

Philadelphia College of Osteopathic Medicine

DigitalCommons@PCOM

PCOM Physician Assistant Studies Student
Scholarship

Student Dissertations, Theses and Papers

1-1-2022

Is Cryoanalgesia an Effective Supplemental Method of Post-Thoracotomy Pain Management?

Jency Boyce

Philadelphia College of Osteopathic Medicine

Follow this and additional works at: https://digitalcommons.pcom.edu/pa_systematic_reviews



Part of the [Mental Disorders Commons](#), and the [Physical Therapy Commons](#)

Recommended Citation

Boyce, Jency, "Is Cryoanalgesia an Effective Supplemental Method of Post-Thoracotomy Pain Management?" (2022). *PCOM Physician Assistant Studies Student Scholarship*. 635.

https://digitalcommons.pcom.edu/pa_systematic_reviews/635

This Selective Evidence-Based Medicine Review is brought to you for free and open access by the Student Dissertations, Theses and Papers at DigitalCommons@PCOM. It has been accepted for inclusion in PCOM Physician Assistant Studies Student Scholarship by an authorized administrator of DigitalCommons@PCOM. For more information, please contact jaclynwe@pcom.edu.

Is Cryoanalgesia an Effective Supplemental Method of Post-Thoracotomy Pain Management?

Jency Boyce, PA-S

A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant Studies

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

November 25, 2021

Abstract

Objective: The objective of this EBM review is to determine if cryoanalgesia is an effective addition to pain management protocols for patients post-thoracotomy.

Study Design: This EBM review examines three randomized controlled trials.

Data Sources: Data was gathered from the three studies found on PubMed and EBSCOhost. Each study was published in a peer reviewed journal, in English between 2010 and 2021.

Outcome Measured: The outcome measured was pain reported by patients using a visual analog scale (VAS). Two studies utilized a 0-10 scale and the third a 0-100mm scale.

Results: In the study by Sepsas et al. it was found that the difference in pain scores between groups was 2.1 on day 1 and 1.1 on day 7, with scores being higher in the control group both days. Both comparisons had a p-value < 0.0001. In the study led by Momenzadeh et al., it was found that the control group had pain scores approximately 1.2 points higher on VAS on both days 1 and 7. P-value was <0.0001 for both data sets. The third study, by Mustola et al., was found to be insignificant with the difference between groups being 0.1 on day 1 and 3.6 on day 7. The scale used in this study was 0-100mm and the p-values for day 1 and 7 were 0.732 and 0.328 respectively.

Conclusions: This EBM reviewed showed that while some studies found significant improvement in pain, evidence is conflicting. As such further, more broad investigation is warranted.

Key Words: Cryoanalgesia, post-operative pain, thoracotomy

INTRODUCTION

A thoracotomy is a type of surgical incision utilized to access the internal wall of the thorax, as well as its contents for biopsies, resections, and explorations.¹ Thoracotomies are used for a variety of diseases and conditions affecting the many structures of the thoracic cage and mediastinal spaces such as the lungs, heart, esophagus, and great vessels.¹ Despite the crucial and lifesaving nature of these procedures, thoracotomies can cause severe pain in the post-operative period. Poorly controlled pain is not only distressing to the patient but can affect pulmonary function and delay ambulation which may lead to poor outcomes and delayed recovery.^{2,3}

In examining the importance of effective pain management for these patients, it is important to discuss the impact that this can have on the patients themselves, as well as the healthcare system. To begin, it is important to look at the large number of patients that this impacts; lung cancer is one of the top three most common types of cancer, and is the leading cause of cancer deaths in the United States.⁴ Surgical resection by means of thoracotomy is the most common treatment for many stages of lung cancer.⁴ In the United States 120,000 lung resections occur each year and despite new technology, an open thoracotomy remains the most commonly used approach.⁵ Meanwhile approximately 4,500 esophagectomies are performed annually in the United States, of which the majority are also done with open thoracotomies.⁵ This is especially important as incidence of esophageal adenocarcinoma is increasing, and surgery is the preferred treatment for this disease.⁵

Another impact is that of cost, a crucial topic in any discussion of treatment methods. Although it varies, medical bills for patients undergoing open thoracotomy can range from \$15,000-31,000.⁵ Longer hospital stays, more pain medications and complications can be

associated with higher costs, and thus reducing these with better pain management would be beneficial to both the patient and the healthcare system. Additional follow ups can also lead to increased cost for the patient, not to mention that they can indicate a slower return to normal life. One study found that 27% of patients who undergo thoracotomy will return to the hospital or emergency department within 6 months of discharge, 54% of whom have a chief complaint of post-operative pain.⁷ Another study found that 16.5% of thoracotomy patients returned to the ED or were re-admitted to the hospital within 30 days of surgery.⁸

A final impact to consider, which affects cost as well as patient quality of life, is opioid use, which can lead to addiction. With the number of opioid related deaths reaching 33,000 annually in the United States, and as much as \$78.5 billion being spent on opioid abuse and overdoses, decreasing the number of opioids prescribed has become an important topic in medicine.⁹ One large study found that thoracic surgery carries the highest risk of all types of surgery for long term opioid use.⁹ This further indicates the importance of pain control.

Typical management of post-thoracotomy pain aligns with general post-operative pain management protocols; this includes regional nerve blocks, epidurals and oral analgesics including NSAIDs, acetaminophen and opioids. Thoracotomy is considered one of, if not the, most painful surgical incisions.³ While traditional pain management protocols are in place, thoracotomy procedures are still associated with high post-operative pain and complications due to decreased pulmonary function, such as infections and atelectasis.³ As such, it is worth considering if there may be effective supplemental methods of pain management that may allow better pain control, such as cryoanalgesia. Cryoanalgesia is a method of applying ice crystals to nerves that causes disruption of the nerve impulses through local damage to the vasculature.⁶ The myelin sheath and endoneurium layer are spared however, which allows the block to be temporary.⁶ While temporary, it still has been known to last weeks and even months.⁶ This is an

advantage over current therapies such as nerve blocks and epidurals, as those either require continuous infusions or repeating the procedure to maintain analgesia for this long.¹⁰ This carries higher risk of inflammation, bacterial colonization and infection.¹⁰ Cryoanalgesia has been used and discussed for many years, but there is still much debate about its overall benefits. The hope is that the addition of this method to current pain management will allow more comfort for the patient, leading to a quicker return to normal breathing and fewer complications.

OBJECTIVE

The objective of this EBM review is to determine if cryoanalgesia is an efficacious method to reduce pain in patients undergoing thoracotomy, which may improve comfort, thereby decreasing complications and required pain medications.

METHODS

These studies were selected from PubMed and Medline, using the key words “cryoanalgesia”, “post-operative pain” and “thoracotomy”. The search parameters also included studies from AMED, Alt Health Watch and CINAHL databases. Each study selected was a randomized controlled clinical trial that was published in a peer-reviewed journal, in English. The articles were selected based on if they were randomized controlled trials that compared cryoanalgesia plus traditional pain management to traditional pain management alone. They also were only selected if they had taken place since 2010, they specifically examined thoracotomies and at least one of the measured outcomes was self-reported patient pain. Any studies that did not meet these criteria were excluded. Among the three articles selected, the population was adult patients undergoing thoracotomy. The intervention was intra-operative cryoanalgesia of intercostal nerves in addition to traditional pain management in comparison to patients who only received traditional pain management. The outcome of patients’ pain was measured by visual analogue scale (VAS). Each study reported p-values between the study and control groups.

MEASURED OUTCOMES

The outcome measured was post-operative pain, which was self-reported by the patient. In each study, the measure was collected by use of VAS, a commonly used tool to quantify pain. VAS is typically a 10-point scale (Momenzadeh & Sepsas) or a 100mm line (Mustola) and a patient indicates the severity of their discomfort along the line, with 0 being no pain and 10 (or 100mm) being severe pain.

Table 1. Demographics and Characteristics of Included Studies

| Study | Type | # Patients | Age (yrs) | Inclusion Criteria | Exclusion Criteria | W/D | Interventions |
|-------------------------------|------------------|------------|---|--|--|-----|--|
| Sepsas, 2013 ¹¹ | Double blind RCT | 50 | Adults under 75 years old (mean age approx 64) | Patients with lung cancer undergoing thoracotomy and lung resection | Patients with ASA \geq 4, over age 75, BMI \geq 35, history of another malignancy, sleep apnea and those who refused to consent | 0 | One, 60 second application of -40°C cryoanalgesia to intercostal nerves at the level of incision and one above and below. |
| Momenzadeh, 2011 ³ | Double blind RCT | 60 | Adults 19-51 years of age, (average 41.3 control, 41.9 trial group) | Adult patients requiring posterolateral thoracotomy, ASA Class I-III. | Patients with ASA \geq 4, history of opioid or illicit drug addiction and those with diabetes for 10+ years | 0 | One, 90 second application of -70°C cryoanalgesia to intercostal nerves at the level of incision, one above and below. |
| Mustola, 2011 ¹² | Single blind RCT | 42 | Adult patients, mean age of study group: 64, mean of control group:59 | Adult patients undergoing posterolateral thoracotomy in ASA groups I-III | ASA \geq 4, those requiring chronic opioids and those with moderate-severe pain (VAS \geq 2) at incision site prior to procedure | 2 | One, 60 second application of -70°C cryoanalgesia to intercostal nerves at the level of incision, one above and one below. |

RESULTS

In Sepsas, et al., researchers evaluated 50 adult patients in the post-operative period, as part of a randomized controlled trial. Half of the patients undergoing thoracotomy received a 60 second application of -40°C cryoanalgesia to 3 intercostal nerves, intraoperatively. The other half did not receive this, while both groups received morphine, paracetamol and tenoxicam intraoperatively and morphine post-operatively as needed.¹¹ Researchers recorded patient pain from self-reported VAS scores. This was done every 6 hours for the first day, ever 12 hours for 3 subsequent days, daily for 3 more days, then 2 weeks later, then monthly for 2 months.¹¹ This EBM review will focus on pain the first day at hour 6 and the 7th post-operative day. While the surgeon was not blinded to which patient received which treatment, the patients and those collecting pain scores were.¹¹ The mean pain score for the control group on day 1 was 3.00 ± 1.00 and on day 7 was 1.2 ± 0.6 , while the study group had a day 1 mean of $0.9 \pm .07$ and a day 7 mean of 0.01 ± 0.03 .¹¹ The difference between groups was 2.1 on day 1 and 1.1 on day 7, with a p-value < 0.0001 for both comparisons. These results can be seen in Table 2.

Table 2. Sepsas Study: Differences in Pain Between Groups

| | Control Group <i>Mean\pmSD</i> | Study Group <i>Mean\pmSD</i> | P-Value |
|------------------------------------|---|---|----------------|
| Mean Pain on Day 1 (Hour 6) | 3.00 ± 1.00 | $0.9 \pm .07$ | $P < 0.0001$ |
| Mean Pain on Day 7 | 1.2 ± 0.6 | $.01 \pm .03$ | $P < 0.0001$ |

Momenzadeh et al. looked at 60 adult patients during their post-operative period following a thoracotomy procedure. Thirty of the patients received a 90 second application of -70°C cryoanalgesia to three intercostal nerves, while the others did not.³ In addition to standard general anesthesia, both groups received pethidine as needed in the post-operative period.³ Nurses recorded the self-reported VAS scores every 2 hours on the first day, every 4 hours on the second day and every 12 hours on days three to seven.³ Again, this EBM review focuses on pain

scores on day 1 and 7. Surgeons were aware of the patients’ treatments but the patients themselves and the nurses recording the scores were not. In the study, the mean pain scores were presented in a line graph; the numerical values in Table 3 have been extrapolated from said figure for the sake of discussion. The approximate mean pain score for the control group on day 1 was 3.9 and on day 7 was 1.9.³ For the study group the mean pain score on day 1 was approximately 2.7 and on day 7 was approximately 0.7.³ The control group scores were 1.2 points higher on day 1 and day 7. P-value was < 0.001 for both sets of data points.

Table 3. Momenzadeh Study: Differences in Pain Between Groups

| | Control Group | Study Group | P-Value |
|---------------------------|----------------------|--------------------|----------------|
| Mean Pain on Day 1 | ≈ 3.9 | ≈ 2.7 | P <0.001 |
| Mean Pain on Day 7 | ≈ 1.9 | ≈ 0.7 | P <0.001 |

Mustola et al. conducted their study using 40 adult patients undergoing thoracotomy. Half of the patients received 60 seconds of -70°C on three intercostal nerves, while the remaining twenty of them did not.¹² Both groups received 3 days of an epidural infusion of ropivacaine, and patients were given oxycodone, tramadol, codeine, NSAIDs or acetaminophen as needed.¹² Pain scores were recorded every 6 hours for 1 day, then daily for 3 days, then again at 1 week, 4 weeks, 8 weeks and 6 months.¹² Patients were unaware of which treatment group they were in. On day 1, the control group’s mean pain score was 11.3 ± 13.1 (CI 95%, 5.4 to 17.3) and on day 7 it was 5.8 ± 9.9 (CI 95%, 1.5 to 10.1).¹² In the group that received cryoanalgesia, day 1 mean score was 11.2 ± 14.9 (CI 95%, 4.4 to 18.0) and day 7 was 9.4 ± 11.6(CI 95%, 4.3 to 14.5).¹² The p-value for day 1 was 0.732 and for day 7 was 0.328.¹² This data can be seen in Table 4.

Table 4. Mustola Study: Differences in Pain Between Groups

| | Control Group <i>Mean ± SD</i> | Study Group <i>Mean ± SD</i> | P-Value |
|------------------------------------|--|--|----------------|
| Mean Pain on Day 1 (Hour 6) | 11.3 ± 13.1 (CI 95%, 5.4 to 17.3) | 11.2 ± 14.9 (CI 95%, 4.4 to 18.0) | P = 0 .732 |
| Mean Pain on Day 7 | 5.8 ± 9.9 (CI 95%, 1.5 to 10.1) | 9.4 ± 11.6 (CI 95%, 4.3 to 14.5) | P = 0.328 |

DISCUSSION

As previously mentioned, thoracotomies, while crucial, are extremely painful surgical incisions and effective pain management can be difficult to achieve.³ If pain control is not adequately managed, patients can suffer not only discomfort but also further surgical complications, higher healthcare cost and are at risk for opioid addiction.^{2,3,9} Cryoanalgesia offers a potential supplemental pain management treatment.

In general, cryoanalgesia has become a useful tool in the management of some types of peripheral nerve pain, and has been determined to be safe, effective, and cost-effective in this area.¹³ The method has only had one report of serious complications being reported and no incidence of permanent nerve damage.¹³ The serious complication was myonecrosis and abscess formation.¹³ The less serious complications include bruising, infection, frostbite, and changes in pigmentation.¹³ There are also relatively few contraindications to the treatment, which also make it desirable. Contraindications include coagulopathies, bleeding disorders, active infections, cold urticaria, cryoglobulinemia and history of Raynaud's syndrome.¹³ Another complication that can occur in surrounding tissue or if the nerve is not properly treated is allodynia.¹³ In the study by Mustola et al. nine of the patients who received cryoanalgesia were experiencing this eight weeks post-operatively.¹² However, allodynia can also occur in patients as a surgical complication. For instance, in the same study, three patients in the control group also had allodynia and the difference between the two groups was not found statistically significant.¹² While useful in peripheral nerve pain, the studies in this EBM review discuss its potential for deep, surgical pain.

The Sepsas et al. study found statistically significant results that pain was decreased in patients who received cryoanalgesia during their procedure.¹¹ The pain scores were lower by approximately 2 points on the first day and 1 point on the seventh, which given the scale is

significant, especially from a patient perspective experiencing the pain. An important limitation of this study is that some patients underwent lobectomy and others a pneumonectomy, and therefore different amounts of tissue were disrupted among patients.¹¹ This could affect results of the study because amount of tissue could impact the baseline level of pain expected.

Momenzadeh et al. also found statistically significant results of pain being approximately 2 points lower on VAS on both day one and day seven for the cryoanalgesia group.³ This further supports the information found in the study by Sepsas et al. One limitation in this study is that the indications for thoracotomy were not discussed. It is possible that different indications could impact expected level of pain, based on if a procedure required tissue removal or was less disruptive such as an exploration or small biopsy. Additionally in this study, although the demographics were comparable among the groups, the trial group had more males. This skew in gender may have impacted pain perception and outcomes.³ In the other two studies, the gender distribution was more equal.

The study led by Mustola et al. yielded insignificant results.¹² Pain scores were relatively equal among both groups suggesting that cryoanalgesia did not have any impact. It is worth considering that in this study, epidurals were used for every patient for the first three days.¹² This varies from the first two where systemic medications were given as needed, rather than this localized form of anesthesia. It is possible that this was a significant source of pain control which had a greater impact than the cryoanalgesia. One limitation of this study is that the pain protocol used in addition to the epidural was a wide variety of pain medications from opioids to NSAIDs to acetaminophen.¹² This allows more variation in pain management and less of a controlled comparison. Although these medications were given based on their VAS score, variation in patients pain tolerance or perhaps judgement of a healthcare worker could impact which medication they received. Another limitation of this study is that it was not discussed if the

researchers collecting pain scores were blinded to the treatment patients had received, which could have led to significant bias. Lastly, it is of note that two participants were lost to follow up in this trial and thus their data was fully excluded from analysis due to concern for lack of data points.¹² The other two studies did not lose any participants.

Important limitations to consider in all the studies examined is that not every researcher was able to be fully blinded, for example the surgeons knew which patients they were performing cryoanalgesia on. One limitations of the patient populations include that most of the patients were older patients, so it is unclear if cryoanalgesia could be beneficial in younger ones. Lastly, it is important to consider that, while VAS is frequently used in medicine, the values may mean different things to different people, or certain patients may have varying thresholds to ask for pain medication.

One limitation of this EBM review as a whole is that it only evaluated three studies, and only pain on the first and seventh post-operative day. There may be other useful studies and outcomes that could be included to help give a more complete answer. Additionally, while this EBM was examining specifically the utility of cryoanalgesia in the more immediate post-operative period, long term pain is worth evaluating further. It also would be valuable to examine exact costs of the two groups, amount of pain medication and long-term outcomes such as post-operative quality of life and long-term addiction outcomes. As mentioned at the beginning, these are important patient-oriented outcomes that are hopefully improved with higher quality pain management.

CONCLUSION

This EBM review has determined that there is conflicting evidence for the effectiveness of cryoanalgesia in post-thoracotomy pain management. While Momenzadeh et al. and Sepsas et al. found the method to significantly improve patient pain, Mustola et al. did not determine any

significant difference.^{3,11,12} It is still notable that pain was improved for many patients and did not seem to be worsened for the patients that did not see benefit. Since cryoanalgesia has few contra-indications and is inexpensive, it is certainly worth further considering for some patients with whom cost and certain health conditions are of concern. In the future, it would also be beneficial to further research epidurals for pain control post-thoracotomy, as the insignificant results in the study by Mustola et al. could be due to the effectiveness of the epidural.

Additionally, thorough allocation concealment for all researchers should be achieved for optimal evaluation and comparison. It would also be prudent for future studies and reviews on cryoanalgesia to include a larger patient population, include younger patients, standardized specific pain medications to be used, and examination of more outcomes such as long-term quality of life, costs, long-term opioid use, pulmonary function, and other surgical complications. With this information, a more complete analysis could be done, providing great benefit for patients undergoing painful procedures.

References

1. Chang B, Tucker WD, Burns B. Thoracotomy. StatPearls. StatPearls Publishing. 2021. <https://www.ncbi.nlm.nih.gov/books/NBK557600/>. Accessed 10/11/2021.
2. Joshi MB, Girish BS, Bonnet F, et al. A systematic review of randomized trials evaluating regional techniques for postthoracotomy analgesia. *Anesth Analg*. 2008;107(3):1026-1040. doi:10.1213/01.ane.0000333274.63501.ff.
3. Momenzadeh S, Elyasi H, Valaie N, et al. Effect of cryoanalgesia on post-thoracotomy pain. *Acta Med Iran*. 2011;49(4):241-245. <https://acta.tums.ac.ir/index.php/acta/article/view/3731/3706>. Accessed 01/06/2021
4. Wang S, Dea T, Cornett P, et al. Cancer. In: Papadakis MA, McPhee SJ, Rabow MW, eds. *Current Medical Diagnosis & Treatment: 2021*. 60th Ed. McGraw-Hill; 2021: 1654-1720.
5. Cools-Lartigue J, Park BJ. Economic assessment in minimally invasive thoracic oncological surgery—USA experience. *Shanghai Chest* 2018; 2:89. doi: 10.21037/shc.2018.11.05
6. Trescot AM. Cryoanalgesia in interventional pain management. *Pain Physician*. 2003 Jul;6(3):345-60.
7. Hazewinkel MHJ, Berendsen RR, van Klink RCJ, et al. Incidence and risk factors of unplanned emergency department visits following thoracic surgery. *J Thorac Cardiovasc Surg*. 2021;8:668-676. doi: <https://doi.org/10.1016/j.xjon.2021.08.020>
8. Shaffer R, Backhus L, Finnegan MA, et al. Thirty-day unplanned postoperative inpatient and emergency department visits following thoracotomy. *J Surg Res*. 2018;230:117-124. doi:10.1016/j.jss.2018.04.065
9. Zhao S, Chen F, Feng A, et al. Risk factors and prevention strategies for postoperative opioid abuse. *Pain Res Manag*. 2019;2019: 1-12. doi: 10.1155/2019/7490801
10. Ilfeld B.M. Continuous peripheral nerve blocks: a review of the published evidence. *Anesth Analg*. 2011;113:904–925. doi: 10.1213/ANE.0b013e3182285e01
11. Sepsas E, Misthos P, Anagnostopulu M, et al. The role of intercostal cryoanalgesia in post-thoracotomy analgesia. *Interact Cardiovasc Thorac Surg*. 2013;16(6):814-818. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3653449/>. Accessed 01/06/2021. doi:10.1093/icvts/ivs516
12. Mustola ST, Lempinen J, Saimanen E, et al. Efficacy of thoracic epidural analgesia with or without intercostal nerve cryoanalgesia for post thoracotomy pain. *Ann Thorac Surg*. 2011;91(3):869-873. <https://www.annalsthoracicsurgery.org/action/showPdf?pii=S0003-4975%2810%2902612-3>. Accessed 01/06/2021. doi:10.1016/j.athoracsur.2010.11.014

13. Filippiadis D, Efthymiou E, Tsochatzis A, Kelekis A, Prologo JD. Percutaneous cryoanalgesia for pain palliation: Current status and future trends. *Diagn Interv Imaging*. 2021;102(5):273-278. doi:10.1016/j.diii.2020.11.007