

Scientific Article

Influence of Caregiver Presence During Physician Office Visits on Patients Undergoing Chemoradiation Therapy for Esophageal Cancer



Joseph K. Ho, MD,^{a,1} Bin Gui, MD,^{b,1} Jennifer Yoon, MD,^a Quan Zhang, MD,^c Sharon L. Manne, PhD,^d and Salma K. Jabbour, MD^{b,*}

^aRutgers Robert Wood Johnson Medical School, Rutgers University, New Brunswick, New Jersey; ^bRutgers Cancer Institute of New Jersey, Department of Radiation Oncology, New Brunswick, New Jersey; ^cFirst People's Hospital of Huaian, Huaian, China; and ^dRutgers Cancer Institute of New Jersey, Department of Population Science, New Brunswick, New Jersey

Received 15 May 2020; revised 6 December 2020; accepted 23 December 2020

Purpose: Although the association of marital status with outcomes for patients with cancer has been widely studied, the mechanisms underpinning the protective effect of marriage are still not fully understood. The social support that marriage imparts is often discussed as an explanation for why patients with cancer who are married have better outcomes. Social support has been difficult to objectively quantify. Accompaniment of the patient at physician visits may be more meaningful than marital status itself. This study investigated the effect of caregiver presence at physician visits on treatment tolerance and outcome in patients undergoing chemoradiation therapy (CRT) for esophageal cancer.

Methods and Materials: Patients who received a diagnosis of esophageal cancer who underwent CRT from January 1, 2005, to January 1, 2016, as part of their curative-intent management were retrospectively reviewed. Data collected included the patients' marital status, caregiver presence at each physician visit, baseline performance status, serum albumin values and leukocyte values throughout treatment, patient weight values throughout treatment, tumor response to therapy, and overall survival. Patients were divided into 2 groups based on frequency of caregiver presence at physician visits (<50% or ≥50% of visits). Using χ^2 tests, Wilcoxon rank sum tests, and log-rank tests, the patients' characteristics, treatment tolerance and treatment outcome, and overall survival, respectively, were compared.

Results: In total, 35 of 59 patients were defined as having frequent caregiver presence at physician visits (≥50% of all documented visits), whereas 24 patients were categorized as having infrequent caregiver accompaniment. No significant difference in performance status or weight loss before the diagnosis of esophageal cancer was found. Patients who had frequent caregiver presence at physician visits maintained body weight better than those who had infrequent caregiver presence (median weight loss of 2.7 kg compared with 4.9 kg; $P = .04$). There was no difference in overall survival between the 2 groups.

Conclusions: Although patients with esophageal cancer undergoing CRT who had frequent caregiver presence at physician visits were not found to have an overall survival benefit, they had less weight loss, which may confer favorable treatment tolerance and maintenance of nutritional status during cancer treatment.

© 2021 Published by Elsevier Inc. on behalf of American Society for Radiation Oncology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Sources of support: This work had no specific funding.

Disclosures: Dr Jabbour reports grants, personal fees, and nonfinancial support from Merck & Co outside the submitted work. No other disclosures were reported.

Data-sharing statement: Research data are stored in an institutional repository and will be shared upon request to the corresponding author with a data sharing agreement.

* Corresponding author: Salma Jabbour, MD; E-mail: jabbousk@cinj.rutgers.edu

¹ J.K.H. and B.G. contributed equally to this work.

<https://doi.org/10.1016/j.adro.2021.100649>

2452-1094/© 2021 Published by Elsevier Inc. on behalf of American Society for Radiation Oncology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

The potential influence of marital status on the survival of patients with cancer has been examined for several cancers. A number of studies have reported that unmarried patients have shorter survival after diagnosis compared with married patients for multiple malignancies, including gastric cancer,¹ colorectal cancer,² and esophageal cancer.^{3,4} Most convincingly, Aizer et al examined the 10 leading causes of cancer-related deaths in the United States in the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) database and found that compared with married patients, unmarried patients with cancer were at significantly greater risk of presenting with metastatic cancer, under-treatment, and death from the cancer for all of the 10 malignancies examined.⁵ Even after adjusting for demographics, stage of cancer, and treatment, marriage was associated with a relative risk reduction in cancer death of 12% to 33%; in fact, esophageal cancer was 1 of the 5 malignancies studied for which the marriage-associated risk reduction in cancer death appeared larger than that of chemotherapy.^{5,6}

Although there is a large body of research showing that being married is correlated with esophageal cancer survival, mechanisms for this finding are still not fully understood.^{3-5,7} One reason that marriage is associated with improved cancer survival may be because married patients are less likely to refuse potentially curative radiation or surgery against the advice of their physicians.^{7,8} It also has been proposed that esophageal cancer may be particularly demanding on social support for optimal care and that spouses may help by improving nutritional intake.⁷ This would be congruent with studies that found poor nutritional status to be associated with lower quality of life, lower tolerability of treatment, and lower overall survival in patients with gastrointestinal malignancies.^{9,10} Increased nutritional risk as calculated by a formula that included serum albumin level and the proportion of the patients' weight at certain timepoints compared with their ideal weight was found by Cox et al to be associated with reduced survival in patients with esophageal cancer treated with chemoradiation therapy (CRT)¹¹; improvement in survival was observed after nutritional interventions that ranged from dietary advice or oral supplementation to major interventions such as enteral feeding or tube placement.¹¹⁻¹³ Similarly, studies by Di Fiore et al found that several markers of nutritional status, including albumin level, could predict benefit from CRT for patients with esophageal cancer, and patients with malnutrition at baseline and during treatment had a significantly lower response rate to CRT and decreased survival.^{14,15}

Social support has been difficult to definitively quantify, and there is no social support measure developed specifically for oncology settings.^{16,17} Marital status may not

always indicate the amount of social support a patient receives, and unmarried patients may in some cases have more social support than married patients. We hypothesized that the frequency of caregiver presence during physician appointments provided evidence of tangible social support that could be quantified and used to further explore how marital status and social support may interact with nutritional status and treatment tolerance to affect the survival of patients with esophageal cancer undergoing CRT.

Materials and Methods

Sample and data collection

Retrospectively, electronic medical records of 59 patients with nonmetastatic locally advanced esophageal cancer pursuing CRT from January 1, 2005, to January 1, 2016, at a single cancer institution were reviewed. We collected patients' data, including age, sex, total visits in which a patient was seen by a physician, total visits in which a patient was accompanied by a relative or friend at a physician encounter, marital status, Eastern Cooperative Oncology Group (ECOG) performance status before treatment, patient weight before and throughout treatment, histology, tumor stage, radiation dose and fractions, chemotherapy, surgical resection, albumin values before and throughout treatment, treatment toxicities, leukopenias, hospitalizations throughout therapy and causes of hospitalizations, and overall survival.

Albumin values compared were albumin values within 10 days before or after the date of initiation of radiation therapy as well as the last date of radiation therapy, with preference given to values closest to the actual date of radiation therapy. Likewise, weight loss in kilograms was determined by subtracting weight values obtained from the patient's last date of radiation therapy from weight values obtained from the initial radiation oncology consultation visit. Each physician visit document was methodically examined for the presence of a caregiver and further verified with documentation from the same visit date by other cancer care staff such as chemotherapy nurses, social workers, and nutritionists. Of note, all patients received consultation with nutritionists per standard practice at the cancer institution for esophageal cancer. Other supportive care measures such as intravenous fluids were given as needed at the independent discretion of physicians involved in each patient's care, but there was no protocol in place to routinely administer these prophylactically. Hematologic toxicity was recorded on the basis of the National Cancer Institute's Common Terminology Criteria for Adverse Events, version 4.0. Patients were divided into 2 groups by the frequency of having companionship at physician medical, surgical, and radiation oncology visits: frequent companionship was

defined as being accompanied at $\geq 50\%$ of visits, and infrequent companionship was defined as being accompanied at $< 50\%$ visits. The Institutional Review Board of Rutgers New Brunswick Health Sciences approved this study. Patients gave consent for standard-of-care therapy. This study was conducted on an institutional review board–approved retrospective study, and patient data were deidentified. The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available owing to privacy or ethical restrictions.

Statistical analysis

Patients’ characteristics, treatment outcome and tolerance, and overall survival were listed and compared between the 2 groups. We used χ^2 tests or Fisher exact tests for categorical variables and Wilcoxon rank sum tests for nonnormally distributed continuous variables. Kaplan-Meier log-rank tests were used to evaluate overall survival. Statistical significance of all tests was assumed at $P < .05$. One-sided P values were reported for outcome analyses. All statistics were calculated using SAS statistical software, University Edition for Mac (SAS Institute Inc, Cary, North Carolina).

Results

Patient characteristics

Table 1 lists baseline patient characteristics and compares patients who had frequent companionship ($n = 35$) versus infrequent companionship ($n = 24$), with frequent companionship defined as documentation that the patient was accompanied by a spouse, relative, or friend at a physician encounter at $\geq 50\%$ of all physician visits. There were no significant differences in patient age, sex, performance status, baseline weight, weight loss before diagnosis, tumor characteristics, or cancer staging between the 2 groups. There were no significant differences in marital status between the 2 groups ($P = .33$). No significant difference in survival was found between married patients compared with nonmarried (single, divorced, or widowed) patients when looking at marital status alone ($P = .37$). All patients were referred for nutrition consultation per standard practice for patients with esophageal cancer at the cancer institution.

Table 2 lists treatment characteristics and compares treatments received by patients who had frequent companionship and those who had infrequent companionship. There were no significant differences in radiation dose, number of radiation fractions, chemotherapy category, or use of surgical resection between the 2 groups.

Table 1 Baseline patient characteristics

Parameter	Infrequent companionship, n (%) (n = 24)	Frequent companionship, n (%) (n = 35)	<i>P</i> value
Age, mean \pm SD, y	62.7 \pm 11.7	68.7 \pm 10.9	.06
Male sex	17 (70.8)	22 (62.9)	.52
Married	15 (62.5)	26 (74.3)	.33
Baseline ECOG performance status (range)	0 (0-2)	0 (0-3)	.40
Prediagnosis weight loss, kg (range)	9.1 (0-29.5)	9.1 (0-27.2)	.50
Baseline weight, kg (range)	85.1 (43.1-147.8)	70.8 (44.5-117.9)	.15
Histology			.44
Adenocarcinoma	16 (66.7)	18 (51.4)	
Squamous cell	8 (33.3)	15 (42.9)	
Small cell	0	2 (5.7)	
Tumor location			.92
Cervical	1 (4.2)	2 (5.7)	
Upper	2 (8.3)	3 (8.6)	
Middle	4 (16.7)	9 (25.7)	
Lower	17 (70.8)	21 (60.0)	
Preoperative clinical stage			.86
I	1 (4.6)	0	
II	7 (31.8)	7 (26.9)	
III	14 (63.6)	18 (69.2)	
IV	0	1 (3.9)	
T classification of TNM staging			.38
1	1 (4.8)	0	
2	5 (23.8)	3 (12.0)	
3	15 (71.4)	21 (84.0)	
4	0	1 (4.0)	
N classification of TNM staging			>.99
0	4 (17.4)	4 (16.7)	
1	15 (65.2)	16 (66.7)	
2	3 (13.0)	4 (16.7)	
3	1 (4.3)	0	

Abbreviation: ECOG = Eastern Cooperative Oncology Group.

Companionship status and patient outcomes

No overall survival difference was demonstrated between patients who had frequent companionship at their physician visits and those who had infrequent companionship ($P = .98$) (Fig 1). However, patients with frequent companionship maintained their weight better than those with infrequent companionship (median weight loss of 2.7 kg vs 4.9 kg; $P = .04$; Fig 2A). When examining weight loss solely based on marital status, irrespective of companionship status, married patients did not maintain

Table 2 Treatment characteristics

Parameter	Infrequent companionship, n (%) (n = 24)	Frequent companionship, n (%) (n = 35)	P value
Radiation dose, Gy (range)	50.4 (45.0-72.0)	50.4 (39.0-66.0)	.80
Radiation fractions (range)	28 (18-34)	28 (13-33)	.59
Treatment duration, days (range)	39 (9-64)	39 (17-60)	.88
Radiation therapy			.55
3D CRT	13 (56.5)	17 (48.6)	
IMRT	10 (43.5)	18 (51.4)	
Chemotherapy types			.73
5-FU and platinum	10 (43.5)	11 (33.3)	
Paclitaxel and platinum	4 (17.4)	6 (18.2)	
Other	9 (39.1)	16 (48.5)	
Surgical resection	14 (58.3)	13 (37.1)	.11

Abbreviations: CRT = chemoradiation therapy; IMRT = intensity modulated radiation therapy.

weight significantly better than nonmarried patients (median weight loss of 3.8 kg vs 3.2 kg; $P = .44$; Fig. 2B). Additionally, patients with frequent companionship had a greater chance of hospitalization after CRT compared with those with infrequent companionship (62.9% vs 37.5%; $P = .049$). There were no differences in grade 3/4 leukopenia or change in albumin throughout the therapy between the 2 groups ($P = .44$ and $P = .21$, respectively) (Table 3).

As expected, patients who had surgical resection of their cancer had longer survival ($P = .0001$). Subgroup analyses of patients based on surgical resection found no overall survival difference between patients with frequent companionship at physician visits versus those with infrequent companionship, both in patients who had surgical resection ($P = .67$) and patients who did not have surgical resection ($P = .23$). Short-term outcomes including hospitalization, weight loss, leukopenia, and albumin decrease did not differ between patients with frequent companionship at physician visits versus those with infrequent companionship, both in patients who had surgical resection and patients who did not have surgical resection (Table 4).

Discussion

To our knowledge, no studies to date have directly examined the effect of the presence of caregivers on the

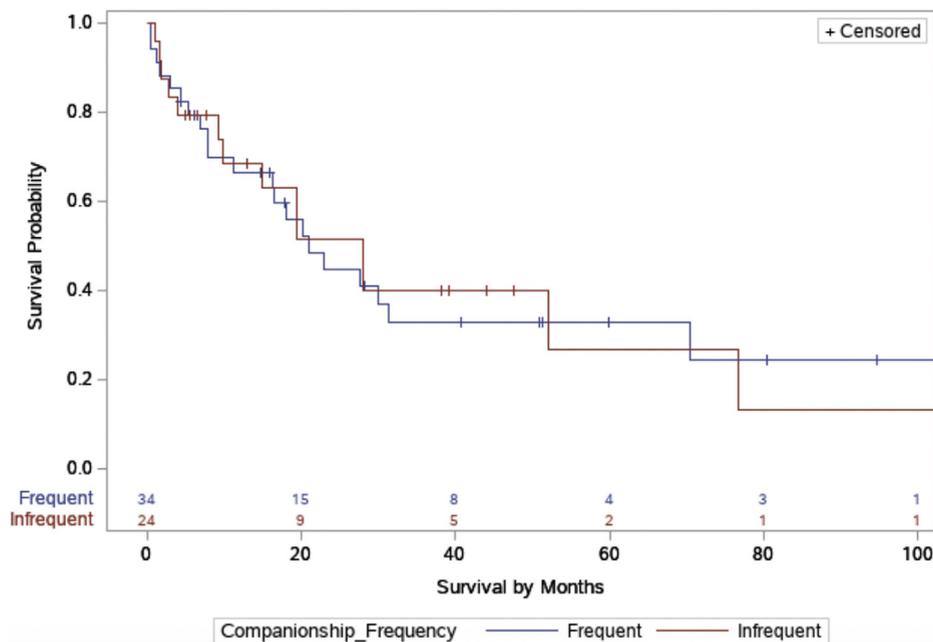


Figure 1 Patients were categorized into 2 groups by the frequency of documented caregiver presence at physician visits: patients with frequent companionship had documented caregiver presence at $\geq 50\%$ of physician visits, and patients with infrequent companionship had documented caregiver presence at $< 50\%$ of physician visits. There was no difference in overall survival between patients who had frequent companionship and patients who had infrequent companionship ($P = .98$).

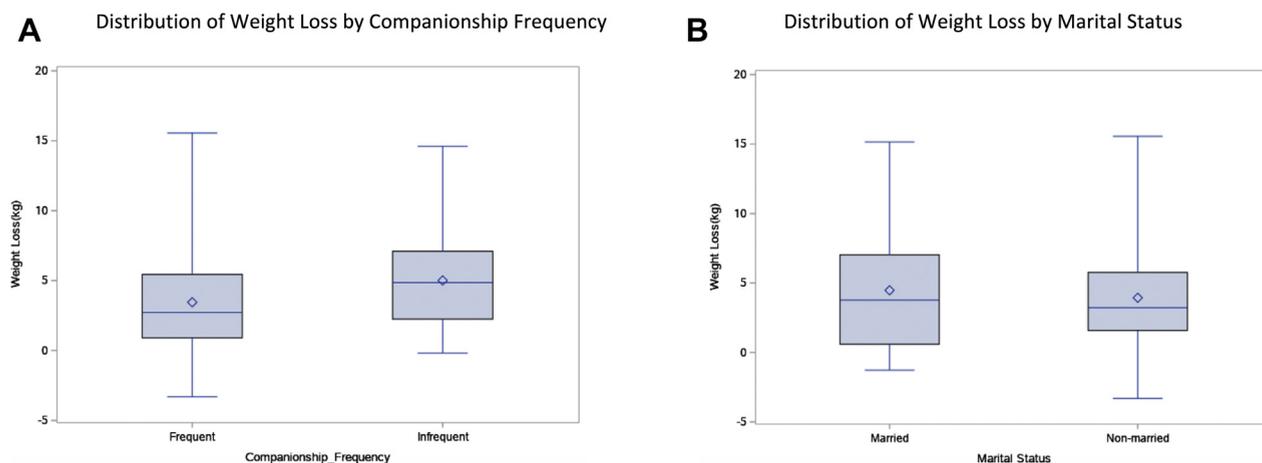


Figure 2 (A) Distribution of weight loss by companionship frequency. (B) Distribution of weight loss by marital status. Negative values for weight loss indicate weight gain. The horizontal line inside each box indicates the median, the top and bottom of the box indicate the interquartile range, the I bars indicate the minimum and maximum values, and the diamond indicates the mean.

outcome of patients with esophageal cancer treated with CRT. It has been suggested that the benefits of marriage on survival in cancer are mediated through improved social support and that providing support to unmarried patients with cancer might significantly reduce differences in survival rates between married and unmarried patients with cancer.⁵

We conducted a retrospective study to examine whether the survival, nutritional status, and treatment tolerance of patients with esophageal cancer undergoing CRT were associated with having caregiver support, defined as having a spouse, family member, or friend attend $\geq 50\%$ of all physician visits. In accordance with our hypothesis, patients who were frequently accompanied at physician visits had less weight loss during CRT. However, there were no significant differences in overall survival or leukopenia. Patients in this study who had surgical resection of their cancer had longer survival; frequency of companionship during physician visits had no influence on survival among the patients in this study who had surgery. This finding is similar to that of a study by Brusselaers et al, which found that marital status had no influence on survival among patients with esophageal cancer undergoing surgery.¹⁸ The sample size in our study, however, was limited and may not shed light on survival status.

In a secondary analysis of data from a randomized controlled trial that sought to examine whether survival of patients with advanced cancer would be associated with having a family caregiver, Dionne-Odom et al found that

Table 3 Patient outcomes

Outcome	Infrequent companionship, n (%)	Frequent companionship, n (%)	P value
Hospitalization	9 (37.5)	22 (62.9)	.049
Weight loss, kg (range)	4.9 (−0.2 to 14.6)	2.7 (−3.3 to 15.5)	.04
CTCAE grade 3/4 leukopenia	9 (45)	12 (38.7)	.44
Albumin decrease, g/dL (range)	0.2 (−0.8 to 1.2)	0.35 (−0.3 to 1.4)	.21

Abbreviation: CTCAE = Common Terminology Criteria for Adverse Events, version 4.0.

Table 4 Patient outcomes based on surgical resection

Outcome	With surgical resection			Without surgical resection		
	Infrequent companionship, n (%)	Frequent companionship, n (%)	P value	Infrequent companionship, n (%)	Frequent companionship, n (%)	P value
Hospitalization	3 (21.4)	6 (46.2)	.17	6 (16)	12 (72.7)	.37
Weight loss, kg (range)	4.9 (−0.2 to 14.6)	2.7 (−3.3 to 15.6)	.09	4.5 (0-8.7)	2.7 (−2.2 to 15.2)	.11
CTCAE grade 3/4 leukopenia	4 (33.3)	4 (33.7)	.61	5 (62.5)	8 (40.0)	.26
Albumin decrease, g/dL (range)	0.1 (−0.1 to 1.2)	0.5 (−0.1 to 1.40)	.21	0.3 (−0.8 to 0.95)	0.3 (−0.3 to 1.4)	.43

Abbreviation: CTCAE = Common Terminology Criteria for Adverse Events, version 4.0.

patients with a caregiver actually had shorter survival compared with those without a caregiver.¹⁹ It is plausible that patients in the current study who were more frequently accompanied during their physician visits had higher daily needs and required family or friends to accompany them to medical visits, perhaps accounting for why patients who were more frequently accompanied had more hospitalizations in this study. However, similar to the study by Dionne-Odom et al, the data we collected on potential markers of disease severity do not support this explanation because there were no differences in ECOG performance status, patient baseline weight and weight loss, cancer staging, and cancer histology (Table 1).

In this study, we found that the mean weight loss was significantly less among patients who were more frequently accompanied during their physician visits. Literature has shown that patients with weight loss have worse outcomes when undergoing chemotherapy for gastrointestinal malignancies and that patients who stop losing weight have better overall survival.⁹ Physicians caring for patients with cancer who are frequently unaccompanied by others at physician visits should thus consider that this specific patient population may especially require formal nutritional intervention or consultation.

This study has potential limitations to be considered. First, the study is retrospective and not a prospective, planned analysis. Second, the study is limited in power and was performed at a single cancer institution, which may have led to selection bias. Third, the presence of a patient's family or friends at a physician visit was consistently documented but is not a required data collection point in the institution's electronic medical record system. Caregiver presence at each physician visit was verified with documentation of visits with other cancer care staff from the same day. Although it is possible that a caregiver was present at the physician visit but not successfully documented in the physician note or the notes of other cancer care staff from the same day, it is likely that a caregiver in such a case would be considered a more passive participant compared with caregivers whose participation in physician visits is readily noted among patients categorized as having frequent caregiver presence at physician visits. Nonetheless, having a spouse, family member, or friend frequently attend physician visits or having a caregiver is not necessarily congruent with the quality of the patient's social support. Further research needs to be performed to examine how social support may be quantified and the effects that specific care or interventions provided by social support may have on patient survival.

This study's finding that frequent companionship at physician visits was associated with less mean weight loss suggests that caregiver presence at physician visits has an important role in helping patients understand the tasks required to maintain nutritional status, which may be

associated with better tolerance of therapy. Of course, there are myriad ways that a spouse or caregiver helps to care for an ailing loved one that have yet to be objectively measured and studied. In a large, single-center, randomized controlled comparison of electronic patient-reported systematic symptom monitoring versus usual care in patients receiving chemotherapy for metastatic solid tumors, Basch et al found that systematic symptom monitoring was associated with increased survival.²⁰ Fatigue, pain, anorexia, dyspnea, neuropathy, and nausea were found to be the most common severe or disabling patient-reported symptoms.²¹ A sensible mechanism proposed by Basch et al for improvement in survival was that clinicians were alerted earlier to patients' symptoms and thus were able to promptly respond and prevent adverse consequences.²¹ Companionship at physician visits may similarly improve communication of patient symptoms to clinicians so that symptoms are managed before serious complications develop.

Conclusions

The medical community increasingly recognizes caregiver burden and aims to mitigate undue burden and caregiver distress.²² This study suggests that caretakers who physically attend physician visits with the patient may have a significant influence on the patient's overall medical care; if feasible, caretakers may want to delegate some of their other tasks and attend physician office visits with the patient to aid in communication of the patient's needs and implementation of physician recommendations. As health care systems consider investing in social support services or interventions to help patients with cancer, they may find it wise to continue to explore whether providing companionship at medical visits influences morbidity or mortality more than simply providing assistance to get to medical appointments.

References

1. Zhang J, Gan L, Wu Z, Yan S, Liu X, Guo W. The influence of marital status on the stage at diagnosis, treatment, and survival of adult patients with gastric cancer: A population-based study. *Oncotarget*. 2017;8:22385-22405.
2. Li Q, Gan L, Liang L, Li X, Cai S. The influence of marital status on stage at diagnosis and survival of patients with colorectal cancer. *Oncotarget*. 2015;6:7339-7347.
3. Zhang Q-W, Lin X-L, Zhang C-H, et al. The influence of marital status on the survival of patients with esophageal cancer: A population-based, propensity-matched study. *Oncotarget*. 2017;8:62261-62273.
4. Du L, Kim JJ, Chen B, Zhu S, Dai N. Marital status is associated with superior survival in patients with esophageal cancer: A Surveillance, Epidemiology, and End Results study. *Oncotarget*. 2017;8:95965-95972.
5. Aizer AA, Chen MH, McCarthy EP, et al. Marital status and survival in patients with cancer. *J Clin Oncol*. 2013;31:3869-3876.

6. Sjoquist KM, Burmeister BH, Smithers BM, et al. Survival after neoadjuvant chemotherapy or chemoradiotherapy for resectable oesophageal carcinoma: An updated meta-analysis. *Lancet Oncol*. 2011;12:681-692.
7. Paniagua Cruz A, Haug KL, Zhao L, Reddy RM. Association between marital status and racial disparities in esophageal cancer care. *JCO Oncol Pract*. 2020;16:e498-e506.
8. Aizer AA, Chen MH, Parekh A, et al. Refusal of curative radiation therapy and surgery among patients with cancer. *Int J Radiat Oncol Biol Phys*. 2014;89:756-764.
9. Andreyev HJN, Norman AR, Oates J, Cunningham D. Why do patients with weight loss have a worse outcome when undergoing chemotherapy for gastrointestinal malignancies? *Eur J Cancer*. 1998;34:503-509.
10. Lee JLC, Leong LP, Lim SL. Nutrition intervention approaches to reduce malnutrition in oncology patients: A systematic review. *Support Care Cancer*. 2016;24:469-480.
11. Cox S, Powell C, Carter B, Hurt C, Mukherjee S, Crosby TD. Role of nutritional status and intervention in oesophageal cancer treated with definitive chemoradiotherapy: Outcomes from SCOPE1. *Br J Cancer*. 2016;115:172-177.
12. Buzby GP, Knox LS, Crosby LO, et al. Study protocol: A randomized clinical trial of total parenteral nutrition in malnourished surgical patients. *Am J Clin Nutr*. 1988;47(2 Suppl):366-381.
13. Veterans Affairs Total Parenteral Nutrition Cooperative Study Group. Perioperative total parenteral nutrition in surgical patients. *N Engl J Med*. 1991;325:525-532.
14. Di Fiore F, Lecleire S, Pop D, et al. Baseline nutritional status is predictive of response to treatment and survival in patients treated by definitive chemoradiotherapy for a locally advanced esophageal cancer. *Am J Gastroenterol*. 2007;102:2557-2563.
15. Di Fiore A, Lecleire S, Gangloff A, et al. Impact of nutritional parameter variations during definitive chemoradiotherapy in locally advanced oesophageal cancer. *Dig Liver Dis*. 2014;46:270-275.
16. Saracino R, Kolva E, Rosenfeld B, Breitbart W. Measuring social support in patients with advanced medical illnesses: An analysis of the Duke—UNC Functional Social Support Questionnaire. *Palliative and Supportive Care*. 2015;13:1153-1163.
17. Broadhead WE, Kaplan BH. Social support and the cancer patient. Implications for future research and clinical care. *Cancer*. 1991;67(3 Suppl):794-799.
18. Brusselaers N, Mattsson F, Johar A, et al. Marital status and survival after oesophageal cancer surgery: A population-based nationwide cohort study in Sweden. *BMJ Open*. 2014;4:e005418.
19. Dionne-Odom JN, Hull JG, Martin MY, et al. Associations between advanced cancer patients' survival and family caregiver presence and burden. *Cancer Med*. 2016;5:853-862.
20. Basch E, Deal AM, Dueck AC, et al. Overall survival results of a trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment. *JAMA*. 2017;318:197.
21. Basch E, Deal AM, Kris MG, et al. Symptom monitoring with patient-reported outcomes during routine cancer treatment: A randomized controlled trial. *J Clin Oncol*. 2016;34:557-565.
22. Adelman RD, Tmanova LL, Delgado D, Dion S, Lachs MS. Caregiver burden: A clinical review. *JAMA*. 2014;311:1052-1060.