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

RYAN D. NIPP, JOSEPH A. GREER, AREEJ EL-JAWAHRI, LARA TRAEGER, EMILY R. GALLAGHER, ELYSE R. PARK, VICKI A. JACKSON, WILLIAM F. PIRL, JENNIFER S. TEMEL

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 were 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].

Correspondence: Ryan D. Nipp, M.D., Massachusetts General Hospital Cancer Center, 55 Fruit Street, Yawkey 7B, Boston, Massachusetts 02114, USA. Telephone: 617-724-4000; E-Mail: RNipp@MGH.Harvard.edu Received September 11, 2015; accepted for publication September 28, 2015; published Online First on November 30, 2015. ©AlphaMed Press 1083-7159/2015/$20.00/0 http://dx.doi.org/10.1634/theoncologist.2015-0232
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. Participants 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 $\chi^2$ 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...
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 \( \chi^2 \) 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 \( \mu = 101.88 \) [SD = 16.57] vs. 86.00 [SD = 16.61], \( p = .002 \)) and TOI scores (mean \( \mu = 56.08 \) [SD = 10.60] vs. 55.85 [SD = 10.14], \( p = .001 \)) 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 \( \mu = 94.97 \) [SD = 13.25] vs. 94.43 [SD = 13.95], \( p = .79 \)) and TOI scores (mean \( \mu = 56.14 \) [SD = 14.36] vs. 56.85 [SD = 14.36], \( p = .79 \)).

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 care groups at week 12, younger patients receiving EPC had lower rates of anxiety symptoms (22.7% vs. 35.6%, \( p = .04 \)).

The \( p \) values were derived from \( \chi^2 \) and Fisher’s exact tests for categorical variables and from independent-sample \( t \) test for continuous variables. Fisher’s exact test comparing rates of patients married to the rates of patients not married.

An 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.

### Table 1. Demographics

| Variable                   | Age \(<65 (n=47)\) | Age \(\geq65 (n=60)\) | \(p\) value | Female \((n=57)\) | Male \((n=50)\) | \(p\) value |
|----------------------------|-------------------|------------------------|-------------|----------------|----------------|-------------|
| Female, no. (%)            | 27 (57.4)         | 30 (50.0)              | .56         | —              | —              | —           |
| Race, no. (%)              | White             | 44 (93.6)              | 60 (100.0)  | 55 (96.5)      | 49 (98.0)      | .92         |
|                            | Black             | 2 (4.3)                | 0 (0.0)     | 1 (1.8)        | 1 (2.0)        | .64         |
|                            | Asian             | 1 (2.1)                | 0 (0.0)     | 1 (1.8)        | 0 (0.0)        | .13         |
| Marital status, no. (%)\(^a\) | Married          | 31 (66.0)              | 36 (60.0)   | 34 (59.6)      | 33 (66.0)      | .28         |
|                            | Single            | 8 (17.0)               | 4 (6.7)     | 5 (8.8)        | 7 (14.0)       | .56         |
|                            | Divorced or separated | 6 (12.8)              | 10 (16.7)   | 7 (12.3)       | 9 (18.0)       | .13         |
|                            | Widowed           | 2 (4.3)                | 10 (16.7)   | 11 (19.3)      | 1 (2.0)        | .67         |
| 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)      | .35         |
|                            | 1                 | 27 (57.4)              | 30 (50.0)   | 31 (54.4)      | 26 (52.0)      | .92         |
|                            | 2                 | 3 (6.4)                | 6 (10.0)    | 5 (8.8)        | 4 (8.0)        | .35         |
| Mood symptoms, no. (%)     |                   |                        |             |                |                | —           |
| HADS                       | Depression subscale | 13 (27.7)             | 11 (18.6)   | 13 (23.2)      | 11 (22.0)      | 1.00        |
|                            | Anxiety subscale  | 22 (46.8)              | 16 (27.1)   | 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 \( \chi^2 \) and Fisher’s exact tests for categorical variables and from independent-sample \( t \) test for continuous variables. Fisher’s exact test comparing rates of patients married to the rates of patients not married.

\(^a\)An 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.
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 \( \times \) group assignment, \( B = 8.09, SE = 3.51, 95\% CI = 1.12 \) to 15.06, \( \beta = .30, p = .02 \)), 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

**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 \( \geq 65 \) | 5.18  | 2.66  | 0.22  | -0.09 to 10.46 | .05           |
| Age \( \times \) group assignment | -8.96 | 3.56  | -0.35 | -16.03 to -1.89 | .01           |
| Gender \( \times \) 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 \( \geq 65 \) | 7.10  | 3.37  | 0.23  | 0.42 to 13.78  | .04           |
| Age \( \times \) group assignment | -12.50 | 4.49  | -0.37 | -21.41 to -3.58 | .01           |
| Gender \( \times \) group assignment | 11.97 | 4.43  | 0.33  | 3.18 to 20.76  | .01           |

**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 \( \geq 65 \) (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 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.
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 therapy [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.

**ACKNOWLEDGMENTS**

This work was supported by an American Society of Clinical Oncology Career Development Award and philanthropic gifts from the Joanne Hill Monahan Cancer Fund and Golf Fights.

©AlphaMed Press 2016
Cancer. Ryan D. Nipp is supported by Training Grant ST32CA071345-18 from the National Institutes of Health. Jennifer S. Temel is supported by National Cancer Institute Career Development Award K24CA181253.

Author Contributions

Conception/Design: Ryan D. Nipp, Joseph A. Greer, Areej El-Jawahri, Lara Traeger, Emily R. Gallagher, Elyse R. Park, Vicki A. Jackson, William F. Pirl, Jennifer S. Temel

Provision of study material or patients: Ryan D. Nipp, Joseph A. Greer, Areej El-Jawahri, Lara Traeger, Emily R. Gallagher, Elyse R. Park, Vicki A. Jackson, William F. Pirl, Jennifer S. Temel

Collection and/or assembly of data: Ryan D. Nipp, Joseph A. Greer, Areej El-Jawahri, Lara Traeger, Emily R. Gallagher, Elyse R. Park, Vicki A. Jackson, William F. Pirl, Jennifer S. Temel

Data analysis and interpretation: Ryan D. Nipp, Joseph A. Greer, Areej El-Jawahri, Lara Traeger, Emily R. Gallagher, Elyse R. Park, Vicki A. Jackson, William F. Pirl, Jennifer S. Temel

Manuscript writing: Ryan D. Nipp, Joseph A. Greer, Areej El-Jawahri, Lara Traeger, Emily R. Gallagher, Elyse R. Park, Vicki A. Jackson, William F. Pirl, Jennifer S. Temel

Final approval of manuscript: Ryan D. Nipp, Joseph A. Greer, Areej El-Jawahri, Lara Traeger, Emily R. Gallagher, Elyse R. Park, Vicki A. Jackson, William F. Pirl, Jennifer S. Temel

Disclosures

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

(C/A) Consulting/advisory relationship; (R) Research funding; (E) Employment; (I) Expert testimony; (H) Honoraria received; (O) Ownership interests; (P) Intellectual property rights/inventor/patient holder; (SAB) Scientific advisory board

References

1. Temel JS, Greer JA, Muzikansky A et al. Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med 2010;363:733–742.

2. Zimmermann C, Swami N, Krzyzanowska M et al. Early palliative care for patients with advanced cancer: A cluster-randomised controlled trial. Lancet 2014;383:1721–1730.

3. Temel JS, Jackson VA, Billings JA et al. Phase II study: Integrated palliative care in newly diagnosed advanced non-small-cell lung cancer patients. J Clin Oncol 2007;25:2377–2382.

4. Bakitas M, Lyons KD, Hegel MT et al. Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer: The Project ENABLE II randomized controlled trial. JAMA 2009;302:741–749.

5. Smith TJ, Temin S, Alexi ER et al. American Society of Clinical Oncology provisional clinical opinion: The integration of palliative care into standard oncology care. J Clin Oncol 2012;30:870–887.

6. Sanson-Fisher R, Girgis A, Boyes A et al. The unmet supportive care needs of patients with cancer. Cancer 2000;88:226–237.

7. Smith DP, Supramaniam R, King MT et al. Age, health, and education determine supportive care needs of men younger than 70 years with prostate cancer. J Clin Oncol 2007;25:2560–2566.

8. Morrison RS, Meier DE. Clinical practice: Palliative care. N Engl J Med 2004;350:2582–2590.

9. Parker PA, Baile WF, de Moor C et al. Psycho-social and demographic predictors of quality of life in a large sample of cancer patients. Psychooncology 2003;12:183–193.

10. Pud D. Gender differences in predicting quality of life in cancer patients with pain. Eur J Ocr Oncol Nurs 2011;15:486–491.

11. Nelson CJ, Weinberger MI, Balk E et al. The chronology of distress, anxiety, and depression in older prostate cancer patients. The Oncologist 2009;14:891–899.

12. Zhang AY, Cooper GS. Recognition of depression and anxiety among elderly colorectal cancer patients. Nurs Res Pract 2010;2010:693961.

13. Rose JH, O’Toole EE, Einastder D et al. Patient age, well-being, perspectives, and care practices in the early treatment phase for late-stage cancer. J Gerontol A Biol Sci Med Sci 2008;63:960–968.

14. Bradley N, Davis L, Chow E. Symptom distress in patients attending an outpatient palliative radiotherapy clinic. J Pain Symptom Manage 2005;30:123–131.

15. Cassileth BR, Lusk EL, Strouse TB et al. Psychosocial status in chronic illness: A comparative analysis of six diagnostic groups. N Engl J Med 1984;311:506–511.

16. Linden W, Vodermair A, Mackenzie R et al. Anxiety and depression after cancer diagnosis: Prevalence rates by cancer type, gender, and age. J Affect Disord 2012;141:343–351.

17. Jordon M, Fayers P, Loge JH et al. Quality of life in advanced cancer patients: The impact of sociodemographic and medical characteristics. Br J Cancer 2001;85:1478–1485.

18. Vodermair A, Linden W, Mackenzie R et al. Disease stage predicts post-diagnosis anxiety and depression only in some types of cancer. Br J Cancer 2011;105:1814–1817.

19. Walsh D, Donnelly S, Rybicki L. The symptoms of advanced cancer: Relationship to age, gender, and performance status in 1,000 patients. Support Care Cancer 2000;8:175–179.

20. Thome B, Halberg IR. Quality of life in older people with cancer: A gender perspective. Eur J Cancer (Engl) 2004;13:454–463.

21. Zimmermann C, Burman D, Swami N et al. Determinants of quality of life in men with advanced cancer. Support Care Cancer 2011;19:621–629.

22. Lundh Hagelin C, Seiger A, Fürst CJ. Quality of life in terminal care: With special reference to age, gender and marital status. Support Care Cancer 2006;14:320–328.

23. Blank TO, Bellizzi KM. A gerontologic perspective on cancer and aging. Cancer 2008;112(suppl):2569–2576.

24. Cheung WY, Le LW, Gagliele L et al. Age and gender differences in symptom intensity and symptom clusters among patients with metastatic cancer. Support Care Cancer 2011;19:417–423.

25. Mor V, Allen S, Malin M. The psychosocial impact of cancer on older versus younger patients and their families. Cancer 1994;74(suppl):2118–2127.

26. Bright N, Balducci L, Blasco G. Cancer in the elderly: Is it time for palliative care in geriatric oncology? J Geriatr Oncol 2014;5:197–203.

27. Novotny PJ, Smith DJ, Guse Let al. A pilot study assessing social support among cancer patients enrolled on clinical trials: A comparison of younger versus older adults. Cancer Manag Res 2010;2:133–142.

28. Chock MM, Lapid MI, Atherton PJ et al. Impact of a structured multidisciplinary intervention on the quality of life of older adults with advanced cancer. Int Psychogeriatr 2013;25:2077–2086.

29. Markson EW. Functional, social, and psychological disability as causes of loss of weight and independence in older community-living people. Clin Geriatr Med 1997;13:639–652.

30. Aass N, Fosså SD, Dahl AA et al. Prevalence of anxiety and depression in cancer patients seen at the Norwegian Radium Hospital. Eur J Cancer 1997;33:1597–1604.

31. Hopwood P, Stephens RJ. Depression in patients with lung cancer: Prevalence and risk factors derived from quality-of-life data. J Clin Oncol 2000;18:893–903.

32. Cella DF, Bonomi AE, Lloyd SR et al. Reliability and validity of the Functional Assessment of Cancer Therapy-Lung (FACT-L) quality of life instrument. Lung Cancer 1995;12:199–220.

33. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361–370.

34. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. J Gen Intern Med 2001;16:606–613.

35. Yanick. R. Cancer burden in the aged: An epidemiologic and demographic overview. Cancer 1997;80:1273–1283.

36. Hurria A, Gupta S, Zauderer M et al. Developing a cancer-specific geriatric assessment: A feasibility study. Cancer 2005;104:1998–2005.

37. Baider L, Perez T, De-Nour AK. Gender and adjustment to chronic disease: A study of couples with colon cancer. Gen Hosp Psychiatry 1989;11:1–8.

38. Broeckel JA, Jacobsen PB, Balducci L et al. Quality of life after adjuvant chemotherapy for breast cancer. Breast Cancer Res Treat 2000;62:141–150.

39. Lapid MI, Atherton PJ, Kung S et al. Does gender influence outcomes from a multidisciplinary intervention for quality of life designed for patients with advanced cancer? Support Care Cancer 2013;21:2485–2490.

40. Bischoff K, Weinberg V, Rabow MW. Palliative and oncologic co-management: Symptom management for outpatients with cancer. Support Care Cancer 2013;21:3031–3037.

41. Akechi T, Okuyama T, Akizuki N et al. Course of psychological distress and its predictors in advanced non-small cell lung cancer patients. Psychooncology 2006;15:463–473.
42. Rose JH, Radziewicz R, Bowmans KF et al. A coping and communication support intervention tailored to older patients diagnosed with late-stage cancer. Clin Interv Aging 2008;3:77–95.

43. Rose JH, Bowman KF, Radziewicz RM et al. Predictors of engagement in a coping and communication support intervention for older patients with advanced cancer. J Am Geriatr Soc 2009;57(suppl 2):S296–S299.

44. Yancik R. Population aging and cancer: A cross-national concern. Cancer J 2005;11:437–441.

45. Champion VL, Wagner LI, Monahan PO et al. Comparison of younger and older breast cancer survivors and age-matched controls on specific and overall quality of life domains. Cancer 2014;120:2237–2246.

46. Fried TR, Bradley EH, Towle VR et al. Understanding the treatment preferences of seriously ill patients. N Engl J Med 2002;346:1061–1066.

47. Hurria A, Dale W, Mooney M et al. Designing therapeutic clinical trials for older and frail adults with cancer: U13 Conference recommendations. J Clin Oncol 2014;32:2587–2594.

48. Puts MT, Hardt J, Monette J et al. Use of geriatric assessment for older adults in the oncology setting: A systematic review. J Natl Cancer Inst 2012;104:1133–1163.

49. Clark MM, Rummans TA, Atherton PJ et al. Randomized controlled trial of maintaining quality of life during radiotherapy for advanced cancer. Cancer 2013;119:880–887.

50. Craike MJ, Hose K, Courneya KS et al. Perceived benefits and barriers to exercise for recently treated patients with multiple myeloma: A qualitative study. BMC Cancer 2013;13:319.

51. Asztalos M, De Bourdeaudhuij I, Cardon G. The relationship between physical activity and mental health varies across activity intensity levels and dimensions of mental health among women and men. Public Health Nutr 2010;13:1207–1214.

52. Curry C, Cossich T, Matthews JP et al. Uptake of psychosocial referrals in an outpatient cancer setting: Improving service accessibility via the referral process. Support Care Cancer 2002;10:549–555.

53. Mystakidou K, Tsilika E, Parpa E et al. Demographic and clinical predictors of spirituality in advanced cancer patients: A randomized control study. J Clin Nurs 2008;17:137–148.

54. Jacobs-Lawson JM, Schumacher MM, Hughes T et al. Gender differences in psychosocial responses to lung cancer. Gend Med 2010;7:137–148.

55. Pollak KI, Arnold RM, Jeffreys AS et al. Oncologist communication about emotion during visits with patients with advanced cancer. J Clin Oncol 2007;25:5748–5752.

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.