ORIGINAL ARTICLE

The potential role for acupuncture in treating symptoms in patients with lung cancer: an observational longitudinal study

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ABSTRACT

Background

Most lung cancer patients experience multiple symptoms related either to the disease or its treatment. The commonly reported symptoms are pain, depression, anxiety, nausea, and poor well-being. The aim of the present study was to evaluate the effect of acupuncture as a potential treatment modality in symptomatic lung cancer patients.

Methods

This prospective observational study enrolled 33 lung cancer patients from the Peter Brojde Lung Cancer Centre between August 2010 and May 2012. All patients received 45-minute sessions of acupuncture, 1–2 times weekly for a minimum of 4 sessions. Symptom severity was assessed using the Edmonton Symptom Assessment System (ESAS) before and after completion of acupuncture.

Results

The study cohort included 30 patients with non-small-cell lung cancer and 3 with small-cell lung cancer. Mean age was 62 years (range: 36–88 years); 17 of the patients were women. Most of the patients had advanced-stage cancer (73%) and good performance status (Eastern Cooperative Oncology Group 0–1: 88%). Of these patients, 67% received anticancer treatment (chemotherapy or radiotherapy, or both) with acupuncture. Of the remaining 10 patients, 8 received acupuncture after a complete surgical resection of their tumour, and because of their advanced age, 2 received acupuncture and best supportive care. The median number of acupuncture sessions was 7 (interquartile range: 4–13 sessions). Statistically significant improvements in pain, appetite, nausea, nervousness, and well-being were observed. A clinically important improvement (2 points on the ESAS) was reported by 61% of patients for pain and by 33% for well-being.

A significant positive correlation between improved well-being and the number of acupuncture sessions was observed. This correlation remained significant even after controlling for treatment and narcotic use. Receiver operating characteristic analysis demonstrated that a minimum of 6 acupuncture sessions are required for a 70% chance of a clinically important improvement in well-being.

Conclusions

The present study is the first to demonstrate that acupuncture may be an effective approach for improving symptoms—in particular, pain and well–being—in lung cancer patients. Acupuncture is a safe and minimally invasive procedure, and it is potentially useful even in patients undergoing anticancer treatment.

KEY WORDS

Acupuncture, lung cancer, Edmonton Symptom Assessment System, ESAS, pain, integrative oncology clinics, narcotics

1. BACKGROUND

Most lung cancer patients experience multiple symptoms related either to the cancer or to treatment side effects. This increase in symptom load includes pain, fatigue, nausea and vomiting, distress, depression, and anxiety, and it contributes to impaired quality of life and decreased functional capacity[1–7]. In response to the severity and persistence of their symptoms, patients often try complementary modalities (CMS) such as mindful meditation, deep relaxation techniques, massage, and acupuncture in conjunction with standard treatments[8–11].

Use of CMS in cancer patients ranges from 7% to 64% in various studies[12], but the additional benefit of various CMS in controlling symptoms in cancer is less

clear. Several studies of varying methodologic rigour suggest that acupuncture can potentially help manage cancer symptoms such as pain, lack of appetite, nausea, emotional distress, depression, and anxiety[13–19]. However, no study has focused exclusively on lung cancer patients, despite that cancer being one of the commonest in men and women alike[20,21]. The aim of the present study was therefore to evaluate the effects of acupuncture as a potential treatment modality for symptom control in lung cancer patients.

2. METHODS

Our study was conducted at the Peter Brojde Lung Cancer Centre (PBLCC) between August 2010 and May 2012. The PBLCC was established in 2009 within the Segal Cancer Centre of the Jewish General Hospital in Montreal. The PBLCC uses an integrative oncology clinic prototype focused on lung cancer patients and seeks to use clinical research to identify how best to combine current medical treatments with CMs to improve outcomes. The CM modalities offered by the PBLCC include nutrition interventions, acupuncture, massotherapy, and physiotherapy.

All patients with lung cancer at the Jewish General Hospital are seen by the Pulmonary Oncology service, and symptomatic patients are referred to the PBLCC integrative oncology clinic. Patients seen in the PBLCC and referred for acupuncture were eligible for inclusion in the current study if they had received a minimum of 4 sessions of acupuncture and had completed a baseline and end-of-treatment Edmonton Symptom Assessment System (ESAS) questionnaire. The study was conducted in adherence to institutional research guidelines, and all patients signed an informed consent that had been approved by the hospital research ethics committee. Acupuncture was provided by the licensed acupuncturist on the interdisciplinary team within the PBLCC integrative oncology clinic.

Acupuncture sessions lasted 45 minutes, and patients were typically treated 1–2 times weekly. Nine acupuncture points were used: 6 body points (Li4, Liv3, St36, Sp6, P6, Lu7) and 3 auricular points (Shenmen, Subcortex, Zero)[22]. The chosen points included at least 1 specific point for each symptom being evaluated. Dry stainless steel needles were inserted in the skin to an estimated depth of 0.5–1 cun (1–2.5 cm) to produce a *de-qi* sensation—that is, a sensation of numbness, distension, or electrical tingling at the needling site, which radiates along the corresponding meridian. The inserted needles were maintained for 30 minutes and turned every 10 minutes. During the session, the acupuncturist observed the patients for side effects, such as a stinging sensation, bruising, fainting, muscle spasms, bleeding, and nerve damage.

The ESAS was used for symptom assessment at the first visit to the acupuncturist (before any treatment) and again after the last treatment. The ESAS is a validated instrument developed to measure 9 symptoms: pain, strength, nausea, depression, anxiety, drowsiness, appetite, shortness of breath, and overall well-being[23]. Patients were asked to rate the severity of each symptom on a scale from 0 to 10, with 10 being most severe.

2.1 Statistical Analysis

Baseline characteristics of the patients were collected from medical charts: age, sex, diagnosis, Eastern Cooperative Oncology Group (ECOG) performance status (PS), stage, medical treatment, and use of narcotics. Binary variables were created for any anticancer treatment or narcotic that was given during acupuncture.

The primary outcome was change in well-being and pain scores. To evaluate the effect of acupuncture, the pre- and post-treatment scores for each symptom were compared using the Wilcoxon signed-rank test. The level of significance was set at $p < 0.05$ (two-tailed). The intensity of symptoms was classified as mild (score = 0–3) or moderate-to-severe (score $\geq$ 4). Chi-square analysis was used to identify the effect of acupuncture on symptom intensity. Recommendations for a minimal clinically important difference on visual analog scales for various symptoms, including pain, are highly variable, ranging from 1.4 to 2.9[24–26]. For the present study, we defined the minimal clinically important change as a 2-point difference in the post- and pre-treatment symptom scores. Patients were categorized as clinically improved (score reduction of 2 points or more); stable (change of between –1.9 and 2.0 points), or clinically worse (score increase by more than 2 points).

The interaction between change in symptom scores and number of acupuncture sessions was tested using a Pearson correlation test. In addition, two separate linear regression models were tested for the differences in pain score and the differences in well-being score (dependent variables). The explanatory variables included in the first model were cancer stage, use of concurrent anticancer treatment, and use of narcotics. The second model included age, sex, and ECOG PS. Variables were selected based on clinical significance, and the number of explanatory variables was limited to 3 to preserve a power of 0.8 and a significance level of 0.05.

All analyses were conducted using the PASW Statistics software application (version 18.0, SPSS, Chicago, IL, U.S.A.).

3. RESULTS

Of the 37 patients referred for acupuncture, 33 (89%) had received 4 or more sessions of acupuncture at the time of analysis. Of the 33 patients analyzed, 30

(91%) had non-small-cell lung cancer, and 3 (9%) had small-cell lung cancer. Mean age was 62 years (range: 36–88 years), and 17 of the patients (52%) were women. Almost three quarters (73%) had advanced lung cancer (stage IIIB, IV, or extensive), and most had an ECOG performance status of 0–1 (88%, Table I). In 23 patients (67%), acupuncture was given while the patient was also undergoing chemotherapy or radiation therapy. Of the remaining 10 patients, 8 received acupuncture after surgical resection of their tumour, and 2 received acupuncture with best supportive care only. No significant side effects attributable to the acupuncture were observed.

The median number of acupuncture sessions was 7 (interquartile range: 4–13 sessions). Statistically significant improvements in pain, appetite, nausea, nervousness, and well-being were observed (Table II). At the end of treatment, pain had improved clinically in 20 patients (61%), remained stable in 11 (33%), and deteriorated in 2 (6%, Figure 1). The 2 patients whose pain deteriorated stopped acupuncture after 4 sessions, one because of cancer progression, and the other because of frailty.

Reported pain intensity improved significantly after acupuncture treatment. Before acupuncture, 22 patients (67%) reported moderate-to-severe pain (score ≥ 4); after acupuncture, the number of patients with moderate-to-severe pain had declined to 11 (33%, chi-square test $p = 0.05$). During acupuncture treatment, 8 patients were taking narcotics for pain. These subjects also reported a statistically significant reduction in mean pain score to 2.25 after treatment from 5.75 before treatment ($p < 0.001$). No

significant correlation was found between change in pain score and number of acupuncture sessions ($r = 0.046$, $p = 0.8$), even after controlling for use of narcotics ($r = 0.043$, $p = 0.814$). Furthermore, other factors, such as cancer stage and concurrent cancer treatment, did not significantly alter the observed effects of acupuncture treatment on pain (Table III).

Similar results were seen for improvements in well-being. (Figure 2). A clinically important improvement in well-being was reported by 11 patients (33%), with 21 patients (64%) remaining stable, and just 1 patient with clear cancer progression feeling worse. Initially, 17 patients (52%) reported a well-being score of 4 or higher. After acupuncture, only 11 patients (33%) reported a score of 4 or higher (chi-square $p = 0.05$). Linear regression modelling for change in well-being score failed to show any significant effect of stage, active treatment, or use of narcotics (Table III). Age, sex, and ECOG PS also had no effect on differences in the well-being score (data not shown). Change in well-being was significantly correlated with the number of acupuncture sessions ($r = -0.438$, $p = 0.012$), and it remained significant even after controlling for anticancer treatment ($r = -0.476$, $p = 0.007$) and use of narcotics ($r = -0.434$, $p = 0.015$). One outlier with 43 acupuncture sessions (>3 standard deviations above the mean) was excluded from this correlation analysis. Receiver operating characteristic analysis demonstrated that a minimum of 6 sessions was required for a 70% chance of a clinically significant (2-point or more) reduction in well-being score.

4. DISCUSSION

To our knowledge, the present study is the first to analyze the efficacy of acupuncture in alleviating symptoms in lung cancer patients. Our results show that acupuncture is feasible, safe, and well tolerated. Furthermore, patients undergoing acupuncture in the PBLCC integrative oncology clinic experienced significant improvements in 5 of 9 symptoms assessed on the ESAS. We focused specifically on two of those symptoms (pain and overall well-being) and showed that, as far as could be assessed using statistical methods, the effect of acupuncture was independent of age, sex, PS, concurrent cancer treatment, and use of narcotics. The number of acupuncture sessions completed was significantly correlated with improvement in well-being (but not pain), and our results suggest that 6 sessions, at a minimum, are needed to achieve a clinically significant effect on well-being.

Being a single-institution nonrandomized observational prospective study, our research has strengths and limitations. Acupuncture was delivered by a single, experienced acupuncturist, and the 9-point acupuncture intervention was standardized for the study. That standardization ensured minimal variability across the acupuncture sessions and, at the same time, created effective patient–acupuncturist

TABLE I   Demographics for the study group

Variable	Value
Patients (*n*)	33
Age (years)	
Mean	62
Range	52
Sex [*n* (%)]	
Female	17 (52)
Male	16 (48)
Cancer type [*n* (%)]	
NSCLC	30 (91)
SCLC	3 (9)
Stage [*n* (%)]	
Early (I–IIIA, limited)	9 (27)
Advanced (IIIB, IV, extensive)	24 (73)
ECOG performance status [*n* (%)]	
0–1	29 (88)
>1	4 (12)

NSCLC = non-small-cell lung cancer; SCLC = small-cell lung cancer; ECOG = Eastern Cooperative Oncology Group.

TABLE II   Outcome of repeated measures presenting the effect of acupuncture on the Edmonton Symptom Assessment System score

	Pre-acupuncture (mean±SD)	Post-acupuncture (mean±SD)	Z Statistic[a]	p Value[b]
Pain	4.79±2.9	2.42±2.6	−3.74	**0.001**
Appetite	3.79±2.9	2.45±2.9	−2.84	**0.005**
Nausea	1.12±2.2	0.24±0.7	−2.37	**0.018**
Nervousness	3.06±2.9	2.15±2.2	−2.08	**0.038**
Well-being	3.76±2.6	2.70±2.2	−2.72	**0.007**
Shortness of breath	3.18±3.1	2.97±2.9	−0.95	0.341
Drowsiness	3.10±3.1	2.42±2.5	−1.41	0.160
Depression	2.03±2.7	1.88±2.0	−0.16	0.877
Strength	3.05±2.8	2.40±2.1	−2.01	0.064

[a]   A negative value indicates an improvement in the symptom score.
[b]   By a Wilcoxon signed-rank test based on positive ranks, two-tailed; bolding indicates significance (<0.05).
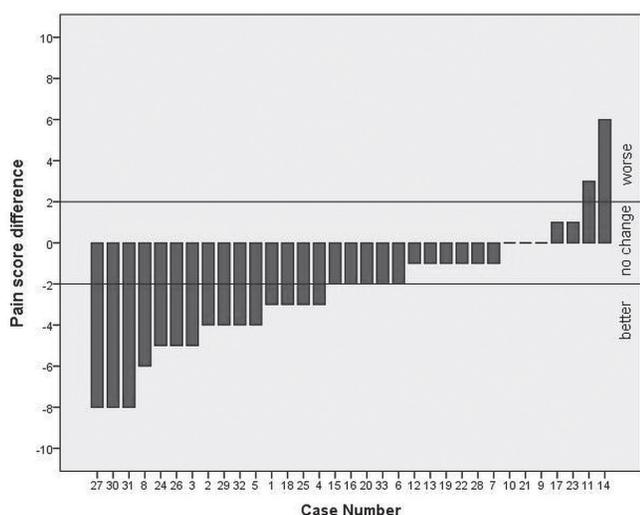SD = standard deviation.

FIGURE 1   *Difference in pain scores pre- and post-acupuncture. Each bar represents a patient. The horizontal lines represent a difference of 2 points, which is considered a minimal clinically important difference. Only 2 patients (case numbers 11 and 14) reported worsening of pain.*

communication and strengthened the subsequent commitment to treatment by the patients. Other aspects of treatment were not standardized; for example, treatment duration varied between 4 and 26 weeks.

Interpretation of the results and some aspects of the statistical analysis are limited by the size of the study and the absence of a control group. Thus, to assess whether our results are reproducible and generalizable, they should ideally be confirmed in a larger randomized controlled trial with multiple acupuncturists.

There is increasing evidence that the use of acupuncture for symptom control in severe or life-threatening illness is plausible. That evidence includes results of earlier clinical trials. For example, a review of 27 randomized controlled trials of acupuncture in palliative care concluded that acupuncture should be included as a modality for use in the palliation of pain[27]. However, the use of acupuncture has not yet been accepted as a standard of care in adjunctive medical treatment. The general applicability of the results from acupuncture studies to date are limited because of the use of different acupuncture techniques (for example, electrical or manual), controls (with or without comparison groups), outcome measures, needle protocols, and duration of treatment[13,15,16,27]. Most importantly from our perspective, no earlier acupuncture trials have focused specifically on lung cancer patients, despite the large numbers of patients diagnosed with lung cancer and their evident need for control of frequent, severe, and debilitating symptoms[28,29]. In a randomized controlled study with two control groups (nonpoint and noninvasive), Alimi and colleagues[15] reported pain improvement in 36% of patients treated with auricular acupuncture. However, that study population consisted of mixed cancer patients with only 2 of 70 being lung cancer patients, both of whom were randomized to placebo.

The mechanisms associated with acupuncture's analgesic action are complex, but appreciation that this treatment modality has physiologically relevant effects is growing and strengthening the case for its use in symptom control. Acupuncture practitioners recognize meridians or energy pathways that correspond to neurovascular connective tissue planes connecting various parts of the body[30–33]. One hypothesis is that acupuncture stimulates a somatosensory system that results in the release of endogenous opioids[34,35]. Acupuncture is known to trigger electrophysiologic changes in various areas of the nervous system, including the autonomic nervous system, the pituitary gland, the hypothalamus, and other parts of the brain, causing the release of neurotransmitters, neuropeptides, and other hormones that can affect a range of bodily functions[36,37]. The proposal is that, through this

TABLE III   Linear model to evaluate the effect of other parameters on improvement in Edmonton Symptom Assessment System score

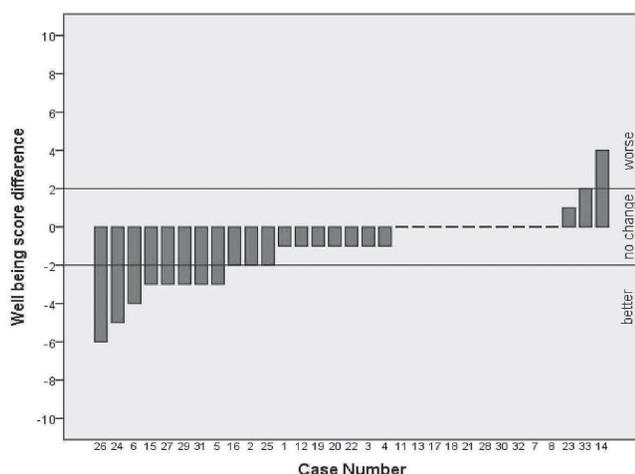|	Difference in pain score[a]		Difference in well-being score[a]	
	Standardized coefficient	p Value	Standardized coefficient	p Value
Treatment[b]	−1.408	0.259	−0.516	0.534
Narcotics[b]	−1.399	0.254	−0.864	0.293
Stage[b]	−0.0612	0.314	0.309	0.444

[a]   Dependent variable.
[b]   Predictor.

FIGURE 2   Difference in well-being scores pre- and post-acupuncture. Each bar represents a patient. The horizontal lines represent a difference of 2 points, which is considered a minimal clinically important difference. Only 1 patient (case number 14) reported worsening of well-being.

biologic response, acupuncture can modulate blood pressure and body temperature, enhance immunity, decrease inflammation, and subsequently improve cancer- and treatment-related symptoms[13,30,31,38].

5.   CONCLUSIONS

This study is the first to demonstrate that acupuncture may be an effective approach for improving symptoms—in particular, pain and well-being—in a lung cancer population. Acupuncture is a safe and minimally invasive modality, and it may have a particularly useful role in patients undergoing anticancer treatment—such as those who constituted the greater proportion of the patients in the present study.

A large-scale randomized controlled trial is needed to confirm the beneficial effects of acupuncture in this population and to gather more precise information about the frequency and duration of acupuncture treatments required to achieve optimal symptom control. Patients and practitioners need answers to important practical questions about the symptoms that are most amenable to relief through acupuncture, and the point in the patient's treatment trajectory when it is best to use acupuncture.

6.   CONFLICT OF INTEREST DISCLOSURES

All persons who have made substantial contributions to the work reported in this manuscript are included as authors, and none have relevant financial interests in this manuscript.

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