Advance Care Planning Improves Psychological Symptoms But Not Quality of Life and Preferred End-of-Life Care of Patients With Cancer

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ABSTRACT

Background: This study was conducted to examine whether a longitudinal advance care planning (ACP) intervention facilitates concordance between the preferred and received life-sustaining treatments (LSTs) of terminally ill patients with cancer and improves quality of life (QoL), anxiety symptoms, and depressive symptoms during the dying process. **Patients and Methods:** Of 795 terminally ill patients with cancer from a medical center in Taiwan, 460 were recruited and randomly assigned 1:1 to the experimental and control arms. The experimental arm received an interactive ACP intervention tailored to participants' readiness to engage in this process. The control arm received symptom management education. Group allocation was concealed, data collectors were blinded, and treatment fidelity was monitored. Outcome measures included 6 preferred and received LSTs, QoL, anxiety symptoms, and depressive symptoms. Intervention effectiveness was evaluated by intention-to-treat analysis. **Results:** Participants providing data had died through December 2017. The 2 study arms did not differ significantly in concordance between the 6 preferred and received LSTs examined (odds ratios, 0.966 [95% CI, 0.653–1.428] and 1.107 [95% CI, 0.690–1.775]). Participants who received the ACP intervention had significantly fewer anxiety symptoms (β , -0.583; 95% CI, -0.977 to -0.189; $P=.004$) and depressive symptoms (β , -0.533; 95% CI, -1.036 to -0.030; $P=.038$) compared with those in the control arm, but QoL did not differ. **Conclusions:** Our ACP intervention facilitated participants' psychological adjustment to the end-of-life (EoL) care decision-making process, but neither improved QoL nor facilitated EoL care honoring their wishes. The inability of our intervention to improve concordance may have been due to the family power to override patients' wishes in deeply Confucian doctrine-influenced societies such as Taiwan. Nevertheless, our findings reassure healthcare professionals that such an ACP intervention does not harm but improves the psychological well-being of terminally ill patients with cancer, thereby encouraging physicians to discuss EoL care preferences with patients and involve family caregivers in EoL care decision-making to eventually lead to patient value-concordant EoL cancer care.

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Background

Improving the quality of end-of-life (EoL) care is a priority in healthcare systems.¹ An essential component of high-quality EoL care is honoring individuals' values and preferences.^{1,2} One strategy to achieve this aim is advance care planning (ACP)³ to explore patient preferences for life-sustaining treatments (LSTs)^{4,5} and clarify misunderstandings⁶ about their efficacy at EoL, actively involve patients in EoL care decision-making, and align EoL care with patients' goals and preferences.^{1,2,4,5} Providing such value-based EoL care to terminally ill patients with cancer may not only "individualize" EoL cancer care² and counteract the international trend toward increasingly aggressive and costly EoL care,^{7–9} but also may facilitate adjustment to the uncertainty inherent in EoL care decision-making, thus alleviating anxiety and depressive symptoms and improving quality of life (QoL).^{10,11} The few randomized controlled trials (RCTs) of ACP studies targeting terminally/seriously ill patients^{12–19} have shown that ACP not only increases physician-patient EoL care discussions,^{12–19} (earlier) completion of advance directives,^{13,16–18} and concordance between preferred and received EoL care,^{13,16} but also does not detrimentally affect patients' anxiety, depression, and QoL.^{14,18,19}

However, the robustness and validity of these ACP RCT findings are threatened by several methodological insufficiencies.^{3,20} First, all but one¹³ of the ACP studies we reviewed provided a single-session intervention^{12,14–19} long before the patient's death,^{12,14,15,18} or few (13.67%^{16–18}, 12.0%¹³) patients died within 6 months after enrollment when concordance between preferred and received EoL care was evaluated. Second, most studies were cross-sectional, with only 2^{14,15} evaluating intervention outcomes more than once to capture changes as death approached, when EoL care decision-making becomes more relevant. Third, study outcomes commonly centered

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on the EoL care process (eg, the content/quality of ACP communication)^{12,14,15,18,19} and the completion of advance directives,^{13,16–18} but rarely on patient outcomes reflecting high-quality EoL care^{1,20} (eg, EoL care honoring patients' wishes^{13,15,16,19}), psychological adjustment to the impending death,^{18,19} and better QoL.¹⁴ Fourth, ACP studies have commonly failed to tailor interventions to participants' readiness to engage in ACP,^{12,13,16,18} directly assess patients' EoL care preferences when evaluating the concordance between preferred and received EoL care,¹⁵ and explicitly indicate how treatment fidelity was ensured/monitored.^{12,13,15–19}

Therefore, this RCT was designed to examine an interactive ACP intervention tailored to participants' readiness to engage in ACP while monitoring/ensuring high treatment fidelity. We hypothesized that our ACP intervention would facilitate concordance between preferred and received LSTs of terminally ill patients with cancer and improve psychologic symptoms and QoL during the dying process compared with an intervention based on symptom management education (control arm).

Patients and Methods

Design, Settings, and Sample

Consecutive adult oncology patients were recruited from April 2013 through June 2017 from a medical center in northwest Taiwan when their oncologist first recognized their cancer as terminal (ie, disease continually progressed with distant metastases and was unresponsive to repeated chemotherapy/targeted therapies). Participant oncologists referred patients to research assistants, who were experienced oncology nurses trained by the principal investigator to enroll subjects and collect data. Patients were excluded if they were diagnosed as cognitively incompetent or with psychiatric disorders, were participating in other trials, or were undergoing palliative care, or if their family caregivers were unavailable or declined to participate. Participants were followed through December 2017. This RCT targeted patient–caregiver dyads; only patients' primary outcomes are reported herein. The study protocol (supplemental eAppendix 1, available with this article at JNCCN.org) was approved by the ethics committee of Chang Gung Memorial Hospital, Linkou, Taiwan, and registered at ClinicalTrials.gov (identifier: NCT01912846). All participants provided written informed consent before enrollment.

Sample Size Calculation, Randomization, and Blinding

Sample size was estimated from observational evidence that patient–physician EoL care discussions (an essential ACP component) increase the likelihood of honoring EoL care preferences of patients with cancer (one of our

primary outcomes).¹¹ This evidence was used because no ACP RCTs for patients with cancer had reported the same outcomes as ours when the current study was launched. Patients with cancer who reported EoL care discussions with their physicians were more likely to receive EoL care consistent with their preferences (odds ratio [OR], 2.04; $P < .0001$).¹¹ A sample of 190 dyads per arm would achieve 85% power to detect a between-arm difference in this primary outcome using 2-sided tests ($P < .05$). We did not adjust the alpha values for comparing between-arm multiple primary outcomes and concordances for multiple received/preferred LSTs. Given the 18.5% attrition in our previous longitudinal study,²¹ 231 dyads per arm were needed.

Participants were randomly assigned 1:1 to the experimental and control arms using a computer-generated random sequence sealed in consecutively numbered opaque envelopes. To ensure blinding of group assignment, the random allocation sequence was independently generated or assigned by researchers not involved in patient recruitment, interventions, clinical care, and data collection.

Treatments

This theory-based, individualized, interactive ACP intervention had 5 major components: (1) repeated assessments of participants' readiness to engage in ACP, (2) specific subinterventions tailored to participants' readiness to engage in ACP, (3) facilitation of physician–patient EoL care discussions, (4) use of a booklet and video educational aid to facilitate understanding of ACP and LSTs at EoL, and (5) psychological support of participants while engaged in EoL care decision-making. During the intervention, participants interacted multiple times with trained interventionists experienced in oncology nursing and palliative care and who were not involved in participants' clinical care. The intervention protocol did not follow a script with prespecified topics. The trained ACP interventionists had the flexibility to provide care tailored to each participant's specific needs at each stage of ACP-engagement readiness and to communicate the patient's concerns and EoL care preferences to clinicians, as needed. Interactions occurred weekly during hospitalization, or monthly at outpatient clinics when participants returned for visits, until they died.

Participants were assessed for ACP-engagement readiness according to the transtheoretical model.²² For participants at the precontemplation stage, the individualized subintervention aimed to address their lack of readiness to engage in ACP and to motivate them to consider its relevance. The interventionists explored the values and EoL care preferences of the contemplation-stage participant, explained the benefits and burdens of applicable treatments, and encouraged the participants

to evaluate the benefits and burdens from their own perspective and communicate their preferences and concerns about treatments with their oncologist. For preparation-stage participants, interventionists clarified any unrealistic expectations of continuing/initiating anticancer treatments or LSTs. For participants ready to act on ACP, the interventionists facilitated communication of EoL care preferences to the oncologists to achieve a consensus on EoL care goals and specific treatments that could be used or withheld. For maintenance-stage participants (those who had consolidated their EoL care decisions), interventionists continually provided reassurance regarding the EoL care decisions and made necessary changes in response to health status.

Control-arm participants received a sham treatment of symptom-management education weekly during hospitalization or monthly at outpatient visits until they died. This treatment included (1) symptom-management education from a trained interventionist experienced in oncology nursing and palliative care, and (2) a booklet and video on symptom management. We hypothesized that despite symptom management being another essential component of high-quality EoL care,¹ participants' receiving education and a booklet and video on symptom management alone would not impact this study's primary outcomes,²³ but would parallelize the education received by both study arms as much as possible. Specific booklets and videos were provided to participants in each arm, and interventionists discussed the relevant booklet and video contents with all participants, as needed. Intervention sessions were not audio- or video-recorded for feasibility considerations, but interventionists recorded intervention-treatment components to later evaluate compliance of intervention delivery with the study protocol (supplemental eAppendix 2). This treatment fidelity was monitored throughout the study.

Outcome Measures

Preferences for LSTs

Preferences for cardiopulmonary resuscitation, intensive care unit care, chest compression, intubation with mechanical ventilation, nasogastric tube feeding, and intravenous nutrition were assessed using an adapted interview protocol (supplemental eAppendix 3). For each LST, patients were asked whether they (1) wanted, (2) did not want, or (3) were undecided about the treatment.

LSTs Received

Data on the receipt of the aforementioned 6 LSTs in patients' last month of life were retrieved from medical records and supplemented by caregivers' reports during bereavement follow-ups.

Quality of Life

Participants' QoL was measured using a modified 13-item McGill QoL Questionnaire (MQoL).²⁴ The original MQoL stresses psychologic, social, and existential well-being. We omitted 3 items (the 3 most distressing symptoms) to avoid overlap with the potential effect of symptom distress on participants' QoL. Total scores for this modified MQoL ranged from 0 to 130; higher scores indicated a better QoL.

Anxiety and Depressive Symptoms

Anxiety and depressive symptoms were measured by the Hospital Anxiety and Depression Scale (HADS).²⁵ The 14-item HADS, the most widely used tool for assessing psychological distress in patients with cancer undergoing palliative care,²⁶ has 7 items measuring anxiety (HADS-A) and 7 measuring depression (HADS-D). HADS assesses psychological symptoms rather than physiological symptoms, thus avoiding confounding measures that may overestimate anxiety or depression severity for patients with cancer who commonly experience multiple physical symptoms. The HADS-A and HADS-D subscales each have a total score ranging from 0 to 21; higher scores indicate more anxiety or depressive symptoms.

Covariate Measures

To evaluate the effectiveness of our ACP intervention, we adjusted for several covariates shown to influence QoL, anxiety symptoms, and depressive symptoms: treatment dose (ie, number of intervention treatments provided), proximity to death^{27,28} (ie, the period between death and assessment [ie, 1–30, 31–90, 91–180, 181–365, 366–545, and ≥ 546 days before death]), which are conventional periods for estimating survival),²⁹ known time-varying covariates that may vary in each assessment (ie, physical symptom distress³⁰ and functional dependence),³¹ and time-invariant variables (ie, comorbidity, age, and sex; see supplemental eAppendix 4).

Data Collection

Participants' characteristics were assessed at baseline (before random assignment). Data on outcome measures (LST preferences, QoL, anxiety symptoms, and depressive symptoms) and time-varying covariates were collected at baseline and every 3 to 4 weeks afterward until participants withdrew or died. Data collectors were blinded to participants' group assignment.

Statistical Analysis

Between-arm homogeneity at baseline was examined by chi-square and independent *t* tests. LST preferences were dichotomized into "want"/"do not want" treatment, with those indicating "undecided" counted as wanting that treatment because the clinical default is to provide LSTs

unless specifically refused.³² Concordance was evaluated by cross-tabulating each LST last reported before death and LST received in participants' last month of life. Concordance was expressed as both a percentage (received/preferred LSTs) and a kappa coefficient for chance-corrected agreement.³³ Kappa values were categorized as poor (≤ 0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), or almost perfect (0.81–1.00).³⁴ Between-arm differences in concordance between preferred and received LSTs were expressed by an OR with 95% CI.

Effects of the ACP intervention on the 3 continuous outcome variables (QoL, anxiety symptoms, depressive symptoms) during the dying process were simultaneously evaluated by intention-to-treat analysis³⁵ using multivariate hierarchical linear modeling (MHLM)³⁶ by HLM 7.0 to control for the inflation of type I errors from multiple outcome comparisons. Furthermore, MHLM allows different waves of data across patients to accommodate variable numbers of follow-up points, inconsistent time intervals between subsequent data collections, and missing data for the dependent variables, eliminating the need to delete observations in analyses.³⁶ MHLM uses random intercepts to account for within-subject correlations of repeated observations from each patient.³⁶ The MHLM in this study controlled for treatment dose, proximity to death, and time-invariant and lagged time-varying covariates (functional dependence, physical symptom distress, anxiety symptoms, depressive symptoms, and QoL measured in the previous wave of assessment) to ensure a clear time sequence of effects on the 3 outcomes.

Results

Patient Characteristics

Of 795 patients approached, 460 (57.86%) were enrolled and randomly assigned 1:1 to the experimental and control arms (Figure 1). Nonenrollment was primarily due to family caregivers' unavailability and patients' weakness. The final sample included 215 participants per arm who died by the end of the study. Between-arm baseline characteristics, LST preferences, QoL, anxiety symptoms, and depressive symptoms were balanced at randomization (supplemental eAppendix 5) and in the final sample (Table 1). Experimental and control arm participants received on average 5.99 ACP intervention sessions (SD, 6.11) and 5.43 sham treatment sessions (SD, 6.45), respectively. After enrollment, experimental and control arm participants survived 147.33 (SD, 155.01) and 127.39 days (SD, 151.66) and were assessed 5.19 (SD, 4.75) and 4.93 times (SD, 5.35), respectively. The last assessment was on average 27.69 days (SD, 52.99) before death.

Figure 1. CONSORT diagram.

Abbreviation: LSTs, life-sustaining treatments.

Preferred and Received LSTs

The ACP intervention did not facilitate concordance between preferred and received LSTs. Concordance between participants' last-assessed LST preferences and LSTs received in the last month was 58.2% to 77.5% and 59.0% to 75.7% for the experimental and control arms, respectively (Table 2), with patients receiving fewer LSTs than they preferred (data not shown). Concordance between preferred and received LSTs was poor to fair for each arm (κ [95% CI], 0.040 [−0.050 to 0.130] to 0.212 [0.098–0.326], and 0.019 [−0.063 to 0.101] to 0.224 [0.110–0.338] for the experimental and the control arms, respectively. Between-arm concordance did not differ significantly for any of the 6 preferred and received LSTs examined (OR [95% CI], 0.966 [0.653–1.428] to 1.107 [0.690–1.775]).

Table 1. Patient Characteristics (N=430)

Variable	Experimental Arm (n=215)		Control Arm (n=215)		P Value
	n	%	n	%	
Age, y					.178
≤55	93	43.3	75	34.9	
56–65	71	33.0	86	40.0	
>65	51	23.7	54	23.1	
Sex					.341
Male	156	72.6	147	68.4	
Female	59	27.4	68	31.6	
Educational level					.433
≤Junior high school	123	57.2	131	60.9	
>Junior high school	92	42.8	84	39.1	
Cancer site					.772
Liver	44	20.5	53	24.7	
Gastrointestinal tract	43	20.0	48	22.3	
Esophagus	35	16.3	34	15.8	
Pancreas	35	16.3	28	13.0	
Lung	13	6.0	14	6.5	
Other	45	20.9	38	17.7	
Metastasis					.674
Yes	202	94.0	204	94.9	
No	13	6.0	11	5.1	
Time from diagnosis, mo					
Mean ±SD	12.03 ± 15.51		10.46 ± 13.47		.264
SDS score: mean ± SD	26.98 ± 6.72		26.69 ± 7.07		.662
ESDS score: mean ± SD	28.28 ± 8.82		27.37 ± 8.60		.282
MQoL score: mean ± SD	89.72 ± 20.12		90.90 ± 18.85		.530
HADS-D score: mean ± SD	11.70 ± 4.33		11.69 ± 4.50		.994
HADS-A score: mean ± SD	6.16 ± 3.79		6.41 ± 3.80		.495
LST preferences					
Cardiopulmonary resuscitation					.913
Yes	69	32.1	65	30.2	
No	129	60.0	132	61.4	
Uncertain	17	7.9	18	8.4	
Intensive care unit care					.918
Yes	85	39.7	85	39.5	
No	113	52.8	116	51.0	
Uncertain	16	7.5	14	6.5	
Chest compression					.774
Yes	70	32.6	67	31.2	
No	129	60.0	135	62.8	
Uncertain	16	7.4	13	6.0	

(continued on next page)

Abbreviations: ESDS, Enforced Social Dependency Scale; HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HADS-D, Hospital Anxiety and Depression Scale-Depression; LST, life-sustaining treatment; MQoL, McGill Quality of Life Questionnaire; SDS, Symptom Distress Scale.

Table 1. Patient Characteristics (N=430) (cont.)

Variable	Experimental Arm (n=215)		Control Arm (n=215)		P Value
	n	%	n	%	
LST preferences (cont.)					.769
Intubation with mechanical ventilation support					.769
Yes	68	31.6	63	29.3	
No	133	61.9	140	65.1	
Uncertain	14	6.5	12	5.6	
Nasogastric tube feeding					.594
Yes	122	56.7	119	55.3	
No	87	40.5	86	40.0	
Uncertain	6	2.8	10	4.7	
Intravenous nutrition support					.305
Yes	180	84.1	173	80.5	
No	32	15.0	36	16.7	
Uncertain	2	0.9	6	2.8	

Abbreviations: ESDS, Enforced Social Dependency Scale; HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HADS-D, Hospital Anxiety and Depression Scale-Depression; LST, life-sustaining treatment; MQoL, McGill Quality of Life Questionnaire; SDS, Symptom Distress Scale.

Anxiety Symptoms, Depressive Symptoms, and QoL

ACP intervention improved anxiety symptoms and depressive symptoms but not QoL that patients preferred regarding their dying process. Unadjusted MQoL, HADS-A, and HADS-D scores for both arms are shown in Figure 2. After controlling for identified covariates, the simultaneous MHLM analysis of the 3 outcomes showed no significant difference in QoL between the experimental and the control arms (Table 3). However, the experimental arm participants reported significantly fewer anxiety symptoms (β [95% CI], -0.583 [-0.977 to -0.189]; $P=.004$) and depressive symptoms (β [95% CI], -0.533 [-1.036 to -0.030]; $P=.038$) than the control arm participants.

Discussion

The results support our hypothesis that an individualized, interactive ACP intervention would lighten anxiety and depressive symptoms in terminally ill patients with cancer who are facing EoL and making EoL care decisions. However, the ACP intervention did not facilitate concordance between patients' preferred and received LSTs, nor did it improve their QoL at EoL. The inability of the ACP intervention to honor participants' LST preferences is consistent with reports on patients with life-limiting noncancer diseases¹⁵ and on overall patient-assessed goal-concordant care,¹⁹ but not with the significant positive impact reported for elderly patients¹³ or nursing home residents.¹⁶ Our finding of poor-to-fair concordance between patients' preferred and received

Table 2. Effectiveness of ACP Intervention in Facilitating Concordance With LSTs

LST	Concordance Between Preferred and Received LSTs							
	Experimental Arm			Control Arm			Arm Difference	
	n	%	κ (95% CI)	n	%	κ (95% CI)	OR (95% CI)	P Value
Cardiopulmonary resuscitation	208	69.7	0.077 (−0.023 to 0.177)	205	68.3	0.061 (−0.029 to 0.151)	1.069 (0.704–1.622)	.755
Intensive care unit care	207	62.3	0.054 (−0.044 to 0.152)	205	61.0	0.030 (−0.060 to 0.120)	1.058 (0.711–1.575)	.779
Chest compression	207	69.6	0.040 (−0.050 to 0.130)	204	69.1	0.019 (−0.063 to 0.101)	1.021 (0.671–1.553)	.922
Intubation with mechanical ventilation	207	69.6	0.080 (−0.045 to 0.205)	205	69.6	0.051 (−0.059 to 0.161)	0.991 (0.651–1.508)	.966
Nasogastric tube feeding	208	58.2	0.212 (0.098–0.326)	205	59.0	0.224 (0.110–0.338)	0.966 (0.653–1.428)	.861
Intravenous nutrition support	200	77.5	0.174 (0.009–0.339)	185	75.7	0.095 (−0.066 to 0.256)	1.107 (0.690–1.775)	.673

Abbreviations: ACP, advance care planning; LSTs, life-sustaining treatments; OR, odds ratio.

Figure 2. Unadjusted mean (95% CI) scores for (A) quality of life, (B) depressive symptoms, and (C) anxiety symptoms during the dying trajectory.

Abbreviations: HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HADS-D, Hospital Anxiety and Depression Scale-Depression; MQL, McGill Quality of Life Questionnaire.²⁴

LSTs may be attributable to the family power to override the autonomy/wishes of conscious, competent patients.³⁷ This power is commonly exercised in medical care decision-making, including EoL care,³⁸ in deeply Confucian doctrine-influenced societies such as Taiwan. In future studies, we will examine how our ACP intervention influenced family caregivers' attitudes toward honoring and supporting their relative's LST preferences. In addition, we repeatedly assessed participants' LST preferences regarding their dying process because the extent to which their EoL care preferences are honored may be distorted if preferences are measured long before death, a common approach of existing research.^{11,13,15} However, this repeated assessment (testing)³⁹ may have threatened the internal validity of our study by sensitizing and motivating control-arm participants to prepare for their EoL care, thereby neutralizing/minimizing the intervention's effectiveness in facilitating concordance between patients' preferred and received LSTs.

The ACP intervention significantly facilitated patients' psychological adjustment while they were deciding about their EoL care. Our results demonstrate that the ACP intervention not only caused no psychological harm, as previously reported,^{18,19} but that it also reduced anxiety and depressive symptoms for those in the experimental arm compared with the control arm. This success is probably attributable to the strategies of actively exploring participants' EoL care values, goals, and preferences; tailoring the ACP intervention to their readiness to engage in ACP; and sensitively providing psychological support for those struggling with making such emotion-laden decisions. Worldwide, especially in Asian countries, well-intentioned physicians tend to omit or delay EoL care discussions with patients to avoid disturbing or overwhelming them,⁴⁰ leading to considerable discrepancies between patients' preferred and actual involvement in EoL care discussions,⁴¹ especially for highly anxious or depressed patients.⁴¹ Avoiding EoL care discussions may in turn predispose patients to experience further anxiety or depressive symptoms. Our intervention may have ended this vicious cycle by facilitating psychological adjustment while patients were making EoL care decisions. However, the intervention did not improve patients' QoL throughout the dying process. Improving QoL at EoL may require components not included in this ACP intervention, such as adequate and effective symptom management⁴² or comprehensive and early integration of palliative care into standard oncology care.⁴³

Strengths of our study include its interactive intervention tailored to participants' readiness to engage in ACP,⁴ intervening throughout the dying process,²⁰ evaluating high-quality EoL care outcomes based on most participants' self-reports, and ensuring internal validity

Table 3. Impact of ACP Intervention on QoL, Anxiety Symptoms, and Depressive Symptoms

	QoL				Anxiety Symptoms				Depressive Symptoms			
Variable	β	95% CI		P Value	β	95% CI		P Value	β	95% CI		P Value
Arm												
Experimental	1.689	−0.578	3.956	.144	−0.583	−0.977	−0.189	.004	−0.533	−1.036	−0.030	.038
Control	Ref				Ref				Ref			
Proximity to death, d												
≤30	Ref				Ref				Ref			
31–90	7.527	5.575	9.478	<.001	−1.082	−1.499	−0.666	<.001	−2.202	−2.678	−1.727	<.001
91–180	12.143	9.999	14.286	<.001	−1.672	−2.121	−1.223	<.001	−3.682	−4.200	−3.164	<.001
181–365	15.548	13.079	18.017	<.001	−2.219	−2.722	−1.717	<.001	−4.411	−5.000	−3.822	<.001
366–545	18.906	15.443	22.369	<.001	−2.957	−3.657	−2.256	<.001	−5.748	−6.573	−4.924	<.001
≥546	18.976	14.518	23.435	<.001	−2.778	−3.675	−1.881	<.001	−5.679	−6.738	−4.620	<.001
Lagged time-varying variables												
Symptom distress ^a	−0.030	−0.163	0.103	.657	0.017	−0.011	0.045	.230	0.030	−0.003	0.062	.070
Functional dependence ^b	0.047	−0.072	0.166	.438	0.017	−0.007	0.041	.169	0.026	−0.003	0.054	.077
QoL ^c	0.383	0.314	0.452	<.001	−0.036	−0.050	−0.022	<.001	−0.003	−0.019	0.014	.748
Depressive symptoms ^d	0.245	−0.031	0.522	.082	−0.026	−0.084	0.031	.366	0.281	0.214	0.347	<.001
Anxiety symptoms ^e	−0.857	−1.173	−0.541	<.001	0.289	0.223	0.355	<.001	0.078	0.002	0.155	.045
Treatment dose	−0.126	−0.280	0.028	.109	0.008	−0.022	0.038	.605	0.012	−0.024	0.048	.525
Sex												
Male	−0.252	−2.717	2.213	.842	−0.531	−0.957	−0.105	.015	−0.080	−0.626	0.465	.773
Female	Ref				Ref				Ref			
Age, y (dichotomized at median age)												
>57	6.254	3.869	8.639	<.001	−0.387	−0.805	0.030	.068	0.157	−0.374	0.688	.562
≤57	Ref				Ref				Ref			
Comorbidities ^f												
0	Ref				Ref				Ref			
1	0.997	−1.795	3.790	.484	−0.028	−0.511	0.454	.909	−0.677	−1.295	−0.059	.032
2	0.367	−2.741	3.475	.817	0.229	−0.307	0.766	.402	−0.206	−0.894	0.481	.566
≥3	2.614	−1.329	6.557	.194	0.088	−0.609	0.785	.805	−0.184	−1.065	0.697	.682

Abbreviations: ACP, advance care planning; QoL, quality of life.

^aMeasured with Symptom Distress Scale.

^bMeasured with Enforced Social Dependency Scale.

^cMeasured with McGill QoL Questionnaire.

^dMeasured with Hospital Anxiety and Depression Scale-Depression.

^eMeasured with Hospital Anxiety and Depression Scale-Anxiety.

^fCharlson-Deyo comorbidity index.

through using a rigorous design and monitoring treatment fidelity. However, this RCT was conducted at a Taiwanese hospital using a sample of terminally ill patients with cancer who had a family caregiver and who were referred to this study by their oncologist, limiting the generalization of these findings to national and international target populations without an available family caregiver. We focused on the patient participants and did not consider family caregivers' perspectives. Future studies should evaluate how ACP interventions influence family caregivers' understanding, support, and

endorsement of patients' LST preferences to achieve patient value-concordant EoL care.⁴⁴ Furthermore, terminally ill patients' indecision when making EoL care choices indicates their ambivalence about LSTs. Categorizing "undecided" responses as treatment preferences may have inflated the preference rate (approximately 10%; see Table 1), but removing them from analyses may not bring undecided patients' preferences to the attention of clinicians, who would miss the opportunity to meet the needs of these patients at EoL. Further research should explore the role of uncertainty

in facilitating or hindering concordance between the preferred and received EoL care of terminally ill patients with cancer and evaluate interventions to eliminate their uncertainty in making EoL care decisions.⁴⁵

Conclusions

This interactive intervention tailored to the readiness of terminally ill patients with cancer to engage in ACP during the dying process facilitated their psychological adjustment to EoL care decision-making despite not influencing concordance between their preferred and received LSTs and not improving their QoL before death. These findings assure healthcare professionals that such an ACP intervention does not harm the psychological well-being of terminally ill patients with cancer but instead improves it. With this assurance, clinicians can systematically adopt and integrate ACP interventions into clinical care⁴⁰ to respect patients' desire for active participation in EoL care discussions⁴¹ and to facilitate

physician–patient EoL care discussions early in the patient's disease trajectory.¹ We suggest involving family caregivers in EoL care decision-making and considering their LST preferences,⁴⁴ which may eventually lead to EoL cancer care that is concordant with patient values.

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