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Original Article

Effects of Acceptance and Commitment Therapy on fatigue interference and health-related quality of life among patients with advanced lung cancer: A pilot randomized controlled trial

Huiyuan Li [a], Xiaohuan Jin [a], Marques Shek Nam Ng [a], Ka Fai Mann [b], Nina Wang [c], Cho Lee Wong [a],*

[a] *The Nethersole School of Nursing, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China*
[b] *School of Continuing and Professional Education, City University of Hong Kong, Hong Kong SAR, China*
[c] *Respiratory Department, Xiangya Hospital Central South University, Changsha, China*

ABSTRACT

Objective: The present study aimed to examine the feasibility and preliminary effects of Acceptance and Commitment Therapy (ACT) on fatigue interference and health-related quality of life in patients with advanced lung cancer.
Methods: In a single-blinded, parallel-group randomized controlled trial, 40 patients with advanced lung cancer were randomized to either the intervention group, which received the four-session individual ACT in 4 weeks, or the control group, which received usual care. The outcomes were evaluated at baseline and one week postintervention.
Results: Intervention feasibility and acceptability were established with a high attendance rate of 88.75% and a high retention rate of 75%. Approximately 95% of the participants reported satisfaction with the intervention. Despite the insignificant effects on fatigue interference, statistically significant interactions effects of ACT for health-related quality of life ($P = 0.001$), cancer-related fatigue ($P < 0.001$), depressive symptoms ($P < 0.001$), anxiety ($P < 0.001$), and distress ($P = 0.003$) were noted.
Conclusions: This pilot trial supports the feasibility and acceptability of conducting ACT for patients with advanced lung cancer. The findings show the potential positive effects of ACT on health-related quality of life. Future studies with full-scale samples are recommended to evaluate the long-term effects of ACT on fatigue interference.

Introduction

Cancer-related fatigue (CRF) is the most common and distressing symptom reported by patients with advanced lung cancer.[1] CRF is defined as a persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion associated with cancer or treatment; however, it is not proportional to recent activities and interferes with usual function.[2] CRF is caused by cancer diagnosis, anticancer treatments, and psychological responses to cancer.[3,4] Patients with lung cancer experience the highest level of CRF.[5] A cohort study also reported CRF as the most serious cause of concern for over 10 years among patients with advanced lung cancer.[1]

CRF has lasting impacts on physical, social, and psychological aspects of daily life, which is also call fatigue interference.[6] The term "fatigue interference" refers to the degree of CRF-associated interference with different aspects of life. In the physical domain, unrelieved CRF causes patients to spend more time in bed, leading to cardiovascular, respiratory, and muscle deconditioning.[7] In addition, CRF diminishes their abilities to participate in social activities (eg. working, leisure, and exercise activities) and sustain meaningful relationships with families and peers.[8] CRF also renders patients dependent on others for home housework, transportation, and simple self-care activities (e.g. cooking and bathing).[9,10,11,12] Moreover, CRF interferes with changes in the psychological health of cancer patients.[13] Emotional responses to cancer, especially the experienced difficulty in accepting cancer diagnosis,[14,15] increases the sense of powerlessness and influences the level of CRF. These further cause patients to constantly worry about their future and blame themselves for becoming a burden on their families.[16] Attempts to

control and being caught up in the internal experience related to CRF lead to high levels of anxiety and depression,[17] which cause the high alert of CRF, bringing about sustained distress during the cancer trajectory.[18] All these aspects influence each other, further exacerbate the level of CRF, and severely affect patients' health-related quality of life.[19] Thus, appropriate interventions that alleviate CRF and fatigue interference among patients with advanced cancer will play a key role in global palliative care.

To date, nonpharmacological interventions, such as physical exercise, complementary interventions and psychological interventions, are mainly used in CRF management. However, these interventions raise different degrees of challenges for patients with advanced cancer.[20] Meta-analyses and reviews showed that exercise interventions can effectively reduce CRF[21,22,23,24] However, these studies did not include patients with advanced cancer who specifically reported CRF, and CRF may be a major obstacle to participation in exercises, especially in advanced subgroups.[25] Acupuncture, an expressive method of complementary interventions, has been increasingly studied. However, results on its effectiveness in improving fatigue were inconsistent.[26,27] Cognitive and behavior therapy (CBT) is a mainstream psychological intervention for CRF and shows promising effects[28]; however, related studies have been criticized for their low reproducibility and low/medium efficacy.[80] This finding is supported the notion that CBT may not be an ideal solution for distressing experiences of cancer patients, especially those in the advanced stage[29,30] Given that CBT aims to identify CRF-related thoughts and correct them through cognitive efforts, the process of eliminating irrational cognition and building new cognition means denying and avoiding one's CRF experience to a certain extent. However, long-term avoidance of CRF-related thoughts and feelings likely suppresses negative emotions, decreases tolerance to physical symptoms and restricts activities, thereby reducing the possibility of living a satisfactory life.[31,32]

Acceptance and Commitment Therapy (ACT), a mindfulness-based behavioral therapy, may be an alternative way to promote CRF management. ACT does not aim to reduce symptoms[31] but to improve functioning and health-related quality of life by increasing psychological flexibility.[33] Psychological flexibility is defined as the ability to be fully in touched with the present moment as a conscious person and commit to achieving valued goals.[34] It involves six core processes: acceptance, defusion, connection with the present moment, self-as-context, values, and committed action.[35] In the context of CRF, ACT may cultivate patients with advanced lung cancer to accept physical sensations and psychological feelings related to CRF, focusing on them without judging or making unnecessary attempts to control CRF[36] and performing tasks that are really important to them. Hence, ACT reduces the fatigue interference on physical and psychosocial well-being and improves the quality of life. ACT shows promising effects on the improvements of functions and quality of life in cancer patients.[37,38,39,40,29,41] However, little research has been conducted on its effectiveness on CRF and fatigue interference, especially in patients with advanced cancer. In a recent systematic review, five pilot randomized controlled trials (RCTs) conducted ACT interventions on patients with advanced cancer.[42] Three of these RCTs examined the feasibility and preliminary effects of ACT on fatigue interference. Several limitations existed among these pilot studies. Firstly, patients with CRF were not recruited as study entry. Thus, the ACT interventions and outcome measurements were untargeted. Moreover, despite the severity of CRF and continuous fatigue interference in patients with advanced lung cancer, few studies examined the effects of ACT on fatigue interference in this population. Although a systematic review reported ACT as an effective way to improving health-related quality of life,[42] studies were conducted in Western countries. Coping strategies for fatigue interference and CRF differ depending on cultural contexts,[43,44] possibly affecting the intervention designs and assistive technology utilization in programs. Thus, the development of a cultural-based ACT intervention and investigation of its feasibility and preliminary effectiveness in non-Western contexts are warranted.

An ACT intervention for patients with advanced lung cancer in China was designed. This pilot study aimed to determine the feasibility and acceptability of the ACT intervention and test its preliminary effects on fatigue interference and health-related quality of life in this population.

Methods

Study design and objectives

A prospective, parallel, single-blinded pilot RCT was designed and conducted from March 2021 to May 2021. The research objectives were as follows:

1) To test the feasibility and acceptability of ACT in patients with advanced lung cancer;
2) To examine the preliminary effects of ACT for patients with advanced lung cancer on fatigue interference and health-related quality of life (primary outcomes), CRF, depressive symptoms, anxiety and distress (secondary outcomes) at one week post-intervention compared with the usual care control group.

This pilot study adhered to the CONSORT Statement.[45]

Participants

Patients meeting the following inclusion criteria were invited to participate in this study: (1) aged 18 years or older; (2) diagnosed with stage III/IV lung cancer through pathological section or cytology; (3) had experienced unexplained fatigue syndrome, with a score of 3 or higher in the Fatigue Symptom Inventory (FSI)[46]; (4) had a reliable internet connection and a mobile smartphone.

Patients were excluded if they were (1) diagnosed with cognitive dysfunction or other mental illnesses that may interfere with the completion of treatment; (2) had a life expectancy of less than 3 months or whose physical conditions were considered extremely weak to participate in the present study according to a physician's assessment; (3) receiving other psychosocial interventions or participating in health promotion programs.

Sample size

The sample size of a pilot trial should be at least 10% of that in the main study.[47] Thus, the sample size of the main RCT of ACT for patients with advanced lung cancer, which was estimated with a medium effect size of 0.5 at a study power of 0.80 and an attrition rate of 20%, was around 160 subjects. Therefore, 40 participants (20 participants per group) were recruited.

Procedure

Fig. 1 shows the procedural flow of this study. Convenience sampling was used to recruit participants from the respiratory department of a university-affiliated hospital in Central China. The participants were identified through medical chart review and approached for eligibility by a clinical nurse. The list of interested participants was recorded to allow researchers to contact them. Potential participants received information about the study and provided written informed consents. The study was halted when the enrollment reached 40.

Randomization and blinding

The randomization procedure was performed by a research assistant who was not involved in the recruitment, enrollment, and treatment
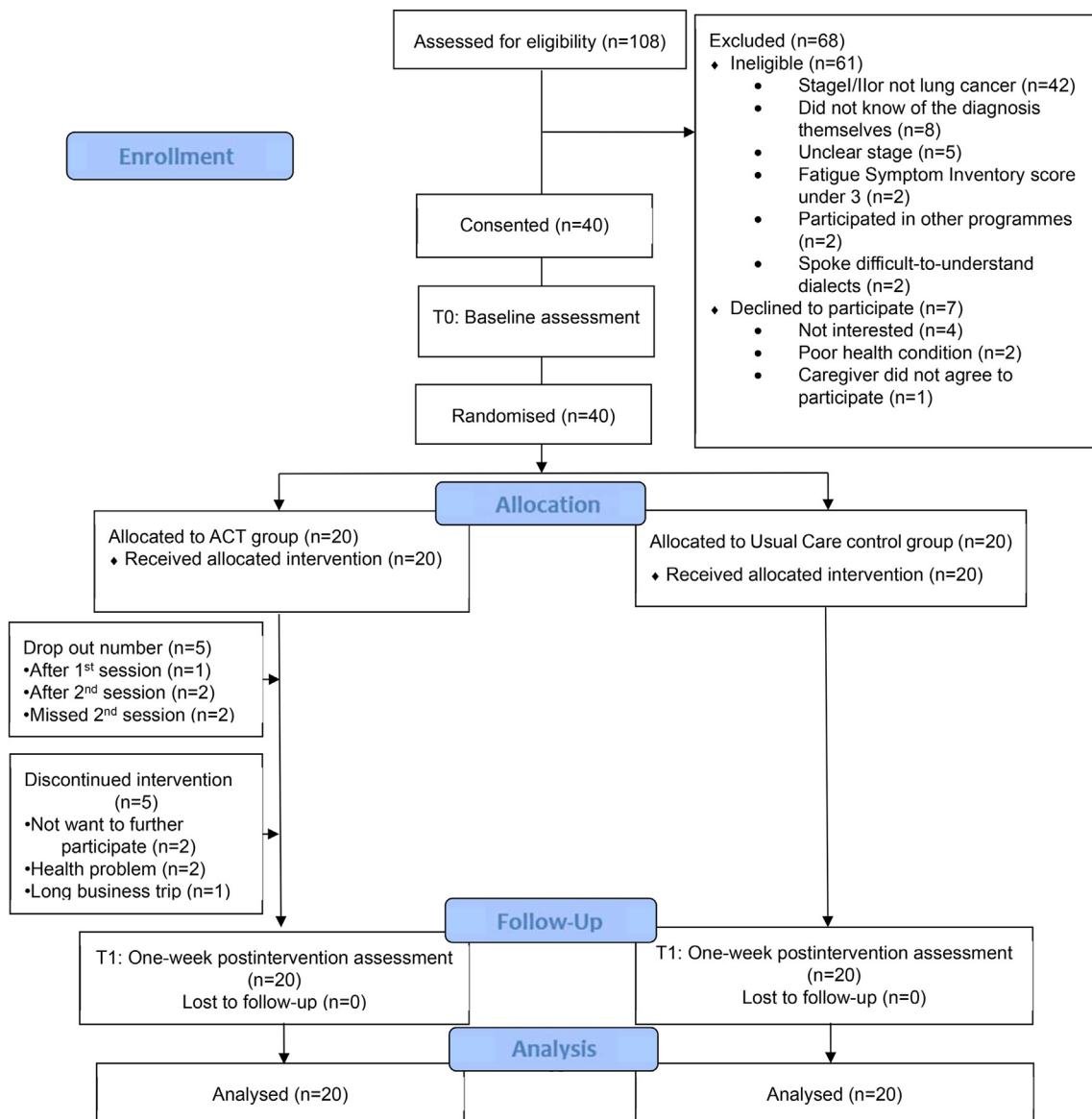
Fig. 1. Flow diagram of this study.

process. The participants were randomized at a 1:1 ratio to the intervention or control group using a permuted block design to generate randomly varying block sizes of 4 and 6 (by an independent statistician). The research assistant who performed randomization informed the participants about the allocation using an opaque and sealed envelope.

Given that this study involved a psychological intervention, the interventionist and participants were impossible to blind. Nevertheless, assessors who collected data and performed data analysis were blinded to group allocation. During the process, participants in both groups were instructed to avoid communicating with others in terms of the intervention content to prevent contamination and not to disclose their allocation to the assessors.

Intervention

ACT group

The ACT intervention was developed in accordance with ACT reference books, training manuals for therapists[48,58,50] and previous ACT intervention research for cancer patients.[51,52,53,54,55,56] The findings of our previous research supplemented the development of the program. On the one hand, this intervention program was designed based on our

previous systematic review,[42] which revealed that a brief ACT intervention with no more than four sessions and an individual format has promising effects on the improvement of health-related outcomes post-intervention in patients with advanced cancer and a reliable adherence rate. On the other hand, the intervention manual was modified based on the results of our qualitative interview of 21 patients with advanced lung cancer. This interview explored the fatigue experience and inflexible coping with fatigue along the treatment trajectory. The results were clustered into categories, such as denial, suspicion and excessive control of fatigue and diagnosis. These avoidant and inflexible behaviors are deeply influenced by traditional Chinese virtues, such as "Endurance,"[57] which provides a cultural context and reveals the necessity to conduct ACT. An expert panel, including two ACT experts, two psychologists, one nursing professor, one respiratory head nurse, and one doctor of respiratory department, was invited to validate the intervention manual.

An individual-based, four-session (60–90 min/session) weekly ACT intervention was adopted for the intervention group. The intervention program consisted of one face-to-face session in an independent meeting room of the respiratory department and three videoconferencing-based sessions via Tencent video conference software in addition to receiving

Table 1
Themes and contents of the intervention.

Themes	Outline	ACT process targeted
Session 1: Living in the moment. Embrace the cancer life	• Self-introduction and introduction of purpose of the program and basic rules (completion of mindful breathing exercise). • Help understand the interference of CRF in the process of suffering from advanced lung cancer and costs of controlling related thoughts and feelings (metaphor: The man in the hole). • Master alternative strategies to cope with fatigue and distressing thoughts, feelings and feelings related to CRF and lung cancer more effectively (completion of 'T' puzzle game; Chinese Finger Trap). • Master the strategies of focusing on the present moment (completion of 'Be focused' exercise).	Contact with the present moment. Acceptance
Session 2: Being kind to yourself. Keeping a distance from your thoughts	• Help separate the thoughts/feelings related to the CRF experience from the facts (mindful drinking exercise; metaphor: Passengers on the bus; experiential exercise: Labeling your thoughts; Milk, Milk, Milk). • Help observe themselves in an objective way, treat the diagnosis of advanced lung cancer and thoughts/feels/feelings related to CRF experience objectively (experiential exercise: The sky and the weather). • Consolidate strategies of acceptance and focus on present moment.	Contact with present moment. Cognitive defusion. Self-as-context
Session 3: Clarifying your values. Putting your values into action	• Consolidate the strategies of acceptance, focus on the present moment, cognitive defusion and self-as-context (Eating a raisin exercise). • Understand the difference between values and goals. • Clarify personal values and their importance (Experiential exercise: 80th Birthday; Value compass). • Setting one smallest value-based goal in SMART format (specific, measurable, achievable, relevant, and time-bound).	Contact with present moment. Values
Session 4: Moving forward with committed action. Living a meaningful cancer life	• Consolidate the strategies of acceptance, focus on the present moment, cognitive defusion and self-as-context (completion of Body scan exercise). • Further clarify personal values and goals. • Share own values with others to promote their action. • Summary and feedback.	Contact with present moment. Committed action

ACT, Acceptance and Commitment Therapy; CRF, Cancer-related fatigue.

usual care from the clinical nurses in charge during hospitalization. The videoconferencing platform is a frequently used social media platform for online communication during the COVID-19 pandemic[60]; it can realize online face-to-face video communication without time and space restrictions. The participants received a reminder of appointments via WeChat (a popular social media software in China) in advance.

Table 1 presents the theme of each session and a summary of session content. The ACT model underpins the intervention for patients with advanced lung cancer. The intervention was designed to reduce fatigue interference and improve health-related quality of life by increasing the psychological flexibility via integrating six core elements. Session 1 included the review of experiences on the struggles with CRF and realization of the consequence of controlling fatigue and cancer experiences, thus introducing acceptance as an alternative. Session 2 aimed to separate thoughts or feelings (ie. depression, anxiety and cancer-related distress) related to the experience of fatigue and lung cancer with literal truth and view them objectively and transcendentally. Session 3 aimed to clarify personal values and present the smallest value-guided goal. Session 4 emphasized the ongoing value-based goals and committed to actions for a meaningful cancer life. After four sessions, the participants were motivated to improve their health-related quality of life by promoting psychological flexibility.

A patient booklet was distributed to the participants before the first session, and a structured practice log was used to record their homework completion, including the time they spent practicing mindfulness weekly, experiences of perceiving inner experience, and using ACT strategies. Several strategies were included to cultivate the process, including mindfulness exercises, metaphors, and experiential exercise. Each session began with a brief mindfulness exercise and review, which helped participants connect with the present moment and focus on the practice. The story-like quality of metaphors, the unique strategy in ACT, provided a rich verbal context that evoked thoughts, feelings, and behaviors similar to those evoked by the participants' actual situation, and in such verbal context, they can explore new behaviors, circumventing the potential traps of learning by rules. The homework helped patients consolidate their skills and actively apply them to daily life. The audiotapes of

mindfulness exercise were sent to them via WeChat at the end of each session to ensure the quality of self-exercise.

Control group

Participants randomized to the control group received care as usual, which involved information about lung cancer-related treatments during hospitalization, medication guidance, health education, such as diet and exercise advice, and reexamination recommendation after discharge. The standardized usual care in the research department was provided face-to-face by the participant's nurse in charge at their bedside during hospitalization.

Treatment fidelity

The intervention was delivered using validated treatment manuals by the first author, a PhD candidate in nursing with experience in oncological and psychological care. The interventionist received ACT trainings from experienced ACT therapists for 15 days, including booster sessions about the theory, didactics, experiential exercises, role play, and online group supervision every 2 weeks. The interventionist practiced the intervention under the supervision by supervisor (CLW) until she had adequate competency to conduct the intervention. During the intervention process, self-evaluation was conducted by the interventionist with a day-to-day diary and a 60-item ACT fidelity checklist (rating scale: 1–7) to assess whether each point occurred in the session recording.[58] The mean rating scores per session ranged from 5.90 to 6.60. Semi-monthly meeting with supervisor (CLW) was held to ensure adherence to the protocol.[59] Randomly selected 20% of the intervention audiotapes were reviewed by ACT practitioners (CLW, XHJ) to provide feedback to adjust the interventionist's skills.

Measures

Demographics

Demographic measures consisted of age, gender, marital status, education level, economic level, classification and stage of lung cancer, and type of treatment.

Feasibility and acceptability

The feasibility of intervention was assessed based on eligible, recruitment, attrition, and adherence rates (the frequency of practicing mindfulness and session attendance). The feasibility of administering the questionnaires was explored in terms of its readability and the time required for completion. Any participants who missed a session or withdrew from the intervention were recorded with detailed reasons. The acceptability was assessed with satisfaction ratings on an eight–item scale from 1 (not agree at all) to 5 (totally agree) for helpfulness of the mindfulness, metaphors, value clarification, and goal setting, the number and length of sessions, intervention format and the extent to which skills can be easily applied to real life on an item from 1 (not at all) to 5 (extremely). Open-ended questions were asked for participants' experiences of ACT and overall satisfaction.

Primary outcomes

Fatigue interference: the Fatigue Symptom Inventory (FSI). The fatigue interference and intensity over the previous 7 days were assessed with the 13-item FSI.[61] With an 11-point Likert scale ranging from 0 (no interference) to 10 (extreme interference), the first four items were used to assess fatigue intensity, and items 5–11 were used to assess the degree to which fatigue in the past week was judged to interfere with different aspects, such as general activity, bathing and dressing ability, work activity, concentration ability, relation with others, enjoyment of life, and mood. Items 12–13 were used in the testing of the frequency of fatigue. The higher the score, the greater the fatigue intensity and interference. Disruption index (ie. fatigue interference) can be computed by summing items 5–11. This study used the FSI–I subscale to test the fatigue interference. The subscale has shown good reliability and validity.[62] The Chinese version of FSI tested in patients with non-small-cell lung cancer[63] also showed a good internal consistency (Cronbach's α = 0.92).

Health-related quality of life: Functional Assessment of Cancer Therapy–Lung, Version 4 (FACT-L). The 36-item FACT-L, including five domains, namely, physical, social, emotional, functional well-being, and additional concerns about lung cancer, was used to assess the quality of life of patients with lung cancer. The items were rated on a 5-point scale from 0 (not at all) to 4 (very much), with high scores indicating a good quality of life. This scale has been widely used among Chinese lung cancer patients with good test–retest reliability and internal consistency coefficients more than 0.75.[64]

Secondary outcomes

CRF: the multidimensional Fatigue inventory (MFI). CRF was evaluated with the Chinese version of MFI, which is a 20-item and 4-point rating scale. It contains three domains: spiritual, physical, and mental fatigue. High scores indicate a high degree of fatigue. The Chinese version of this scale has been tested in cancer patients, indicating a good reliability with a Cronbach's alpha of 0.89.[65]

Depressive symptoms: the patient Health Questionnaire (PHQ-9). The severity of depressive symptoms was measured by PHQ-9, in which each item can be scored from 0 (not at all) to 3 (nearly every day).[66] The cut-off points can be used to divide the total score into no depression (0–4), mild (5–9), moderate (10–14), moderate-severe (15–19), and severe depression (20–27) categories. High scores indicate increased levels of depressive symptoms. The Chinese version of PHQ-9 showed an acceptable internal consistency with a Cronbach's alpha of 0.86 within a Chinese community sample.[67]

Anxiety: Generalized Anxiety Disorder Scale (GAD-7). The participants' level of anxiety was measured by the GAD-7. Scores of 5, 10, and 15 were used as the cut-off points for mild, moderate, and severe anxiety,

respectively. High scores indicate high levels of anxiety. The Chinese version of GAD-7 was validated in general hospital outpatients and showed good reliability with a Cronbach's alpha of 0.898.[68]

Cancer-specific distress: Impact of Events Scale-Revised (IES-R). Cancer-specific distress was assessed by the 22-item IES-R, a measurement for assessing the impact of traumatic life events.[69] The scale contains three domains, namely, intrusion, avoidance, and hyperarousal via a 5-point Likert scale ranging from 0 (not at all) to 4 (extremely). High scores indicate increased levels of distress. The Chinese version of IES-R was validated in victims who had experienced life-threatening events requiring accident and emergency services, showing good internal consistency (Cronbach's α: 0.83–0.89).[70]

Data collection

Baseline assessment (T0) was conducted before randomization by an independently trained assessor who was blinded to the study. The baseline data, including information about demographic and clinical characteristics, were collected face-to-face in the respiratory department. Postintervention data were collected at oneweek postintervention (T1) by the same assessor via telephone call. The participants in the intervention group were asked about the intervention acceptability via WeChat on the same day.

Ethical consideration

The study was approved by the Joint Chinese University of Hong Kong–New Territories East Cluster Clinical Research Ethics Committee (2020.581) and a research hospital in Mainland China. Written informed consent was obtained from participants before formal participation. The participants were informed about confidentiality and their right to leave the study at any time without any penalty.

Data analysis

IBM SPSS 24.0 was used for data analysis by a statistician blinded to the allocation. Baseline differences between groups regarding demographics and disease-related data were examined using *t*-test for continuous variables and Chi-square, Fisher's exact test, or Mann–Whitney U test for categorical variables. All data analyses were performed following the intention-to-treat principle.[71] Descriptive analysis adopted percentage, mean, and standard deviation (SD). A generalized estimating equation (GEE) model was used to compare the differential change in each outcome post-intervention with respect to the baseline between groups. The GEE model was fitted for repeated data to analyze the overall treatment effects over time, with adjustment of outcomes at the baseline level, relaxing the distribution assumption and incorporating the covariates.[72,73] Two-sided *p* values of 0.05 or less were considered statistically significant. Effect sizes (Cohen's *d*) of 0.2, 0.5, and 0.8 were considered small, moderate, and large group differences, respectively.[74]

Results

Characteristics of participants

Table 2 summarizes the demographic characteristics of the 40 participants. The mean age of the participants was 56.90 years (SD: 7.05). The majority of the participants were males (72.50%), married (97.50%), and diagnosed with non-small-cell lung cancer (72.50%). On average, the participants had been diagnosed with advanced lung cancer for 9.48 months. Their mean baseline FSI score was 32.98 (SD: 18.05). No significant differences in demographic characteristics were found between the two groups at baseline.

Table 2
Characteristics of the participants.

Characteristics	All ($n = 40$)	ACT group ($n = 20$)	UC group ($n = 20$)	P
Age (years), mean (SD)	56.90 (7.05)	54.75 (7.81)	59.05 (5.60)	0.052[a]
Gender, n (%)				0.288[b]
Male	29 (72.50)	13 (65.00)	16 (80.00)	
Female	11 (27.50)	7 (35.00)	4 (20.00)	
Marital status, n (%)				1.000[c]
Married	39 (97.50)	19 (95.00)	20 (100.00)	
Divorced	0 (0.00)	0 (0.00)	0 (0.00)	
Widowed	1 (2.50)	1 (5.00)	0 (0.00)	
Educational level, n (%)				0.332[d]
Primary school or below	10 (25.00)	4 (20.00)	6 (30.00)	
Junior high school	14 (35.00)	7 (35.00)	7 (35.00)	
High school	14 (35.00)	7 (35.00)	7 (35.00)	
Tertiary or above	2 (5.00)	2 (10.00)	0 (0.00)	
Residence, n (%)				0.710[c]
City	9 (22.50)	4 (20.0)	5 (25.00)	
Town	17 (42.50)	10 (50.0)	7 (35.00)	
Rural	14 (35.00)	6 (30.0)	8 (40.00)	
Employment status, n (%)				0.294[c]
Employed	5 (12.50)	4 (20.00)	1 (5.00)	
Unemployed	5 (12.50)	4 (20.00)	1 (5.00)	
Retired	14 (35.00)	6 (30.00)	8 (40.00)	
Farming	16 (40.00)	6 (30.00)	10 (50.00)	
Income per month (¥), n (%)				0.303[d]
< 1000	11 (27.50)	3 (15.00)	8 (40.00)	
1000–3000	14 (35.00)	10 (50.00)	4 (20.00)	
3000–5000	10 (25.00)	3 (15.00)	7 (35.00)	
> 5000	5 (12.50)	4 (20.00)	1 (5.00)	
Type of lung cancer, n (%)				0.288[b]
SCLC	11 (27.50)	4 (20.00)	7 (35.00)	
NSCLC	29 (72.50)	16 (80.00)	13 (65.00)	
Type of NSCLC, n (%)				0.219[b]
Adenocarcinoma	17 (58.62)	11 (68.75)	6 (46.15)	
Squamous carcinoma	12 (41.38)	5 (31.25)	7 (53.85)	
Stage of SCLC, n (%)				–
Extensive stage	11 (100.00)	4 (100.00)	7 (100.00)	
Limited stage	0 (0.00)	0 (0.00)	0 (0.00)	
Stage of lung cancer, n (%)				0.088[c]
IIIA	3 (7.50)	1 (5.00)	2 (10.00)	
IIIB	1 (2.50)	0 (0.00)	1 (5.00)	
IVA	26 (65.00)	11 (55.00)	15 (75.00)	
IVB	10 (25.00)	8 (40.00)	2 (10.00)	
Length of diagnose (month), Mean (SD)	9.48 (7.07)	9.35 (6.93)	9.60 (7.38)	0.913[a]
Cancer treatment received, n (%)				0.252[c]
Chemotherapy	15 (37.50)	5 (25.00)	10 (50.00)	
Surgery and chemotherapy	2 (5.00)	0 (0.00)	2 (10.00)	
Chemotherapy and radiotherapy	1 (2.50)	1 (5.00)	0 (0.00)	
Chemotherapy and targeted therapy	5 (12.50)	4 (20.00)	1 (5.00)	
Chemotherapy and immunotherapy	11 (27.50)	7 (35.00)	4 (20.00)	
Surgery, chemotherapy, and targeted therapy	2 (5.00)	1 (5.00)	1 (5.00)	
Surgery, chemotherapy, and immunotherapy	1 (2.50)	0 (0.00)	1 (5.00)	
Chemotherapy, radiotherapy, and immunotherapy	2 (5.00)	1 (5.00)	1 (5.00)	
Chemotherapy, radiotherapy, and targeted therapy	1 (2.50)	1 (5.00)	0 (0.00)	

ACT, Acceptance and Commitment Therapy; NSCLC, non-small-cell lung cancer; SCLC, small-cell lung cancer; SD, standard deviation; UC, usual care.

[a] Independent t-test.
[b] Chi-squared test.
[c] Fisher's exact test.
[d] Mann–Whitney U test.

Feasibility

Fig. 1 shows the flow for the study, where 108 patients were assessed for eligibility. Among them, 61 participants did not meet the inclusion criteria, and the eligible rate was 43.52%. A total of 40 of the remaining 47 eligible participants consented, accounting for a recruitment rate of 85.11%. Seven participants declined to participate because they had little interest ($n = 4$) and experienced poor health condition ($n = 2$), and their caregiver disagreed with their participation ($n = 1$). All participants completed the baseline and postintervention assessments. Exactly, 15 of the 20 participants in ACT group participated in all four sessions. All participants in the ACT group completed the first face-to-face-session. As for the last three videoconferencing-based sessions, five of them dropped

out because of long business trip ($n = 1$), health problem ($n = 2$), and unwillingness to continue the intervention ($n = 2$). The session attendance rate for the ACT group was 88.75%. All 40 participants received the scheduled usual care. The adherence rate was 75% in the ACT group, and the overall adherence rate was 87.5%. No adverse events were found. The participants in the ACT group completed an average of 5.95 out of 8 homework (SD: 1.91), and the average duration of practicing mindfulness at home was 36 min per week.

Acceptability

The mean satisfaction score in the ACT group was 4.94 (SD: 0.11). Overall, 95% of the participants were totally satisfied with the whole

Table 3

ACT intervention satisfaction.

Item	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1. I can understand the content of the whole program.	0 (0%)	0 (0%)	0 (0%)	1 (5%)	19 (95%)
2. The content of the whole program can meet my needs.	0 (0%)	0 (0%)	0 (0%)	2 (10%)	18 (90%)
3. Some metaphorical stories and mindfulness exercises are helpful to me.	0 (0%)	0 (0%)	0 (0%)	2 (10%)	18 (90%)
4. Setting goals and committed action are helpful to me.	0 (0%)	0 (0%)	0 (0%)	0 (0%)	20 (100%)
5. I can easily apply the skills I have learned in the program into my real life.	0 (0%)	0 (0%)	0 (0%)	3 (15%)	17 (85%)
6. The format of the whole program is appropriate and reasonable.	0 (0%)	0 (0%)	0 (0%)	0 (0%)	20 (100%)
7. The number of sessions and the duration of each session of the program are appropriate and reasonable.	0 (0%)	0 (0%)	1 (5%)	2 (10%)	17 (85%)
8. Overall, I am satisfied with the content and design of the whole program.	0 (0%)	0 (0%)	0 (0%)	1 (5%)	19 (95%)

ACT, Acceptance and Commitment Therapy.

program (Table 3). The hybrid form (face-to-face and virtual conferencing formats) was recognized by all participants. They agreed that committed actions with valued goals were helpful. The majority of them completely understood the content of the whole program (95%), which can meet their needs (90%). Ninety percent of participants strongly agreed that several metaphors and mindfulness exercises were helpful. Most of them (85%) agreed that the number of sessions and the length and pace of each session were appropriate and were willing to apply ACT strategies to actual life. One participant suggested that the duration of each session should be shorter. Participants stated the content of the questionnaire was easy to understand. The questionnaire was completed within 30–40 min. In the open-ended questions, several participants noted that the program was user friendly and provided multiple strategies. Most participants mentioned that they continued to perform mindfulness exercise and goal setting after the intervention ($n = 5$). A participant expressed his wish to continue learning this method.

Preliminary effects of the intervention

Table 4 presents the descriptive statistics for outcomes at T0 and T1 and the results of the GEE model for the outcomes in groups across time. No significant differences were found in the outcomes between the two groups at baseline.

The GEE analysis showed that the interactions effects were statistically significant in the total score of health-related quality of life ($B = 8.267$; 95% confidence interval [CI] = 3.305–13.229; $P = 0.001$; $d = 0.73$). Participants in the ACT group also showed statistically significant changes in the scores of emotional and functional well-being subscales at postintervention (P ranged from <0.001 to 0.017). Nevertheless, nonsignificant change with a medium effect size was observed in the scores of fatigue interference ($B = -4.950$; 95% CI = 10.621–0.721; $P = 0.087$; $d = -0.54$; Table 4).

Regarding secondary outcomes, statistically significant changes were observed in the scores of CRF and one of its subscales between the groups at T1 (total score: $B = -5.700$; 95% CI = −[8.252–3.148]; $P < 0.001$; $d = -0.83$; spiritual fatigue: $B = -4.050$; 95% CI = −[5.596–2.504]; $P < 0.001$; $d = -1.29$). Statistically significant decreases in depressive symptoms and anxiety were found in the groups from baseline to postintervention (depressive symptoms: $B = -3.400$; 95% CI = −[4.728–2.072]; $P < 0.001$; $d = -1.32$; anxiety: $B = -2.700$; 95% CI = −[3.818–1.582]; $P < 0.001$; $d = -0.88$). Furthermore, statistically significant interaction effects were indicated at T1 in the total score of cancer-specific distress and two subscales: intrusion and avoidance (total score: $B = -5.300$; 95% CI = −[8.852–1.748]; $P = 0.003$; $d = -0.76$; intrusion: $B = -2.200$; 95% CI = −[3.989–0.411]; $P = 0.016$; $d = -0.57$; avoidance: $B = -2.450$; 95% CI = −[3.778–1.122]; $P < 0.001$; $d = -1.05$; Table 4).

Discussion

This pilot study examined the feasibility and preliminary efficacy of a four-session ACT intervention compared with the usual care for fatigue interference and health-related quality of life in patients with advanced lung cancer. The findings suggest that the intervention is feasible and acceptable for the target population with high attendance (88.75%) and retention (75%) rates. These results provided early evidence that participants with advanced lung cancer under ACT reported significantly fewer depressive symptoms, lower levels of anxiety, distress and fatigue and better health-related quality of life than those who received usual care.

Several aspects demonstrate the strengths and feasibility of this study. Compared with previous studies on ACT for patients with advanced cancer,[54,55] this work showed high attendance and retention rates. Such finding was observed because for patients with advanced cancer, a brief intervention (four sessions) is appropriate to traditional healthcare settings (i.e. complex and long-term treatments) and requires less resource investment from patients and providers.[75,29] In addition, short-session programs may increase adherence because they ensure that each participant receives intervention sessions as much as possible despite the physical deterioration and treatment side effects.

Individual format increases the participants' self-disclosure to a great extent, consistent with the results of a systematic review.[42] Patients with advanced lung cancer in different gender and age groups suffer from diverse psychosocial burdens. Compared with group modality, the individual format provides a comfortable space for each to recount personal experiences, avoiding the circumstances in which participants evaded expressing their views because of differences in life experiences. Moreover, the combined online–offline intervention optimizes the intervention form and enhances its reach and effectiveness under the current epidemic situation, where face-to-face contact needs to be minimized, thus ensuring engagement.[76] The first face-to-face session built a good relationship between the interventionist and participants. The last three online sessions reduced the barriers caused by distance and time issues. Except for the time spent in hospital for treatment, most of the time, patients suffered from the side effects of treatments and encountered various psychosocial problems at home. The videoconferencing-based sessions not only provide patients at home with continuous psychological support, especially those in rural areas, but may also have practical application prospects to those who are already financially strained[60]).

Furthermore, the core of the ACT intervention is closely consistent with several qualities of the Chinese culture and a collectivistic culture. In the Chinese culture, people tolerate internal experience or avoid inappropriate emotions, and this tendency is regarded as an important virtue.[57] In a collectivistic culture, harmony is advocated by avoiding personal feelings and emotions to prevent interpersonal conflict.[77] Patients with advanced cancer continue to undertake family or work responsibilities by tolerating their painful sensations and avoiding feelings related to fatigue and cancer.[78] However, controlling or avoiding internal experience implies severe fatigue interference and poor quality of life. ACT provides an alternative way to help patients with advanced lung cancer shift from avoidance to acceptance. Hence, the study design of the ACT program was receptive and feasible for patients with advanced cancer in the context of Asian culture.

Helping participants realize the friendly nature of the process and emphasizing the benefit of participation using well-specified manuals are

Table 4
Changes in the outcome variables in the study groups across time using GEE model.

	T0 Mean (SD)	T1 Mean (SD)	T1 B (95%CI)	T1 P	Group B (95%CI)	Group P	Group*T1 B (95%CI)	Group*T1 P	Cohen's d[a]
Fatigue interference			1.300 (−4.039, 6.639)	0.633	−1.450 (−7.123, 4.223)	0.616	−4.950 (−10.621, 0.721)	0.087	−0.54
ACT group ($n = 20$)	11.70 (8.42)	8.05 (5.10)							
UC group ($n = 20$)	13.15 (10.27)	14.45 (10.90)							
Health-related quality of life			1.692 (−2.543, 5.927)	0.434	−3.026 (−9.673, 3.621)	0.372	8.267 (3.305, 13.229)	0.001*	0.73
ACT group ($n = 20$)	76.44 (10.82)	86.40 (10.31)							
UC group ($n = 20$)	79.47 (11.18)	81.16 (12.38)							
PWB			0.850 (−1.179, 2.879)	0.412	0.550 (−1.818, 2.918)	0.649	0.850 (−1.576, 3.276)	0.492	0.20
ACT group ($n = 20$)	15.50 (3.91)	17.20 (3.58)							
UC group ($n = 20$)	14.95 (3.93)	15.80 (5.06)							
SWB			0.992 (−0.721, 2.705)	0.256	−1.226 (−3.664, 1.212)	0.324	1.167 (−0.738, 3.072)	0.230	0.28
ACT group ($n = 20$)	17.09 (4.61)	19.25 (4.95)							
UC group ($n = 20$)	18.32 (3.37)	19.31 (3.81)							
EWB			−1.950 (−3.268, −0.632)	0.004*	−2.000 (−4.253, 0.253)	0.082	4.100 (2.648, 5.552)	<0.001*	1.13
ACT group ($n = 20$)	13.80 (4.15)	15.95 (4.26)							
UC group ($n = 20$)	15.80 (3.25)	13.85 (2.70)							
FWB			0.600 (−0.635, 1.835)	0.341	0.800 (−1.212, 2.812)	0.436	1.800 (0.322, 3.278)	0.017*	0.52
ACT group ($n = 20$)	9.85 (2.98)	12.25 (3.97)							
UC group ($n = 20$)	9.05 (3.65)	9.65 (2.78)							
LCS			1.200 (−0.197, 2.597)	0.092	−1.150 (−3.085, 0.785)	0.244	0.350 (−1.137, 1.837)	0.645	0.12
ACT group ($n = 20$)	20.20 (3.11)	21.75 (2.69)							
UC group ($n = 20$)	21.35 (3.30)	22.55 (2.95)							
Cancer-related fatigue			1.000 (−1.004, 3.004)	0.328	−2.200 (−5.697, 1.297)	0.218	−5.700 (−8.252, −3.148)	<0.001*	−0.83
ACT group ($n = 20$)	50.80 (5.94)	46.10 (7.42)							
UC group ($n = 20$)	53.00 (5.64)	54.00 (7.41)							
Spiritual fatigue			0.250 (−0.949, 1.449)	0.683	−0.900 (−2.538, 0.738)	0.282	−4.050 (−5.596, −2.504)	<0.001*	−1.29
ACT group ($n = 20$)	18.80 (2.97)	15.00 (3.69)							
UC group ($n = 20$)	19.70 (2.43)	19.95 (3.15)							
Mental fatigue			0.500 (−0.475, 1.475)	0.315	0.300 (−0.661, 1.261)	0.541	−0.950 (−2.023, 0.123)	0.083	−0.51
ACT group ($n = 20$)	12.30 (1.75)	11.85 (1.95)							
UC group ($n = 20$)	12.00 (1.41)	12.50 (2.14)							
Physical fatigue			0.250 (−0.508, 1.008)	0.518	−1.600 (−3.253, 0.053)	0.058	−0.700 (−1.602, 0.202)	0.128	−0.23
ACT group ($n = 20$)	19.70 (2.85)	19.25 (3.02)							
UC group ($n = 20$)	21.30 (2.62)	21.55 (3.47)							
Depressive symptoms			−0.650 (−1.795, 0.495)	0.266	0.750 (−0.995, 2.495)	0.400	−3.400 (−4.728, −2.072)	<0.001*	−1.32
ACT group ($n = 20$)	7.05 (2.80)	3.00 (1.81)							
UC group ($n = 20$)	6.30 (2.98)	5.65 (2.25)							
Anxiety			−0.500 (−1.278, 0.278)	0.208	0.800 (−1.183, 2.783)	0.429	−2.700 (−3.818, −1.582)	<0.001*	−0.88
ACT group ($n = 20$)	6.90 (3.58)	3.70 (2.76)							
UC group ($n = 20$)	6.10 (2.95)	5.60 (2.80)							
Cancer-specific distress			2.850 (−0.374, 6.074)	0.083	2.450 (−1.554, 6.454)	0.230	−5.300 (−8.852, −1.748)	0.003*	−0.76
ACT group ($n = 20$)	35.80 (6.33)	33.35 (8.40)							
UC group ($n = 20$)	33.35 (6.92)	36.20 (5.44)							
Intrusion			1.700 (0.156, 3.244)	0.031*	1.600 (−0.513, 3.713)	0.138	−2.200 (−3.989, −0.411)	0.016*	−0.57
ACT group ($n = 20$)	16.10 (3.17)	15.60 (5.06)							
UC group ($n = 20$)	14.50 (3.27)	16.20 (2.98)							
Avoidance			1.400 (0.229, 2.571)	0.019*	0.700 (−0.687, 2.087)	0.322	−2.450 (−3.778, −1.122)	<0.001*	−1.05
ACT group ($n = 20$)	12.20 (1.70)	11.15 (2.52)							
UC group ($n = 20$)	11.50 (2.76)	12.90 (1.92)							
Hyperarousal			−0.250 (−1.267, 0.767)	0.630	0.150 (−1.178, 1.478)	0.825	−0.650 (−1.840, 0.540)	0.285	−0.29
ACT group ($n = 20$)	7.50 (2.09)	6.60 (2.52)							
UC group ($n = 20$)	7.35 (2.30)	7.10 (2.00)							

Notes: T0: baseline; T1: one-week post-intervention. Baseline and post-intervention scores reported as mean and SD.
ACT, Acceptance and Commitment Therapy; CI, confidence interval; EWB, emotional well-being; FWB, functional well-being; GEE, generalized estimating equation model; LCS, lung cancer subscale; PWB, physical well-being; SWB, social/family well-being; UC, usual care.
B: average difference on outcome variables with reference to the baseline measurement.
[a]Cohen's d effect size was calculated for the between-group effects based on the change score of means and SDs of the two groups at one week postintervention with respect to the baseline.
*P < 0.05.

good ways to maintain intervention fidelity. A majority of the participants were satisfied with the intervention. They particularly valued the mindfulness practice (especially mindful breathing) and value orientation work. Several participants reported that the exercises enable them to actively adjust themselves back to the present and mobilize themselves to actively perform meaningful tasks. This finding is in line with cultivating awareness of the present moment without judgment in ACT. Mindfulness exercises can gradually cultivate the ability to experience any sensation due to CRF and its treatments without excessive emotional reactivity.[59,79] Although the sensations are not reduced, suffering may be alleviated.

Evidence of preliminary effectiveness of ACT was obtained. No significant changes in fatigue interference were found between the two study groups, which was supported by a previous preliminary study involving advanced breast cancer.[51] The possible reason is that symptom interference is currently measured in pilot studies. However, this notion does not mean that the ACT intervention program is ineffective in helping patients with advanced lung cancer manage their fatigue interference. Small sample sizes and short follow-up period may have limited the measure's sensitivity to change. The other possible reason is that lung cancer treatment usually lasts for approximately 6 months. The intervention process was aligned to the participants' treatments. Lung cancer and its treatments

can result in sustained degree of fatigue interference in daily life,[3,4] and this process may have weakened the effect of intervention. The persistence of symptomatic interference is an expression of the need for ACT. ACT may better represent the individualistic and dynamic nature of cancer adjustment compared with other cancer-based interventions.[29] Thus, large-scale studies with long-term follow-ups are warranted to determine the potential benefits of ACT to alleviate fatigue interference.

ACT also demonstrated significant improvements on the overall score of health-related quality of life and reductions in depressive symptoms, anxiety, overall score of cancer-specific distress, and CRF among the participants compared with the control group. These findings were supported by those of previous similar studies,[80,54,81] the evidence from a systematic review of patients with advanced cancer,[42] and two reviews concerning cancer patients.[40,29] The probable reason is that ACT helps participants cultivate a positive state, that is, helping them recognize the normal state of distressful experiences in the trajectory of cancer treatments, thereby freeing up resources, improving the functioning of physical diseases, engaging in meaningful activities, and maximizing the quality of life.[38,29] Mindfulness exercise, as a core technique of ACT, may be the other potential mechanism by which the intervention reduces the perceptions of symptom severity and promotes the appropriate contact with the present moment.[82] However, the effects need to be interpreted with caution because of the small sample size.

Limitations

Limitations of this study should be noted. First, the small sample size weakened the statistic power for detecting effects. Second, the participants were recruited from a single hospital only, limiting the generalizability of the findings. Third, given that the intervention was synchronized with the patients' treatment course (especially chemotherapy), the participants who attended the sessions may experience serious side effects after completing chemotherapy, and thus, the effect size of the intervention was weakened. Finally, this study did not include follow-up assessments postintervention. Given that ACT involves gradual skills development, it will be more verifiable when longer follow-up assessments are added to prove changes among patients.[51]

Research and clinical implications

This study provided insights into the intervention design and process. First, as the pilot test results usually inform treatment acceptability and feasibility rather than efficacy, the preliminary findings warranted a full-scale powered study for evaluating the therapeutic effects of ACT on fatigue interference and health-related quality of life in patients with advanced lung cancer. Second, previous ACT research emphasized the importance of long-term follow-up for capturing unexpected improvements over time and maintenance effects compared with comparator conditions.[83] Future studies will benefit from increased follow-up assessments to examine the efficacy of ACT. Third, the promotion of skills is related to the in-session realization of ACT components, and psychotherapy research has shown that patients who improve their skills (such as acceptance and cognitive defusion) during the process show better treatment outcomes.[84] Given that the functional outcome (fatigue interference) may not be sensitive to capture changes in the short term, a participant comprehension check can be adopted to test whether the degree of the six components of ACT is realized during the sessions, which is beneficial to understanding the participants' level of skill acquisition and further optimization of interventions.[75] Moreover, changes in acceptance and mindfulness are potential mechanisms underlying the mental health benefits of mindfulness- and acceptance-based interventions[85,86] thus, whether certain ACT component, mindfulness, or a combination of the aforementioned is a critical mechanism of change that deserves further discussion. In summary, after the designed ACT intervention program has been proven feasible and acceptable, we will conduct a large-sample, prospective RCT to verify the effects of ACT on

the improvement of fatigue interference and health-related quality of life in patients with advanced lung cancer. The further full-scale RCT study was already registered online in ClinicalTrials.gov (NCT04869267).

The results also revealed potential clinical implications. The patient engagement and frequency used in mindful exercises and value-oriented actions reflect the patients' desire for psychological support. Focusing on meaningful living rather than delving into the distress of cancer is valuable to end-of-life care in the population. Owing to cultural adaptability, ACT can fulfill the need of and help patients with advanced lung cancer accept early the normal nature of symptom interference and cancer, thus helping them realize psychosocial adjustment to cancer and take effective actions based on the life that they want as early as possible. Numerous studies demonstrated the practicality of ACT implemented by clinical nurses for inpatients.[87,88] This evidence may support that an individual psychosocial support by trained nurses can be a realistic alternative to psychologists in routine cancer care.[89] Nurses have the most immediate opportunity to provide patients with psychological support and initially attend to their needs. Thus, increasing ACT trainings appropriately and infusing brief but focused interventions into daily care may enrich the clinical role and strengthen the specialist capacity of oncology nurses. Further, ACT applications are needed to clarify the value of ACT delivered by nurses.

Conclusions

This study supports the feasibility and acceptability of a four-session ACT intervention for fatigue interference and health-related quality of life in patients with advanced lung cancer. The findings showed that the intervention is potentially effective in remitting depressive symptoms, anxiety, distress, and fatigue and improving health-related quality of life in this population. Preliminary effect size estimates suggest that ACT deserves full-scale studies, especially with respect to fatigue interference.

Ethics statement

The study was approved by the Joint Chinese University of Hong Kong–New Territories East Cluster Clinical Research Ethics Committee (Approval No.2020.581) and a research hospital in Mainland China. Written informed consent was obtained from participants before formal participation.

Declaration of competing interest

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.apjon.2022.100102.

Authors' contributions

Conceived and designed the analysis: Huiyuan LI, Marques Shek Nam NG, Cho Lee WONG
Collected the data: Huiyuan LI, Nina WANG Contributed data or analysis tools: Xiaohuan JIN, Ka Fai MANN
Performed the analysis: Huiyuan LI

Wrote the paper: Huiyuan LI, Xiaohuan JIN, Marques Shek Nam NG, Cho Lee WONG

Revise the paper: Huiyuan LI, Xiaohuan JIN, Marques Shek Nam NG, Ka Fai Mann, Nina WANG, Cho Lee WONG.

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