

**Acupuncture is a feasible treatment for post-thoracotomy pain:
Results of a prospective pilot trial**

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Abstract

OBJECTIVE: Thoracotomy is associated with severe pain that may persist for years.

Acupuncture is a complementary therapy with a proven role in pain control. A randomized trial showed that acupuncture was effective in controlling pain after abdominal surgery, but the efficacy of this technique for the treatment of thoracotomy pain has not been established. We developed a novel technique for convenient application of acupuncture to patients undergoing thoracotomy, and in a prospective Phase II trial evaluated the safety of this intervention and the feasibility of doing a randomized trial.

METHODS: Adult patients scheduled for unilateral thoracotomy with preoperative epidural catheter placement received acupuncture immediately prior to surgery. Eighteen semi-permanent intradermal needles were inserted on either side of the spine, and four were inserted in the legs and auricles. All needles were kept in place for four weeks. Using a numerical rating scale, pain was measured on the first five postoperative days. After discharge, pain was assessed using the Brief Pain Inventory at 7, 30, 60 and 90 days.

RESULTS: Thirty-six patients were treated with acupuncture. Of these, 25, 23, and 22 patients provided data at 30, 60, and 90 days, respectively. The intervention was well tolerated by patients with only one minor and transient adverse event of skin ulceration.

CONCLUSIONS: The rate of data completion met our predefined criterion for determining a randomized trial to be feasible. This novel intervention is safe and acceptable to patients undergoing thoracotomy and does not interfere with standard preoperative care. We are now

testing the hypothesis that acupuncture significantly adds to standard perioperative pain management in a randomized trial.

Introduction

Thoracotomy is a common procedure employed for primary lung cancer, with almost 30,000 performed annually in the United States (Source: Agency for Healthcare Research and Quality). The procedure is extensive and can be associated with severe pain in patients already compromised by numerous other co-morbidities such as chronic obstructive pulmonary disease. Uncontrolled pain can have devastating consequences on post-operative recovery; consequently, extensive measures such as epidural catheters, local anesthetic infiltration and nonsteroidal-anti-inflammatory drugs (NSAIDs), are used to maximize analgesia and minimize side effects. [1,2]. Acupuncture represents a modality providing analgesia with a paucity of side effects; however, acupuncture needles can potentially overlap with the surgical field and also hamper epidural catheter placement, making acupuncture impractical. We undertook a single-arm, open-label, clinical trial to assess: 1) the feasibility of employing pre-operative acupuncture needles with thoracic surgery for post-operative analgesia, 2) the acceptance by patient's of a non-traditional technique in the treatment of a diagnosis as ominous as cancer, 3) the percentage of patients providing evaluable pain data at the first post-operative visit (approximately 30 days post surgery), and, 4) the occurrence of any adverse effects. Here we describe the results of this study undertaken to determine the feasibility of a randomized trial, to determine the optimal timing of outcome assessments, to provide data to aid trial design (e.g., sample size calculations) and to suggest modifications of our standard treatment strategy to facilitate execution. We specified that we would consider the trial "feasible:" if at least 75% of patients tolerated the intervention; if the intervention did not interfere with surgery and routine post-operative care; if at least 75% of

patients provided evaluable data at the first post-operative visit; and, if reported adverse events were acceptable. Furthermore, accrual needed to be sufficiently rapid so that, after appropriate sample size calculations, a randomized trial could be completed in less than two years.

Methods

The study was approved by the Institutional Review Board (IRB) at Memorial Sloan-Kettering Cancer Center in accordance with an assurance filed with and approved by the Department of Health and Human Services. Written informed consent was obtained from each participant.

Eligibility Criteria

We recruited adult patients at Memorial Sloan-Kettering Cancer Center who were scheduled to receive a unilateral, posterolateral thoracotomy with analgesia using an epidural catheter.

Patients excluded from the study were those scheduled to undergo "hemiclamshell" or "clamshell" thoracotomy, extrapleural pneumonectomy, or esophagectomy. Patients who had received acupuncture within the previous six weeks, or who had heart valve dysfunction (a contraindication to the use of intradermal acupuncture needles) were also excluded. Patients with a coagulopathy precluding insertion of an epidural catheter were also ineligible. All of the patients entered on this study were operated on by a single surgeon (VR), which allowed for uniformity of surgical technique and perioperative care.

Acupuncture Needle Insertion and Management

Epidural catheters were placed in all patients in a pre-operative holding area. An iodine antiseptic was used to sterilize both the field for epidural placement and acupuncture placement. Eighteen semi-permanent intradermal acupuncture needles were inserted approximately 2.5cm lateral to the lower border of spinous process of the T2 - 10 vertebrae immediately after placement of the epidural catheter (see Figure 1). Subsequently, both the epidural catheter and acupuncture needles were covered simultaneously by an occlusive "Tegaderm" dressing. In addition, one needle was placed in each leg at the "ST36" point and one in each auricle at the "Shenmen" point. We initially used "Japanese" style needles, as described by Kotani et al.[3], but found these time-consuming to apply and switched to stainless steel AcuMedic intradermal needles (AcuMedic Ltd., London, UK). These are thumbtack-shaped and consist of a 2mm x 0.28mm acupuncture needle attached to a metal ring embedded in surgical tape.

The epidural catheter and acupuncture needles were both removed after removal of the chest tube, typically 3 to 7 days post surgery. All needles were replaced after the epidural catheter was removed, typically 24 to 48 hours before discharge from the hospital. No restrictions were placed on patients' activity level or showering. Patients were asked to remove the leg and auricular needles a week after discharge. Needles on the back were removed by an acupuncturist at the first follow-up visit, usually 3 to 4 weeks postoperatively. Patients who remained in pain at this time were offered further acupuncture treatment consisting of stainless steel, 15mm x 0.16mm Seirin auricular needles placed bilaterally for 20-25 minutes at the Shenmen, brain and adrenal points in the ear. In addition, up to two needles were placed at auricular points corresponding to the sites where patients were experiencing most pain (e.g. chest, abdomen or

ribs). Following this treatment, acupressure metal balls were applied at the same points, and patients were taught to press each point for two minutes twice a day. They were also instructed to press on the points if they experienced exacerbation of pain. The metal balls typically remained in place in place for 4-7 days. These were used in preference to intradermal needles for this stage of treatment as they do not penetrate the skin and there is no risk of infection.

Acupuncture Quality Control

Immediately after each needle insertion, acupuncturists completed an audit sheet verifying the acupuncture points used. These records were routinely reviewed and acupuncturists were found to have followed the acupuncture point prescription. Study acupuncturists are certified by the National Certification Commission for Acupuncture and Oriental Medicine (NCCAOM) and are licensed to practice acupuncture in New York State. They have used acupuncture in clinical practice for 3 - 25 years. All were employees of the Integrative Medicine Service at Memorial Sloan-Kettering Cancer Center.

Primary outcome

We specified that we would consider the trial "feasible:" if at least 75% of patients tolerated the intervention; if the intervention did not interfere with surgery and routine post-operative care; if at least 75% of patients provided evaluable data at the first post-operative visit; and, if reported adverse events were acceptable. We also wanted insure that accrual was sufficiently rapid so that, after appropriate sample size calculations, a randomized trial could be completed in less than two years.

Pain Assessment

Pain in the immediate postoperative period was assessed by a 0–10 point numerical rating scale (NRS) marked "no pain" at one end and "worst pain" at the other. Patients were evaluated between 4:00 pm and 6:30 pm on the evening of their operation surgery, at least two hours after leaving the Operating Room. Those not leaving by 4.30 pm had their first pain evaluation on the following day. On the first postoperative day, patients were evaluated in the morning and late afternoon. The first pain evaluation assessed pain at rest, on movement and on coughing “since you woke up from your operation.” Subsequent evaluations (post-operative days 2, 3, 4 and 5) evaluated pain at rest, on movement and with coughing since the previous evaluation.

After discharge from the hospital, pain was assessed 1 week from removal of the epidural catheter (11–18 days after surgery) and then approximately 30, 60 and 90 days postoperatively. The 11–18 day follow-up was conducted by a research study assistant by telephone; all others were conducted when patients returned for routine post-discharge appointments. Pain was evaluated using a modified Brief Pain Inventory (BPI), a validated pain measurement tool that measures both the intensity of pain (sensory dimension) and interference of pain in the patient's life (reactive dimension)[4]. The number of needles remaining in place at the postoperative visit (day 30) was recorded.

Data Analysis

Data were analyzed using Stata 8.2 (Stata Corp., College Station, TX). We chose an actual sample of 25 patients. Our stopping rule was for the trial to cease once 25 patients had provided data at the 30 day follow-up.

Results

Patient Accrual and Adverse Events

Thirty nine patients were accrued between August 2002 and September 2003. Participant flow is shown in Figure 2. Accrual was limited for this pilot study because patients were accrued only from a single clinician (VR) for operation on a single day of the week. Patient acceptance was very good, with fewer than five patients refusing participation in the trial.

Twenty-five patients (64%) provided evaluable data at the first post-operative visit (approximately 30 days). Seven patients were withdrawn from the study by investigators for protocol reasons such as the epidural catheter was not used, or was removed early due to inadequate analgesia. None of these terminations would occur in a randomized trial due to the “intent-to-treat” principle. Of the patients who were not withdrawn, 25 of 32 provided evaluable data, a 78% data completion rate, which meets our predefined criterion for doing a subsequent randomized trial. Of the four patients who opted to withdraw, one patient expressed distrust of hospital staff, one reported no pain, one did not want to deal with needles after discharge and one withdrew without giving a reason.

Table 1 provides basic demographic information about study participants. Most patients (62%) were women in their 60s, undergoing lobectomy for primary lung cancer. There was a tendency for greater drop-out among men and patients undergoing procedures other than lobectomy.

None of the remaining patients requested or required removal of the acupuncture needles before discharge. Of the 25 patients with 30-day data, there were no data on needle retention for two: one patient received follow-up care at a different institution and one was discharged before reinsertion of needles. Of the 23 remaining patients, 12 (52%) either retained 16 or more needles out of 18; 4 patients (18%) retained fewer than half the needles and were thus defined as not tolerating the intervention.

Treatment was very well tolerated, with no patient complaining of discomfort from the needles or the Tegaderm. Seven adverse events were reported to the IRB of which six had clearly had no relationship to acupuncture. One patient was noted to have a 1 cm in diameter superficial skin ulcer at 30 day follow-up. This was under the Tegaderm but away from the acupuncture needles. The Tegaderm was removed, the ulcerated area cleaned and Bacitracin ointment applied. The ulceration healed within four days.

After changing from the “Japanese” style to the Acumedic needles (see Methods), application of needles in the pre-operative period was rapid, and did not interfere with routine care.

Results of Pain Assessment

Pain data for the immediate postoperative period are shown in table 3; table 4 shows data for post-discharge follow-ups. Although data from this single arm feasibility trial does not permit assessment of the efficacy of acupuncture in the management of post-thoracotomy pain, examination of the tables shows decreasing severity of pain over time. Twenty-two of 25 patients who provided data at day 30 also provided data at day 90, suggesting that obtaining evaluable data from patients over time is excellent. The apparently higher pain scores at day 90 compared to day 60 probably do not indicate increasing pain as it is well within typical statistical variation.

Comment

There are multiple possible sources of post thoracotomy pain, including the skin incision, muscle division, rib fracture or resection, costochondral dislocation, neuroma formation and, less commonly, infection or tumor recurrence. Uncontrolled acute pain in post-operative period may lead to chronic pain characterized as “the post-thoracotomy pain syndrome.” This is defined as an aching or burning pain that persists or recurs along a thoracotomy scar two months or more after surgery. Several studies estimate the prevalence of short-term post thoracotomy pain at 50% to 80% [5,6]. Approximately 5% of all patients undergoing thoracotomy suffer severe or incapacitating pain that interferes significantly with their daily activities. After an initial decline, there is little evidence demonstrating an appreciable diminishment of post thoracotomy pain over time. Although one study reported the prevalence of pain falling from 80% at 3 months post-surgery to 61% at 1 year[6] a longitudinal study examined patients 1 to 5 years post-surgery and found stable pain intensity over the course of follow-up, with approximately 50% patients reporting some level of pain[7].

Absolute control of pain following thoracotomy using traditional analgesics can be associated with many side-effects, some of which (like sedation) can have devastating consequences on patients with co-morbidities such as lung disease and heart disease.. Acupuncture is a well-known complementary treatment for pain[8] with few to no side effects, and data from recent meta-analyses suggest that it can relieve both acute and chronic pain[9]. In this study we employed it pre-operatively in a pre-emptive fashion because of ease of placement compared to post-operative placement.

Recent data suggest that acupuncture is effective in relieving pain following abdominal surgery[3]. In that study, 185 patients scheduled for surgery were randomized to receive true or placebo acupuncture. In the true acupuncture group, 5mm semi-permanent acupuncture needles were inserted preoperatively at 14 points in the back and fixed in place with surgical tape. Patients assigned to the control group had needles placed perpendicularly so that they did not penetrate the skin. Pain control was superior in the acupuncture group; the percentage of patients with moderate or severe pain at rest on the day immediately following surgery was 72% in the control group but only 47% in those receiving true acupuncture. Patients in the acupuncture group also received approximately 25% less morphine during the first four postoperative days than did placebo patients.

Although these data are promising, we were concerned that the severity and duration of pain reported after abdominal surgery was somewhat less than is typical after thoracotomy. We felt it would be necessary to provide acupuncture stimulation over a longer period of time than attempted by Kotani et al. and hypothesized that 30 days would be ideal. Therefore, we inserted

needles immediately preoperatively, changed them before discharge from the hospital and then did not remove them until the first follow-up visit approximately 3 to 4 weeks postoperatively. This entails needles being retained for three weeks or more.

In this study, we demonstrated that a novel acupuncture intervention was safe and acceptable to staff and patients. To our knowledge, this is the first reported clinical trial to evaluate acupuncture in the management of post-thoracotomy pain. The acupuncture procedure took only five minutes to complete and did not interfere with standard preoperative care, such as placement of the epidural catheter. Although fewer patients than intended provided follow-up data, the predicted rate of data completion for the randomized trial met our predefined criterion. We propose that the BPI pain intensity score be used as our primary endpoint as this had the lowest coefficient of variation. We also propose 30 day follow-up as the primary endpoint. Although we are also interested in chronic post-thoracotomy pain, this ideal has to be considered against the potential of increased patient drop-out over time. From these and others' data[10], pain at 30 days appears reasonably predictive of longer-term outcome.

Accrual was relatively slow because this pilot of a novel technique accrued patients only from a single clinician, a maximum of one day each week. A preliminary sample size calculation for the subsequent randomized trial showed 100 evaluable patients, or 140 randomized to account for a 25% drop-out rate. The Thoracic Service at MSKCC performs an average of 550 thoracotomies annually that would meet study eligibility criteria. We would need to accrue 13% of patients to meet our target sample within two years, or 9% to meet accrual targets within three years. The randomized trial has been approved by our Institutional Review Board and has been

initiated. The results of this randomized trial will determine whether acupuncture plus standard continuous epidermal or intravenous analgesia is superior to standard systemic analgesia alone.

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FIGURE LEGENDS

Figure 1. Intradermal acupuncture needles used in this study.

Figure 2. Participant flow through the trial.

Table 1: Baseline Patient Data

| | Completed day 30 data (n=25) | Did not provide day 30 data (n=14) | All |
|---------------------|---------------------------------|---------------------------------------|----------|
| Age | | | |
| less than 60 | 8 (32%) | 3 (21%) | 11 (28%) |
| 60-70 | 12 (48%) | 8 (57%) | 20 (51%) |
| greater than 70 | 5 (20%) | 3 (21%) | 8 (21%) |
| Female | 18 (72%) | 6 (43%) | 24 (62%) |
| Diagnosis | | | |
| Primary lung cancer | 23 (92%) | 13 (93%) | 36 (92%) |
| Lung metastases | 2 (8%) | 1 (7%) | 3 (8%) |
| Procedure | | | |
| Exploration only | 2 (8%) | 2 (14%) | 4 (10%) |
| Pneumonectomy | 0 (0%) | 2 (14%) | 2 (5%) |
| Lobectomy | 18 (72%) | 7 (50%) | 19 (64%) |
| Wedge resection | 5 (20%) | 3 (22%) | 8 (21%) |

Table 2: Pain scores in the immediate postoperative period. Results are given as mean (SD)

| Day | Pain at rest | Pain on movement | Pain on cough |
|-----|-------------------|-------------------|-------------------|
| 0 | n=8: 5 (2.39) | n=7: 5.86 (2.97) | n=4: 5.75 (4.35) |
| 1 | n=34: 2.5 (2.15) | n=34: 4.38 (2.74) | N=31: 5.08 (2.97) |
| 2 | n=32: 1.97 (1.86) | n=32: 3.66 (2.32) | N=22: 5.68 (2.25) |
| 3 | n=29: 2.32 (2.25) | n=29: 4.48 (2.44) | N=20: 5.55 (2.63) |
| 4 | n=15: 2.00 (2.00) | n=15: 3.20 (2.11) | n=8: 3.63 (3.07) |
| 5 | n=9: 1.78 (2.22) | n=9: 4.00 (2.45) | n=5: 5.20 (2.77) |

Table 3. Pain scores after discharge

| Day | Pain from operation | BPI total | BPI pain intensity | BPI pain interference | BPI relief |
|-----|---------------------|-------------------|--------------------|-----------------------|-------------------|
| 7 | 28 (97%) | n=29: 3.88 (1.91) | n=29: 3.6 (1.52) | n=28: 3.94 (2.42) | n=24: 7.25 (2.27) |
| 30 | 21 (84%) | n=25: 2.92 (1.79) | n=25: 2.62 (1.49) | n=25: 3.09 (2.25) | n=20: 7.4 (2.14) |
| 60 | 16 (70%) | n=23: 1.75 (1.96) | n=23: 1.72 (1.76) | n=23: 1.78 (2.21) | n=8: 7 (2.2) |
| 90 | 11 (50%) | n=22: 2.17 (2.36) | n=22: 2.13 (1.98) | n=22: 2.18 (2.79) | n=9: 7.22 (1.72) |



Figure 1

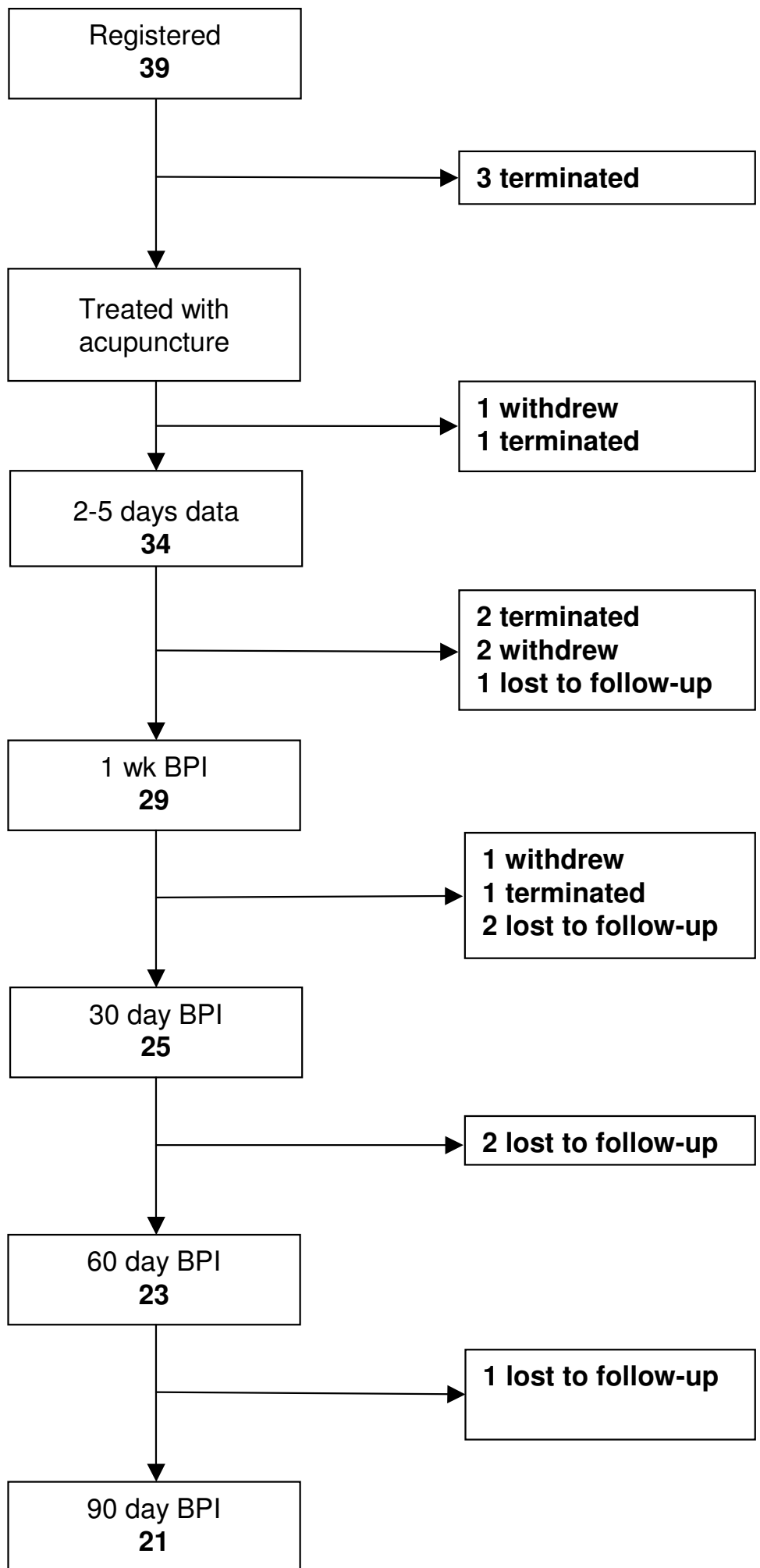


Figure 2