A Nurse Practitioner Directed Intervention Improves the Quality of Life of Patients with Metastatic Cancer: Results of a Randomized Pilot Study

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Abstract

Background: There is a paucity of randomized studies evaluating the value of palliative interventions on a prospective basis in newly diagnosed oncology patients. We sought to prospectively evaluate quality of life (QoL) outcomes in advanced cancer patients who received discussion-based palliative care interventions from an advanced registered nurse practitioner (ARNP) integrated into the oncology team, and compare these outcomes with a control population.

Methods: Patients with metastatic cancer were randomized to standard care or an ARNP-directed intervention that included discussions of the benefits of hospice, discussions on living wills and advanced directives (Five Wishes document) along with an assessment of QoL. Relevant endpoints included change from baseline QoL and improvement in hospice knowledge.

Results: From November 13, 2008, through July 28, 2009, 26 patients were accrued at the Mayo Clinic in Jacksonville, Florida. The study closed early due to published data demonstrating the benefits of early palliative care interventions in the management of metastatic cancer patients. Statistically significant improvements from baseline were noted in emotional and mental QoL assessments in the intervention group that were not seen in the control group. Patients found it useful to have the living will and Five Wishes documents offered as part of the ARNP intervention.

Conclusions: An ARNP-directed intervention that explains the benefits of hospice and addresses advanced directives early in the course of metastatic cancer patients' treatment, is well received by the patients and their relatives and leads to measurable improvement in the patient's emotional and mental QoL.

Introduction

ADVANCED CANCER PATIENTS who are still receiving disease-specific management may often have unmet psychological, social and spiritual needs because efforts are concentrated on the medical management of the malignancy (such as with chemotherapy and radiation therapy).¹ Additionally, active treatment of the cancer has significant burdens that may manifest as depression, fatigue, anxiety and emotional trauma.^{2,3} Typically the patient and family are focused on the pathway to cure. Regrettably, the patient's spiritual needs are frequently not assessed or addressed at this time.⁴ The inattention to the spiritual, social, rehabilitative and psychological needs of the patients and their families are missed opportunities for interventions that may bring significant palliative benefits.

Hospice provides care to patients with a terminal illness and a predicted survival of less than 6-12 months. Timeliness of hospice enrollment for patients with terminal cancer could be improved in the United States, given that 30% of patients referred to hospice die within 7 days and median length of stay in hospice in the United States is 21 days.^{5,6} Patients who do not experience timely hospice referral benefit less from the financial, social and psychological services that hospice provides, including evaluation and treatment of symptoms utilizing palliative principles.

There are multiple potential explanations for delay in hospice referrals, both patient driven and physician driven. In many cases, patients may be overestimating their chances for extended survival, which can result in a resistance to interventions focused more on palliation of symptoms rather than disease-specific management.⁷ Also, many academic medical

centers and private oncology practices do not offer ongoing care and support upon hospice enrollment, patients and/or their families may be reluctant to enlist the assistance of hospice because of a strong attachment to their current caregivers and perceived sense of abandonment. Patients may also have inherent fears related to overuse of narcotics, or of death itself. On the other hand, physicians may be reluctant to discuss hospice with patients because of difficulty communicating that a disease-specific treatment is futile or no longer effective, or they simply may not feel the patient will be understanding or receptive to the idea of palliative care or hospice.⁸ Despite perceptions of the clinician regarding timing of hospice referral, retrospective studies have demonstrated that hospice referrals that are made too early are very rare, and are far outnumbered by referrals that come too late.^{1,6}

Recent data showed that a phone ARNP intervention can mitigate the decline in psychological well-being experienced by metastatic cancer patients.⁹ A recently published randomized trial in patients with metastatic lung cancer showed that patients who received palliative care had an improvement in overall survival in addition to improvement in their quality of life as compared with a control, no-intervention group.¹⁰ Previous investigations have mostly focused on either comprehensive inpatient services or a team-based, multidisciplinary outpatient approach, which have been shown to be effective for reducing pain and other symptoms as well as increasing patient and caregiver satisfaction.¹¹ However, there are drawbacks to utilizing these models in a conventional oncology practice structure. Specifically, many of these interventions can be costly and time intensive; reimbursement models are often suboptimal for palliative care services rendered; and palliative care teams are often separate and not fully integrated with the oncology care team. Therefore, it would be of interest to demonstrate a discernible benefit with simple interventions, such as those provided by an oncology ARNP who is a member of the oncology practice and who provides care to oncology patients under physician supervision. We report the results of a pilot randomized trial evaluating the benefits of this ARNP-directed palliative intervention that included discussions of the benefits of hospice and advanced directives using a clear and concise living will document, "Five Wishes." The goal of this study was to determine if an intervention with a palliative ARNP would lead to improvement in the patients' QoL, improvement in knowledge about hospice, earlier referral to hospice services, and decreased sense of abandonment from the oncology practice upon hospice referral.

Methodology

This study was initially designed as a randomized phase 2 trial with a goal of accruing 100 patients with metastatic cancer (50 patients per arm). Patients were randomized to either a control arm or an intervention arm. The control group completed baseline and one month later (or at the time of hospice referral if that occurred earlier) hospice knowledge questionnaires (HKQ) and QoL tools, including the Functional Assessment of Cancer Therapy-General [FACT-G] and the Linear Analogue Self Assessment scale (LASA), but did not receive any mandatory palliative care intervention. These patients had access to palliative care consultations and hospice referrals as deemed indicated by their oncology team. Patients on the in-

tervention arm, in addition to completing the questionnaires and QoL tools at baseline (pre-intervention) and one month later (post-intervention), had an initial and a one-month follow-up consultation with an oncology ARNP who taught them about hospice, helped fill out the Five Wishes and living will forms, and assessed their psychological, physical, intellectual/cognitive, social, and spiritual needs.

The FACT-G assessment tool has been widely used and prospectively validated as a measure for QoL endpoints.¹² It is a survey with 27 questions distributed among physical, social/family, emotional, and functional categories. Each question is answered in a linear scale from 0 to 4, creating a maximum score of 108 (28 each for physical, social, and functional, and 24 for emotional). The LASA is a 12-question survey, with each question designed to assess multiple QoL parameters on a linear scale of 1-10. Its use has also been validated in multiple previous palliative care interventions.¹³ It was decided to use these two QoL tools in this pilot study in order to assess whether one of them will be preferable to the other for future studies. The Five Wishes document is a living will written in layperson's language which assists patients in answering five fundamental questions regarding their end of life care: identifying a health care surrogate, the kind of medical treatment desired, desire for comfort measures, how the patient wishes to be treated, and what the patient wants his or her family to know at the time of their death.¹⁴ Spiritual needs were assessed through direct questioning of patients' preferences and their satisfaction with their spiritual life. Sense of abandonment from the oncology practice was assessed via a supplementary questionnaire. Patients in the intervention arm also were followed by the ARNP following hospice referral.

This study was opened from November 3, 2008 through July 28, 2009 and was closed after the first 26 patients were entered in view of the finding of the positive effects of a nurse intervention in terminal cancers as reported by Bakitas and colleagues,⁹ and in view of the preliminary data analysis of the patients offered participation in this study that showed that many patients refused study participation as a result of the control arm and their desire to receive the ARNP intervention.

Eligibility criteria for study participants included: age greater than 18 years, a diagnosis of metastatic cancer, a strong expectation of hospice referral within 12 months of enrollment as determined by their treating oncologist, willingness to participate in two palliative care consultations with an ARNP prior to hospice enrollment, willingness to undergo visits by the ARNP after hospice enrollment, ability to complete questionnaire(s) alone or with assistance, willingness and ability to provide informed verbal consent, and having an identifiable primary caregiver. Patients were excluded from participating if they were planning to enter hospice care with other hospice providers instead of the Community Hospice of Northeast Florida (CHNEF), which was a partner for this study.

Statistical analysis for questionnaire data from the FACT-G and LASA surveys was performed with all questionnaire item responses tabulated separately for each group, using median and range. Pre/post changes in overall (functional) QoL, as measured by the FACT-G functional well-being subscale score, were compared between arms A and B using the Wilcoxon rank-sum (Mann-Whitney U) test. Secondary analyses

TABLE 1. DEMOGRAPHIC VARIABLES

	<i>Intervention (N=12)</i>	<i>No intervention (N=14)</i>	<i>Total (N=26)</i>	
Age				<i>p</i> = 0.6993
Mean (SD)	66.7 (16.3)	64.9 (7.5)	65.7 (12.2)	
Range	(38.0-91.0)	(51.0-82.0)	(38.0-91.0)	
Gender				<i>p</i> = 0.5551
Male	3 (25%)	5 (35.7%)	8 (30.8%)	
Female	9 (75%)	9 (64.3%)	18 (69.2%)	
Patient's living situation				<i>p</i> = 0.3996
Alone	3 (30%)	2 (15.4%)	5 (21.7%)	
With caregiver	7 (70%)	11 (84.6%)	18 (78.3%)	
Data not available	2	1	3	
Caregiver relationship to patient				<i>p</i> = 0.0604
Spouse	4 (33.3%)	11 (84.6%)	15 (60%)	
Daughter	4 (33.3%)	0 (0%)	4 (16%)	
Son	0 (0%)	1 (7.7%)	1 (4%)	
Parent	1 (8.3%)	0 (0%)	1 (4%)	
Other relative	2 (16.7%)	1 (7.7%)	3 (12%)	
Other	1 (8.3%)	0 (0%)	1 (4%)	
Data not available	0	1	1	
Cancer type				<i>p</i> = 0.2592
Breast	7 (58.3%)	5 (35.7%)	12 (46.2%)	
Lung	0 (0%)	2 (14.3%)	2 (7.7%)	
Prostate	1 (8.3%)	0 (0%)	1 (3.8%)	
Other	4 (33.3%)	7 (50%)	11 (42.3%)	
Cancer grade				<i>p</i> = 0.9817
Missing	0 (0%)	1 (7.1%)	1 (3.8%)	
2	2 (16.7%)	2 (15.4%)	4 (16%)	
3	4 (33.3%)	4 (30.8%)	8 (32%)	
4	6 (50%)	7 (53.8%)	13 (52%)	
Performance score				<i>p</i> = 0.5612
0	1 (8.3%)	1 (7.1%)	2 (7.7%)	
1	7 (58.3%)	10 (71.4%)	17 (65.4%)	
2	4 (33.3%)	2 (14.3%)	6 (23.1%)	
3	0 (0%)	1 (7.1%)	1 (3.8%)	

utilized the remainder of the domains for each submeasure. Descriptive secondary questionnaire items scored on an ordinal scale were reported using median and range, and analyzed using the Wilcoxon rank-sum test. For the Hospice Knowledge Questionnaire, correct responses were assigned a value of 1, incorrect responses a value of -1, and responses of "do not know" a value of 0. The hospice knowledge survey responses were descriptively tabulated according to randomization group (A/B) and time of survey administration (pre/post). To determine whether arms A and B differ with respect to hospice knowledge as a result of the intervention, the pre/post difference in the scored survey responses were compared between groups using the nonparametric Wilcoxon rank sum (Mann-Whitney U) test.

The study was approved by the Mayo Clinic institutional review board (IRB). Given the minimal risk associated with the study, verbal consent was obtained from all participants as determined by the IRB. Protocol was listed in clinicaltrials.gov as protocol number NCT00896792.

Results

This study was opened from November 3, 2008 through July 28, 2009 and was closed after the first 26 patients were enrolled. Demographics of the study participants are summarized on

Table 1 below. There were no significant differences between the groups. Final questionnaire data could not be analyzed for eight patients, two in the intervention group and six in the control group. Two patients, both in the control group, were too ill to complete the baseline and follow-up questionnaires. Two participants withdrew because of lack of compliance with the required visits and consultations. One of them had expressed interest in the intervention arm and was not interested in participating in the control portion of the study after randomization. Four patients died prior to completing the follow-up survey (one in intervention group, three in control group). In addition, patients reported to the study personnel that it was very useful to have the living will and Five Wishes documents completed as part of the ARNP intervention.

Although an original primary endpoint of the study was to assess time to hospice referral in the two groups, the frequently prolonged period to hospice referral, relatively short study follow-up, and small sample size made it difficult to assess this outcome. By the same token, sense of abandonment upon hospice referral, which was a secondary endpoint of the study, could not be properly evaluated from the data collected.

Despite the fact that the study was closed early with only 26 patients randomized (12 to the intervention arm and 14 to the control arm), there was a statistically significant improvement in the FACT-G emotional domain in the intervention group as

TABLE 2. FACT-G DOMAIN CHANGES FROM BASELINE

	<i>Intervention (N=12)</i>	<i>No intervention (N=14)</i>	<i>Total (N=26)</i>	<i>p value</i>
FACT-G Physical: Change from baseline				<i>p</i> = 0.9289
N	10	8	18	
Mean (SD)	0.3 (5.12)	-0.4 (3.54)	0.0 (4.38)	
Range	(-6.7-9.0)	(-7.0-5.0)	(-7.0-9.0)	
FACT-G Social/Family: Change from baseline				<i>p</i> = 0.3244
N	10	8	18	
Mean (SD)	0.4 (5.80)	0.8 (2.65)	0.6 (4.56)	
Range	(-6.0-14.0)	(-2.8-6.0)	(-6.0-14.0)	
FACT-G Emotional: Change from baseline				<i>p</i> = 0.0106
N	10	6	16	
Mean (SD)	1.2 (2.94)	-4.5 (4.54)	-0.9 (4.49)	
Range	(-5.0-5.0)	(-11.0-0.0)	(-11.0-5.0)	
FACT-G Functional: Change from baseline				<i>p</i> = 0.7671
N	9	6	15	
Mean (SD)	-0.8 (5.08)	0.8 (2.99)	-0.2 (4.31)	
Range	(-11.0-5.0)	(-2.0-6.0)	(-11.0-6.0)	
FACT-G Total: Change from baseline				<i>p</i> = 0.3121
N	9	6	15	
Mean (SD)	1.2 (12.15)	-3.9 (4.97)	-0.8 (9.99)	
Range	(-16.7-22.0))	(-9.2-2.0)	(-16.7-22.0)	

SD, Standard deviation.

compared with baseline assessment which was not seen in the control group ($p=0.0106$) (Table 2). None of the additional FACT-G domains had statistically significant differences between groups.

Table 3 shows the results of the LASA scale administered to patients in both cohorts. There were no significant differences between the groups at baseline (data not shown). The change from baseline mental QoL was statistically improved in the

TABLE 3. LASA QUESTIONNAIRES CHANGE FROM BASELINE (POSITIVE S=IMPROVED QoL)

	<i>Intervention (N=12)</i>	<i>No intervention (N=14)</i>	<i>Total (N=26)</i>	
Overall QOL				<i>p</i> = 0.2762
N	10	8	18	
Mean (SD)	2.0 (25.73)	-8.8 (21.67)	-2.8 (23.96)	
Range	(-50.0-40.0)	(-60.0-10.0)	(-60.0-40.0)	
Overall mental				<i>p</i> = 0.0219
N	10	8	18	
Mean (SD)	19.0 (32.47)	-10.0 (16.04)	6.1 (29.73)	
Range	(-10.0-100.0)	(-40.0-10.0)	(-40.0-100.0)	
Overall physical				<i>p</i> = 0.8886
N	10	8	18	
Mean (SD)	7.0 (21.11)	3.8 (9.16)	5.6 (16.53)	
Range	(-20.0-40.0)	(-10.0-20.0)	(-20.0-40.0)	
Overall emotional				<i>p</i> = 0.0724
N	10	8	18	
Mean (SD)	13.0 (19.47)	-6.3 (20.66)	4.4 (21.75)	
Range	(-20.0-40.0)	(-50.0-10.0)	(-50.0-40.0)	
Social activity				<i>p</i> = 0.2554
N	10	8	18	
Mean (SD)	2.0 (25.30)	-2.5 (12.82)	0.0 (20.29)	
Range	(-60.0-30.0)	(-20.0-20.0)	(-60.0-30.0)	
Overall spiritual				<i>p</i> = 0.2767
N	10	8	18	
Mean (SD)	7.0 (13.37)	-2.5 (16.69)	2.8 (15.26)	
Range	(-10.0-30.0)	(-30.0-20.0)	(-30.0-30.0)	
Pain frequency				<i>p</i> = 0.3848
N	10	8	18	
Mean (SD)	-5.0 (27.59)	7.5 (17.53)	0.6 (23.88)	
Range	(-70.0-30.0)	(-20.0-40.0)	(-70.0-40.0)	

(continued)

TABLE 3. (CONTINUED)

	Intervention (N=12)	No intervention (N=14)	Total (N=26)	
Average pain				$p=0.8885$
N	10	8	18	
Mean (SD)	7.0 (15.67)	6.3 (15.98)	6.7 (15.34)	
Range	(-20.0-40.0)	(-20.0-30.0)	(-20.0-40.0)	
Average fatigue				$p=0.3213$
N	10	7	17	
Mean (SD)	0.0 (27.89)	-8.6 (36.25)	-3.5 (30.81)	
Range	(-70.0-30.0)	(-50.0-60.0)	(-70.0-60.0)	
Level of support				$p=0.1444$
N	9	7	16	
Mean (SD)	3.3 (25.00)	-5.7 (11.34)	-0.6 (20.16)	
Range	(-50.0-40.0)	(-30.0-0.0)	(-50.0-40.0)	
Financial concerns				$p=0.5013$
N	10	7	17	
Mean (SD)	-1.0 (12.87)	-8.6 (42.20)	-4.1 (27.85)	
Range	(-20.0-30.0)	(-100.0-30.0)	(-100.0-30.0)	
Legal concerns				$p=0.4381$
N	10	7	17	
Mean (SD)	-10.0 (20.6)	-22.9 (36.8)	-15.3 (28.1)	
Range	(-50.0-20.0)	(-100.0-0.0)	(-100.0-20.0)	

SD, standard deviation.

intervention group as compared to the control group (19 versus 10, $p=0.02$). No other variables achieved statistical significance. Table 4 shows the hospice knowledge questionnaire data, which did not attain statistical significance for difference in change from baseline in the two groups.

Discussion

Recent evidence has shown that early palliative care can improve certain outcome measures such as increased patient satisfaction. Concurrent with this is an interest in developing

models of care delivery that can result in meaningful improvements while keeping implementation simple. We set out to demonstrate that QoL outcomes can be improved with ARNP-directed education and follow-up. The results of our FACT-G and LASA surveys, which assess a broad range of QoL measures, including physical, social, emotional, and functional well-being, showed significant improvement in the emotional and mental well-being of the patients following the intervention as determined by the FACT-G and LASA questionnaires which was not observed in the control group. Emotional quality of life was measured by the FACT-G questionnaire based on questions regarding feelings of sadness, anxiety (in general and about death specifically), and coping. The LASA tool is a much shorter tool which includes only one question for each domain; for example, mental well-being is determined by how patients answer the following question on a 10 point scale: "How would you describe your overall mental (intellectual) well-being?" We suspect that, despite the semantic differences, both of these domains were interpreted by patients as being similar, especially when compared to other parameters such as physical and functional well-being. Ultimately, participants had no difficulties completing the FACT-G questionnaire, and therefore, given the more detailed and the more comprehensive nature of this tool as compared to the LASA tool, we have decided to use the FACT-G in future studies.

Despite the encouraging results, there are some important limitations to our study. The most significant limitation is the small size of the cohort. Due to published results demonstrating improvement in outcomes from a nurse-driven intervention, in addition to patient feedback encouraging more widespread adoption of the intervention, it was felt unethical to continue to accrue to a control population without the potential benefits from the ARNP intervention. Of course, having a control group would be useful for demonstration of tangible QoL benefits going forward, but future studies will likely need to focus on different types and schedules of

TABLE 4. HOSPICE KNOWLEDGE QUESTIONNAIRE (HKQ): TOTAL SCORES (-100%) AND CHANGE FROM BASELINE (-100%)

	Intervention (N=12)	No intervention (N=14)	Total (N=26)	
Total HKQ score: baseline				$p=0.4654$
N	11	11	22	
Mean (SD)	43.4 (26.93)	36.4 (27.75)	39.9 (26.92)	
Range	(0.0-84.6)	(0.0-92.3)	(0.0-92.3)	
Total HKQ score: cycle 1				$p=0.3225$
N	10	7	17	
Mean (SD)	61.5 (25.64)	46.2 (33.23)	55.2 (29.07)	
Range	(15.4-84.6)	(-15.4-84.6)	(-15.4-84.6)	
Change from baseline				$p=0.1848$
N	9	7	16	
Mean (SD)	13.7 (20.63)	1.1 (23.68)	8.2 (22.20)	
Range	(-23.1-38.5)	(-23.1-46.2)	(-23.1-46.2)	
p value	0.1032	0.3856		

HKQ, hospice knowledge questionnaire; SD, standard deviation.

interventions, rather than completely excluding one group of patients from receiving ARNP counseling and education. Alternatively, future studies could use an immediate versus delayed intervention group, with surveys conducted prior to the delayed group receiving their intervention. The study endpoints pertaining to hospice utilization and sense of abandonment were not able to be properly assessed, primarily due to low sample size and a prolonged time to hospice referral. A future analysis with a larger cohort would be helpful, but would likely need to compare to historical controls as opposed to a true control group.

In summary, our pilot study demonstrated that a simple ARNP-directed intervention focusing on early palliative care, hospice education and quality of life assessments improves the emotional well-being and mental quality of life of patients with metastatic cancer as determined by the FACT-G and LASA tools. The success of this study brings a simple way to introduce advanced directives discussions and symptom assessment early in the clinical course of metastatic cancer patient care by a professional (in this case the ARNP) who is part of the oncology team. Also, advanced care planning and informed discussions about end-of-life issues were well received by patients despite the fact that they were incorporated into the first consultation visit. It has been previously suggested that advanced directive discussion be reserved for a second (or later) palliative care consultation visit in order to focus on other aspects of patient care, such as symptom management, and to allow providers and patients to develop a relationship.¹⁵

In the future, we plan to explore the use of this intervention in broader study populations, with special attention to underserved and minority subgroups, given the reports of underutilization and decreased awareness of palliative care and hospice services in this population.¹⁶ In addition, it would be of interest to apply this ARNP intervention to specific disease subtypes, and tailor palliative care education to disease-specific concerns (such as cough or dyspnea in advanced lung carcinoma, for instance). Future studies are needed to better understand the impact of these types of palliative care interventions on QoL-related outcomes, and to broaden our utilization of them in patients who may benefit.

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