Published in final edited form as:

Ann Thorac Surg. 2009 September ; 88(3): 903–910. doi:10.1016/j.athoracsur.2009.04.139.

A Randomized Controlled Trial of Bupivacaine Through Intracostal Catheters for Pain Management After Thoracotomy

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Abstract

Background—Optimal management of pain after thoracotomy can be challenging. Continuous infusion of local anesthetic into the incision may help reduce the amount of narcotics required to control postoperative pain. To address this issue, we performed a randomized, double-blinded, controlled trial of infusion of bupivacaine versus placebo through intercostal and subcutaneous catheters after thoracotomy.

Methods—From April 2006 to June 2007, 124 patients had intercostal catheters placed at thoracotomy and connected to continuous infusion pain pumps. Each patient had catheters placed in the intercostal space near the head of the rib and subcutaneously beneath the incision; both were connected to an infusion pump through a Y connector. Patients were randomly assigned to receive placebo (normal saline solution) or 0.25% bupivacaine as a 4 cc per hour infusion for 100 hours after thoracotomy. All personnel caring for the patients were blinded to the content of the infusion. Demographic information, visual analog pain scores, and oral morphine equivalent usage was recorded for each patient. In addition to the infusion catheters, all patients had epidural analgesia that remained in place until postoperative day 3.

Results—There were 60 patients in the bupivacaine arm and 64 in the placebo group. Overall mean age was 64.7 years and 65 (52.4%) were men. Mean body mass index was 28.8 kg/m². There were no statistical differences in any demographic parameter except that there were more men in the placebo group. Pulmonary resection was performed in 100 patients, an antireflux procedure in 16, and other miscellaneous procedures in 8. There was no statistical difference in the morphine equivalent usage between the two groups. There was also no difference between the average daily pain scores between the two groups. Length of stay was not significantly different between groups: mean (SD) of 6.2 (3.4) and 6.7 (5.0) for placebo and bupivacaine, respectively ($p = 0.51$). There was no operative mortality, and complications occurred in 28% of patients (placebo group, 25%; bupivacaine group, 32%; $p = 0.41$).

Conclusions—This randomized, double-blinded, controlled trial demonstrated that the infusion of local anesthetic into the subcutaneous area and around the rib fracture site in addition to epidural analgesia did not reduce the amount of narcotic usage after a thoracotomy, nor did it affect visual analog pain scores. Pain control with intercostal catheters infusing local anesthetics did not produce a measurable pain relief beyond that provided by epidural analgesia.

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Presented at the Poster Session of the Forty-fifth Annual Meeting of The Society of Thoracic Surgeons, San Francisco, CA, Jan 26–28, 2009.

Management of pain after a thoracotomy can be challenging. Traditionally, pain relief has been accomplished with narcotic analgesics delivered through an epidural or intravenous route. It is unknown whether direct infusion of local anesthetic into the area of the incision is efficacious after a thoracotomy.

We performed a double-blinded, randomized, controlled trial to measure the efficacy of an intercostal catheter infusion with bupivacaine after a thoracotomy.

Material and Methods

Patients who underwent a standard posterolateral thoracotomy had a Stryker (Kalamazoo, MI) pain pump placed and were then randomly allocated to have an infusion of either 400 mL 0.25% bupivacaine or normal saline solution. All patients also had an epidural catheter placed before the thoracotomy for postoperative analgesia and removed on postoperative day 3. Epidurals were managed by a dedicated pain service. All patients were 18 years old or more, signed an informed consent agreement, and were able to take oral medications preoperatively and postoperatively. Patients were excluded if they were less than 18 years old or more than 80 years old, American Society of Anesthesiology class IV or higher, allergic to bupivacaine or other local anesthetics, currently using opioids, sedatives, or hypnotics, were pregnant, or were undergoing a redo thoracotomy or other major concomitant procedure at the time of thoracotomy. The Mayo Foundation Institutional Review Board approved this study.

At the time of thoracotomy closure, two Stryker Exfen 2.5-inch catheters were placed in the incision. One catheter was placed in the intercostal space near the head of the rib, and another was placed in the subcutaneous tissue beneath the skin incision (Fig 1). These were connected to a Stryker pain pump. The pump had been prefilled with either 400 mL normal saline solution or 400 mL 0.25% bupivacaine. The surgeon, patient, and all allied staff (resident, fellow, nursing, physician assistant, respiratory therapist, and so forth) caring for the patient did not know whether a patient was receiving saline (placebo) or bupivacaine. The patient's ribs were approximated with no. 1 Vicryl (Ethicon, Cincinnati, OH) peri-costal sutures. One to three chest tubes were placed at closure. The sizes of the chest tubes included 28F, 32F, and 38F. The chest tubes were removed when drainage was 300 mL or less in 24 hours and there was no air leak.

We prospectively collected age, sex, race, height, weight, and Eastern Cooperative Oncology Group (ECOG) performance score preoperatively. Intraoperative data recorded included surgeon, type of surgical procedure, duration of procedure, number of ribs cut or broken, width of maximum chest opening, and length of skin incision.

All patients received standard pain management which included an epidural catheter, intravenous patient-controlled analgesia or oral narcotics, or both, as necessary. A dedicated pain team managed the epidural analgesia according to a predetermined order set (see Appendix A). All narcotics used, including those used in the epidural, were recorded and converted into morphine equivalents (Table 1). Patients had visual analog pain scores recorded by the nursing staff in the postoperative period, usually every 2 hours for the first 3 days postoperatively and then every 4 hours, as per our Mayo Clinic thoracic surgery quality initiative protocol previously described [1]. If pain was not controlled by the initial epidural settings, the rate of infusion was increased in a stepwise fashion.

Pain pumps were begun when the incision was closed and run at 4 mL per hour (2 cc per hour in each limb of the catheter) until all 400 mL were administered (100 hours or approximately 4 postoperative days). Data were collected until discharge or postoperative day 10.

Statistics

Descriptive statistics are reported as either mean (SD) or number (%) as appropriate. Comparisons between treatment arms (placebo versus bupivacaine) for dichotomous variables were assessed using a χ^2 test, and continuous measures were assessed using a two-sample *t* test assuming unequal variances. The visual analog pain scores for each day were averaged, and total daily oral morphine equivalents use were recorded for each patient. The overall comparison of treatment arms for patient pain score, as well as the in-hospital narcotic usage, from the day of surgery (day 0) through postoperative day 10 were performed using a generalized linear model, accounting for correlated measurements within a patient across the days of hospitalization. The model also included the day of hospitalization to account for the varying lengths of hospital stay in patients. Because there was a difference between treatment arms for sex, in spite of a random assignment of patients to the study arms, we also ran the analyses including sex as an added covariate. The associations of treatment arm with narcotics use and pain remained unchanged; therefore, we have chosen to report results from the simpler models. Additionally, for each day of hospitalization, the patient pain score and the narcotic usage was compared between treatment arms using a two-sample *t* test assuming unequal variances. (The *p* values reported in Tables 4 and 5 are unadjusted for multiple comparisons.) The power of this study to detect a treatment difference can be estimated using the observed effect size (β) and standard error (*sep*). This study estimated the effect size for bupivacaine usage as approximately 11 units. Given the observed standard error of 17.9 units, this study had 80% power to detect a difference in narcotic usage between treatment arms of 50 units. The alpha-level was set at 0.05 for statistical significance. All analyses used SAS version 9 data sets (SAS Institute, Cary, NC) for analysis.

Results

From April 2006 to June 2007, 124 patients were enrolled and randomized. There were 60 patients in the bupivacaine arm and 64 in the placebo arm. Mean (SD) age was 64.7 (10.4) years, and 65 (52.4%) were men. The mean (SD) body mass index was 28.8 kg/m² (5.8 kg/m²), and 99% had an ECOG performance score of 0 or 1. There were significantly more males randomized to the placebo group (62.5%) than to the bupivacaine arm (41.7%; *p* = 0.02). There were no other significant differences in other demographic variables between the control and bupivacaine groups (Table 2). Pulmonary function testing was available in 98 patients (79.0%). There was no statistically significant difference between the two groups. Mean (SD) forced expiratory volume in 1 second (FEV₁) for the placebo group was 2.5 (0.9) and 2.2 (0.9) for the bupivacaine group (*p* = 0.19). Mean (SD) FEV_{1%} predicted for the placebo group was 82.0% (24.4) and 76.8% (21.1) for the bupivacaine group (*p* = 0.27).

Pulmonary resection was performed in 100 patients, including lobectomy in 65, wedge resection in 18, segmentectomy in 12, bilobectomy in 4, and pneumonectomy and sleeve resection in 1 each. A Belsey Mark IV fundoplication was performed in 16 patients, pleural biopsy in 1, and other miscellaneous procedures in 5. Mean (SD) maximum rib spreading width was 9.4 cm (1.9; range, 6 to 18 cm), and mean (SD) length of skin incision was 20 cm (5 cm; range, 9 to 34 cm). There was no difference in any of these variables between groups. A single rib was cut in 107 patients, two ribs in 3, none in 11, and not recorded in 3 patients. In the placebo group, one chest tube was placed in 17 patients, and two were placed in 47 patients. In the bupivacaine group, one chest tube was placed in 21 patients, two were placed in 37, and three were placed in 2 patients. Size 28F chest tubes were used in 71.9% of placebo patients and in 76.6% of controls. Size 32F chest tubes were used in 26.6% of placebo patients and in 23.3% of bupivacaine patients. Only 1 patient who had a 38F chest tube placed was in the placebo group. None of these differences was statistically significant (*p* = 0.76). All patients had epidural catheters for postoperative analgesia; 108 were placed before the induction of

anesthesia and 16 in the immediate postoperative period. The epidural catheters were in the thoracic area in 121 patients and in the lumbar area in 3. Medications infused through the epidural catheter included fentanyl, bupivacaine, hydromorphone, and morphine sulfate.

Mean (SD) hospital length of stay was 6.4 days (4.2; range, 2 to 36), and did not differ between the two groups ($p = 0.51$). There was no operative mortality, and complications occurred in 28.2% of patients (25.0% placebo and 31.7% bupivacaine, $p = 0.41$). Complications included atrial fibrillation in 17 patients, pneumonia in 7, air leaks lasting longer than 7 days in 6, atelectasis requiring bronchoscopy in 6, blood transfusion in 6, chest tube drainage more than 7 days in 5, respiratory failure requiring prolonged ventilation in 5, chylothorax in 2, acute renal failure in 1, and other complications in 7 (Table 3).

Overall, there was no significant difference in the amount of morphine equivalents used during the hospital stay between the two groups ($p = 0.53$; Table 4, *p*Fig 2). When comparing the total morphine equivalents used during the first 4 days postoperatively (the time when the pump was infusing local anesthetic), there was also no significant difference between the two groups ($p = 0.19$): mean (SD) of 466 (287) and 408 (229) for the placebo and bupivacaine groups, respectively. There also was no difference in the average daily pain score between the two groups ($p = 0.64$; Table 5, Fig 3). Including sex as a covariate in the analyses did not alter the nonsignificant difference for either narcotic use or the pain scores between the treatment arms.

Comment

There are many methods for pain control after thoracotomy, including epidural analgesia, intrapleural infusion of local analgesics, and intermittent or continuous intercostal nerve blocks. Epidural analgesia often results in relatively good pain control, but is associated with side effects including pruritis, nausea, constipation, mental status changes, urinary retention, and somnolence. Somnolence can reduce the tidal volume and cough reflex of patients, thus increasing the risk for atelectasis and pneumonia. Nonnarcotic analgesics can be used to reduce the narcotic requirements and decrease the risk of somnolence; however, use of these nonnarcotic analgesics is often limited by side effects.

Another potential analgesic adjunct is infusion of local anesthetic directly into the thoracotomy incision. That can be accomplished by placing thin catheters into the intercostal space as the thoracotomy incision is closed. These catheters are then perfused with a local anesthetic at low volume. Current technology employs a microprocessor-controlled pump to infuse 4 to 6 mL per hour over a 3- to 4-day period. Since a majority of the pain from a thoracotomy is thought to come from cutting and spreading the ribs, controlling the bone pain by direct inhibition of pain fiber transmission should significantly reduce pain medication requirement.

This double-blinded, controlled randomized trial compared epidural analgesia plus continuous intercostal nerve block with epidural analgesia alone. We were unable to demonstrate a significant reduction in the amount of morphine equivalents use with the addition of a continuous intercostal nerve block.

This is one of the few randomized, blinded controlled trials of intercostal catheters for pain control after thoracotomy. Debrecei and colleagues [2], from Hungary, randomly allocated 50 patients to receive bupivacaine through a T7-9 epidural or through an intercostal catheter. They found that patients in the intercostal catheter group had a higher visual analog pain score 4, 8, and 12 hours after surgery, and they required more narcotic for breakthrough pain. There was no demonstrable difference in the postoperative pulmonary function between the two groups. They concluded that epidural analgesia is better than intercostal catheter analgesia after a thoracotomy. Perttunen and coworkers [3] in 1995 randomly assigned patients to a single intrathoracic block, epidural analgesia, or continuous paravertebral infusion of bupivacaine.

They found no difference in pain, morphine consumption, respiratory function, or adverse events. A small difference was seen in a study that randomly assigned 100 patients to either thoracic epidural bupivacaine or thoracic paravertebral bupivacaine [4]. This study found minimally lower pain scores with paravertebral infusion, but the specific number was not reported. They did report lower use of morphine in the first and second 24-hour period for the paravertebral infusion group than the epidural group (105 ± 20 mg and 262 ± 67 mg versus 86 ± 30 mg and 211 ± 64 mg, respectively). However, the data collection was carried out in a non-blinded fashion by the nursing staff, the concentration of bupivacaine was 0.25% in the epidural group and 0.5% in the paravertebral group, and mortality was 4.4% in the epidural group and 10% in the paravertebral group. These factors present potential confounding biases in the study design, and therefore raise questions as to the validity of the conclusions.

The other randomized trials are small. Kaiser and coinvestigators [5] allocated only 13 patients in each arm to compare continuous extrapleural intercostal nerve blockade (T3 thru T6) to bupivacaine and fentanyl through a thoracic epidural catheter; and Chan and colleagues [6] allocated only 20 patients to receive intermittent injections of either bupivacaine or saline through an intercostal catheter. Owing to such small patient cohorts, it is difficult to rely on any conclusions reached in these studies.

In a recent review of intercostal nerve blocks for postthoracotomy analgesia, Detterbeck [7] stated: "Continuous intercostal nerve blockade after thoracotomy using an extrapleural catheter results quite consistently in better pain relief and preservation of pulmonary function than systemic narcotics, and appears to be at least as good as an epidural approach. The ease of the extrapleural approach and the low incidence of complications suggest this technique should be used more frequently." Although our technique was slightly different than the extrapleural approach, our findings in this relatively large randomized, double-blinded, controlled trial would not support this statement. We did not find a benefit of adding a continuous infusion of bupivacaine for patients who had an epidural catheter. Of note, in the Detterbeck [7] review, four of the nine quoted studies that compare narcotics with intercostal infusion are all from the same institution, and all show benefit. Of the other five quoted studies, only two show any benefit.

We recognize that our outcome could be falsely negative for a variety of reasons. We did not tunnel the catheter under the pleura above and below the opened interspace as others have done. We placed the catheter in the subcutaneous tissue under the incision and in the intercostal space right next to the cut end of the rib posteriorly. That may have prevented the bupivacaine from reaching the affected areas; however, the cut rib and the area under the skin incision must generate a significant amount of pain, which should be blocked by local anesthetic infusion into the area. In our design, the effects of the epidural analgesia may have overwhelmed the effects of the intercostal catheters. The study was designed to determine whether the addition of an intercostal infusion would help postoperative pain control, not to determine whether it was better than epidural analgesia. We did not think it ethical to withhold epidural analgesia and rely only on the intercostal catheter for pain relief.

We did use pericostal sutures for closure in all patients. We did not add any rib drilling or intercostal muscle detachment or other such methods. Whether addition of these techniques would change our results is not known. We did not have any complications attributable to the intercostal catheters. Others have reported complications, including an infected rib that required subsequent resection [2].

We did see a increase in the need for morphine after the intercostal catheter was removed in the group that received bupivacaine. It is unclear why this occurred, but it was not statistically

significant. It remains unknown whether there was sensitization from the bupivacaine or whether the bupivacaine irritated the nerve leading to an increased morphine requirement.

There was a maldistribution of men versus women in the two arms of the trial that occurred despite randomization. However, that should not have affected the outcome, as there was no difference in the morphine equivalent use in men versus women nor was there any difference in the pain scores between the sexes.

In conclusion, this randomized, double-blinded, controlled trial demonstrated that the infusion of local anesthetic into the subcutaneous tissue and near the transected rib in addition to epidural analgesia did not reduce the amount of narcotic usage after a thoracotomy, or affect visual analog pain scores. Pain control with intercostal catheters infusing local anesthetics did not produce a measurable pain relief beyond that provided by epidural analgesia.

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Fig 1.
The positions of the two catheters that infused either saline or bupivacaine are demonstrated.

Fig 2.
Average daily narcotic usage. (Bupivacaine = solid line; placebo dotted line.)

Fig 3.
Average daily pain score. (Bupivacaine = solid line; placebo dotted line.)

Table 1**Narcotic Conversion Chart for Bupivacaine Pump Study**

Drug (Listed in Same Order as in Access Database)	Conversion Factor
Fentanyl epidural (µg)	0.422
Fentanyl IV/SQ/IM/patch (µg)	0.1
Oxycodone PO (mg)	1.5
MSO4 IV/SQ/IM/patch (mg)	0.41
MSO4 PO (mg)	1
Hydromorphone epidural (µg)	0.06
Hydromorphone IV/SQ/IM/patch (mg)	10
Hydromorphone PO (mg)	10
Oxymorphone IV/SQ/IM/patch (mg)	0.166
Codeine PO (mg)	0.1
Nalbuphine (Nubaine) PO/IV (mg)	1
MSO4 epidural (mg)	3
Propoxyphene (Darvon) PO (mg)	0.3
Hydrocodone PO (mg)	1.5

To get oral morphine equivalent multiply the amount by the factor eg, fentanyl epidural 345 µg * 0.422 = 145.59 oral morphine equivalents.

IM = intramuscular; IV = intravenous; MSO4 = morphine sulfate; PO = oral; SQ = subcutaneous.

Table 2

Demographics

Variable	All Patients (n = 124)	Bupivacaine (n = 60)	Placebo (n = 64)	p Value
Age, years				
Median (min-max)	64.7 (10.4)	64.8 (9.8)	64.6 (11.1)	0.90 ^a
BMI, kg/m ²				
Median (min-max)	28.8 (5.8)	28.7 (6.2)	28.8 (5.4)	0.60 ^a
Sex				
Male, n (%)	65 (52.4%)	25 (41.7%)	40 (62.5%)	0.02 ^b
Race				
Caucasian, n (%)	121 (97.6%)	60 (100%)	61 (95.3%)	0.09 ^b
Hispanic, n (%)	2 (1.6%)	0	2 (3.1%)	
Native American, n (%)	1 (0.8%)	0	1 (1.6%)	
ECOG-Zubrod				
Zubrod = 0, n (%)	79 (63.7%)	40 (66.7%)	39 (60.9%)	0.51 ^b
Zubrod = 1, n (%)	44 (35.5%)	20 (33.3%)	24 (37.5%)	
Zubrod = 2, n (%)	1 (0.8%)	0	1 (1.6%)	

^aSignificance tested using a two-sample *t* test, assuming unequal variances.

^bSignificance tested using a χ^2 test.

BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; min-max = minimum-maximum.

Table 3**Complications**

Complication	All Patients (n = 124)	Placebo (n = 64)	Bupivacaine (n = 60)
Atrial fibrillation	17	10	7
Air leak longer than 7 days	6	4	2
Atelectasis requiring bronchoscopy	6	4	2
Prolonged ventilation	5	2	3
Chest tube drainage more than 7 days	5	1	4
Hemorrhage requiring transfusion	6	0	6 ^a
Pneumonia requiring antibiotics	7	3	4
Acute renal failure	1	0	1 ^b
Chylothorax	2	0	2 ^c
Recurrent laryngeal nerve injury	1	0	1
Ventricular fibrillation	1	0	1
Myocardial infarction	1	0	1
Wound infection	1	1	0
Sepsis	1	0	1
ARDS	1	0	1
Urinary tract infection	1	0	1
Psychosis	1	0	1
Fever of unknown origin	1	0	1

Note, a single patient may have had more than a single complication.

^aOne patient required reoperation.

^bOne patient required dialysis.

^cOne patient required reoperation.

ARDS = adult respiratory distress syndrome.

Table 4

Morphine Equivalent Usage

	Treatment						p Value ^a	
	Day	Placebo			Bupivacaine			
		n	Mean	SD	n	Mean		SD
	0	64	90.7	42.6	60	83.2	41.1	0.32
	1	64	145.4	102.9	60	115.9	62.7	0.06
	2	64	139.0	114.7	60	113.9	70.4	0.14
	3	63	92.3	65.5	60	94.6	95.8	0.88
	4	59	56.1	60.4	59	63.9	124.1	0.67
	5	37	58.2	69.3	37	85.4	186.9	0.41
	6	26	58.3	59.2	26	106.2	199.4	0.25
	7	22	35.6	41.4	18	125.9	222.2	0.11
	8	15	32.6	45.6	13	146.4	235.5	0.11
	9	9	46.7	51.0	11	120.3	188.3	0.24
	10	8	38.8	64.4	7	147.6	229.5	0.27
Total use 0 to 3		64	465.9	287.4	60	407.6	228.9	0.19

^aTreatment arm comparison made using two-sample *t* test assuming unequal variances. Overall comparison between treatment arms for morphine equivalent usage during hospitalization, *p* = 0.53.

Table 5

Pain Scores

Day	Treatment					
	Placebo			Bupivacaine		
	n	Mean	SD	n	Mean	SD
0	64	3.36	1.91	60	2.87	1.87
1	63	2.88	1.27	60	3.14	1.41
2	64	2.62	1.34	59	2.40	1.29
3	62	2.84	1.43	59	2.78	1.30
4	58	3.21	1.53	58	3.17	1.63
5	36	3.33	1.44	35	2.72	1.63
6	26	3.37	1.57	24	3.02	1.83
7	22	2.98	1.61	15	2.69	1.99
8	15	2.80	1.24	10	3.43	1.82
9	9	3.00	1.34	8	3.12	1.61
10	8	2.20	1.95	4	2.07	2.04
Average use 0 to 3	64	2.92	1.12	60	2.79	1.16
						0.52

^aTreatment arm comparison made using two-sample *t* test assuming unequal variances. Overall comparison between treatment arms for reported pain during hospitalization, $p = 0.64$.