)**	0 (0.0)	3 (1.6)	9 (5.14)**
Dysphagia	-1 (-1.0)	0 (-2.1)	2 (1.4)*	-1 (-2.0)	-2 (-4.0)	5 (2.7)*	-2 (-4.-1)	-3 (-5.-1)*	7 (4.10)**
Eating difficulties	1 (0.1)	2 (1.3)*	1 (0.3)	0 (0.0)	2 (1.3)*	3 (1.5)*	0 (0.0)	2 (1.3)*	3 (1.6)*
Reflux	1 (-1.2)	1 (-1.4)	1 (-1.4)	0 (-2.1)	6 (3.10)**	3 (0.7)	-1 (-3.1)	10 (6.15)***	3 (0.6)
Choking	1 (-1.2)	2 (0.5)	2 (-1.4)	0 (-2.1)	2 (-2.6)	0 (0.0)	-1 (-3.0)	1 (-3.5)	-2 (-4.1)
Dry mouth	4 (2.7)*	1 (-1.2)	3 (0.6)	-1 (-2.1)	4 (0.7)	1 (-2.5)	0 (-1.2)	6 (2.10)**	4 (1.7)

*T1 represents before primary treatment; T2, 1 month after treatment; T3, 6 months after treatment; and T4, 12 months after treatment. *p<0.01 alone; **p<0.01 and difference between means>5; ***p<0.01 and difference between means>10

much change. Scores for insomnia symptom increased in both the early stage and advanced cancer groups (Table 2).

At 12 months after treatment, patients with early stage and advanced cancer still had lower global QoL scores than those with precursor lesion (difference between means>5, p<0.01) (Table 2). There were no significant differences in all measures compared to baseline levels in the precursor lesion group (p>0.01). However, appetite loss, reflux, and dry month in the early stage cancer group, role function, financial difficulties, and dysphagia in the advanced cancer group, and global QoL, social function, pain, and insomnia in both groups showed significantly worse results than the baseline (difference between means>5, p<0.01) (Table 3).

Comparisons of QoL scores for patients at different time points

In the precursor lesion group, function and symptom scores did not change over time, except fatigue, pain, insomnia, appetite loss, and dry month (p<0.01) (Table 3). In the early stage cancer group, some measures were worse at 1 month after treatment, and then gradually recovered, but some constantly deteriorated, such as appetite loss and reflux. Patients with advanced cancer consistently reported problems with insomnia, appetite loss, financial difficulties, dysphagia, eating, reflux, and choking, for which mean scores exceeded 15 points throughout the study. The early stage cancer group scored better than the advanced cancer group for most function and symptom measures (p<0.01), although the global QoL scores in both groups were similar between 1 month to 1 year after treatment, which were lower than those in the precursor lesion group (difference between means>5, p<0.01) (Table 2). Scores for constipation, diarrhea, saliva problems, taste, cough, and speech difficulties in three groups were around zero and did not change much over time, and thus were not presented in tables. Nausea/vomiting and esophageal pain results showed similar trends as those

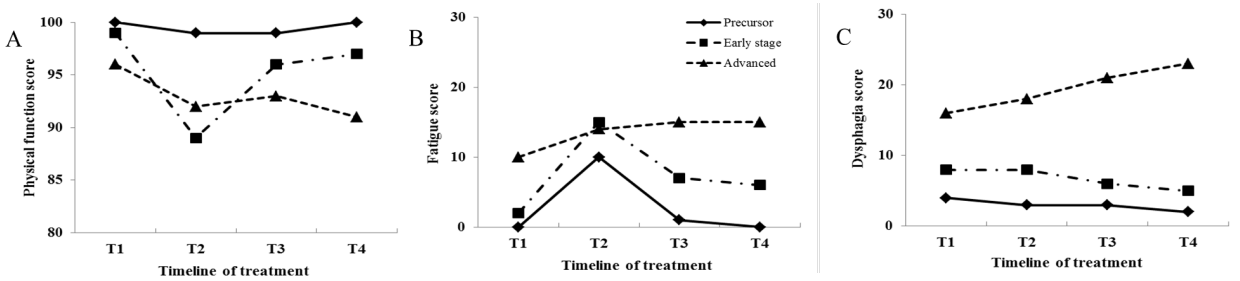

Figure 1. Changes in Mean Scores for Representative QoL Domains for Different Clinical Stage Groups Along the Timeline of Treatment. A: Physical function; B: Fatigue; C: Dysphagia. (T1, before primary treatment; T2, 1 month after treatment; T3, 6 months after treatment; and T4, 12 months after treatment)

of eating difficulties and pain measures. Figure 1 shows changes in mean scores for representative QoL domains (physical function, fatigue, and dysphagia) for 3 groups along the timeline of treatment.

Discussion

In the context of bio-psychosocial medical model, patients' QoL is evolving into a key issue in modern cancer research and clinical practice (Farooqui et al., 2013). QoL outcomes provide information about patients' subjective feeling of physical and psychosocial health as well as indications of prognosis (Gockel et al., 2010; Djarv and Lagergren, 2011; Quinten et al., 2014). QoL measures with survival and mortality data reflect curative effects on malignancies and rehabilitation, inform treatment choices, and improve doctor-patient communication (Velikova et al., 2004; Lin et al., 2012). In the current study, although the pretreatment QoL scores for all measures did not significantly differ between the precursor lesion and early stage cancer groups, patients with precursor lesion scored better than those with early stage cancer in most function and symptom measures at time points following treatment. The advanced cancer group always had the worst QoL scores among the three. In addition, the measures which deteriorated at 1 month after treatment in the precursor lesion group finally recovered to baseline at last assessment, while some measures in the early cancer group did not return to baseline values. In the advanced cancer group, some measures did not demonstrate much change during the follow-up period, while others continually deteriorated.

In most measures, the precursor lesion and early cancer groups reported superior QoL scores to the advanced cancer group throughout the study. This discrepancy was probably due to significant variability among patients' baseline condition, treatment approaches, demographic characteristics, and mental states. Before primary treatment, precursor lesion and early esophageal/gastric cardia cancer are usually asymptomatic and do not affect daily activities of patients, while advanced cancer is always accompanied by a series of symptoms, like eating difficulties, reflux, and pain in the chest and back. Besides, different treatment approaches may have differing effects on patients' QoL. Our patients diagnosed with precursor lesion usually received endoscopic treatments such as EMR and APC, which are effective, minimally invasive, and cost-effective (Peters et al., 2005), while those with esophageal/gastric cardia cancer were treated with surgery alone or combined with neoadjuvant radiotherapy and/or chemotherapy, and advanced cancer often needed a longer period of treatment. As the patients with advanced cancer were older than those with early stage lesions, tumor biology and therapeutic methods may have a larger impact on them. Moreover, advanced cancer patients usually suffer greater shock and concern, which is reflected by the fact that emotional function scores in this group were lower than those in the other two groups throughout the current study. All these led to inferior QoL in advanced cancer patients. Since most precursor lesion and early cancer patients were identified through the screening program, while most advanced cancer patients were referred to the hospital with typical symptoms, it is important to note that better QoL will be achieved if esophageal/gastric cardia lesions are detected at an early stage. In addition, our study showed that the advanced cancer group reported more problems with financial difficulties than the other two groups during the follow-up. The mean scores for financial difficulties in this group gradually increased (got worse) over time. These may resonate with an early observation that screening, early diagnosis and treatment for esophageal/gastric cardia cancer could provide great cost savings (Wei et al., 2011a; Yang et al., 2011).

QoL scores showed distinct patterns of change along the timeline of treatment for different clinical stages of esophageal/gastric cardia lesions. For patients with precursor lesion or early esophageal/gastric cardia cancer, some QoL domains, like fatigue and pain, deteriorated in the first month after primary treatment and gradually improved during the remaining follow-up period. We presume that prescribed treatment modalities for esophageal/gastric cardia cancer are related to marked injuries of body and psychology during the months following treatment; for example, dyspnea in patients treated with surgery may be associated with reduced lung volume due to the presence of an intrathoracic stomach (Lagergren et al., 2007). As a result, early posttreatment QoL scores are impaired in comparison to baseline levels, which is consistent with other studies (Reynolds et al., 2006; Lagergren et al., 2007; Parameswaran et al., 2010). With fading immediate side effects of treatments and an increased tolerance towards residual symptoms with time, QoL for patients with early stage lesions would improve within 6 to 12 months after treatment. But for advanced cancer patients, some QoL measures did not change much and some gradually got worse over

time. So it is important to inform patients with different clinical stages what problems may occur and what to except after treatment. Most patients with early stage lesions can expect a generally good QoL. For advanced cancer patients who consistently report problems in some QoL domains, physicians should take corresponding measures and offer extra counseling to relieve their concern and improve their QoL (Azmawati et al., 2014). Timely supportive interventions may help patients to cope with their posttreatment problems more easily. Besides, since QoL has prognostic value and may be associated with mortality and survival (Djarv and Lagergren, 2011; Quinten et al., 2014), health care providers should focus on not only clinical parameters but also patients' perception of their QoL. Clinicians must realize that the patient-reported QoL is one of the most important considerations, and QoL assessments should be incorporated into routine clinical practice to guide decisions.

It seems unusual that although most measures in the early cancer group were better than those in the advanced cancer group after treatment, patients in both groups had similar global QoL scores. Besides, changes of many QoL measures between baseline and 1 month after treatment in early stage cancer patients were larger than those in advanced cancer patients. These may be explained by response shift. Adjustments to impairments of physical function and esophageal/gastric cardia cancer symptoms experienced before primary treatment may lead to reevaluation of internal standards in advanced cancer patients. As a result, an adaptation of the perception of QoL (i.e. response shift) may occur, and many measures, including global QoL scale, in the advanced cancer group would be affected after treatment (Sprangers and Schwartz, 1999; Blazeby et al., 2005). There may be much larger score change associated with patients who reported worsening in this group. Response shift is an important confounding factor in current QoL research and difficult to measure. Even using a combination of generic and disease-specific tools, it may be still too crude to detect discrepancies between patients with different clinical stages (Blazeby et al., 2005).

The study is subject to certain limitations. Firstly, because of a small sample size and incomplete information, we were not able to quantify the effects of treatments and other clinical characteristics as contributing factors to the variation of QoL scores in the follow-up and between different stages of esophageal/gastric cardia lesions. Based on this study, large-scale and long-period follow-up investigations should be conducted to evaluate the QoL and its influential factors for patients with different clinical stages of esophageal/gastric cardia cancer. Secondly, at baseline, patients had already been diagnosed with esophageal/gastric cardia lesions, and their QoL may be affected by tumor biology and psychosocial factors in an unpredictable and individual way, so using pretreatment data as comparator values to assess changes in QoL may lead to inherent flaws (Derogar and Lagergren, 2012). However, a true baseline (i.e. before the disease has occurred) is not feasible to obtain.

In conclusions, the QoL was better for patients at an early stage of esophageal/gastric cardia lesions. At 12 months after treatment, all measures in the precursor lesion group showed no significant differences compared with pretreatment values, while some measures in advanced esophageal/gastric cardia cancer patients gradually deteriorated. Our results indicate that screening, early diagnosis and effective treatment among high risk populations enhance the QoL for esophageal/gastric cardia cancer patients. As QoL plays an important role in clinical practice, QoL assessments should be incorporated into routine health care and guide clinical decisions together with mortality and survival. Target intervention and counseling should be given by health care providers during treatment and follow-up to facilitate the QoL improvement.

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References

Aaronson NK, Ahmedzai S, Bergman B, et al (1993). The European organization for research and treatment of cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*, **85**, 365-76.

Avery KN, Metcalfe C, Barham CP, et al (2007). Quality of life during potentially curative treatment for locally advanced oesophageal cancer. *Br J Surg*, **94**, 1369-76.

Azmawati MN, Najibah E, Hatta MD, Norfazilah A (2014). Quality of life by stage of cervical cancer among Malaysian patients. *Asian Pac J Cancer Prev*, **15**, 5283-6.

Blazeby JM, Conroy T, Hammerlid E, et al (2003). Clinical and psychometric validation of an EORTC questionnaire module, the EORTC QLQ-OES18, to assess quality of life in patients with oesophageal cancer. *Eur J Cancer*, **39**, 1384-94.

Blazeby JM, Sanford E, Falk SJ, et al (2005). Health-related quality of life during neoadjuvant treatment and surgery for localized esophageal carcinoma. *Cancer*, **103**, 1791-9.

Chen Z (2008). Third National Retrospective Sampling Survey of Death Causes Report in 2004-2005 of China. peking union medical college press, Beijing (in Chinese).

Darling GE (2013). Quality of life in patients with esophageal cancer. *Thorac Surg Clin*, **23**, 569-75.

Derogar M, Lagergren P (2012). Health-related quality of life among 5-year survivors of esophageal cancer surgery: a prospective population-based study. *J Clin Oncol*, **30**, 413-8.

Djarv T, Lagergren P (2011). Six-month postoperative quality of life predicts long-term survival after oesophageal cancer surgery. *Eur J Cancer*, **47**, 530-5.

Farooqui M, Hassali MA, Knight A, et al (2013). Cross sectional assessment of health related quality of life (HRQoL) among patients with cancer in Malaysia. *Asian Pac J Cancer Prev*, **14**, 3017-21.

Fayers PM, Aaronson NK, Bjordal K, et al (2001). EORTC QLQ-C30 scoring manual, 3rd edn. European Organisation for Research and Treatment of Cancer, Brussels.

Ferlay J, Soerjomataram I, Ervik M, et al (2013). GLOBOCAN 2012 v1.0, Cancer incidence and mortality worldwide: IARC

CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer. Available from: http://globocan.iarc.fr, Accessed on 18/3/2014.

Gockel I, Gonner U, Domeyer M, et al (2010). Long-term survivors of esophageal cancer: disease-specific quality of life, general health and complications. *J Surg Oncol*, **102**, 516-22.

Jemal A, Siegel R, Ward E, et al (2006). Cancer statistics, 2006. *CA Cancer J Clin*, **56**, 106-30.

Lagergren P, Avery KN, Hughes R, et al (2007). Health-related quality of life among patients cured by surgery for esophageal cancer. *Cancer*, **110**, 686-93.

Lin JY, Wang MS, Dong LP, et al (2012). Influence of personal character on quality of life of patients with esophageal cancer in north Henan province and influencing factors. *Asian Pac J Cancer Prev*, **13**, 5415-20.

Osoba D, Rodrigues G, Myles J, et al (1998). Interpreting the significance of changes in health-related quality-of-life scores. *J Clin Oncol*, **16**, 139-44.

Parameswaran R, Blazeby JM, Hughes R, et al (2010). Health-related quality of life after minimally invasive oesophagectomy. *Br J Surg*, **97**, 525-31.

Peters FP, Kara MA, Rosmolen WD, et al (2005). Endoscopic treatment of high-grade dysplasia and early stage cancer in Barrett's esophagus. *Gastrointest Endosc*, **61**, 506-14.

Quinten C, Martinelli F, Coens C, et al (2014). A global analysis of multitrial data investigating quality of life and symptoms as prognostic factors for survival in different tumor sites. *Cancer*, **120**, 302-11.

Reynolds JV, Mclaughlin R, Moore J, et al (2006). Prospective evaluation of quality of life in patients with localized oesophageal cancer treated by multimodality therapy or surgery alone. *Br J Surg*, **93**, 1084-90.

Rouvelas I, Zeng W, Lindblad M, et al (2005). Survival after surgery for oesophageal cancer: a population-based study. *Lancet Oncol*, **6**, 864-70.

Scarpa M, Saadeh LM, Fasolo A, et al (2013). Health-related quality of life in patients with oesophageal cancer: analysis at different steps of the treatment pathway. *J Gastrointest Surg*, **17**, 421-33.

Sprangers MA, Schwartz CE (1999). The challenge of response shift for quality-of-life-based clinical oncology research. *Ann Oncol*, **10**, 747-9.

Tomizawa Y, Wang KK (2009). Screening, surveillance, and prevention for esophageal cancer. *Gastroenterol Clin North Am*, **38**, 59-73, viii.

Velikova G, Booth L, Smith AB, et al (2004). Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. *J Clin Oncol*, **22**, 714-24.

Wan CH, Chen MQ, Zhang CZ, et al (2005). The Chinese version of EORTC QLQ-C30 form in evaluation of quality of life for patients with cancer. *J Practical Oncol*, **20**, 353-5.

Wang GQ, Jiao GG, Chang FB, et al (2004). Long-term results of operation for 420 patients with early squamous cell esophageal carcinoma discovered by screening. *Ann Thorac Surg*, **77**, 1740-4.

Wang X, Song ZF, Xie RM, et al (2013). Analysis of death causes of in-patients with malignant tumors in Sichuan Cancer Hospital of China from 2002 to 2012. *Asian Pac J Cancer Prev*, **14**, 4399-402.

Wei WQ, Yang CX, Lu SH, et al (2011a). Cost-benefit analysis of screening for esophageal and gastric cardiac cancer. *Chin J Cancer*, **30**, 213-8.

Wei WQ, Yang J, Zhang SW, et al (2011b). Esophageal cancer mortality trends during the last 30 years in high risk areas in China: comparison of results from national death surveys conducted in the 1970's, 1990's and 2004-2005. *Asian Pac J Cancer Prev*, **12**, 1821-6.

Xu WX, Qian Y, Chen ZD (2007). Development and evaluation on measurement instrument of quality of life for patients with esophageal cancer Chinese version of EORTC QLQ-OES18. *Modern Oncol*, **15**, 1792-94 (in Chinese).

Yang J, Wei WQ, Niu J, et al (2011). Estimating the costs of esophageal cancer screening, early diagnosis and treatment in three high risk areas in China. *Asian Pac J Cancer Prev*, **12**, 1245-50.

Zapletal C, Heesen C, Origer J, et al (2014). Quality of life after surgical treatment of early Barrett's cancer: a prospective comparison of the Ivor-Lewis resection versus the modified Merendino resection. *World J Surg*, **38**, 1444-52.

Zeng J, Liu JS (2012). Quality of life after three kinds of esophagectomy for cancer. *World J Gastroenterol*, **18**, 5106-13.