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Original Article

Impacts of physically active and under-active on clinical outcomes of esophageal cancer patients undergoing esophagectomy

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Abstract: Physical activity has been reported to positively influence quality of life and survival in certain cancers. However, the associations between them in esophageal cancer are previously undefined. The aims of this study are to investigate whether physically active esophageal cancer patients have improved quality of life and lower risk of recurrence as well as death compared with physically inactive patients. We evaluated the relationships between postoperative leisure time physical activity and quality of life and recurrence and death among patients diagnosed with esophageal cancer. We respectively used generalized estimating equations and Cox proportional regression to analysis quality of life and survival, adjusting for known potential confounding factors. Comparing esophageal cancer patients reporting more than 9 MET hours per week of postoperative leisure time physical activity with those reporting less, we found improved quality of life. Additionally, we also found that postoperative leisure time physical activity ≥9 MET hours per week, compared with less, was associated with a 23% lower risk of all-cause mortality (HR, 0.666; 95% CI, 0.481-0.921; *P*=0.014) and a 53% lower risk of recurrence (HR, 0.306; 95% CI 0.218-0.429; *P*<0.001). Leisure time physical activity was significantly associated with quality of life and risk of recurrence and death of esophageal cancer patients. Clinicians should consider increasing physical activity, regardless of previous behaviors, as a part of primary cancer treatment. The ultimate goal is to improve quality of life and prolong survival of cancer survivors.

Keywords: Physical activity, quality of life, survival, esophageal cancer

Introduction

Esophageal cancer (EC) has been one of the leading malignancies influencing public health around the world. An estimated 455,800 new EC cases and 400,200 EC-caused deaths occurred in 2012 worldwide [1]. Esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (AC) are the two major histologic forms of it [2]. Due to lack of clinical symptoms in early stage, the majority of individuals presenting with EC are diagnosed with advanced disease. Even though these patients may benefit from esophagectomy and perioperative sequential or concurrent chemoradiotherapy, the outcomes are still relatively poor, with unsatisfactory quality of life (QOL) and 5-year survival rates around 15-20% [3].

Physical activity, with its contributions towards supportive care outcomes in cancer patients including QOL, physical fitness, physical function and cancer-related fatigue has been well reported in previous literatures [4-7]. Additionally, several large observational studies have also reported that physical activity could improve pulmonary and cardiovascular function, strengthen muscle, affect body image and mood, strengthen immunity, maintain independence and mobility, thus reducing the physical and psychological symptoms and improving QOL during cancer treatment [8-12]. Because of benefitting from physical activity, it is more likely to facilitate greater physical and psychological developments during the recovery process of cancer treatment, which takes place following surgery, radiotherapy and chemotherapy.

Moreover, epidemiological data documented that physical activity has been strongly linked to cancer risk including breast cancer [13], lung cancer [14], colorectal cancer [15], pancreatic cancer [16], endometrial cancer [17] and bladder cancer [18]. These studies consistently concluded that increasing physical activity level

was associated with meaningful reductions in risk of cancer. In this way, there was reason to believe that physical activity might extend survival in cancer patients. To date, this hypothesis has been demonstrated in several crucial studies, which have reported that physical activity could decrease cancer recurrence and death to prolong overall survival (OS) and disease-free survival (DFS) [19-23].

It is critical for cancer patients and clinicians to know how they can improve QOL and enhance survival during cancer treatment and recovery phases, and whether behavioral choice, for example leisure time physical activity, can provide benefit. The countless beneficial effects of physical activity have already been observed. However, no previous studies have assessed the associations between leisure time physical activity and QOL and survival of EC patients undergoing esophagectomy after diagnosis. We are the first to evaluate that the impact of leisure time physical activity level on QOL and survival in EC patients. Our hypotheses are that patients who have higher levels of leisure time physical activity postoperative will: (1) have better health-related QOL; (2) have longer DFS and OS. Once these hypotheses will be demonstrated, our results indicate that clinicians should consider increasing leisure time physical activity, regardless of previous behaviors, as a part of primary cancer treatment to improve QOL and prolong survival of EC cancer survivors.

Materials and methods

Study population

Patients were eligible for inclusion in this study: (1) if they had undergone esophagectomy with curative intent due to a newly diagnosed EC on between January 2012 and December 2012 at the Department of Thoracic Surgery, Qilu Hospital of Shandong University; (2) their complete clinical and pathological data could be collected. Patients were excluded if they received preoperative adjunctive therapy or if they were lost to follow-up. This study was approved by Qilu Hospital of Shandong University's Ethics Review Committee. All participants provided written informed consent.

Data collection

The complete clinical and pathological data were obtained from patients' medical records. The conditions of education and income, the patients' postoperative weight were obtained via telephone interviews inquiring patients or their kin. All tumors were staged in accordance with the American Joint Committee on Cancer staging manual [24]. The cutoff point of alcohol was based on the 2011 Chinese Inhabitant Dietary Guideline. The cutoff values of tumor length and the lymph node ratio were in accordance with previous article [25].

Physical activity assessment

We assessed leisure time physical activity in metabolic equivalent task (MET) hours per week after esophagectomy. Every EC patient or their kin was asked "what was average time per week spent at each of the following activities after operative"? Choices included walking at normal pace, jogging (≤10 minutes per mile), running (>10 minutes per mile), bicycling, swimming or water exercises, ball sports, exercise classes, social dancing, and other activities. These activities were the most common ones in China. Each reported activity was converted into MET score on the basis of the classification by Ainsworth et al. [26]. One MET is defined as the energy cost for sitting quietly and is set at 3.5 ml/kg per minute of oxygen. MET score is the ratio of the associated metabolic rate for a specific activity to the resting metabolic rate. The scores for MET hours per week for each activity were calculated from the self-reported hours per week participated in that activity multiplied by the associated MET score. Eventually, the score from the each activity was summed for a total MET hours per week score. For the classification of levels of physical activity, two groups were divided: <9 MET hours per week group and ≥9 MET hours per week group. The cutoff value of physical activity is based on previous articles [22, 27, 28], consistently reporting that more than 9 MET hours per week of physical activity has been linked to developed cancer outcomes. Moreover, the cutoff point is also depended on the health guidelines about physical activity for health proposed by the World Health Organization [29].

QOL assessment

The primary end point of this study was the QOL of EC survivors at 3 years after surgery. The QOL was assessed at diagnosis and 36 months among EC survivors postoperative. To evaluate

Table 1 Patients characteristics

Characteristics	Postoperative leisure time physical activity, MET-h/wk (n=303)		*p* value
	<9 (n=157)	≥9 (n=146)	
Age (years)	65.006±7.449	63.685±7.581	0.127
Gender (M:F)	135:22	117:29	0.174
Education			
High school and below	133 (84.713%)	122 (83.562%)	0.784
Some college and above	24 (15.287%)	24 (16.438%)	
Income (RMB/month)			0.422
<1000	56 (35.669%)	61 (41.781%)	
1000~2000	47 (29.936%)	35 (23.973%)	
>2000	54 (34.395%)	50 (34.246%)	
BMI (kg/m^2)	21.848±2.889	21.142±3.241	0.046
Smoking (pack-year)			0.226
<20	86 (54.777%)	90 (61.644%)	
≥20	71 (45.223%	56 (38.356%)	
Alcohol (kg/day)			0.660
≤0.025	106 (67.516%)	102 (69.863%)	
>0.025	51 (32.484%)	44 (30.137%)	
Past medical history			
HBP	31 (19.745%)	28 (19.178%)	0.901
CAD	9 (5.732%)	11 (7.534%)	0.528
Diabetes	5 (3.185%)	8 (5.479%)	0.325
Tumor information			
Pathology			0.027
SCC	140 (89.172%)	140 (95.890%)	
AC	17 (10.828%)	6 (4.110%)	
Histological grade			0.475
Well	28 (17.834%)	19 (13.014%)	
Moderately	61 (38.854%)	57 (39.041%)	
Poorly/undifferentiated	68 (43.312%)	70 (47.945%)	
Location			0.609
Cervical/upper/middle	97 (61.783%)	86 (58.904%)	
Low	60 (38.217%)	60 (41.096%)	
Length<3 cm	58 (36.943%)	69 (47.260%)	0.069
T category			0.798
0	3 (1.911%)	5 (3.425%)	
1	22 (14.013%)	21 (14.384%)	
2	46 (29.299%)	46 (31.507%)	
3	80 (50.955%)	71 (48.630%)	
4	6 (3.822%)	3 (2.054%)	
TNM stage			0.195
0/I/II	93 (59.236%)	97 (66.438%)	
III/IV	64 (40.764%)	49 (33.562%)	
Lymph node metastasis	74 (47.134%)	62 (42.466%)	0.414
No. of metastatic lymph nodes	1.783±3.325	1.356±2.961	0.240
Ratio of lymph node<0.2	116 (73.885%)	123 (84.247%)	0.027
Type of surgery			0.881
L-thoracic esophagectomy	128 (81.529%)	120 (82.192%)	
R-thoracic esophagectomy	29 (18.471%)	26 (17.808%)	
Treatment regimen			0.987
S	92 (58.599%)	84 (57.534%)	
S plus postoperative R	14 (8.917%)	12 (8.219%)	
S plus postoperative C	27 (17.197%)	26 (17.808%)	
S plus postoperative CRT	24 (15.287%)	24 (16.439%)	

M, male; F, female; BMI, body mass index; HBP, high blood pressure; CAD, coronary artery disease; SCC, squamous cell carcinoma; AC, adenocarcinoma; *L*, left; *R*, right; S, surgery; R, radiotherapy; C, chemotherapy; CRT, chemoradiotherapy.

Table 2. Multivariable-adjusted association between post-operative leisure time physical activity and quality of life assessed by EORTC QLQ-C30 and QLQ-OES18 over 3 years of follow up

	β coefficient	95% CI	*p* value
QLQ-C30 Functional Scales			
Physical Functioning	-6.003	-11.809, -0.197	0.043
Role Functioning	-2.216	-8.560, 4.128	0.494
Emotional Functioning	-8.198	-15.813, -0.582	0.035
Cognitive Functioning	-1.656	-10.554, 7.242	0.715
Social Functioning	-8.548	-16.632, -0.464	0.038
Global Health	-5.764	-10.172, -1.356	0.010
QLQ-C30 Symptom Scales			
Fatigue	4.161	-3.251, 11.573	0.271
Nausea/vomiting	-0.718	-7.083, 5.647	0.825
Pain	4.745	-3.723, 13.212	0.272
Dyspnoea	2.032	-4.903, 8.967	0.566
Insomnia	9.029	-0.409, 17.649	0.040
Appetite	17.351	2.699, 32.003	0.020
Constipation	0.776	-14.045, 15.596	0.918
Diarrhoea	0.230	-5.921, 6.380	0.942
Financial difficulties	1.291	-7.875, 10.457	0.782
QLQ-OES18			
Dysphagia Scale	3.112	-9.929, 16.153	0.640
Eating Scale	11.507	1.689, 21.325	0.022
Reflux Scale	13.274	0.525, 26.024	0.041
Pain Scale	0.792	-6.316, 7.900	0.827
Trouble swallowing saliva	-0.958	-6.875, 4.959	0.751
Choking when swallowing	-0.109	-6.787, 6.570	0.975
Dry mouth	-0.405	-4.813, 5.623	0.879
Trouble with taste	16.350	2.777, 29.915	0.018
Trouble with coughing	0.689	-6.101, 7.479	0.842
Trouble with talking	0.779	-8.212, 6.654	0.837

CI, confidence interval.

QOL specifically in patients undergoing EC treatment, the widely used European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire QLQ-C30 and oesophagus-specific module QLQ-OES18 were chosen. The EORTC QLQ-C30 [30] includes five functional scales (physical, role, emotional, cognitive and social), three symptom scales (fatigue, nausea/vomiting and pain), six single items (dyspnoea, insomnia, appetite, constipation, diarrhea and financial difficulties) and a global health scale. The oesophagus-specific module QLQ-OES18 [31] measures oesophageal cancer-specific symptoms and ascertains four symptom scales (dysphagia, eating, reflux and pain) and six single items (trouble swallowing saliva, choking when swallowing, dry mouth, trouble with taste, trouble with cough and trouble with talking).

Before analysis, both the QLQ-C30 and OES-18 questionnaire responses were linearly transformed into a 0-100 score in accordance with the EORTC scoring manual [30]. High scores in the function scales and the global QOL scale indicate better function and QOL, respectively, while high scores in the symptom scales and items represent more severe symptoms.

Survival assessment and follow-up

The secondary end points for the present study were 3-year DFS and 3-year OS. DFS was defined as the time of surgery to the time of tumor recurrence. OS was calculated from the date of surgery to the date of death or to last follow-up. Every patient was informed routinely examined in our outpatient clinics every 3 months for the first 2 years after operative and every 6 months interval or until death thereafter. Physical examination, laboratory tests, barium meal fluoroscopy, esophagoscopy, computed tomography scans or some other tests were alternative used during follow-up. We eventually obtain patients' recurrence condition or death condition by regular follow-up. The follow-up end point was death or January 2016.

Statistical analysis

Baseline patient-related, surgical and oncological characteristics were presented as mean ± standard deviation or proportion by physical activity levels (<9 MET hours per week group versus ≥9 MET hours per week group). These characteristics were compared between the two groups using either the Student's *t*-test or χ^2 test where appropriate. The generalized estimating equations (GEEs) were used for QOL analyses. The survival analyses were described by the Kaplan-Meier curves and log-rank tests. The Cox regression model was used in the univariate and multivariate analyses. The variables having statistically significant in the univariate

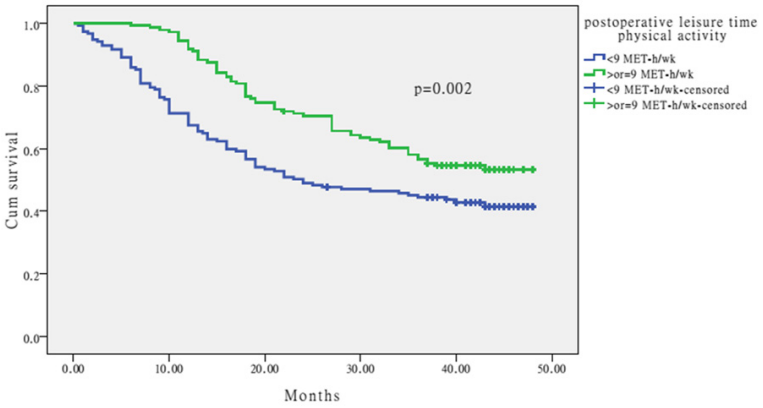

Figure 1. OS related to postoperative leisure time physical activity.

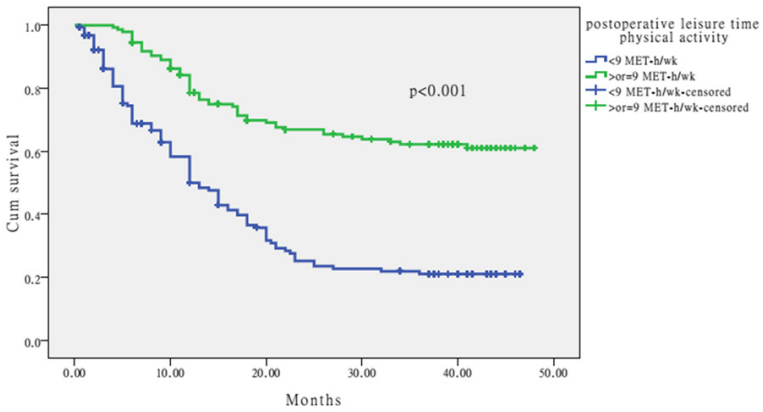

Figure 2. DFS related to postoperative leisure time physical activity.

analysis were selected into the multivariable analysis. All *p* values were two-sided and $P<0.05$ was considered statistically significant.

All data were performed using the Statistical Package for Social Science program (SPSS for Windows, version 17.0, SPSS Inc., Chicago, IL).

Results

In summary, a total of 303 EC patients (252 males and 51 females) were included in our study. There were 157 patients in the <9 MET hours per week group and 146 patients in the ≥9 MET hours per week group. In addition, there were only 146 EC survivors, accounting for 48.18%, at 3 years of follow-up. Among them, 67 cases reported their physical activity levels were less than 9 MET hours per week, whereas 79 reported their activity levels were 9 or more MET hours per week. Patients who engaged in more physical activity were likely to have a lower BMI ($P=0.046$), have been ESCC individuals ($P=0.027$) and report lower ratio of positive lymph node ($P=0.027$). The covariates according to category of physical activity levels are shown in **Table 1**.

Table 2 presents the association between leisure time physical activity and QOL over 36 months of follow-up. After adjustment for potential confounders, which are age, gender, education, income, BMI, smoking, alcohol, past medical history, tumor information, type of surgery, treatment regimen and QOL at diagnosis, the positive relationships were found between leisure time physical activity and certain aspects of QOL, including global health ($\beta=-5.764$, 95% CI -10.172- -1.356, $P=0.010$), physical functioning ($\beta=-6.003$, 95% CI -11.809- -0.197, $P=0.043$), emotional functioning ($\beta=-8.198$, 95% CI -15.813- -0.582, $P=0.035$), social functioning ($\beta=-8.548$, 95% CI -16.632- -0.464, $P=0.038$), insomnia ($\beta=9.029$, 95% CI -0.409-17.649, $P=0.040$) and appetite ($\beta=17.351$, 95% CI 2.699-32.003, $P=0.020$) assessed by QLQ-C30 as well as eating ($\beta=11.507$, 95% CI 1.689-21.325, $P=0.022$), reflux ($\beta=13.274$, 95% CI 0.525-26.024, $P=0.041$) and trouble with taste ($\beta=16.350$, 95% CI 2.777-29.915, $P=0.018$) assessed by QLQ-OES18.

Additionally, significant associations were also found between leisure time physical activity and risk of recurrence or all-cause mortality. The 3-year OS and DFS associated with levels of physical activity, calculated by Kaplan-Meier analysis, are shown in **Figures 1** and **2**. Compared with inactive ones, patients who had more activity tended to prolong OS ($P=0.002$) and DFS ($P<0.001$). The factors related to OS and DFS on univariate analysis are shown in **Table 3**. In univariate analysis, physical activity, pathology type, tumor length, T stage, TNM

Table 3. Univariate analysis of factors associated with OS and DFS

	OS			DFS		
	p value	HR	95% CI	*p* value	HR	95% CI
Age	0.161	1.015	0.994-1.036	0.075	1.019	0.998-1.039
Male	0.023	0.566	0.346-0.926	0.619	0.900	0.595-1.361
Education	0.775	1.063	0.698-1.620	0.250	1.262	0.849-1.877
High school and below						
Income						
<1000 RMB/month	0.335	Ref.		0.571	Ref.	
1000~2000	0.152	1.330	0.901-1.965	0.957	0.989	0.664-1.474
>2000	0.319	1.208	0.833-1.753	0.356	1.183	0.828-1.690
BMI	0.557	0.985	0.937-1.036	0.906	1.003	0.954-1.054
Smoking	0.996	1.001	0.729-1.373	0.626	1.081	0.791-1.476
<20 pack-year						
Alcohol	0.299	0.831	0.587-1.178	0.310	0.837	0.593-1.180
≤0.025 kg/d						
Past medical history						
HBP	0.672	1.089	0.735-1.613	0.409	0.840	0.556-1.271
CAD	0.687	0.877	0.462-1.664	0.855	0.944	0.512-1.742
Diabetes	0.981	0.991	0.464-2.115	0.991	0.996	0.467-2.124
Tumor information						
Pathology	0.026	1.798	1.071-3.017	0.003	2.172	1.311-3.598
SCC						
Histological grade						
Well	0.119	Ref.		0.452	Ref.	
Moderately	0.300	1.315	0.783-2.208	0.762	0.930	0.582-1.487
Poorly/undifferentiated	0.054	1.634	0.991-2.696	0.536	1.153	0.735-1.809
Location	0.794	0.958	0.696-1.320	0.548	0.908	0.662-1.245
Cervical/upper/middle						
Length <3 cm	<0.001	0.430	0.305-0.607	<0.001	0.540	0.391-0.747
T category						
0	0.016	0.076	0.009-0.615	0.056	0.259	0.065-1.038
1	<0.001	0.114	0.041-0.317	0.001	0.207	0.078-0.546
2	0.013	0.363	0.163-0.806	0.103	0.494	0.211-1.153
3	0.118	0.542	0.251-1.169	0.238	0.607	0.265-1.391
4	<0.001	Ref.		0.002	Ref.	
TNM stage	<0.001	2.906	2.116-3.991	<0.001	2.452	1.793-3.355
0/I/II						
Lymph node metastasis	<0.001	2.772	2.003-3.838	<0.001	2.093	1.531-2.860
No. of metastatic lymph nodes	<0.001	1.102	1.068-1.137	<0.001	1.116	1.078-1.154
Ratio of lymph node <0.2	<0.001	0.454	0.323-0.639	<0.001	0.412	0.291-0.582
Type of surgery						
*L*eft-thoracic esophagectomy	0.303	1.226	0.832-1.808	0.263	1.251	0.845-1.852
Treatment regimen						
S	0.013	Ref.		0.004	Ref.	
S plus postoperative R	0.003	2.130	1.287-3.522	0.042	1.774	1.020-3.085
S plus postoperative C	0.155	1.358	0.891-2.070	0.098	1.419	0.937-2.149
S plus postoperative CRT	0.040	1.556	1.021-2.371	0.001	1.976	1.327-2.942
Physical activity	0.003	0.618	0.450-0.848	<0.001	0.314	0.225-0.437

HR, hazard ratio; CI, confidence interval; BMI, body mass index; HBP, high blood pressure; CAD, coronary artery disease; SCC, squamous cell carcinoma; S, surgery; R, radiotherapy; C, chemotherapy; CRT, chemoradiotherapy.

Table 4. Multivariate analysis of factors associated with OS and DFS

	OS			DFS		
	p value	HR	95% CI	*p* value	HR	95% CI
Male	0.101	0.653	0.393-1.086	—	—	—
Length <3 cm	0.117	0.742	0.511-1.078	0.202	0.788	0.546-1.136
T category						
0	0.122	0.179	0.020-1.582	0.738	0.768	0.164-3.606
1	0.006	0.192	0.059-0.621	0.164	0.430	0.131-1.410
2	0.100	0.450	0.174-1.165	0.778	0.859	0.298-2.473
3	0.168	0.549	0.234-1.288	0.713	0.834	0.317-2.193
4	0.052	Ref.		0.299	Ref.	
TNM stage	0.912	0.967	0.536-1.746	0.356	1.341	0.719-2.500
0/I/II						
Lymph node metastasis	0.053	1.737	0.992-3.042	0.893	0.961	0.540-1.709
No. of metastatic lymph nodes	0.068	1.049	0.996-1.105	0.005	1.082	1.024-1.144
Ratio of lymph node <0.2	0.565	0.882	0.574-1.355	0.425	0.838	0.543-1.293
Treatment regimen						
S	0.309	Ref.		0.148	Ref.	
S plus postoperative R	0.071	1.611	0.960-2.702	0.122	1.563	0.888-2.751
S plus postoperative C	0.863	0.962	0.621-1.491	0.303	1.250	0.818-1.911
S plus postoperative CRT	0.805	1.057	0.683-1.635	0.044	1.534	1.011-2.327
Physical activity	0.014	0.666	0.481-0.921	<0.001	0.306	0.218-0.429

HR, hazard ratio; CI, confidence interval; S, surgery; R, radiotherapy; C, chemotherapy; CRT, chemoradiotherapy.

stage, lymph node metastasis, the number of lymph node metastases, positive lymph node ratio and treatment regimen (all $P<0.05$) were associated with both OS and DFS. The results of multivariate Cox regression analysis of the factors related to OS and DFS are shown in **Table 4**. According to this analysis, physical activity was independent prognostic factors for OS ($P=0.014$; HR, 0.666; 95% CI, 0.481-0.921) and DFS ($P<0.001$; HR, 0.306; 95% CI, 0.218-0.429).

Discussion

In this retrospective study of patients undergoing esophagectomy with EC, we found that leisure time physical activity ≥9 MET hours per week was associated with improved QOL. Physically active patients were more likely to have energy, enjoy their life, sleep well, and have good mood as well as few feelings of appetite loss. Moreover, we also found that more leisure time physical activity was associated with a 23% lower risk of all-cause mortality and a 53% lower risk of recurrence. Generally speaking, more leisure time physical activity can not only develop QOL, but also prolong DFS and OS of cancer patients.

Our findings, indicating that more leisure time physical activity after surgery were associated with better QOL over 36 months of follow-up, is similar to previously reported associations. In a randomized study, 108 breast cancer patients were assessed QOL post-diagnosis after undergoing 24 weeks of physical training. Results detected a positive correlation between physical activity and improved QOL [32]. Similar results were found in another study that analyzed 373 colorectal cancer patients, 2-10 post-diagnosis, for QOL. It showed that substituting sedentary behavior with physical activity was associated with higher QOL in colorectal cancer survivors [33]. Additionally, some another previous studies have also reported that physical activity can affect QOL of cancer patients, since it reduces the side effects during treatment and preserves physical ability [34, 35].

Moreover, our findings on leisure time physical activity and survival confirm and extend previous findings. Michelle D. et al. [22] found higher physical activity was associated with a reduced risk of an adverse breast cancer outcome. Patients who walked ≥1 hours per week had better survival compared with those who

walked <1 hours per week or not at all. Additionally, Arem et al. [23] analyzed the associations between post-diagnosis leisure time physical activity and mortality among colorectal cancer patients. Compared with none, post-diagnosis leisure time physical activity of ≥7 h/wk was related to a 31% lower all-cause mortality risk.

There are several biologic mechanisms explaining the association between QOL, survival and physical activity. One is that physical activity could develop insulin resistance and reduction hyperinsulinemia [36]. Moreover, it can also increase insulin sensitivity [37] and change insulin-like growth factor (IGF) levels [28]. Higher circulating insulin and IGF-1 have been associated with cancer risk [38-40] and with angiogenesis, tumor growth, and antiapoptotic activity in vivo [41]. While, physical activity could affect these important physiological events to improve symptoms, affect QOL, and modify cancer risk or disease progression. Another mechanism is that physical activity changes adipocytokine levels by increasing anti-inflammatory cytokines and decreasing inflammatory adipocytokines, both of which could influence cancer incidence and mortality [42]. Additionally, physical activity could also regulate immune to improve poor outcomes of cancer. It has been reported by Pedersen et al., and they revealed that activity reduces tumor incidence and growth by over 60% through directly regulating NK cell mobilization and redistribution in an epinephrine- and IL-6-dependent manner [43]. Although studies have strongly proved that physical activity could result in beneficial changes in the circulating level of insulin, inflammation, and immunity, the evidence is still preliminary. More biologic mechanisms will be further studied in future.

To date, previous studies on leisure time physical activity and QOL and survival of cancer are still limited as well as controversy. No literatures have focused on QOL and long-term survival between physically active and underactive EC patients undergoing esophagectomy. Our study added information to the literature. This is the first article that has examined the relationship between leisure time physical activity and QOL and survival of EC patients. What's more, this study used two validated inventories for assessing QOL.

However, our study has several limitations. First, it is a retrospective study and the collected information was somewhat limited. Secondly, we assessed only leisure-time physical activity regardless of occupational and household activity. However, both of them may also affect risk of adverse outcomes of cancer. Therefore, the association incorporating all types of physical activity may be even stronger. Thirdly, confounding variables could not be completely considered into our study even though we tried our best to include extensive adjustments in our analysis.

In conclusion, more leisure time physical activity after esophagectomy were associated with better QOL as well as lower recurrence and mortality risks in our study population. Our results are very promising for patients with EC, and indicate that clinicians should consider adding physical activity as a part of primary cancer treatment. Besides, these findings also encourage cancer patients to change behaviors to positively improve QOL and longevity.

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Disclosure of conflict of interest

None.

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