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Quality of life in patients with esophageal cancer receiving definitive chemoradiotherapy or esophagectomy

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Abstract. The aim of the present study was to assess the variation in the quality of life (QOL) of patients with esophageal cancer receiving definitive chemoradiotherapy or esophagectomy, and to explore the main factors that affects QOL. A total of 102 patients with esophageal cancer receiving definitive chemoradiotherapy or esophagectomy were assessed using a QOL questionnaire, and a numeric score was calculated in each conceptual area and compared with reference data by a statistical method. With regards to the impacts on the QOL, the chemoradiotherapy had less of an impact compared with esophagectomy. The QOL declined following the two treatments, but was restored in a specific period of time. In the present study, the main factors that affected the QOL of patients included physical function, fatigue and pain. Definitive chemoradiotherapy is therefore superior to esophagectomy with regard to its effect on the QOL. The two treatments had an effect on the QOL of patients, but this effect was temporary and was resumed after a period of time.

Introduction

Esophageal cancer is a common type of cancer, particularly in China. There are ~310,000 new esophageal cancer patients annually worldwide, with half of the cases originating from China. Currently, the treatments include esophagectomy, radiotherapy, chemotherapy or a combination thereof. However, the prognosis of patients with esophageal carcinoma is generally poor (1). As is widely known, any therapeutic schedule injures the normal tissue whilst simultaneously killing cancer cells, and this has a negative effect on the quality of life (QOL) for patients. The QOL in patients is a concept introduced by the European Organization for cancer research, which can be measured by a questionnaire known as the QOL questionnaire core 30 (QLQ-C30) (2). QOL is based on the subjective feelings of the individuals involved. However, the validity and sensitivity of QLQ-C30 has been previously confirmed by a number of institutes and therefore serves as a useful tool for obtaining objective information (3). The QLQ-C30 questionnaire has been used as one type of indicator for physical activity, psychological disorder and social adjustment in numerous countries, and it explores the variation of the QOL of patients with cancer (4,5). Prolonging the life span as well as improving the QOL of patients is important. However, patients with cancer usually have a poor QOL due to physical and psychological disorders. Therefore, identifying the therapy that has less of an effect on the QOL is important, particularly for older patients. The present study aimed to provide a fundamental basis for improving the QOL of patients.

Patients and methods

Study design. The QLQ-C30 questionnaire was used to investigate sampled patients during various time periods. The five function domains assessed were physical, role, emotional, cognitive and social function, nine symptom domains, including fatigue, nausea and vomiting, pain, dyspnea, insomnia, anorexia, constipation, diarrhea and economic difficulty, as well as one general health situation in the questionnaire. The higher the scores in the function field and general health situation, the better the QOL. The scores for the symptom field represented the opposite. Information concerning the general characteristics of patients, such as age, gender and the pathology of the tumor, was also collected. In order to avoid misconception, the investigator explained the meaning of each QOL questionnaire item to the patients prior to the study. Data were collected by the investigator after patient approval was obtained. Demographic and treatment information was obtained from a clinical chart.

Patient selection criteria and treatment administration. Between June 2011 and January 2013, 102 patients with esophageal cancer were sampled and required to complete the QOL questionnaire at the Qianfoshan Hospital (Jinan, Shandong, China). All the patients were voluntary in attending the questionnaire investigation and it was their first time receiving therapy. The questionnaire was completed before, 1 month after and 6 months after the two treatments. None of the patients had any severe illness in previous medical records, such as myocardial infarction, and had a Karnofsky performance

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score of ≥70 and no distant metastasis. Subsequently the patients were provided a semi-liquid diet. All the patients were divided into two groups according to their willingness and physical condition. One group was provided precise radiotherapy (including three dimensional-conformal radiotherapy and intensity-modulated radiotherapy; n=52), and were simultaneously administered 4 cycles of concurrent chemotherapy, consisting of intravenous daily cisplatin (12.5 mg/m^2/day; days 1-5) and docetaxel (60 mg/m^2/day; day 1), with the next cycle being initiated 21 days later. Chemotherapy was initiated on the first day of radiotherapy. The second group was administered an esophagectomy (n=50). Precise radiotherapy was based on three-dimensional computer tomography planning, and was applied using a treatment planning system (XiO 4.2; Elekta., Stockholm, Sweden; or Eclipse 10.0; Varian Medical Systems, Palo Alto, CA, USA). Following the formation of a plan, radiotherapy was administered at a dose of 60-66 Gy in 6-6.5 weeks; 2 Gy/fraction/day, 5 fractions/week. A total of 50 patients underwent thoracotomy for curative resection by esophagectomy.

Ethics Statement. Ethics approval was obtained from Qianfoshan Hospital. Quality of life in patients with esophageal cancer receiving definitive chemoradiotherapy or esophagectomy was maintained. Data were collected following patient's concent.

Statistical analysis. All the data were analyzed by SPSS 17.0 (SPSS, Inc., Chicago, IL, USA), the significance of all observed data was determined on the basis of P<0.05, which was considered to indicate a statistically significant difference, with the exception of the data shown in Table VI (P<0.01). The χ^2 test was used to compare the general characteristics of patients for the different treatments. Independent t-test was used to calculate the average scores of function scales for the different treatment. The rank-sum test was used to calculate the difference between the symptom domains, denoted by Z. Data from the symptom domains were presented as the median, 25% percent of values and 75% percent of values. Analysis of variance was used to compare the difference between the function domains during different time periods. Multiple stepwise regression was used to explore the main factors that affect general health.

Results

All the patients finished the QOL questionnaire within the designed experimental period. There were a total of 69 male patients and 33 females, with a mean age of 53.5 years (range, 39-85 years). In the study, 52 patients were administered concurrent chemoradiotherapy (51%, group 1) and 50 patients underwent surgery (49%, group 2). Approximately half of the patients came from the countryside, and had little knowledge of their illness. A total of four-fifths of the patients had various financial difficulties.

The χ^2 test was used to explore the general characteristics of the radiation and surgery groups. Comparing the two groups, the difference between gender, age, clinical staging, location of neoplasm, pathological type, smoking and drinking had no statistical significance (Table I). The difference in the function and symptom domains had no statistical significance

Table I. Difference between the general characteristics for patients undergoing radiation or surgical treatment.

Characteristics	Radiation	Surgery	χ^2	P-value
Gender				
Male	38	33	0.60	0.44
Female	14	17		
Age				
<65	23	28	1.41	0.23
≥65	29	22		
Pathological				
Squamous	45	42	0.73	0.69
Adenocarcinoma	5	7		
Others	2	1		
Location				
Upper	19	9	4.60	0.10
Middle	21	24		
Low	12	17		
Staging				
0-I	5	8	4.57	0.21
II	16	22		
III	20	15		
IV	11	5		
Smoking				
Yes	33	27	0.94	0.33
No	19	23		
Drinking				
Yes	29	26	0.15	0.70
No	23	24		

Table II. Difference between function domains for treatments.

Function domain	Radiation	Surgery	t-test	P-value
Prior to therapy				
Physical	75.34±22.64	73.27±22.58	0.46	0.64
Role	72.75±20.62	69.20±22.00	0.84	0.40
Emotional	72.44±22.36	60.50±22.82	2.67	0.01
Cognitive	74.52±22.35	76.50±23.24	-0.44	0.66
Social	69.23±25.70	61.17±24.72	1.61	0.11
General health	65.55±23.74	62.50±23.82	0.64	0.52
1 month after therapy				
Physical	67.69±20.67	58.13±18.62	2.44	0.02
Role	67.31±23.79	62.00±18.47	1.26	0.21
Emotional	75.48±20.77	65.50±19.19	2.52	0.01
Cognitive	76.60±21.58	77.67±21.06	-0.25	0.80
Social	71.31±23.48	64.17±19.80	1.66	0.10
General health	58.36±20.04	50.17±19.67	2.09	0.04
6 months after therapy				
Physical	83.14±12.48	81.67±14.97	0.54	0.59
Role	78.20±17.32	80.00±16.50	-0.53	0.59
Emotional	81.28±14.50	72.50±20.91	2.47	0.02
Cognitive	78.36±18.40	80.83±18.92	-0.67	0.51
Social	80.61±19.58	72.67±24.63	1.81	0.07
General health	76.28±17.80	75.50±16.70	0.23	0.82

Data are presented as mean ± standard deviation.

Table III. Difference between the symptom domains for patients undergoing radiation or surgical treatment.

Symptom domain	Radiation	Surgery	Z	P-value
Prior to therapy				
Fatigue	22.22 (11.11, 33.33)	22.22 (11.11, 36.11)	0.08	0.78
Nausea	0.00 (0.00, 16.66)	0.00 (0.00, 33.33)	0.48	0.49
Pain	0.00 (0.00, 33.33)	0.00 (0.00, 33.33)	0.78	0.38
Dyspnea	0.00 (0.00, 33.33)	0.00 (0.00, 33.33)	0.03	0.86
Insomnia	0.00 (0.00, 58.33)	0.00 (0.00, 33.33)	1.30	0.25
Anorexia	0.00 (0.00, 33.33)	0.00 (0.00, 33.33)	0.00	0.97
Constipation	0.00 (0.00, 66.66)	0.00 (0.00, 33.33)	0.67	0.41
Diarrhea	0.00 (0.00, 0.00)	0.00 (0.00, 33.33)	0.57	0.45
Economic situation	0.00 (0.00, 66.66)	0.00 (0.00, 66.66)	0.23	0.63
One month after therapy				
Fatigue	33.33 (13.89, 55.55)	33.33 (22.22, 55.55)	0.83	0.36
Nausea	0.00 (0.00, 33.33)	0.00 (0.00, 33.33)	0.73	0.39
Pain	33.33 (0.00, 33.33)	33.33 (16.66, 66.66)	4.62	0.03
Dyspnea	0.00 (0.00, 33.33)	0.00 (0.00, 33.33)	0.20	0.66
Insomnia	0.00 (0.00, 33.33)	0.00 (0.00, 33.33)	0.55	0.46
Anorexia	0.00 (0.00, 33.33)	33.33 (0.00, 66.66)	4.20	0.04
Constipation	0.00 (0.00, 33.33)	0.00 (0.00, 33.33)	0.25	0.62
Diarrhea	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.15	0.70
Economic situation	0.00 (0.00, 66.66)	0.00 (0.00, 33.33)	1.87	0.17
Six months after therapy				
Fatigue	22.22 (0.00, 33.33)	27.77 (0.00, 33.33)	0.10	0.75
Nausea	0.00 (0.00, 12.50)	0.00 (0.00, 33.33)	0.34	0.56
Pain	25.00 (0.00, 33.33)	0.00 (0.00, 50.00)	3.10	0.08
Dyspnea	0.00 (0.00, 33.33)	0.00 (0.00, 33.33)	0.26	0.61
Insomnia	0.00 (0.00, 33.33)	0.00 (0.00, 33.33)	0.08	0.77
Anorexia	0.00 (0.00, 25.00)	0.00 (0.00, 33.33)	1.77	0.18
Constipation	0.00 (0.00, 33.33)	0.00 (0.00, 33.33)	0.07	0.79
Diarrhea	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	1.01	0.32
Economic situation	0.00 (0.00, 66.66)	0.00 (0.00, 33.33)	2.74	0.10

prior to therapy, except for the emotional function domain (Tables II and III). The mean score of the emotional function domain in the surgery group was significantly lower than the radiation group prior to therapy (Table II). The difference of the two groups was statistically significant in the domains of physical function, emotional function, general health situation, pain and anorexia 1 month after therapy. The difference for the other domains 1 month after therapy were not statistically significant (Tables II and III). The scores of the two groups for all the domains had no statistically significant difference 6 months after therapy, except for the emotional domain, which was $P<0.05$. The variation of the two groups during the different time periods are shown in Tables IV and V. The scores of the function and symptom domains were different at the various periods; the scores of the majority of function domains reduced following treatment, but restored in the 6 months after treatment. The differences in the radiotherapy group in the various periods had statistical significance in the domains of physical, role, social, general health, fatigue and pain (Tables IV and V). In the surgery group, the scores of all function domains, except the domain of cognitive, had statistical significance (Table IV). The scores in the symptom domain were only statistically significant for the fatigue, pain and anorexia domains (Table V).

The scores of the general health situation were established as the dependent variable, and the scores of the function and symptom domains were the independent variable. Multiple linear regression was used to explore all the data. It was shown that the effects on the general health, physical function and fatigue prior to radiation; social function, fatigue and pain 1 month after radiation; and physical function in the 6 months after radiation had statistical significance ($P<0.01$). In the second group, physical function and fatigue prior to surgery; physical function, fatigue and pain 1 month after surgery; and physical and role function in the 6 months after surgery had an important effect on the general health ($P<0.01$). The factors that affect general health are shown in Table VI.

Discussion

The number of patients with esophageal cancer is currently on the increase. Esophageal cancer is usually associated with a poor prognosis due to a high local recurrence rate or distant metastasis (6). Although surgery alone or chemoradiotherapy have been widely accepted as the standard treatment for esophageal cancer, the 5-year survival rate is only 20-30% (7,8). The most efficient treatment remains uncertain as there are only a few clinical trials that have compared chemoradiotherapy and

Table IV. Difference between function domains for patients undergoing radiation or surgical treatment.

Function domain	Prior to therapy	One month after therapy	Six months after therapy	F	P-value
Radiation					
PF	75.34±22.64	67.69±20.67	83.14±12.48	8.47	0.00
RF	72.75±20.62	67.31±23.79	78.20±17.32	3.59	0.03
EF	72.44±22.36	75.48±20.77	81.28±14.50	2.76	0.07
CF	74.52±22.35	76.60±21.58	78.36±18.40	0.44	0.64
SF	69.23±25.70	71.31±23.48	80.61±19.58	3.59	0.03
TH	65.55±23.74	58.36±20.04	76.28±17.80	9.89	0.00
Surgery					
PF	73.27±22.58	58.13±18.62	81.67±14.97	19.74	0.00
RF	69.20±22.00	62.00±18.47	80.00±16.50	11.22	0.00
EF	60.50±22.82	65.50±19.19	72.50±20.91	4.11	0.02
CF	76.50±23.24	77.67±21.06	80.83±18.92	0.56	0.57
SF	61.17±24.72	64.17±19.80	72.67±24.63	3.32	0.04
TH	62.50±23.82	50.17±19.67	75.50±16.70	19.52	0.00

PF, physical function; RF, role function; EF, emotional function; CF, cognitive function; SF, social function; TH, total health.

Table V. Difference between emotional domains for various treatment periods.

Emotion domain	Prior to T	One month after T	Six months after T	Z	P-value
Radiation					
Fatigue	74.21	92.36	68.93	7.91	0.02
Nausea	78.38	81.67	75.45	0.78	0.68
Pain	77.07	92.61	65.83	10.71	0.01
Dyspnea	79.50	80.13	75.87	0.39	0.82
Insomnia	84.62	77.56	73.33	2.18	0.34
Anorexia	86.53	80.49	68.48	5.79	0.06
Constipation	81.62	76.57	77.32	0.53	0.77
Diarrhea	76.40	79.21	79.88	0.33	0.85
Economic	77.10	79.95	78.45	0.12	0.94
Surgery					
Fatigue	67.30	91.43	67.77	10.56	0.01
Nausea	75.40	79.53	71.51	1.20	0.55
Pain	59.92	94.76	71.82	18.61	0.00
Dyspnea	77.19	73.29	76.02	0.30	0.86
Insomnia	78.20	74.60	73.30	0.44	0.80
Anorexia	67.70	88.32	70.58	8.33	0.02
Constipation	74.14	74.90	77.46	0.25	0.88
Diarrhea	79.22	75.37	71.91	1.42	0.49
Economic	79.47	75.48	71.55	1.10	0.58

Data are presented as the mean of the rank-sum test. T, therapy.

esophagectomy (9,10). It is well known that radiotherapy can cause numerous complications, including radiation esophagitis, radiation pneumonitis and anorexia (10,11). During radiotherapy, dysphagia of patients may become aggravated due to radiation edema of the esophagus, which induces a feeding disturbance. Patients who have undergone esophagectomy also suffer from continual problems associated with the function domains and specific symptoms. Particular studies have indicated that surgery also has an effect on the QOL (12-14). QOL is one of the important factors for patients choosing to undergo therapy, particularly for older patients. Therefore, it is important to determine the variation in QOL for different treatments, and investigation of the factors that affect the QOL is necessary to provide a reference for clinicians to improve the QOL for patients. Since the 1990s, the potential contribution of the QOL for cancer therapy evaluation has gained increasing recognition. QOL assessment has been used to identify the optimal therapy, estimate the efficiency of drugs and as one type of indicator for the prognosis of cancer. A study by Dancey *et al* (15) used the QLQ-C30 to evaluate the QOL of 851 patients with cancer, and the higher score of the general health situation was found to be associated with a longer life span. The QOL is also applied as an indicator for the prognosis of esophageal cancer (16). Fang *et al* (17) found that the physical function of the QOL was the most important indicator of prognosis for patients receiving radiation for treatment of esophageal cancer. The Food and Drug Administration of America have confirmed QOL as one important index for assessment of novel anticancer drugs (18). However, there are few studies regarding QOL variation following different esophageal cancer treatments (19,20). In order to find the variation of QOL, the present study aimed to compare the QOL between concurrent chemoradiotherapy and surgery for patients with esophageal cancer during the same time period.

As well as being an important endpoint in clinical trials, measures of the QOL are currently used to define the psychosocial aspects of disease and its treatment, which may be as important

Table VI. Factors affecting general health.

Domain	R^2	F	P-value
Prior to radiation			
PF	0.44	39.25	0.00
Fatigue	0.40	33.53	0.00
One month after radiation			
SF	0.51	51.34	0.00
Fatigue	0.45	41.96	0.00
Pain	0.30	21.71	0.00
Six months after radiation			
PF	0.62	80.62	0.00
Prior to surgery			
PF	0.63	82.44	0.00
Fatigue	0.58	67.57	0.00
One month after surgery			
PF	0.66	90.94	0.00
Fatigue	0.43	36.95	0.00
Pain	0.24	15.32	0.00
Six months after surgery			
PF	0.75	145.54	0.00
RF	0.47	42.48	0.00

PF, physical function; SF, social function; RF, role function.

as the physical effects (21). About half of the Chinese patients in the present study originate from the countryside, and have little knowledge with regards to cancer. There is evidence that patients with esophageal cancer usually undergo feelings that include nervousness and depression (22,23). These psychological disorders affect the acceptance of treatment and the curative effect of patients. Therefore, offering knowledge regarding the treatment and providing therapy to relieve psychological disorders was beneficial for patients. In the present study, the score of the emotional function was lowest prior to treatment, and 1 month after treatment the score was higher but remained lower than the score 6 months after treatment. The emotional disorder of patients recovered with time (Table V). Psychological education is important for patients, and by explaining the various ways to deal with psychological problems and encouraging participation in social activities can improve the faith of patients in defeating illness and improve QOL.

Results of the present study show that the QOL of patients following therapy is worse than prior to therapy, but is resumed 6 months after treatment. The mean score of the surgery group was significantly lower than that of the radiation group, which indicates that the patients had a greater fear to surgical treatment. The general health situation of the two groups after 6 months of treatment was improved compared to the prior to treatment period. With regards to the QOL, chemoradiotherapy had a lower impact than surgery, particularly in the domains of physical function, emotional function and general health situation. Therefore, the study has shown that undergoing chemoradiotherapy is more efficient than surgery due to the lower effect on the QOL, particularly for older patients. There were numerous factors that affect QOL, and the disorders of physical function and fatigue played significant roles. The QOL scores declined 1 month after administration of the two treatments, both of which had an impact on the QOL. The reduction of the QOL may affect the daily lives of patients. Patients usually feel pain and an obstruction in esophagus subsequent to receiving the two treatments, and even reject feeding and continuing radiation. In order to improve the QOL of patients, it is necessary to administer antibiotics and hormones to relieve tissue edema and constriction of the esophagus during the treatment. In addition, encouraging patients to participate in social activity, form good eating habits and overcome mental handicaps is important. Avoiding spicy food, wine and tobacco is beneficial for patients (?). Patients with cancer usually have a poor QOL and short life spans. Therefore, selection of the most efficient treatment for patients, while improving the QOL as much as possible is crucial. However, how the QOL of patients with cancer may be improved has not induced enough attention from doctors. The present study suggests that the two treatments can reduce the QOL of patients. As the subjective feelings of patients are as important as the curative effect, doctors should administer more attention to the QOL with the aim of improving it in the future.

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