Influence of acupuncture on bioelectrical impedance measures in patients with gastrointestinal cancer: results of a pilot study

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ABSTRACT

Background Patients with gastrointestinal cancers often suffer from malnutrition and cachexia caused by inflammatory processes due to malignancy and therapeutic intervention. Evaluation of nutritional status and well-being of patients is essential to prevent or slow down the progression of cachexia. In addition, acupuncture as a complementary intervention may help reduce cachexia and unintentional weight loss.

Methods Seven patients with cancers of the gastrointestinal tract enrolled in this pilot study were provided with eight acupuncture sessions in addition to their regular treatment schedule. Bioelectrical impedance analysis (BIA) measurements were taken at every other acupuncture session to evaluate the body composition of patients. BIA is a fast, inexpensive and non-invasive method for evaluating fluid, fat and muscle mass distribution which correlates with nutritional status.

Results All patients enrolled in the pilot study completed the acupuncture intervention and BIA measurements. The average weight loss and reduction in body weight was 1.3%, which is less than the average weight loss of 5% reported in the literature. Both phase angle and fat-free mass decreased in patients, indicating a worsening of the condition. However, a shift from intracellular to extracellular fluid was not observed, which is usually associated with a loss of cell integrity.

Conclusions This pilot study indicates that patients tolerate acupuncture treatments well. The BIA results should be interpreted with caution due to the small sample size. A larger randomised placebo-controlled study is currently being conducted to further investigate the influence of acupuncture and to provide insights into BIA as a reliable tool for evaluating body composition in patients with gastrointestinal cancers.

INTRODUCTION

The occurrence of gastrointestinal cancers is widespread. It accounts for one in four deaths worldwide,1, 2 17.5% of newly diagnosed cases, and is second only to genitourinary cancer incidence in the USA. Although the prevalence of late-stage diagnosis of gastrointestinal cancers has significantly decreased, the burden to patients and caregivers remains high, particularly regarding the side effects of treatment and comorbidities that accompany malignancy. One such comorbidity, cancer cachexia,3 is a debilitating syndrome of progressive weight loss, anorexia and decreased lean body mass that commonly affects patients with both early- and late-stage disease.4 It serves as a predictor of survival and outcome and, in more advanced stages, can interfere with the treatment protocol leading to delays in therapy, poor outcomes and reduced quality of life. However, patients who maintain a normal diet during chemotherapy for gastrointestinal cancers have significantly better outcome and quality of life measures than those who develop malnutrition and devolve to cancer cachexia.5 Thus, preventing or reducing cancer cachexia and malnutrition in patients with gastrointestinal cancer is vital to improving outcomes and quality of life.

Currently, the most common approaches to cancer-related anorexia are pharmacological management such as megestrol acetate, corticosteroids and nutritional supplements to the diet regimen. However, these treatments have limitations and side effects such as Cushing’s syndrome, oedema, immune system suppression and fat redistribution.
Other therapies that may be considered include acupuncture, which has been practised for many centuries as a traditional Chinese medicine (TCM) approach and is now regarded as a well-established complementary and alternative medicine approach in the Western world. Acupuncture has been evaluated as an adjuvant therapy in cancer patients for a variety of symptoms such as pain, nausea, hot flashes, fatigue, postoperative ileus, sleep disturbances and mood disorders.\(^{6,7}\) To date, the best evidence exists for the benefits of acupuncture treatment in the prevention of nausea and vomiting associated with chemotherapy, as it appears to be as effective as pharmacotherapy in reducing the incidence of symptoms.\(^{8,9}\)

Acupuncture seems to work by influencing a number of physiological parameters that are directly involved with control of gastrointestinal functions such as release of serotonin, dopamine, ghrelin, leptin and substance P.\(^{10–12}\) For example, a study evaluating delayed gastric emptying in 30 critically ill patients found that acupuncture was more effective in increasing gastric emptying than standard pharmacological treatment.\(^{13}\) Similarly, an increase in ghrelin production, a hormone secreted by the stomach which induces hunger, has been observed following acupuncture treatment in obese women.\(^{14}\) In this study, acupuncture treatment also decreased the level of the satiety hormone leptin which is produced by adipose tissue in response to food consumption. As a result of this research, scientists have proposed that several factors can influence the homeostasis in hunger and satiety signalling via leptin and ghrelin, one of which is an increase in proinflammatory cytokines that is characteristic of both malignant tumours and a common side effect of chemotherapy treatment.\(^{15}\) More specifically, increases in the amounts of proinflammatory cytokines interleukin 1\(\alpha\), 1\(\beta\) and 6, as well as tumour necrosis factor \(\alpha\), have been reported in a number of trials involving cancer patients.\(^{16–18}\) It appears that inflammation leads to higher stress hormone levels which, in turn, results in decreased ghrelin levels and increased leptin levels leading to cancer cachexia (figure 1). Thus, acupuncture may restore homeostasis by reducing proinflammatory mediators and cortisol levels as well as balancing the secretion of ghrelin and leptin.\(^{12,14}\)

Based on the current knowledge, this pilot study investigated the use of targeted acupuncture to reduce the symptoms of cancer cachexia. Bioelectrical impedance analysis (BIA) served as an objective instrument to evaluate whether acupuncture specifically prevents weight loss and changes in body composition in patients with gastrointestinal cancers undergoing chemotherapy treatment. BIA is a non-invasive, rapid and inexpensive method of evaluating the health status of patients through measurement of resistance and reactance from which body composition can be derived. It is commonly used in a number of conditions to evaluate body water distribution, fat and fat-free mass, and the phase angle (PA) that can provide insights into health status and prognosis of a patient.\(^{19–22}\) Due to its frequent and widespread use as well as predictive value for disease status, progression and outcomes, BIA measurements were central to the objective measurements used in this pilot study.

**MATERIALS AND METHODS**

The design of the pilot study was a pre- and post-intervention single group design in seven patients diagnosed with gastric or colorectal cancer. All patients were evaluated before the start of the acupuncture intervention to establish a baseline. Measurements were collected over the course of 8 weeks and eight acupuncture sessions. Each subject was provided with acupuncture treatments weekly including pre- and post-chemotherapy sessions if the subject was scheduled for chemotherapy. It was estimated that eight acupuncture sessions would cover usually two chemotherapy cycles. Subjects were recruited from the cancer care unit in the North Central Florida region by the cancer care coordinator and the attending oncologist.

**Inclusion criteria**

Subjects were invited to participate in the study if they met the following inclusion criteria:

- At least 21 years of age
- Medical diagnosis of gastric or colorectal cancer
- Weight loss of 5% or more since diagnosis
- No surgery within past month
- Not scheduled for radiation therapy for the duration of the trial or for the next 3 months
- Able to speak or understand English
- Able and willing to follow the research protocol.

**Exclusion criteria**

Upon initial evaluation, patients were excluded from entering the study if they met any of the following criteria:

- Do not have chemotherapy scheduled after surgery
- Will have radiation therapy alone or in combination with chemotherapy
- Have a pre-existing or comorbid disorder that may interfere with the measurements (eg, HIV, infections, hepatitis, Alzheimer’s disorder, movement disorders, acute myocardial infarction within the last 3 months)
- Have burn sites or open and infected wounds
- Have life expectancy of less than 3 months as evaluated by attending physician.

If a subject met the inclusion and exclusion criteria they were provided with an informed consent form and initial baseline measures were taken followed by scheduling the acupuncture sessions.
Study population
Seven patients (4 women, 3 men; age range 34–82 years) enrolled and completed the study. All were undergoing chemotherapy treatment for gastric or colorectal cancer at the time of the study. No subject withdrew from the study.

Treatment and procedures
All patients were provided with an informed consent form that outlined the procedures. Initial baseline measures included demographic information, medical history and current medication and supplement use, appetite visual analogue scale (VAS), BIA, Karnofsky performance scale, amended symptoms and concerns checklist, and the Simplified Nutritional Appetite Questionnaire (SNAQ). Acupuncture treatment schedules were arranged between the patient and the qualified acupuncturist based on the chemotherapy schedule and availability. In most cases, eight acupuncture treatments were provided over the course of 6–8 weeks with BIA and questionnaire evaluations every other treatment.

Acupuncture treatments were administered by a qualified acupuncturist at his private practice. The Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) recommendations were used as a guideline in order to improve appraisal, interpretations and challenges unique to acupuncture research. The rationale for selection of acupuncture points is based on TCM and Auricular Medicine from the works of Nogier and Bahr. Acupuncture needles used were single-use sterile stainless steel and disposable. All subjects received the same primary acupuncture points including both auricular and body acupuncture points that were based on general principles of TCM and Auricular Medicine. In addition to the primary protocol acupuncture points (for further information on acupuncture point selection, please contact the author), each participant received additional acupuncture intervention, which consisted of secondary acupuncture points, to address any specific symptoms that occurred to participants during the study and affected weight loss as well as appetite. For instance, if participants experienced fatigue due to loss of appetite or due to nausea/vomiting, they were treated for management of the specific symptom. Points were located using their standard anatomical location, needles were retained for 15–20 min and the needling (de qi) sensation did not need to be obtained.

Measures
One of the main clinical outcome measures for this study was the BIA for determination of total body water, intracellular fluid, extracellular fluid, fat-free mass, fat mass and PA. The body mass index (BMI) was calculated based on weight and height of the patient at each of the BIA measurements. Body composition was measured by multifrequency BIA (MF-BIA) using the ImpediMed Imp SFB7 (ImpediMed, Eight Mile Plains, Queensland, Australia) which scans 256 frequencies between 4 and 1000 kHz and estimates body.

Figure 1  Framework for the effects of chemotherapy and gastrointestinal cancers on inflammation and metabolism. The bioelectrical impedance analysis parameters that relate to the body composition changes are listed. BMI, body mass index; ECF, extracellular fluid; FFM, fat-free mass; 5-HT, serotonin; HPA, hypothalamic-pituitary-adrenal axis; ICF, intracellular fluid; IL, interleukin; TBW, total body water; TNF, tumour necrosis factor.
composition using Cole modelling with Hanai mixture theory. The PA was reported at 50 kHz. BIA was measured every other visit (total of 4–5 times) at the acupuncture physician’s office. All derived measurements were based on equations for healthy volunteer populations, which is a limiting factor for accurate determination of BIA measurements but has been commonly employed.24

Questionnaires were used to evaluate the change in dietary habits of patients and the overall symptoms. A VAS was used to evaluate appetite over a 10 cm range ranging from poor to good appetite as described previously in the literature. The amended symptoms and concerns checklist was used to evaluate quality of life. This questionnaire has been validated extensively for use in cancer patients. The Karnofsky performance scale was also used to evaluate the functional ability of patients using an 11-point scale with 10% increments. Lower values indicate less functional ability while 100% indicates no functional impairment, complaints or indications of disorders. The scale has been validated and applied to a number of settings with reproducible results. An additional validated and reliable four-item survey, the Simplified Nutritional Appetite Questionnaire (SNAQ), was used to evaluate weight loss and nutritional status of patients. The questionnaire results have been published separately from the BIA findings of this pilot study. Research assistants or the acupuncturist administered the questionnaires and BIA measurements at every other acupuncture treatment for a total of five evaluations including baseline and at acupuncture treatments 2, 4, 6 and 8.

**Statistical analysis**

The BIA measurements for each time point were standardised to baseline measures and calculated as percentage change. Because of the small sample size, only descriptive analysis of data was performed by averaging the percentage change in BIA parameters, BMI and PA for all measurements per patient. Demographic data were analysed by descriptive data.

**RESULTS**

All seven patients entering the pilot study completed at least four BIA measurements including the baseline measure before and after at least one chemotherapy cycle. No patient withdrew from the study, which serves as an indication that the use of acupuncture in patients with gastrointestinal cancers is feasible. BMI, PA and fat mass all decreased over time (figure 2). All other measures—namely, total body water, extracellular fluid, intracellular fluid and fat-free mass—remained stable during the intervention period (table 1). Due to the small sample size and significant variability of the obtained data within and between patients, inferential statistics were not conducted.

The percentage change in BMI ranged from −4% to +4% compared with baseline across measurements with an average change of only −1% (absolute mean ±SD change in BMI −0.37±0.59), which is less than the defined 5% that established progression towards cancer cachexia.

The percentage change in PA from baseline ranged from −16% to +8% across measurements with an average reduction of −7% (absolute mean±SD change in PA −0.32±0.52). Of note, the SD of the average reduction was actually higher, again highlighting the significant variability between patients in this small pilot study.

The percentage change in fat mass ranged from −50% to +27% compared with baseline, with an average reduction of −6%. The relative wide variability is probably due to the small sample size and the various cancer and chemotherapy stages of the patients.

Changes in extracellular and intracellular fluid levels increased slightly over the course of the study indicating a proinflammatory response while at the same time maintaining cellular integrity. Although the sample size in this pilot study was small, these changes may indicate a trend revealing the inflammatory processes as well as maintenance of lean muscle mass (fat-free mass). The PA serves as an overall indicator of nutritional status and cell integrity. Although it decreased over the course of treatment in six of the seven patients, the relative small decrease compared with other studies may provide a marker for the effectiveness of acupuncture in this patient population.

**DISCUSSION**

The results of this pilot study indicate that acupuncture in patients with gastrointestinal cancer undergoing chemotherapy is well tolerated and feasible; indeed, no patients withdrew from the study during the intervention period. Although the small sample size of this pilot study does not allow for extrapolation or generalisation of results to patients with gastrointestinal cancer, BIA findings indicate that acupuncture may be able to reduce the progression and severity of cancer cachexia. Fat mass, BMI and PA all decreased over the course of the intervention; however, the average percentage reduction in PA in the seven subjects after the fifth measurement was only 7%, which is less than expected based on published data on patients with gastrointestinal cancers.21 Of note, the changes in PA are mostly based on healthy individuals and may differ in specific populations. It is therefore essential to follow patients and evaluate each patient and changes in PA individually. Loss of fat-free mass typically indicates that proteins are being used in the proinflammatory cascade instead of maintaining muscle mass, which is a hallmark of cancer cachexia.25 However, in this study, fat-free mass remained at relatively constant levels throughout the intervention period, indicating that the body was...
able to maintain normal metabolic activity. Similarly, although the BMI decreased over time, the observed 1% reduction in BMI and 1.3% decrease in absolute body weight is significantly less than the BMI and weight changes of patients with cancer cachexia in other studies.25 The loss of fat mass may indicate that

Figure 2  Percentage change in bioelectrical impedance analysis (BIA) measurements of (A) fat mass, (B) body mass index and (C) phase angle compared with baseline (measurement 1). Shown are individual percentage changes for each subject as well as the average and SDs at each measurement point.
the body is first reducing the fat resources, which is a natural reaction if a person is not able to consume their normal diet.²⁶ Finally, cancer and chemotherapy are often accompanied by an increase in immune system response and the eventual release of proinflammatory mediators; these help shift intracellular fluid to extracellular fluid due to the inflammatory process, which consists of increased histamine release, cell lysis and the development of oedema.²¹ In this study, both the extracellular and intracellular fluid remained stable over the course of the intervention. The total body water remained stable throughout the intervention period. This indicates that the release of proinflammatory mediators was suppressed and did not lead to the usual inflammation process with the resulting shift in fluid balance.

CONCLUSIONS

This study evaluated the feasibility of acupuncture and the utility of BIA measurements as an objective indicator of symptom management in patients with gastrointestinal cancers and cachexia undergoing chemotherapy. None of the patients enrolled in the study withdrew during the course of the intervention. The results of this study are limited due to small sample size and should not serve to extrapolate or predict the influence of acupuncture on cancer cachexia in patients with gastrointestinal cancer. With this limitation in mind, the results of BIA measurements indicated that acupuncture may be able to reduce or halt the progression of weight loss and preserve a normal metabolism as indicated by fat-free mass maintenance. Although the PA and BMI decreased slightly, the decrease was less pronounced compared with other studies that have evaluated patients with gastrointestinal cancers who were not treated with acupuncture.

Overall, this study is promising both for the use of BIA to evaluate the health status of patients and for the application of acupuncture as an adjunct treatment to reduce cancer cachexia. Based on these results, a larger study is currently being conducted which compares acupuncture use with sham acupuncture (ie, a placebo group) in patients with cancer cachexia being treated for gastrointestinal cancers.

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<th>Summary points</th>
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<tr>
<td>- Bioelectrical impedance analysis (BIA) can identify subtle changes in body water and fat, such as in patients with gastric carcinoma.</td>
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<td>- Acupuncture treatment may counteract the cachexia.</td>
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<td>- This pilot study showed that acupuncture is both acceptable and promising.</td>
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Contributors SLY, OG and JJW conceptualised the study. SLY and JJW conducted the study. OG, SLY and JJW analysed the data and contributed to the manuscript.

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Competing interests None.

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