

Age and Gender Moderate the Impact of Early Palliative Care in Metastatic Non-Small Cell Lung Cancer

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Palliative care • Quality of life • Mood • Advanced cancer • Gender • Geriatrics

ABSTRACT

Background. Studies demonstrate that early palliative care (EPC) improves advanced cancer patients' quality of life (QOL) and mood. However, it remains unclear whether the role of palliative care differs based upon patients' demographic characteristics. We explored whether age and gender moderate the improvements in QOL and mood seen with EPC.

Methods. We performed a secondary analysis of data from a randomized controlled trial of patients with metastatic non-small cell lung cancer. Patients received either EPC integrated with oncology care or oncology care alone. We assessed the degree to which QOL (Trial Outcome Index [TOI]) and mood (Hospital Anxiety and Depression Scale [HADS] and Patient Health Questionnaire 9 [PHQ-9]) outcomes at week 12 varied by patient age (<65) and gender. The week 12 data of 107 patients are included in this analysis.

Results. At 12 weeks, younger patients receiving EPC reported better QOL (TOI mean = 62.04 vs. 49.43, $p = .001$) and lower rates of depression (HADS–Depression = 4.0% vs. 52.4%, $p < .001$; PHQ-9 = 0.0% vs. 28.6%, $p = .006$) than younger patients receiving oncology care alone. Males receiving EPC reported better QOL (TOI mean = 58.81 vs. 48.30, $p = .001$) and lower rates of depression (HADS–Depression = 18.5% vs. 60.9%, $p = .002$; PHQ-9 = 3.8% vs. 34.8%, $p = .008$) than males receiving oncology care alone. At 12 weeks, QOL and mood did not differ between study groups for females and older patients.

Conclusion. Males and younger patients who received EPC had better QOL and mood than those who received oncology care alone. However, these outcomes did not differ significantly between treatment groups for females or older patients. *The Oncologist* 2016;21:119–126

Implications for Practice: This study found that early palliative care improves patients' quality of life and mood differentially based on their age and gender. Specifically, males and younger patients receiving early palliative care experienced better quality of life and mood than those receiving oncology care alone. Conversely, females and older patients did not experience this treatment effect. Thus, palliative care interventions may need to be tailored to patients' age- and gender-specific care needs. Studying how patients' demographic characteristics affect their experience with palliative care will enable the development of interventions targeted to the distinct supportive care needs of patients with cancer.

INTRODUCTION

Patients with advanced cancer who receive early palliative care (EPC) experience improvements in their quality of life (QOL), mood, and possibly even survival [1–4]. Thus, the American Society of Clinical Oncology (ASCO) now recommends involvement of palliative care early in the course of illness for patients with metastatic cancer and/or a high symptom burden [5]. As the evidence mounts demonstrating the benefits of integrated palliative and oncology care and organizations such as ASCO and the American Cancer Society express support for this care model, we need to consider how to

tailor this model to deliver care aligned with each individual's care needs.

Although research has clearly demonstrated the role of targeted therapies based upon a patients' tumor genetics, we lack sufficient data about how to best personalize the provision of palliative care in patients with cancer. Studies suggest that patients' supportive care needs differ according to their demographic and clinical characteristics [6, 7], and palliative care providers often tailor their services according to the specific symptoms or care needs of each individual patient [8].

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Despite palliative care clinicians' efforts to tailor their services, little research has been done to determine how patients' demographic and clinical factors influence their experience with palliative care. In order to provide patients with the most appropriate and efficacious palliative care, we must first understand how the role of EPC differs across specific subpopulations.

Although several of the randomized controlled trials (RCTs) of EPC have been conducted in patients with a number of different advanced cancer diagnoses [2, 4], we have not yet identified whether certain subgroups of patients are more or less likely to benefit from the integrated care model. For example, patient age and gender may influence the impact of EPC, because patients' QOL and mood vary based upon these demographic factors [6, 9–22]. Data suggest that both the physical and psychological effects of cancer vary with age and gender [10, 16, 17, 20, 23, 24]. Specifically, older adults with cancer tend to report lower pain symptoms [24], less emotional distress [16], and fewer negative psychosocial consequences [25] related to their disease. Additionally, studies suggest that older patients with cancer experience better QOL than younger patients [17, 21, 22]. Although older patients with cancer have different physiologic, psychological, and social characteristics compared with younger patients, research regarding the supportive care needs of older versus younger patients is lacking [17, 23, 24, 26–29].

Studies have also shown that women with cancer report lower QOL [10, 16, 20] and higher rates of anxiety [30] and depression [16, 31], compared with men. A study examining factors associated with QOL in patients with advanced cancer demonstrated worse physical and emotional well-being among women [21]. Additionally, women with cancer report greater supportive care needs regarding their emotions, coping, social support, and sexuality [6]. Although data support the notion that gender is associated with cancer patients' QOL and mood, how gender relates to patients' response to EPC is not yet known. Therefore, research is needed to determine whether the impact of EPC is influenced by patient gender.

In the present analysis, we sought to explore whether the improvements in patients' QOL and mood seen with EPC are moderated by demographic characteristics, specifically age and gender. By studying how the impact of EPC varies based on patients' age and gender, we hope to begin to define the role of these characteristics in the care of patients with advanced cancer and to establish a framework for personalized palliative care.

MATERIALS AND METHODS

Study Design

We conducted a secondary analysis of data collected from an RCT assessing EPC integrated with standard oncology care [1]. The study procedures have been previously described [1]. In brief, we randomly assigned patients with metastatic non-small cell lung cancer (NSCLC) to receive EPC integrated with oncology care or oncology care alone. Patients assigned to EPC met with a member of the palliative care team, which consisted of board-certified palliative care physicians and

advanced-practice nurses, within 3 weeks after enrollment and at least monthly thereafter in the outpatient setting until death. Patients assigned to oncology care were not referred to palliative care unless requested by the patient, family, or oncologist. The Dana-Farber/Partners Cancer Care institutional review board approved the study protocol, and all participants provided written informed consent.

Study Sample

The study sample consisted of patients with newly diagnosed metastatic NSCLC presenting to the outpatient thoracic oncology clinic at the Massachusetts General Hospital Cancer Center (Boston, MA) from June 2006 to July 2009. The week 12 data of 107 patients are included in this analysis. Patients were eligible if they had pathologically confirmed metastatic NSCLC diagnosed within the previous 8 weeks; an Eastern Cooperative Oncology Group performance status of 0, 1, or 2; and the ability to read and respond to questions in English. Patients who were already receiving palliative care services were not eligible to participate in the trial.

Outcome Measures

We assessed patients' QOL at baseline and at week 12 using the Functional Assessment of Cancer Therapy–Lung (FACT-L) [32]. The FACT-L assesses physical, functional, emotional, and social well-being during the previous week. In addition, the FACT-L contains a lung cancer subscale evaluating seven symptoms specific to lung cancer. The Trial Outcome Index (TOI) is the sum of the scores on the physical well-being, functional well-being, and lung cancer subscales of the FACT-L. Scores on the FACT-L range from 0 to 136, and scores on the TOI range from 0 to 84, with higher scores indicating a better QOL.

We measured patients' mood symptoms at baseline and at week 12 using the Hospital Anxiety and Depression Scale (HADS) and the Patient Health Questionnaire 9 (PHQ-9) [33, 34]. The HADS is a 14-item questionnaire that contains two 7-item subscales assessing depression and anxiety symptoms during the past week. Scores on each subscale range from 0 to 21, with a score higher than 7 denoting clinically significant depression or anxiety. The PHQ-9 contains 9 items that evaluate symptoms of major depressive disorder. Patients who report at least 5 of the 9 symptoms of depression over the past 2 weeks, with 1 of the 5 being anhedonia or depressed mood, are considered to meet screening criteria for a major depressive syndrome.

Statistical Analyses

We used descriptive statistics to analyze the frequencies, means, and standard deviations of the study variables stratified by age (<65 and ≥65 years) and gender. The majority of studies examining older patients with cancer use an age cutoff of ≥65 years [23, 26, 35, 36]. We assessed differences in baseline characteristics and clinical variables by age and gender, using χ^2 or Fisher's exact test for the categorical variables and independent sample Student's *t* tests for the continuous variables. To assess the degree to which patient age and gender moderated the effect the EPC intervention on QOL (FACT-L and TOI) at week 12, we computed linear regression models adjusting for baseline QOL scores, group assignment, the moderating variables, and computed variables representing

Table 1. Demographics

Variable	Age < 65 (n = 47)	Age ≥ 65 (n = 60)	p value	Female (n = 57)	Male (n = 50)	p value
Female, no. (%)	27 (57.4)	30 (50.0)	.56	—	—	—
Age, mean (median)	55.32 (58.0)	71.35 (71.0)	<.01	64.40 (65.0)	64.20 (66.0)	.92
Race, no. (%)			.14			.64
White	44 (93.6)	60 (100.0)		55 (96.5)	49 (98.0)	
Black	2 (4.3)	0 (0.0)		1 (1.8)	1 (2.0)	
Asian	1 (2.1)	0 (0.0)		1 (1.8)	0 (0.0)	
Marital status, no. (%) ^a			.09			.32
Married	31 (66.0)	36 (60.0)		34 (59.6)	33 (66.0)	
Single	8 (17.0)	4 (6.7)		5 (8.8)	7 (14.0)	
Divorced or separated	6 (12.8)	10 (16.7)		7 (12.3)	9 (18.0)	
Widowed	2 (4.3)	10 (16.7)		11 (19.3)	1 (2.0)	
Children, no. (%)	36 (76.6)	52 (88.1)	.13	47 (82.5)	41 (83.7)	1.00
ECOG, no. (%) ^b			.68			.94
0	17 (36.2)	24 (40.0)		21 (36.8)	20 (40.0)	
1	27 (57.4)	30 (50.0)		31 (54.4)	26 (52.0)	
2	3 (6.4)	6 (10.0)		5 (8.8)	4 (8.0)	
Mood symptoms, no. (%)						
HADS						
Depression subscale	13 (27.7)	11 (18.6)	.35	13 (23.2)	11 (22.0)	1.00
Anxiety subscale	22 (46.8)	16 (27.1)	.04	19 (33.9)	19 (38.0)	.69
PHQ-9 major depressive syndrome	7 (14.9)	8 (13.3)	1.00	6 (10.5)	9 (18.0)	.28
QOL, mean (SD)						
FACT-L	91.89 (16.55)	93.77 (15.91)	.55	92.46 (17.10)	93.50 (15.13)	.74
TOI	55.96 (13.60)	56.08 (12.95)	.96	56.14 (14.36)	55.90 (11.38)	.92

The *p* values were derived from χ^2 and Fisher's exact tests for categorical variables and from independent-sample *t* test for continuous variables.

^aFisher's exact test comparing rates of patients married to the rates of patients not married.

^bAn ECOG PS of 0 indicates that the patient is asymptomatic; 1 indicates that the patient is symptomatic but fully ambulatory; and 2 indicates that the patient is symptomatic and in bed less than 50% of the day.

Abbreviations: ECOG, Eastern Cooperative Oncology Group; FACT-L, Functional Assessment of Cancer Therapy–Lung; HADS, Hospital Anxiety and Depression Scale; PHQ-9, Patient Health Questionnaire 9; QOL, quality of life; TOI, Trial Outcome Index.

the interaction between group assignment and the moderating variables, with a 2-sided $p < .05$. We compared week 12 QOL (FACT-L and TOI) and mood (HADS and PHQ-9) between study groups, stratified by age and gender, using independent sample Student's *t* tests and χ^2 tests, respectively. We performed our statistical analyses using SPSS version 17.0 (SPSS, Chicago, IL, <http://www-01.ibm.com/software/analytics/spss/>).

RESULTS

Patient Characteristics

Of the 107 patients in the study, 47 (43.9%) were age <65, and 50 (46.7%) were male. We found no significant between-group differences across age and gender for baseline demographic and clinical variables (Table 1). Baseline patient-reported measures were also not significantly different, except that older patients had lower rates of anxiety symptoms compared with younger patients (27.1% vs. 46.8%, $p = .04$). We found no significant differences in QOL and mood between the EPC and oncology care groups at baseline across age and gender.

Quality-of-Life and Mood Outcomes by Age

Using linear regression, we found that patient age moderated the effects of EPC on QOL (age \times group assignment, unstandardized

coefficient [B] = -8.96 , SE = 3.56, 95% confidence interval [CI] = -16.03 to -1.89 , $\beta = -0.35$, $p = .01$), thus prompting further analysis of the association stratified by patient age (Table 2). Comparing week 12 QOL between study groups and controlling for baseline QOL, we found that younger patients assigned to EPC had significantly higher FACT-L (mean = 101.88 [SD = 16.57] vs. 86.00 [SD = 16.61], $p = .002$) and TOI scores (mean = 62.04 [SD = 12.35] vs. 49.43 [SD = 12.39], $p = .001$) than younger patients assigned to oncology care (Fig. 1). However, older patients' QOL did not differ between the EPC group and the standard care group (FACT-L mean = 94.97 [SD = 13.27] vs. 95.92 [SD = 13.97], $p = .79$; TOI mean = 56.59 [SD = 10.60] vs. 55.85 [SD = 10.14], $p = .79$).

Comparing the results of week 12 mood symptoms between study groups, controlling for baseline mood, we found significantly lower rates of depressive symptoms for younger patients receiving EPC compared with younger patients receiving oncology care for both the HADS depression subscale (4.0% vs. 52.4%, $p < .001$) and the PHQ-9 (0.0% vs. 28.6%, $p = .006$) (Fig. 2). We found no significant difference between the EPC and oncology care groups in the rates of depressive symptoms among older patients at week 12 (HADS, depression subscale: 25.0% vs. 26.9%, $p = .87$; PHQ-9: 6.3% vs. 7.7%, $p = .83$). Using the anxiety subscale of the HADS to compare rates of anxiety symptoms in the EPC and oncology

Table 2. Regression models

Variable	B	SE	Beta	95% CI	p value
Week 12 TOI					
Baseline TOI	0.48	0.07	0.53	0.35 to 0.62	<.01
Early palliative care group assignment	6.31	3.03	0.26	0.30 to 12.32	.04
Male gender	-8.76	2.63	-0.37	-13.97 to -3.54	<.01
Age ≥ 65	5.18	2.66	0.22	-0.09 to 10.46	.05
Age × group assignment	-8.96	3.56	-0.35	-16.03 to -1.89	.01
Gender × group assignment	8.09	3.51	0.30	1.12 to 15.06	0.02
Week 12 FACT-L					
Baseline FACT-L	0.55	0.07	0.57	0.42 to 0.69	<.01
Early palliative care group assignment	6.52	3.82	0.21	-1.05 to 14.09	.09
Male gender	-12.63	3.31	-0.40	-19.19 to -6.07	<.01
Age ≥ 65	7.10	3.37	0.23	0.42 to 13.78	.04
Age × group assignment	-12.50	4.49	-0.37	-21.41 to -3.58	.01
Gender × group assignment	11.97	4.43	0.33	3.18 to 20.76	.01

Abbreviations: B, unstandardized coefficient; CI, confidence interval; FACT-L, Functional Assessment of Cancer Therapy–Lung; SE, standard error; TOI, Trial Outcome Index.

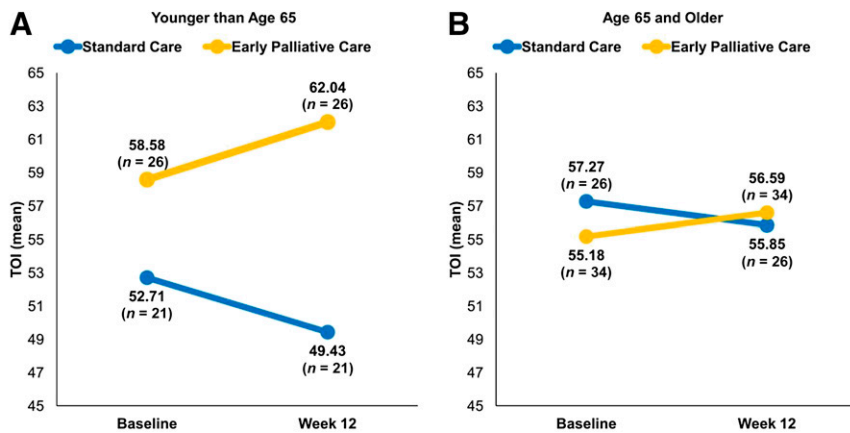


Figure 1. Quality-of-life scores from baseline to week 12 stratified by age. Using TOI scores, participants' quality-of-life from baseline to week 12 are shown for age <65 (A) and age ≥65 (B).

Abbreviation: TOI, Trial Outcome Index.

care groups at week 12, we found no significant treatment differences for older (25.0% vs. 15.4%, $p = .38$) or younger patients (24.0% vs. 47.6%, $p = .10$).

Quality-of-Life and Mood Outcomes by Gender

Using linear regression, we found that patient gender moderated the effects of EPC on QOL (gender × group assignment, $B = 8.09$, $SE = 3.51$, $95\% \text{ CI} = 1.12 \text{ to } 15.06$, $\beta = 0.30$, $p = .02$), thus prompting further analysis of the association stratified by patient gender. Comparing week 12 QOL scores between study groups and controlling for baseline QOL, we found that male patients assigned to EPC had significantly higher FACT-L (mean = 98.44 [SD = 13.72] vs. 85.00 [SD = 11.25], $p < .001$) and TOI scores (mean = 58.81 [SD = 10.85] vs. 48.30 [SD = 8.76], $p = .001$) than male patients assigned to oncology care (Fig. 3). Conversely, female patients in the EPC group did not have significantly different QOL compared with female patients assigned to oncology care (FACT-L mean = 97.58 [SD = 16.27] vs. 97.71 [SD = 17.27], $p = .99$; TOI mean = 59.06 [SD = 12.37] vs. 57.46 [SD = 12.24], $p = .63$).

We found significantly lower rates of depressive symptoms at week 12 for male patients in the EPC group compared with male patients in the oncology care group using both the HADS depression subscale (18.5% vs. 60.9%, $p = .002$) and the PHQ-9 (3.8% vs. 34.8%, $p = .008$) (Fig. 4). We found no significant difference between the EPC and oncology care groups in the rates of depressive symptoms among female patients at week 12 (HADS, depression subscale: 13.3% vs. 16.7%, $p = .73$; PHQ-9: 3.2% vs. 0.0%, $p = .38$). Using the anxiety subscale of the HADS to compare rates of anxiety symptoms in the EPC and oncology care groups at week 12, we found no significant treatment differences among males (26.1% vs. 25.9%, $p = .99$) or females (23.3% vs. 33.3%, $p = .42$).

DISCUSSION

In this exploratory analysis of data from an RCT assessing the impact of EPC integrated with oncology care, we found that age and gender moderated several of the outcomes evaluated with the integrated care model. We demonstrated that younger patients assigned to EPC had better QOL and mood at 12 weeks

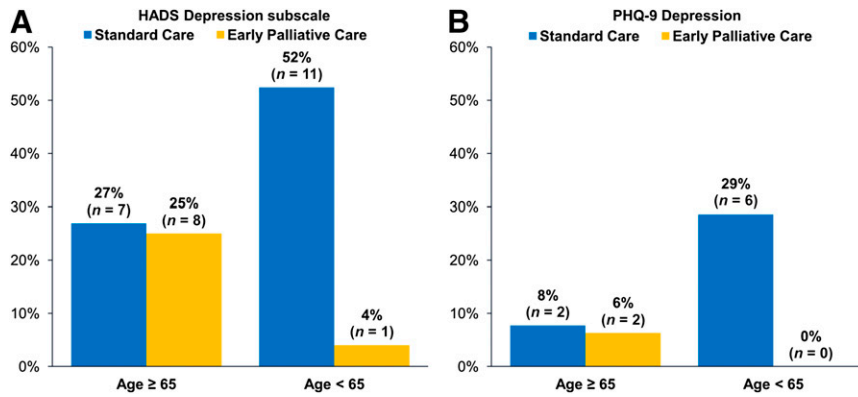


Figure 2. Week 12 depressive symptoms stratified by age. Stratified by age < 65, week 12 depressive symptoms across study arms are shown according to the HADS depression subscale (A) and the PHQ-9 (B).

Abbreviations: HADS, Hospital Anxiety and Depression Scale; PHQ-9, Patient Health Questionnaire 9.

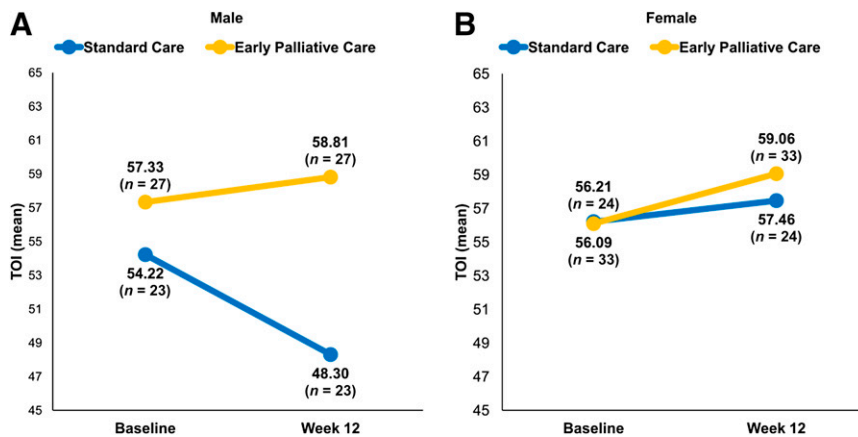


Figure 3. Quality-of-life scores from baseline to week 12 stratified by gender. Using TOI scores, participants’ quality-of-life from baseline to week 12 are shown for male patients (A) and female patients (B).

Abbreviation: TOI, Trial Outcome Index.

than younger patients assigned to oncology care, yet this treatment effect was not present for older patients. We also demonstrated that male patients assigned to EPC had better week 12 QOL and mood compared with males treated with oncology care alone. Conversely, treatment assignment did not significantly affect female patients’ QOL and mood. Collectively, these data suggest that patients’ age and gender qualified their experience with EPC.

RCTs of EPC interventions have consistently demonstrated improvements in patients’ QOL and depression [1–4]. We now report novel findings that these outcomes with EPC differ based on patients’ age and gender. Although prior research has found a relationship between demographic data and patient-reported outcomes [9, 13–15, 37–39], studies had not yet shown that the impact of palliative care interventions differentially vary across subgroups of patients with cancer [40]. Further, despite prior studies demonstrating that cancer patients’ QOL and mood often differ by age and gender [10, 16, 17, 20, 23, 24], we found minimal differences in baseline patient-reported measures across age and gender in our sample. This likely reflects the fact that we obtained patients’ baseline data near the time of diagnosis of advanced cancer, before differences between groups may have become evident

[41]. Thus, our results merit confirmation and if replicated support the need to identify age- and gender-specific palliative care needs. Ultimately, this will guide the development of tailored interventions aimed at meeting the distinct supportive care needs of all patients with cancer [42, 43].

Cancer disproportionately impacts older adults [44], yet few investigators have tested age-specific interventions to improve older patients’ QOL and mood. Our discovery that older patients did not report improvements in their QOL or mood with EPC expands upon the existing literature showing that older patients with cancer experience less emotional variation compared with younger patients [13–15, 23, 36, 45]. Prior data have suggested that younger patients report greater unmet supportive care needs, and this may help explain why younger patients in our study experienced significant benefits from EPC [6]. In addition to QOL and mood, outcome measures used to demonstrate successful supportive care for elderly cancer patients should also include age-specific outcomes such as functional status, treatment tolerability, and social support [46–48]. Additionally, the geriatric cancer population may require tailored interventions that focus on these and other age-specific outcomes while also addressing their competing comorbidities. Therefore, should the findings hold in a confirmatory study,

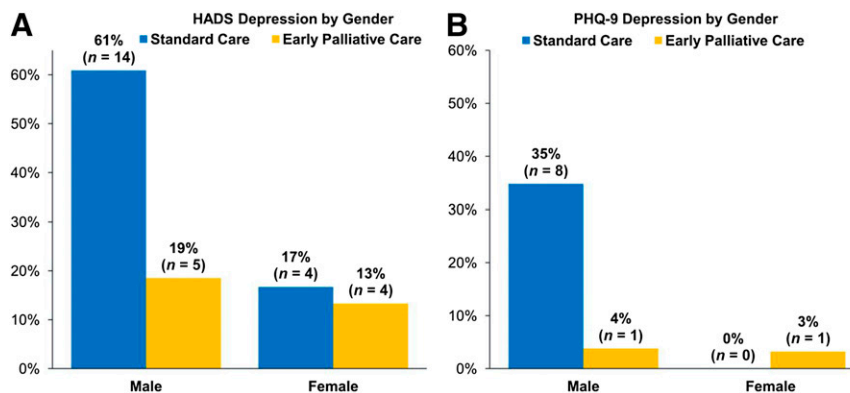


Figure 4. Week 12 depressive symptoms stratified by gender. Stratified by gender, participants' week 12 depressive symptoms across study arms are shown according to the HADS depression subscale (A) and the PHQ-9 (B).

Abbreviations: HADS, Hospital Anxiety and Depression Scale; PHQ-9, Patient Health Questionnaire 9.

future studies of palliative care interventions for older adults should seek to tailor the interventions to the unique needs of the geriatric cancer population and also consider age-specific outcomes when measuring treatment efficacy.

In addition to their age, patients' palliative care needs may depend on their gender. Our findings differ from the results of a prior randomized trial evaluating a multidisciplinary team intervention, including physical therapy, cancer education, psychiatry, and chaplaincy services versus standard care in patients with advanced cancer receiving radiation therapy [49]. This study demonstrated a significant improvement in QOL for females assigned to the intervention, but not for the males [39]. A potential reason for the contrasting results in our analysis and those of this trial is the different patient populations included in the studies. The previous study included a majority of patients with gastrointestinal and brain tumors undergoing radiation [49]. Moreover, the composition of the two interventions was quite distinct. The multidisciplinary program included physical therapy, psychiatry, and chaplain services, all of which were not components of the EPC study and thus may have impacted males and females differentially. For example, women with cancer experience more emotional benefits from physical therapy than men [50, 51]. Additionally, women with cancer accept psychosocial support [52] and spiritual counsel [53, 54] more readily than men. Thus, our findings that women did not experience significant QOL and mood differences with EPC suggest that they may need services in addition to EPC or, conversely, that they receive sufficient support from their oncology team.

Although males who were randomized to the intervention in the previous study did not experience improvement in their QOL, they did maintain their QOL throughout the study period [39]. Similarly, men in our study who received EPC also maintained their QOL at 12 weeks, yet those who received oncology care alone experienced a marked decline in their QOL at that time point, accounting for the observed significant difference between the study groups. Potential explanations for these findings include the existence of gender differences in the receipt of supportive care from the oncology team and/or in the way that patients express their need for supportive care [55]. Notably, women in our study in both the intervention group and the control group maintained their QOL and mood,

which likely limited our ability to show a treatment effect. These results support the consideration of gender when addressing the supportive care needs of patients with cancer.

Although our findings provide valuable new insights regarding differential age and gender outcomes with EPC, several limitations of our study warrant discussion. First, this was an exploratory analysis that requires confirmation in follow-up study. Second, our study included a homogenous patient sample with limited racial and ethnic diversity in a single, tertiary cancer center with a specialized group of palliative care clinicians. Therefore, the degree to which our results would generalize to other oncology patients and palliative care clinicians requires further investigation. Third, we evaluated one model of EPC in which patients only met with palliative care physicians and advanced practice nurses. Thus, our results may not apply to patients receiving alternative palliative care models or care from other supportive care clinicians. Finally, we cannot account for unmeasured confounders such as social support, frailty, or mental capacity, but future efforts to better understand our observed differences should consider these and other specific variables related to patient age and gender when studying palliative care interventions.

CONCLUSION

Integration of EPC with oncology care for patients with metastatic NSCLC improves QOL and mood differentially based on patient age and gender. Identifying how patients' clinical characteristics influence the role of EPC will help us establish a framework for more personalized palliative care interventions. Our study suggests that cancer patients' age and gender may modify both their experience with cancer and their palliative care needs. Similar to cancer directed therapy, which is determined based on both clinical and disease-specific factors, EPC may need to be tailored to individuals' clinical characteristics and care needs. By improving our understanding of these different palliative care needs, we can develop and test interventions specifically targeted to each individual with cancer.

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DISCLOSURES

Jennifer S. Temel: Helsin Therapeutics (RF). The other authors indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (ET) Expert testimony; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

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For Further Reading:

David Hui, Yu Jung Kim, Ji Chan Park et al. Integration of Oncology and Palliative Care: A Systematic Review. *The Oncologist* 2015;20:77–83.

Implications for Practice:

This systematic review identified 38 indicators of integration of oncology and palliative care (PC). On further validation, these indicators may facilitate benchmarking, prioritization, quality improvement, and accountability. Specifically, these indicators may facilitate (a) referring physicians, patients, and caregivers to identify the centers that offer a high level of access to PC services; (b) policy makers and administrators to benchmark their level of integration nationally and internationally, standardize their services, and allocate appropriate resources toward quality improvement; (c) organizations to provide special designations based on the level of integration; and (d) researchers to examine how the extent of integration is associated with various health care outcomes.