Factors Affecting the Quality of Life in Esophageal Cancer Patients

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Abstract: Objective The aim of the study was to assess the quality of life (QoL) of patients with esophageal cancer, and to explore the main socioeconomic factors that affect the QoL. **Method** A multicenter cross-sectional study design was used. Data were collected using scales including the interviewer-administered general situation questionnaire designed by the authors, the Quality of Life Questionnaire-core 30 Version 3 in Chinese (QLQ-C30), and the Patient-generated Subjective Global Assessment (PG-SGA) from a nationwide survey conducted previously in China. The role of each covariate in the full model was assessed using the QoL as the primary outcome in a multilevel ordinal logistic regression analysis. **Results** In total, 1223 patients were included, among whom 1009 (82.5%) were males, and 504 (41.2%) were older than 65 years old. The findings indicate that patients with esophageal cancer in China face a poor quality of life with a mean global quality of life scored of 58.33 (66.67). The most significant factors influencing quality of life were the nutritional support, PG-SGA scores and level of education. Compared with patients who had a PG-SGA score ≥ 9 , patients with scores between 0-1 had significantly better scores in five scales: the PF (physical functioning), RF (role functioning), CF (cognitive functioning), EF (emotional functioning) and SF (social functioning) (OR: 4.75, 4.84, 2.12, 2.81, and 3.00). **Conclusion** Nutritional support and PG-SGA scores significantly influenced the quality of life of patients with esophageal cancer. It appears that most patients with esophageal cancer are in urgent need of symptom alleviation and/or concurrent intervention.

Key words: Esophageal cancer; Quality of life; Malnutrition; Nutritional support; PG-SGA

Introduction

Esophageal cancer is the eighth most common cancer worldwide (456,000 new cases in 2012; 3% of all cancers in 2012) [1] and is known for its marked variation by geographic region, ethnicity, and gender [2]. The incidence rates are significantly higher among men than women. It is rare among persons aged < 50 years [2], and incidence rates gradually increase with age. It is expected that the incidence of esophageal cancer will continue to rise [3] with the continuous development of industrialization and urbanization in China [4], becoming a major threat to human health. Because esophageal cancer is usually diagnosed in advanced stages [5], it has ranked sixth among cancer deaths worldwide (400,000 deaths in 2012) [6]. In the past decade, the patient quality of life (QoL) has been an important focus for evaluating the outcomes of therapy for esophageal cancer, particularly due to its low cure rate despite aggressive treatment [7].

The QoL is a concept introduced by the European

Organization for Cancer Research, which is based on the subjective feelings of the individuals involved and can be measured by a validated questionnaire known as the QoL Questionnaire Core 30 (QLQ-C30) [8]. QLQ-C30 includes 5 functional scales, 3 symptom scales, 6 single-item questions and questions about the global QoL. Quality of Life questionnaires can be used as screening tools to identify those who might benefit from psycho-social intervention [9]. The QoL of patients is significantly affected by esophageal cancer. There is also evidence indicating that a poor QoL is associated with poorer long-term survival in esophageal cancer patients [10]. Thus, it is important to identify the most prominent factors influencing QoL to provide better care that can improve the QoL among patients with esophageal cancer.

Material and Methods

Study design

This cross-sectional study was conducted to assess the QoL of patients with esophageal cancer, and to explore the main factors that affect the QoL of these patients. After receiving approval from the Research Ethics Board of the First Hospital of Hebei Medical University, face-to-face interviews are carried out from October 2011 to June 2016

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for a total of 1508 patients with malignant tumors from 52 hospitals in China.

Subjects

Patients pathologically diagnosed with esophageal cancer and aged at least 18 years old were eligible for inclusion in the study. Data collection was attributed to individual patients rather than individual admissions. The exclusion criteria were: 1) patients who were unwilling to participate in the study, 2) patients aged < 18 or > 90 years, 3) patients with physical or cognitive impairment, 4) patients with AIDS and recipients of organ transplants. Only the patients who met the inclusion criteria and provided signed consent were invited to participate in this study.

Instruments

A set of questionnaires was used to obtain information from the subjects. Demographic data were obtained through a questionnaire (including the patient's name, sex, age, education level, cancer stage, pathological type, etc.) designed by the authors. The PG-SGA [11], which was developed especially for cancer patients, covers seven items: body weight, food intake, symptoms, activities and function, disease and its relation to nutritional requirements, metabolic demand and the results of a physical examination to produce a global assessment of well-nourished or anabolic (A), moderate or suspected malnutrition (B) or severe malnutrition (C). For the global and functional scales, a higher score indicates better global and physical functioning; while for the symptom scale, a higher score indicates worse symptoms. The European Organization of Research and Treatment of Cancer Quality of Life questionnaire (EORTC QLQ-C30) was used to assess the patient quality of life. This instrument is a 30-item multi-dimensional cancer-specific questionnaire developed to assess the QoL of cancer patients in the following domains: functional scales, symptom scales, global QoL and single items. It contains five functional scales (physical, role, cognitive, emotional and social), symptom scales (appetite loss, nausea, vomiting, pain, dyspnea, constipation, diarrhea, fatigue, insomnia, financial difficulties) with one global health scale (GHS) and six single items assessing symptoms and the financial impact of the disease.

Statistical analysis

Information collected from patients at the interview included their age, sex, occupation, permanent residence, educational background, type of health insurance, staging of cancer, pathological type and PG-SGA. A numeric score was calculated in each dimension area of the QLQ-C30. Descriptive data were presented using medians (2nd quartile). For the multivariate analysis, the role of each covariate in the full model was assessed using the QoL as the primary outcome in a multilevel ordinal logistic regression analysis. The SPSS software (SPSS Inc., version 13.0) was utilized for the analyses. Values of $P < 0.05$ were considered to be

statistically significant.

Results

Patient characteristics

Interviews were conducted as face-to-face inquiries by professionals who were trained uniformly between June 2013 and June 2014. A total of 1508 patients were enrolled in the study, and 1223 had complete baseline information. Among these 1223 adults age > 18 years who resided in China, there were 1009 (82.5%) men and 214 (17.5%) women. Interviews were conducted in Chinese. Data were weighted to reflect their proportions in the population. Weighted variables included gender, age, permanent residence, health insurance, occupation, education, staging of cancer, and several other variables, the details of which are shown in Tables 1 and 2.

Table 1 Basic information of the study patients with esophageal cancer ($n = 1223$).

Characteristic	<i>n</i>	%
Gender		
Male	1009	82.5
Female	214	17.5
Age (years)		
< 65	719	58.8
≥ 65	504	41.2
Permanent residence		
Urban ¹	635	51.9
Rural ²	588	48.1
Health insurance		
Medicaid	1087	88.9
Self-pay	136	11.1
Occupation		
Worker ³	74	6.1
Farmer	523	42.8
Cadre ⁴	181	14.8
Retiree + others ⁵	445	36.4
Education		
Primary school or below	574	47.0
Junior/ high school or above	569	46.5
University	80	6.5

¹The patient's residence is municipalities or established towns;

²Patients are non-urban residence; ³Personal files are managed by the ministry of human resources and social security; ⁴Personal files are managed by the city's human resources department; ⁵Retiree or a patient who has worked in any job

Health-related quality of life in patients with esophageal cancer

Esophageal cancer seriously affects the QoL of patients. The scores of the physical functioning (PF), role functioning

(RF), cognitive functioning (CF), emotional functioning (EF) and social functioning (SF) scales were 86.67 (100.00), 83.33 (100.00), 91.67 (100.00), 100.00 (100.00) and 66.67 (100.00), respectively. The scores of three symptom domains (fatigue, nausea and vomiting, pain) were 22.22 (33.33), 0.00 (16.67) and 0.00 (33.33), respectively. Table 3 displays the values for each domain of the QLQ-C30 questionnaire. A multivariate ordinal logistic regression analysis of the main factors that affect the QOL showed that the general quality of life among patients with junior /high school or above-level education was higher than that of the patients with a primary school education or lower (OR: 1.44). Patients with nutritional support also had better general quality of life scores (OR: 1.91), and the PG-SGA scores were correlated with the quality of life, with odds ratios of 4.85, 2.79, 2.30, and 1.0, respectively, for PG-SGA scores of 0-1, 2-3, and 4-8 and ≥ 9 (Table 4). Variables are represented by M (Q).

Table 2 The clinical characteristics in patients with esophageal cancer ($n = 1223$).

Characteristic	<i>n</i>	%
Staging		
0	459	37.5
I	70	5.7
II	204	16.7
III	300	24.5
IV	190	15.5
Pathological typing		
Squamous cell	1033	84.5
Adenocarcinoma	79	6.5
Small cell	21	1.2
Mucinous	2	0.2
Other	88	7.2
Cancer treatment		
Surgery	270	22.1
Chemo-radiotherapy	332	27.1
Chemotherapy + surgery	291	23.8
No treatment	180	14.7
Other	150	12.3
PG-SGA		
0~1	73	6.0
2~3	96	7.9
4~8	179	14.6
≥ 9	875	71.5
NRS 2002		
< 3	612	50.0
≥ 3	608	49.7
Missing	3	0.03

Table 3 The quality of life in esophageal cancer patients ($n=1223$).

Variable	1st quartile	2nd quartile ¹	3rd quartile	4th quartile
General quality of life				
Global quality of life	50.00	58.33	66.67	100.00
General function				
Physical	73.33	86.67	100.00	100.00
Role	66.67	83.33	100.00	100.00
Emotional	75.00	91.67	100.00	100.00
Cognitive	83.33	100.00	100.00	100.00
Social	66.67	66.67	100.00	100.00
General symptom				
Fatigue	0.00	22.22	33.33	100.00
Nausea and vomiting	0.00	0.00	16.67	100.00
Pain	0.00	0.00	33.33	100.00
Dyspnea	0.00	0.00	33.33	100.00
Insomnia	0.00	0.00	33.33	100.00
Appetite loss	0.00	0.00	33.33	100.00
Cough	0.00	0.00	0.00	100.00
Diarrhea	0.00	0.00	0.00	100.00
Financial problems	0.00	33.33	66.67	100.00

¹Quartile is a numerical value in which all values are arranged from small to large in statistics and are divided into four equal positions. 2nd quartile is the median of all the values in the sample.

Table 4 The results of a multilevel ordinal logistic regression analysis of global health.

Factor	OR	P	95%CI
Education			
Junior /high school or above	1.44	0.003	1.13~1.83
Primary school or below	1.00		
Nutritional support			
Yes	1.91	0.000	1.52~2.41
No	1.00		
PG-SGA			
0~1	4.85	0.000	3.10~7.59
2~3	2.79	0.000	1.89~4.11
4~8	2.30	0.000	1.71~3.08
≥ 9	1.00		

Explanatory variables of the qoL: results of the multilevel ordinal logistic regression analysis

The results of the multilevel ordinal logistic regression analysis for global health are presented in Table 4. The total model likelihood ratio test is a comparative model that uses only the intercept. In our analysis, the -2 Log Likelihood decreased from 4072.715 to 3900.669 ($\chi^2 = 172.046$, $P < 0.0001$), indicating that at least one overall regression

coefficient of the independent variables was non-0, and the model was a good fit. The general quality of life among patients who had a junior /high school or above-level education was higher than that of the patients with primary school or lower-level education, with an *OR* value of 1.44.

The measurements for the 14 dimensions were all statistically compared. The impact of each item on the functional domains is shown in Table 5. Only items that had a significant impact on the functional domains of QoL were included. The impact of cancer treatments on patient outcomes and their quality of life was already well-recognized, and not surprisingly was confirmed in our population (functional domains *OR*: 2.38, 2.19, 1.47, 1.48, 1.54). In addition, we found that age has an impact on the PF, EF and CF (*OR*: 1.40, 0.80 and 1.27); occupation has a significant effect on the PF, EF, and CF (*OR*: 1.93, 2.38, 2.68); and nutritional support (*OR*: 2.61, 3.55, 1.92, 1.96 and 1.88) and the PG-SGA score (*OR*: 4.75, 4.84, 2.12, 2.81 and 3.00) have significant effects on the PF, RF, EF, CF and SF functional domains. Indicators that had a significant impact on symptom domains are shown in Table 6.

Table 5 The significance of factors based on a multilevel ordinal logistic regression analysis for the functional domains.

Variable	OR (95%CI)	P
Physical		
Age		
< 65 years	1.40 (1.12~1.74)	0.003
≥ 65 years	1.00	
Gender		
Female	0.65 (0.49~0.86)	0.003
Male	1.00	
Occupation		
Worker	1.93 (1.19~3.15)	0.014
Farmer	1.00	
Cancer treatment		
Other	2.38 (1.79~3.16)	0.000
Chemo + surgery	1.00	
Nutritional support		
Yes	2.61 (2.07~3.29)	0.000
No	1.00	
PG-SGA		
0~1	4.75 (2.85~5.63)	0.000
2~3	3.30 (2.11~4.37)	0.000
4~8	3.01 (2.14~3.84)	0.000
≥ 9	1.00	
Role		
Cancer treatment		
Other	2.19 (1.62~2.96)	0.000
Chemo-radiotherapy	1.41 (1.05~1.88)	0.020
Chemo + surgery	1.00	

Table 5 (Continued)

Health insurance		
Self-pay	0.68 (0.48~0.95)	0.025
Medical insurance	1.00	
Nutritional support		
Yes	3.55 (2.77~4.54)	0.000
No	1.00	
PG-SGA		
0~1	4.84 (2.70~8.67)	0.000
2~3	2.36 (1.52~3.67)	0.000
4~8	2.45 (1.76~3.42)	0.000
≥ 9	1.00	
Emotional		
Age		
< 65 years	0.80 (0.64~0.99)	0.049
≥ 65 years	1.00	
Occupation		
Worker	2.38 (1.45~3.92)	0.001
Retiree + others	1.54 (1.17~2.03)	0.002
Farmer	1.00	
Cancer treatment		
Other	1.47 (1.11~1.95)	0.007
Chemo-radiotherapy	1.57 (1.19~2.08)	0.001
Chemo + surgery	1.00	
Nutritional support		
Yes	1.92 (1.52~2.43)	0.000
No	1.00	
PG-SGA		
0~1	2.12 (1.32~3.41)	0.002
2~3	2.18 (1.43~3.33)	0.000
4~8	2.13 (1.55~2.92)	0.000
≥ 9	1.00	
Cognitive		
Age		
< 65 years	1.27 (1.01~1.6)	0.044
≥ 65 years	1.00	
Occupation		
Worker	2.68 (1.54~4.66)	0.000
Farmer	1.00	
Cancer treatment		
Other	1.48 (1.10~1.99)	0.010
Chemo + surgery	1.00	
Nutritional support		
Yes	1.96 (1.54~2.50)	0.000
No	1.00	
PG-SGA		
0~1	2.81 (1.62~4.87)	0.000
2~3	2.06 (1.32~3.20)	0.001

Table 5 (Continued)

4~8	2.23 (1.59~3.13)	0.000
≥ 9	1.00	
Social		
Cancer treatment		
Other	1.54 (1.16~2.05)	0.003
chemotherapy + surgery	1.00	
Health insurance		
Self-pay	0.67 (0.48~0.93)	0.017
Medical insurance	1.00	
Nutritional support		
Yes	1.88 (1.48~2.38)	0.000
No	1.00	
PG-SGA		
0~1	3.00 (1.85~4.63)	0.000
2~3	2.12 (1.73~2.92)	0.000
4~8	1.92 (1.40~2.58)	0.000
≥ 9	1.00	

Note: we analyzed the impact of all factors on quality of life, but only listed meaningful groups in each functional domain.

Table 6 The significance of factors after a multilevel ordinal logistic regression analysis for the symptom domains.

Variable	OR (95%CI)	P
Fatigue		
Gender		
Female	1.39 (1.04~1.84)	0.024
Male	1.00	
Occupation		
Worker	0.61 (0.38~0.99)	0.046
Farmer	1.00	
Cancer treatment		
Other	0.46 (0.34~0.60)	0.000
Chemo + surgery	1.00	
Nutritional support		
Yes	0.47 (0.37~0.59)	0.000
No	1.00	
PG-SGA		
0~1	0.24 (0.15~0.38)	0.000
2~3	0.27 (0.18~0.41)	0.000
4~8	0.37 (0.27~0.50)	0.000
≥ 9	1.00	
Nausea and vomiting		
Gender		
Female	1.46 (1.03~2.08)	0.033
Male	1.00	
Occupation		
Retiree + others	0.61 (0.43~0.88)	0.007

Table 6 (Continued)

Farmer	1.00	
Cancer treatment		
Other	0.49 (0.34~0.73)	0.000
Chemo + surgery	1.00	
Nutritional support		
Yes	0.53 (0.40~0.70)	0.000
No	1.00	
PG-SGA		
0~1	0.31 (0.14~0.64)	0.002
2~3	0.32 (0.17~0.62)	0.001
4~8	0.29 (0.18~0.47)	0.000
≥ 9	1.00	
Pain		
Cancer treatment		
Other	0.58 (0.43~0.79)	0.001
Chemo + surgery	1.00	
Nutritional support		
Yes	0.57 (0.45~0.72)	0.000
No	1.00	
PG-SGA		
0~1	0.24 (0.13~0.44)	0.000
2~3	0.35 (0.22~0.51)	0.000
4~8	0.45 (0.32~0.64)	0.000
≥ 9	1.00	
Dyspnea		
Cancer treatment		
Other	0.39 (0.25~0.56)	0.000
Chemo-radiotherapy	0.62 (0.41~0.86)	0.005
Chemo + surgery	1.00	
Nutritional support		
Yes	0.54 (0.41~0.72)	0.000
No	1.00	
PG-SGA		
0~1	0.46 (0.22~0.93)	0.030
≥ 9	1.00	
Insomnia		
Gender		
Female	1.37 (1.01~1.86)	0.043
Male	1.00	
Permanent residence		
Urban	1.49 (1.15~1.94)	0.003
Rural	1.00	
Occupation		
Worker	0.56 (0.33~0.97)	0.037
Farmer	1.00	
Nutritional support		
Yes	0.56 (0.43~0.71)	0.000

Table 6 (Continued)

No	1.00	
PG-SGA		
0~1	0.29 (0.16~0.52)	0.000
2~3	0.51 (0.32~0.81)	0.004
4~8	0.55 (0.39~0.77)	0.001
≥ 9	1.00	
Appetite loss		
Occupation		
Worker	0.56 (0.31~0.99)	0.048
Farmer	1.00	
Cancer treatment		
Other	0.41 (0.29~0.58)	0.000
Chemo + surgery	1.00	
Nutritional support		
Yes	0.55 (0.42~0.71)	0.000
No	1.00	
PG-SGA		
0~1	0.16 (0.08~0.33)	0.000
2~3	0.10 (0.04~0.20)	0.000
4~8	0.24 (0.16~0.36)	0.000
≥ 9	1.00	
Cough		
Gender		
Male	1.47 (1.00~2.15)	0.048
Female	1.00	
Nutritional support		
Yes	0.59 (0.43~0.81)	0.001
No	1.00	
PG-SGA		
0~1	0.16 (0.05~0.52)	0.002
2~3	0.42 (0.23~0.56)	0.014
4~8	0.31 (0.18~0.55)	0.000
≥ 9	1.00	
Diarrhea		
Cancer treatment		
Other	0.38 (0.22~0.66)	0.001
Chemo-radiotherapy	0.42 (0.25~0.71)	0.001
Chemo + surgery	1.00	
PG-SGA		
0~1	0.20 (0.05~0.83)	0.027
≥ 9	1.00	
Financial problems		
Age		
< 65 years	1.56 (1.25~1.96)	0.000
≥ 65 years	1.00	
Permanent residence		
Urban	0.72 (0.56~0.92)	0.008

Table 6 (Continued)

Rural	1.00	
Education		
Primary school or below	0.57 (0.35~0.92)	0.023
University	1.00	
Occupation		
Cadre	0.65 (0.45~0.94)	0.021
Worker	0.52 (0.32~0.85)	0.008
Retiree + others	0.56 (0.42~0.74)	0.000
Farmer	1.00	
Cancer treatment		
Other	0.69 (0.52~0.92)	0.011
Surgery	0.68 (0.48~0.96)	0.026
Chemo + surgery	1.00	
PG-SGA		
0~1	0.37 (0.23~0.58)	0.000
2~3	0.38 (0.25~0.57)	0.000
4~8	0.49 (0.36~0.67)	0.000
≥ 9	1.00	

Note: we analyzed the impact of all factors on symptom domains of QoL, but only listed meaningful groups to avoid the complexity of the table.

Discussion

Quality of Life is a multidimensional concept emphasizing the subjective feelings and functional status of patients, with dimensions encompassing physical, social, and psychological functioning [12]. Previous studies have shown that the physical, societal, emotional and other functions of esophageal cancer patients were significantly decreased, and their quality of life was lower than that of healthy subjects [13]. Although it is well-known that symptoms related to esophageal cancer, such as dysphagia, reflux, eating difficulties, diarrhea, appetite loss, are contributors to a poorer QoL [14], the relative influence of other factors, such as the patient demographics and socioeconomic status, have rarely been evaluated. To assess the importance of these factor and implement further targeted interventions, we evaluated the relationships between the nutritional status, demographic information, and socioeconomic variables to all dimensions of the QoL in individuals with esophageal cancer.

Previous studies suggested that 50%~90% of oncology patients have some degree of malnutrition [15]. In the current study, the PG-SGA revealed that only 6.0% of the patients were well-nourished, which was consistent with the results reported by Quyen TC et al. [16], indicating that esophageal cancer patients are more likely to suffer from malnutrition than those with other types of cancers. Decreased dietary intake, metabolic changes, cancer cachexia, and esophageal cancer-related symptoms may synergistically contribute to cancer-related malnutrition in cancer patients [17]. Lis CG et al. demonstrated a strong associa-

tion between the nutritional status and QoL in patients with head and neck cancer, gastrointestinal cancer, lung cancer and gynecological cancer by reviewing extensive available literature [18]. The results of our current ordinal logistic regression analysis showed that malnutrition is one of the main causes of the decline in QoL among esophageal cancer patients. Not surprisingly, the QoL of the well-nourished patients was higher than that of the patients who were malnourished (as defined by PG-SGA score > 2).

We then analyzed the potential influence of nutritional support. The results demonstrated that patients who were provided with nutritional support had better PF, RF, CF, EF and SF scales, with OR values ranging from 1.86 to 3.50, and these patients were less likely to have high symptomatic risk (except for diarrhea and economic difficulties) than those without nutritional support (OR: 0.45 - 0.58). Senesse P et al. [19] also found that home parenteral nutrition (HPN) could benefit the quality of life for malnourished patients with gastrointestinal cancer. In patients with advanced cancer, the PG-SGA is a reliable and effective nutritional screening index, and has the advantages of being a rapid, noninvasive and easy-to-perform test to dynamically evaluate the nutritional status of patients.

A few studies have suggested that a poor QoL is associated with poorer long-term survival in esophageal cancer patients [20]. Additionally, clinicians must take the patients' perception of their QoL into consideration. Decision-making and the management of esophageal cancer would be best performed by a multidisciplinary committee and should be personalized for the specific circumstances of each case [21,22]. Identifying the factors that influence the patient QoL and then giving the necessary treatment and nursing measures are vitally important for patients with esophageal cancer [23].

There are a few limitations of this study that require attention or improvements. The cross-sectional nature of this project makes it impossible to make any causal inferences regarding the relationship between malnutrition and QoL. Further studies are needed to assess whether the QoL and the survival rate of the patients with esophageal cancer were improved after nutritional intervention. Secondly, there were significantly more men ($n = 1009$) than women ($n = 214$) in this study. In 2016, the National Central Cancer Registry (NCCR) collected registration data for 2013 from local cancer registries to estimate the cancer incidence rates in China. The age-standardized incidence rate of esophageal cancer in China was 13.82/100,000 (20.14/100,000 men and 7.65/100,000 women). Therefore, there is a certain selection bias in this study due to the gender-specific incidence rates.

In summary, we found that nutritional support and the PG-SGA score variables were significantly associated with the QoL in patients with esophageal cancer.

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Conflict of Interests

The authors declare no conflict of interest.

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