

Longitudinal Changes in Function, Symptom Burden, and Quality of Life in Patients with Early-Stage Lung Cancer

Marianna Koczywas, MD¹, Anna Cathy Williams, RN, BSN, PHN², Mihaela Cristea, MD¹, Karen Reckamp, MD¹, Frederic W. Grannis Jr., MD³, Brian L. Tiep, MD⁴, Gwen Uman, PhD⁵, and Betty Ferrell, PhD, FAAN, FPCN²

¹Medical Oncology and Therapeutics Research, City of Hope, Duarte, CA; ²Nursing Research & Education, Department of Population Sciences, City of Hope, Duarte, CA; ³Thoracic Surgery, City of Hope, Duarte, CA; ⁴Pulmonary Critical Care, Department of Respiratory Diseases, City of Hope, Duarte, CA; ⁵Vital Research, Los Angeles, CA

ABSTRACT

Background. Emerging evidence supports the integration of palliative care concurrently with disease-focused care in patients with serious illnesses, such as lung cancer. This paper describes how longitudinal changes in physical function, symptom burden, and QOL of patients with early-stage non-small cell lung cancer (NSCLC) informed the development of an interdisciplinary, tailored palliative care intervention.

Methods. Patients with early stage (I–IIIB) NSCLC were accrued into the usual care phase (Phase 1) of an NCI-funded Program Project Grant. Baseline and longitudinal (up to 52 weeks post-accrual) physical function, symptoms, and QOL were assessed in the thoracic ambulatory clinics of one NCI-designated Comprehensive Cancer Center. Outcome measures included geriatric assessments, psychological distress, symptoms, and QOL. The association between disease stage (I–II vs. III) and longitudinal changes in these domains was evaluated.

Results. A total of 103 patients were accrued. Stage I–II patients were significantly more likely to complete the study ($p = 0.005$). The stages (I–II vs. III) were equivalent at baseline on all demographic variables, clinical, and functional status. Physical function fluctuated longitudinally and was higher at 6 and 24 weeks than at baseline and 12 weeks. There was a longitudinal decrease in total number of symptoms ($p < 0.001$). Physical and social/family QOL fluctuated longitudinally ($p < 0.001$ and $p = 0.016$, respectively).

Conclusions. Patients with early-stage NSCLC report a significant longitudinal decrease in physical QOL, and fluctuations in objective and subjective measures of physical function over time were observed regardless of disease stage category. An interdisciplinary palliative care intervention is currently being tested to decrease symptom burden and improve QOL.

An evolving body of evidence supports the value of integrating palliative care into disease-focused care in patients with serious illness, such as lung cancer.^{1–3} Data strongly support that patients with non-small cell lung cancer (NSCLC) experience high symptom burdens, many comorbidities, and psychosocial-spiritual concerns related to the diagnosis.^{4–10} The key study by Temel and colleagues¹¹, reporting on NSCLC patients receiving concurrent palliative care, gained much attention when their outcomes revealed not only improved symptoms but prolonged survival. This evolving evidence has led organizations, such as American Society of Clinical Oncologists to issue statements regarding the inclusion of palliative care for all NSCLC patients at the time of diagnosis.¹² Other investigators and organizations also have strongly supported the integration of palliative care into routine lung cancer care.^{2,3}

The investigators in this study have conducted previous studies adding to the recognition of needs for lung cancer patients across all stages.^{13–15} Whereas the palliative care needs for those with stage IV is well established, the authors' research have documented that patients with stages I–III disease also experience multiple symptoms, psychosocial needs, and living with the uncertainty of possible recurrence. These previous studies led to funding from the National Cancer Institute for a Program Project Grant (P01) to develop a palliative care intervention for

lung cancer and compare it across three populations of early stage (stage I–III), late stage (stage IV), and family caregivers. This paper reports on the usual care phase of the early-stage project and how the findings informed the development of the palliative care intervention.

METHODS

Design

The Program Project includes three prospective longitudinal studies addressing early stage (stages I–III), late stage (stage IV), and family caregivers in NSCLC.

Patient Selection

Study participants were recruited from the Medical Oncology and Surgical Oncology Ambulatory Clinics at an NCI-designated Comprehensive Cancer Center. Eligibility criteria included a diagnosis of stage I–III NSCLC, no other cancer diagnosis within the past 5 years, and aged 18 years or older. Eligible patients were recruited to assess Usual Care in Phase 1 of this two-phase Program Project Grant.

Procedure

The study protocol was approved by the institutional review board. Research nurses approached all eligible individuals during a regularly scheduled clinic visit, and written informed consent was obtained from all patients. Following informed consent, patients completed baseline assessment that included basic demographics, geriatric assessments (physical function, cognitive status, social activities and support, nutritional status), symptoms, psychological distress, and overall quality of life (QOL). An objective measure of physical function (Timed “up and go”) was completed by the research nurse. All outcome measures were repeated at 6, 12, 24, 36, and 52 weeks after accrual. A chart audit was conducted at 52 weeks to collect data regarding treatment variables.

Instruments

Key demographic, disease, and treatment variables were captured through chart audit. Physical function and cognitive status were assessed by: (1) The Instrumental Activities of Daily Living (IADL) Scale, which consists of seven questions rated on a three-point Likert scale of degree to which the activity required to maintain independence at home and in the community can be performed independently. Norms are available and based on 2,146

elderly community residents^{16,17} (2) The Activities of Daily Living (ADL) Scale contains six questions regarding the ability to complete basic self-care skills, such as bathing or dressing, and are rated on a three-point Likert¹⁸ (3) The Blessed Orientation-Memory-Concentration Test consists of six questions designed to screen for gross cognitive impairment. A score >11 signifies potential cognitive impairment. The test has excellent validity as a screening instrument, correlates highly with clinicians’ ratings of dementia severity ($r = 0.89$), and discriminates between patients with mild, moderate, and severe cognitive deficits^{19,20} (4) The Timed “Up and Go” is a performance based measure of function. The test, measured in seconds, is the time it takes for an individual to stand up from a standard arm-chair (approximate seat height of 46 cm), walk a distance of 3 m (10 feet), turn, walk back to the chair, and sit down again²¹; and (5) percent unintentional weight loss and body mass index (BMI) were used to determine nutritional status. Patients were asked to quantify the amount of unintentional weight loss for the past 6 months.

Social activities and support were assessed by: (1) The Medical Outcomes Study (MOS) Social Activity Limitations Scale is a four-item scale that assesses the extent to which physical or emotional problems have interfered with social activities. All items are rated on a five-point Likert scale. The mean of the total score is transformed to a scale of 0–100, with a higher number indicating greater support²²; and (2) The MOS Social Support Survey: Emotional/Information and Tangible Subscales were used to determine access to material aid/behavioral assistance and advice, information, guidance, or feedback from others. The items are rated on a five-point Likert scale.²²

Symptom characteristics were assessed by using the Memorial Symptom Assessment Scale (MSAS). The MSAS is a 32-item tool used to measure the prevalence, characteristics, and distress of common symptoms. Validity testing has included correlation with the RAND Mental Health Inventory well-being subscale, RAND distress subscale, Symptom Distress Scale, Functional Living Index-Cancer, Karnofsky Performance Scale, and Memorial Pain Assessment Card. Reliability and validity have been reported in studies with cancer patients.²³

QOL was assessed by the Distress Thermometer, which is an efficient, low subject burden method to evaluate psychological distress during the past week, based on a scale of 1 to 10. A score of 5 or above indicates a need for intervention.²⁴ The Functional Assessment of Cancer Therapy-Lung (FACT-L, version 4) tool is a 37-item instrument that measures multidimensional QOL.²⁵ This tool is comprised of five subscales: physical, social/family, emotional, functional well-being, and the lung cancer symptom index (LCS). Each item is rated on a five-point

TABLE 1 Demographics

	Stages I and II N (%)	Stage III N (%)	Total N (%)	p value
Gender				
Male	24 (44.4)	24 (49)	48 (46.6)	0.695
Female	30 (55.6)	25 (51)	55 (53.4)	
Age range 34–92 (x = 65.69, SD 11.84)				
Race				
White	43 (79.6)	41 (83.7)	84 (81.6)	0.848
African American	4 (7.4)	4 (8.2)	8 (7.8)	
Asian	6 (11.1)	3 (6.1)	9 (8.7)	
Other	1 (1.9)	1 (2.0)	2 (1.9)	
Ethnicity–Hispanic/Latino				
Yes	5 (9.3)	2 (4.1)	7 (6.8)	0.441
No	49 (90.7)	47 (95.9)	96 (93.2)	
Religious preference				
Protestant	25 (47.2)	17 (34.7)	42 (41.2)	0.407
Catholic	7 (13.2)	7 (14.3)	14 (13.7)	
Jewish	5 (9.4)	2 (4.1)	7 (6.9)	
Other	1 (1.9)	2 (4.1)	3 (2.9)	
None	15 (28.3)	21 (42.9)	36 (35.3)	
Marital status				
Single	2 (3.7)	8 (16.3)	10 (9.7)	0.171
Separated/divorced	10 (18.5)	9 (18.4)	19 (18.4)	
Widowed	7 (13)	4 (8.2)	11 (10.7)	
Married/partnered	35 (64.8)	28 (57.1)	63 (61.2)	
Education				
Elementary school	0 (0)	1 (2)	1 (1)	0.569
Secondary/high school	22 (40.7)	19 (38.8)	41 (39.8)	
College	32 (59.3)	29 (59.2)	61 (59.2)	
Income				
<\$10 K	3 (5.6)	0 (0)	3 (2.9)	0.124
\$10 K–\$30 K	5 (9.3)	11 (22.4)	16 (15.5)	
\$30 K–\$50 K	12 (22.2)	13 (26.5)	25 (24.3)	
>\$50 K	29 (53.7)	19 (38.8)	48 (46.6)	
Preferred not to answer	5 (9.3)	6 (12.2)	11 (10.7)	
Employment status				
Employed	17 (31.5)	12 (24.5)	29 (28.2)	0.546
Unemployed	2 (3.7)	1 (2)	3 (2.9)	
Retired	23 (42.6)	18 (36.7)	41 (39.8)	
Homemaker	9 (16.7)	15 (30.6)	24 (23.3)	
Other	3 (5.6)	3 (6.1)	6 (5.8)	
Smoking history				
Current smoker	1 (1.9)	4 (8.2)	5 (4.9)	0.329
Former smoker	42 (77.8)	36 (73.5)	78 (75.7)	
Nonsmoker	11 (20.4)	9 (18.4)	20 (19.4)	

Likert scale.^{26–28} The Functional Assessment of Chronic Illness Therapy–Spirituality Tool (FACIT–Sp–12) is a 12-item tool that assesses spiritual well being using a five-point Likert scale. The tool generates a total score as well as two subscale scores (meaning and faith). Psychometric properties of the FACIT–Sp–12 was tested in a separate study containing 1,617 subjects of whom the majority had a diagnosis of early stage or metastatic cancer (83.1%).²⁹

Data Analysis

Scannable data forms developed using the Remark system were completed by patients and analyzed using SPSS (version 19.0). Missing values analysis was conducted using the 103 patients who completed the six sets of measures (baseline through 52 weeks) or who did not drop out due to mortality or severe illness. Values were found to be missing completely at random, thus allowing for imputation using the estimation-maximization method.^{30,31} The data were analyzed according to cancer stage group, comparing those with stage I and II disease ($n = 54$, 52.4%) with those having stage III disease ($n = 49$, 47.6%). Descriptive statistics were computed for all variables; contingency table analysis and the chi-square statistic were used to test for association between cancer stage group and categorical variables, whereas two-way repeated measures analysis of variance (ANOVA) was used to test for change over time and time by stage interactions for all continuous predictor and outcome variables.

RESULTS

Demographics and Disease Characteristics

A total of 103 patients were accrued (stage I = 34, stage II = 20, and stage III = 49). Six of these patients died, three patients dropped out of the study before 52 weeks due to severe illness, and six were lost to follow-up (Table 1). For the 49 stage III patients, 21 were no evidence of disease (NED), 12 had metastatic disease, five died, four had stable disease, four had progressive disease, and 3 had recurrence or a new primary while enrolled in the study. Patient age ranged from 34–92 years [mean = 65.69, standard deviation (SD) = 11.86]; 48 (46.6%) were younger than age 65 years, 35 (34%) were 66–74 years, and 20 (19.4%) were aged 75 years and older. Approximately 46.6% of the sample was male. Patients were predominantly Protestant (41.2%); 6.8% were Hispanic/Latino, an additional 8.7% were Asian, 7.8% African American, 1.9% other, and 74.8% Caucasian/non-Hispanic. Just over half of patients

TABLE 2 Geriatric assessment findings

	Stages I and II N (%)	Stage III N (%)	Total N (%)	p value
Functional status				
Activities of daily living (ADL)				
Needs assist (<7)	6 (11.1)	2 (4.2)	8 (7.8)	0.276
Independent	48 (88.9)	46 (95.8)	94 (92.2)	
Instrumental activities of daily living (IADL)				
Needs assist (<14)	15 (27.8)	17 (34.7)	32 (31.1)	0.525
Independent	39 (72.2)	32 (65.3)	71 (68.9)	
Timed up and go				
<10 seconds	44 (81.5)	33 (67.3)	77 (74.8)	0.116
≥10 seconds	10 (18.5)	16 (32.7)	26 (25.2)	
Karnofsky performance status—rated by healthcare team				
Unable to work, lives at home (50–70)	8 (14.8)	8 (16.3)	16 (15.5)	1.000
Normal activities (80–100)	46 (85.2)	41 (83.7)	87 (84.5)	
Karnofsky performance status—self-reported by patients				
Unable to work, lives at home (50–70)	2 (3.7)	6 (12.2)	8 (7.8)	0.146
Normal activities (80–100)	52 (96.3)	43 (87.8)	95 (92.2)	
Routinely exercise				
Yes	20 (38.5)	24 (50.0)	44 (44.0)	0.314
No	32 (61.5)	24 (50.0)	56 (56.0)	
Cognition				
Blessed Orientation-Memory-Concentration Test				
Possible impairment (≥ 11)	1 (1.9)	1 (2.0)	2 (1.9)	1.000
Normal (< 11)	53 (98.1)	48 (98.0)	101 (98.1)	
Comorbidity				
Previous cancer Dx				
Yes	16 (29.6)	13 (26.5)	29 (28.2)	0.827
No	38 (70.4)	36 (73.5)	74 (71.8)	
Other chronic illness				
Yes	50 (92.6)	41 (83.7)	91 (88.3)	0.221
No	4 (7.4)	8 (16.3)	12 (11.7)	
Nutrition				
Body mass index: weight/height ²				
Normal weight	21 (38.9)	22 (44.9)	43 (41.7)	0.277
Overweight	17 (31.5)	19 (38.8)	36 (35.0)	
Obese	16 (29.6)	8 (16.3)	24 (23.3)	
Weight increase or decrease over 6 months				
Increase	3 (42.9)	8 (72.7)	11 (61.1)	0.332
Decrease	4 (57.1)	3 (27.3)	7 (38.9)	
Food intake in the past month				
Unchanged	41 (75.9)	29 (60.4)	70 (68.6)	0.07
More than usual	2 (3.7)	8 (16.7)	10 (9.8)	
Less than usual	11 (20.4)	11 (22.9)	22 (21.6)	

had some college education. Patients aged 65 and older were significantly more likely to be widowed. Just over one third of the patients were retired. Stage I–II patients reported significantly more chronic illnesses than stage III patients ($p = 0.03$). More than three-quarters were former smokers (75.7%), 4.9% were currently smoking, and 19.4% never smoked. On average, patients had been diagnosed approximately 18 months before accrual, which did not differ between disease stage groups. A total of 72 patients (69.9%) had surgery before or during the course of the study, which was significantly more likely to occur for stage I–II patients (79.6%) than for stage III patients (59.2%; $p = 0.032$). Stage III patients (69.4%) were significantly more likely to have chemotherapy and/or radiation than stage I–II patients (25.9%; $p < 0.001$).

As shown in Table 2, the majority of patients across both groups were independent or within normal limits in their ADL (92.2%), IADL (68.9%), Timed Up and Go test (74.8%), objective and subjective Karnofsky Performance Status (84.5 and 92.2%, respectively), and cognition (98.1%). For patients with stage III disease, 65% reported being independent with IADLs and 95% reported independence with ADLs, suggesting that this is a highly functional cohort of patients with locally advanced disease. Functional status was comparable to patients with stage I and II disease. None of the patients was underweight according to their BMI, and 53% were overweight or obese; 61.1% had experienced a weight increase in the past 6 months, but 21.6% report eating less than usual in the past month. Twelve patients reported having no chronic illnesses (11.7%), but all patients were found, upon chart review, to have one or more comorbidities (average of 3.8 comorbidities per patient). The circulatory (60.4%), endocrine (49.5%), respiratory (41.6%), and “mental disorder,” which includes anxiety and depression (36.6%), systems were most frequently involved. Number of medications taken at baseline was equivalent for the two groups (6.9 vs. 7.12, respectively), but after 12 weeks, stage III patients took significantly more medications (9.73 vs. 7.57, $p = 0.025$).

Longitudinal Change in Geriatric Assessment Scores by Stage of Disease

IADL was significantly lower (more dependent) at 52 weeks than at all other time periods except 6 weeks, regardless of stage ($p = 0.012$; Table 3). Objective KPS significantly decreased after baseline at all time points, regardless of stage ($p = 0.001$). Subjective KPS was significantly lower at 36 and 52 weeks than at baseline and 12 weeks, regardless of stage ($p = 0.044$). In contrast to those three measures suggesting that function declined over

TABLE 3 Longitudinal changes in geriatric assessment data by disease stage

Disease stage	Baseline		6 Weeks		12 Weeks		24 Weeks		36 Weeks		52 Weeks		Main effect	Interaction
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Functional status														
Activities of daily living (ADL)														
I & II	6.90	0.3	6.86	0.41	6.85	0.72	6.92	0.27	6.84	0.46	6.84	0.46	0.059	0.089
III	6.91	0.6	6.9	0.36	6.85	0.51	6.9	0.42	6.93	0.24	6.94	0.32		
Total	6.91	0.46	6.88	0.39	6.85	0.63	6.91	0.34	6.88	0.37	6.89	0.41		
Instrumental activities of daily living (IADL)														
I & II	13.17	1.86	12.98	1.82	12.92	2.42	13.01	2.14	12.88	2.16	12.61	2.49	0.012	0.122
III	12.75	2.50	12.74	2.19	13.37	1.42	13.32	1.69	13.36	1.42	12.17	2.72		
Total	12.98	2.17	12.87	1.99	13.13	2.04	13.15	1.95	13.09	1.87	12.41	2.59		
Karnofsky performance status (rated by healthcare team)														
I & II	88.68	11.44	85.05	14.17	86.42	11.94	86.05	11.99	85.63	12.29	86.4	11.79	0.001	0.294
III	87.95	11.93	83.12	11.13	84.59	10.43	83	9.03	81.92	10.46	80.52	10.76		
Total	88.35	11.61	84.18	12.85	85.59	11.26	84.66	10.81	83.95	11.59	83.73	11.65		
Karnofsky performance status (self-rated)														
I & II	87.55	12.07	84.64	12.01	85.85	11.51	84.47	11.29	85.55	10.31	85.84	10.28	0.044	0.191
III	84.32	14.85	82.45	11.49	84.74	10.02	82.82	10.55	80.78	9.05	79.4	13.02		
Total	86.08	13.43	83.65	11.76	85.34	10.82	83.72	10.93	83.38	10	82.92	11.98		
Timed up and go														
I & II	15.37	6.31	14.63	5.95	13	4.85	13.22	4.28	12.9	3.9	13.05	4.99	0.008	0.241
III	14.71	6.02	14.54	5.68	13.89	4.24	12.75	3.40	12.46	2.86	13.86	3.91		
Total	15.1	6.16	14.59	5.8	13.36	4.6	13.03	3.92	12.72	3.50	13.38	4.57		
Nutrition														
Body mass index														
I & II	27.20	5.60	26.78	5.36	26.96	5.56	26.89	5.46	27.01	5.64	31.14	18.78	0.379	0.071
III	26.21	5.02	26.22	4.84	26.19	4.83	26.02	4.85	26.42	4.98	24.77	11.49		
Total	26.75	5.34	26.53	5.11	26.61	5.23	26.50	5.19	26.74	5.33	28.25	16.14		
Cognition														
Blessed Orientation-Memory-Concentration Test														
I & II	0.49	2.09	0.51	1.15	0.64	1.44	0.38	1.29	0.36	0.95	0.39	2.07	0.42	0.963
III	0.8	2.11	0.71	1.63	0.89	1.8	0.43	1.26	0.5	1.21	0.62	1.92		
Total	0.63	2.1	0.6	1.38	0.76	1.61	0.4	1.27	0.42	1.07	0.49	2		
Social activities and support														
Medical Outcomes Study social activities														
I & II	43.75	12.5			43.99	10.18	45.45	10.16	45.04	8.81	47.59	9.83	0.172	0.319
III	43.18	10.6			42.86	12.12	43.84	8.58	39.92	9.07	43.41	11.49		
Total	43.49	11.62			43.47	11.06	44.72	9.46	42.72	9.24	45.7	10.76		
Medical Outcomes Study tangible support														
I & II	74.29	33.83	75.35	32.18	72.29	34.27	71.63	36.64	74.02	35.58	72.99	38.39	0.586	0.658
III	79.69	27.13	75.31	31.75	76.22	32.86	77.07	34.24	76.56	36.63	71.47	39.1		
Total	76.74	30.93	75.33	31.82	74.07	33.52	74.1	35.49	75.17	35.9	72.30	38.52		
Medical Outcomes Study emotional/informational support														
I & II	72.82	29.42	66.36	32.92	70.64	31.02	70.78	32.72	73.48	31.04	74.93	32.56	0.342	0.158
III	76.42	27.03	77.38	26.91	79.71	27.14	83.31	24.97	80.7	27.1	74.83	30.61		
Total	74.45	28.27	71.36	30.69	74.75	29.52	76.47	29.98	76.76	29.4	74.88	31.53		
Medical Outcomes Study social support														
I & II	73.31	27.46	69.36	30.01	71.19	29.2	71.06	32.14	73.66	30.18	74.29	32.28	0.622	0.309
III	77.54	24.86	76.69	27.1	78.55	27.25	81.23	25.92	79.32	28.84	73.71	31.6		
Total	75.23	26.26	72.68	28.81	74.53	28.42	75.67	29.77	76.23	29.56	74.02	31.81		

TABLE 4 Longitudinal changes in symptoms and QOL by disease stage

Psychological distress														
Distress thermometer														
I & II	3.49	2.78	3.49	2.65	3.53	2.9	3.28	2.85	3.55	2.8	3.51	2.56	0.693	0.577
III	3.94	2.47	4.31	2.3	3.43	2.5	4.17	2.68	4.2	2.7	4.29	2.8		
Total	3.68	2.65	3.84	2.53	3.49	2.72	3.66	2.8	3.83	2.76	3.84	2.68		
Symptoms														
Memorial Symptom Assessment Scale (global distress index)														
I & II	1.42	0.77	1.42	0.72	1.31	0.74	1.28	0.72	1.18	0.74	1.24	0.77	0.053	0.559
III	1.56	0.77	1.46	0.63	1.51	0.72	1.45	0.79	1.45	0.72	1.26	0.79		
Total	1.48	0.77	1.44	0.68	1.4	0.73	1.36	0.76	1.3	0.74	1.25	0.78		
Memorial Symptom Assessment Scale (physical symptom subscale)														
I & II	1.66	0.93	1.88	0.93	1.69	0.82	1.75	0.91	1.76	0.8	1.85	0.56	0.658	0.22
III	1.75	0.84	1.59	0.74	1.77	0.73	1.74	0.77	1.92	0.76	1.79	0.63		
Total	1.7	0.89	1.75	0.86	1.72	0.78	1.75	0.84	1.83	0.78	1.82	0.59		
Memorial Symptom Assessment Scale (psychological symptom subscale)														
I & II	1.21	0.76	1.16	0.74	1.05	0.81	0.99	0.81	1	0.77	1.03	0.84	0.059	0.766
III	1.27	0.77	1.25	0.72	1.15	0.78	1.15	0.78	1.19	0.87	1.01	0.83		
Total	1.24	0.76	1.2	0.73	1.1	0.8	1.07	0.8	1.09	0.82	1.02	0.83		
Memorial Symptom Assessment Scale (total number of symptoms)														
I & II	10.57	5.5	10.26	4.83	9.48	5.14	8.22	4.43	7.22	4.24	6.59	3.98	<0.001	0.345
III	11.47	5.24	11.80	6.47	11.18	5.59	9.88	5.45	7.22	4.91	6.55	5.50		
Total	11	5.37	10.99	5.7	10.29	5.4	9.01	4.98	7.22	4.55	6.57	4.74		
Quality of life														
Functional Assessment of Cancer Therapy—lung (total score)														
I & II	100.97	18.81	98.48	18.49	100.87	20.51	98.73	21.11	101.21	21.37	103	19.85	0.52	0.703
III	98.04	19.68	94.21	21.93	92.96	23.99	95.63	23.1	94.32	20.92	95.98	19.81		
Total	99.72	19.12	96.65	20.01	97.49	22.27	97.41	21.89	98.27	21.33	100	20.02		
Functional Assessment of Cancer Therapy – physical well-being														
I & II	22.71	6.18	21.42	6.38	21.29	7.9	21.82	5.90	23.86	5.05	24.16	4.04	<0.001	0.823
III	22.42	5.97	19.56	7.68	19.92	6.83	20.14	6.11	21.83	5.11	22.57	4.94		
Total	22.58	6.05	20.58	7.02	20.67	7.43	21.06	6.02	22.94	5.15	23.44	4.52		
Functional Assessment of Cancer Therapy—social/family well-being														
I & II	19.75	5.97	20.01	7.06	20.04	6.7	18.06	7.8	18.31	8.79	18.07	9.29	0.016	0.863
III	20.14	7.04	20.77	6.83	20.16	7.23	19.52	8.19	19.35	7.89	18.14	8.57		
Total	19.93	6.45	20.35	6.93	20.09	6.91	18.72	7.98	18.78	8.37	18.1	8.92		

TABLE 4 continued

Functional Assessment of Cancer Therapy—emotional well-being														
I & II	18.51	4.46	18.42	4.14	18.51	5	19.14	5.36	19.03	6.09	19.29	5.70	0.532	0.195
III	17.93	5.16	18.32	4.56	16.98	5.44	17.60	5.5	15.84	5.83	17.19	6.95		
Total	18.25	4.77	18.37	4.32	17.82	5.24	18.44	5.45	17.58	6.15	18.34	6.35		
Functional Assessment of Cancer Therapy—functional well-being														
I & II	15.04	4.62	14.64	5.26	14.73	4.99	14.72	5.41	14.59	4.88	14.19	4.99	0.092	0.731
III	15.23	5.13	14	5.04	14.6	4.72	14.39	4.63	13.73	4.08	12.94	5.52		
Total	15.12	4.84	14.35	5.14	14.67	4.85	14.57	5.05	14.2	4.53	13.62	5.25		
Functional Assessment of Cancer Therapy—lung cancer subscale														
I & II	23.8	5.87	23.22	5.07	23.6	5.25	23.68	4.86	24.48	4.78	24.65	5.07	0.143	0.476
III	24.21	4.96	22.27	5.5	22.51	5.8	23.37	5.87	23.46	4.94	22.93	5.19		
Total	23.99	5.46	22.79	5.26	23.11	5.5	23.54	5.31	24.02	4.85	23.87	5.17		
Functional Assessment of Chronic Illness Therapy—spirituality subscale total score														
I & II	35.08	7.73	32.31	7.76	33.46	9.16	33.35	9.74	32.35	8.84	32.49	9.88	0.059	0.623
III	34.23	9.06	33.79	8.05	34.01	9.5	33.07	9.61	33.03	8.78	31.91	11.29		
Total	34.69	8.33	32.98	7.89	33.71	9.27	33.23	9.63	32.66	8.78	32.23	10.5		
Functional Assessment of Chronic Illness Therapy—spirituality subscale meaning														
I & II	25.21	4.84	23.63	5.45	24.18	5.77	24.24	6.35	23.81	5.35	24.29	6.3	0.057	0.233
III	24.98	5.52	24.55	4.92	24.23	6.24	24.1	6.31	23.53	5.29	22.36	7.17		
Total	25.1	5.14	24.04	5.21	24.2	5.95	24.17	6.3	23.68	5.29	23.41	6.74		
Functional Assessment of Chronic Illness Therapy—spirituality subscale faith														
I & II	9.87	5	8.64	4.95	9.28	5.57	9.11	5.93	8.37	5.76	8.22	6.05	0.262	0.379
III	9.25	5.29	9.3	5.21	9.78	5.34	8.97	4.77	9.26	5.26	9.2	6.34		
Total	9.59	5.12	8.94	5.05	9.51	5.54	9.05	5.4	8.78	5.53	8.67	6.17		

TABLE 5 Symptom prevalence over time (%)

Symptom	Baseline	6 Weeks	12 Weeks	24 Weeks	36 Weeks	52 Weeks
Lack of energy	81.6	89.3	90.3	88.3	76.7	74.8
Worrying	74.8	67	58.3	56.3	50.5	44.7
SOB	74.5	76.7	80.6	78.6	72.8	68
Difficulty sleeping	71.8	69.9	62.1	56.3	55.3	53.4
Cough	69.9	65	67	56.3	46.6	46.6
Dry skin	66	60.2	57.3	50.5	32	23.3
Pain	64.1	64.1	66	58.3	53.4	51.5
Feeling nervous	59.2	59.2	49.5	51.5	44.7	36.9
Feeling sad	55.3	53.4	52.4	40.8	35.9	37.9
Difficulty concentrating	53.4	61.2	56.3	50.5	47.6	36.9
Feeling irritable	39.8	37.9	31.1	31.1	18.4	14.6
Numbness	38.8	37.9	33.0	36.9	33.0	26.2
Lack of appetite	38.8	37.9	37.9	34	22.3	18.4
Itching	34	35	27.2	21	9.7	8.7
Nail changes	33	33	33	24.3	20.4	13.6
Problems with urination	31.1	26.2	27.2	23.3	21.4	12.6
Dry mouth	29.1	25.2	20.4	16.5	7.8	7.8
Feeling drowsy	26.2	26.2	22.3	16.5	5.8	5.8
Problems with sexual interest	25.5	21.4	20.4	14.5	17.5	23.3
Difficulty swallowing	23.3	18.4	15.5	12.6	5.8	5.8
Nausea	22.3	31.1	22.3	13.6	4.9	5.8
Dizziness	20.4	29.1	20.4	15.5	10.7	9.7
Sweats	14.6	13.6	8.7	4.9	2.9	2.9
Diarrhea	13.6	17.5	20.4	19.4	16.5	11.7
Feeling bloated	11.7	14.6	14.6	8.7	3.9	4.9
Vomiting	9.7	5.8	9.7	7.8	1.9	2.9
Rash on my body	8.7	9.7	11.7	4.9	1.9	3.9
Rash on my face	4.9	5.8	5.8	1.9	1.9	1.9
Crusting on my skin	4.9	6.8	7.8	5.8	12.6	2.9

time, the 12-, 24-, and 36-week Timed Up and Go tests were significantly faster than baseline and 6-week tests, regardless of stage ($p = 0.008$).

Longitudinal Changes in Symptoms and QOL by Stage of Disease

Overall symptom distress, as measured by the MSAS Global Distress Index, decreased significantly at 52 weeks compared with baseline and 6 weeks, regardless of stage ($p = 0.053$; Table 4). The total number of symptoms reported decreased significantly from 11.00 at baseline to 6.57 at 52 weeks, regardless of stage ($p < 0.001$). Total

symptom scores (total MSAS) and psychological distress remained stable, and none of the scores had significant time by stage interactions. The most prevalent symptoms (Table 5) included lack of energy, worrying, shortness of breath, difficulty sleeping, and cough, all with prevalence of greater than 69% at baseline.

Physical well-being score (as measured by the FACT-L) decreased significantly between baseline and 24 weeks and increased significantly to surpass baseline levels from 12 weeks to 52 weeks, regardless of stage ($p < 0.001$). Social/family well-being increased from baseline to 12 weeks, and then declined from 24 to 52 weeks ($p = 0.16$). All other QOL scores remained statistically stable (Table 4), as did psychological distress and spirituality.

Chart Audit Findings

It was possible to audit 101 of the 103 patient charts at the end of their study participation. Overall, the use of support services was very low considering the complex and multiple needs of these patients. Overall, only 28 patients had referrals to supportive care services, and there were 49 referrals (approximately 1.75 referrals each) to institutional services. These included 13 referrals to social work, 11 each to pulmonary rehabilitation and nutrition, and 5 to PT/OT. In addition, there were five external referrals to home health, PRS, financial counseling, and a combination of medical specialties. The primary reason for an encounter was for symptom management (92.3%), including pain (61.5%), dyspnea/cough/hemoptysis (30.8%), and fever (30.8%). Seventeen patients (16.8%) were admitted to the inpatient setting while on study. The majority of these admissions were unscheduled (76.5%), largely due to need for symptom management. Posthospital disposition included independently at home (86.7%), skilled nursing facility (6.7%), and one in-hospital death (6.76 %).

Intervention Development

The usual care phase findings informed the development of the interdisciplinary palliative care intervention. The Phase 2 (experimental phase) of this Program Project Grant tests a palliative care intervention. Core elements of the intervention consist of an Interdisciplinary Care Conference (ICC) that is conducted for each patient, with attendance by the treating oncologist and thoracic surgeon, nurse, and key supportive care experts (social work, nutrition, pulmonary and physical rehabilitation, pain and palliative medicine, chaplain, and psychologist). Before each ICC, a research nurse gathers all patient baseline assessment data, reviews the responses, and transcribes assessment results onto an interdisciplinary care plan.

Information from the care plan is then presented to the ICC team by the research nurse. The ICC then makes palliative care-related recommendations, which are all documented on the care plan and referrals to supportive care services are initiated. The research nurse conducts follow-up evaluations with each patient, and communicates with the patient's treating oncologist to review the patient's status and to determine whether further recommendations are needed. This phase of the study will continue for 2 years.

In addition to the interdisciplinary care, all patients receive educational materials and participate in four educational sessions that are administered in face-to-face or telephone format by the nurse. The session contents are divided into four QOL domains: physical, psychological, social, and spiritual well-being. Supplemental materials are available that address preoperative issues for patients who are accrued before surgery is scheduled. During each session, the patient identifies topics of interest, and these topics are then discussed during the sessions, allowing for tailoring of content that is pertinent to each patient's needs. The research nurse provides recommended resources to help patients manage palliative care-related issues and initiates any further referrals to palliative care services if needed.

DISCUSSION

A major study limitation is the potential selection bias in a cohort of patients who are highly functional, and therefore, study findings should be interpreted with caution in terms of its generalizability. Findings from this study indicate that patients with the symptom and QOL concerns of early stage NSCLC patients vary across time in association with their treatments. This usual care phase has led to a palliative care intervention, which we hypothesize will improve outcomes for these patients through a consistent assessment of needs, proactively, by an interdisciplinary team.

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