Thoracostomy Tube Irrigation: A Multi-Center Trial Investigating its Efficacy in the Reduction of Secondary Intervention for the Management of Retained Hemothorax

Study Protocol

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Purpose:
Tube thoracostomy (TT) is the most common procedure performed to treat traumatic pneumothorax (PTx), hemothorax (HTx), and hemopneumothorax (HPTx).[1] While the majority of hemothoraces are successfully managed with TT placement, retained HTx may occur in up to 20% of patients, resulting in significant morbidity and mortality.[2-8] There is abundant research on the optimal management of retained collections,[9-17] however, few studies have focused on prevention of retained hemothorax. A pilot study using thoracic irrigation performed at the time of TT placement resulted in fewer secondary interventions for retained hemothorax.[22] This was expanded to a single institution prospective comparative study that yielded similar findings. Based on these promising results, it is necessary to validate the efficacy of thoracic cavity irrigation to prevent retained HTx requiring secondary intervention in a larger, multi-institutional patient population.

Background:
Most thoracic trauma resulting in the formation of pneumothorax (PTx), hemothorax (HTx), or hemopneumothorax (HPTx) is successfully managed with thoracostomy tube (TT) placement to evacuate blood and / or air from the pleural space.[1] Thoracostomy tubes have been a staple of hemothorax management for years, with successful management remaining stable at 80% for decades.[2-5] When TT fails, however, the resulting retained collection can lead to complications such as empyema and fibrothorax.[3,6-8]

A majority of thoracic trauma research has focused on the timing and treatment of these retained collections. Compared to traditional thoracotomy, Video Assisted Thoracoscopic Surgery (VATS) was revolutionary in decreasing morbidity associated with such complications.[8-17] However, early VATS does nothing to prevent the formation of retained collections. There is little published data on thoracic irrigation at the time of TT placement. A study published in 1991 looked at penetrating gastric injuries and demonstrated an increased rate of empyema amongst these patients, especially with associated diaphragm injury.[18] The study suggested that pleural lavage could possibly help decrease complications rates in combined gastric and diaphragm patients. Additionally, a pilot study published in 2012 examined 10 patients in whom suction catheter was utilized for hemothorax evacuation prior to thoracostomy tube placement.[19] This study found a 45% decrease in their secondary intervention rate (18.2% vs. 10%), increased percentage of total TT output in first 24 hours (72.7% vs. 46.2%, $p < 0.0059$), and shorter overall TT duration (4.2 days vs. 5.8 days, $p = 0.04$). However, when Savage and colleagues then evaluated 99 consecutive patients treated with suction evacuation prior to TT placement, they demonstrated a significant reduction in recurrent PTx, but no significant reduction in retained HTx or rate of secondary intervention.[20] These studies suggest that improving pleural fluid evacuation may be beneficial in preventing the complications of retained hemothorax and empyema. The first study lays the basis for pleural irrigation as a means of improving outcomes, while the second study has conflicting results in the literature.

Some of the faculty members in the Medical College of Wisconsin (MCW) Division of Trauma and Acute Care Surgery routinely perform TT irrigation, while others practice selective irrigation. There have been two trials conducted at this institution investigating TT irrigation. The pilot study, published in 2016, was a prospective

observational trial of 20 patients who underwent thoracic irrigation at the time of TT placement.[21] This study demonstrated a 75% reduction in our secondary intervention rate (from 20% to 5%). This was then expanded to a single institution prospective comparative study, which consisted of a non-irrigation control arm and a thoracic irrigation experimental arm. Again, secondary intervention rates were significantly lower within the irrigation group, 5.6% vs 21.8%. Given these promising results, it is essential to expand this study to multiple institutions to validate the data our institution has established.

Hypothesis

Thoracic cavity irrigation at the time of initial thoracostomy tube placement will decrease the secondary intervention rate for retained hemothorax.

Specific Aims:

1) Determine the efficacy of thoracic cavity irrigation to prevent secondary interventions for retained hemothorax.

Methods

Study Design

All trauma patients ages 18 years or older presenting within 24 hours of blunt or penetrating injury resulting in traumatic hemothorax or hemopneumothorax will be eligible for enrollment. Inclusion and exclusion criteria are listed below. This prospective comparative study will consist of a non-irrigation control arm and a thoracic irrigation experimental arm. Thoracic irrigation is performed at the time of the initial TT placement, and is done at the discretion of the attending Trauma surgeon. All patients enrolled will be entered in a prospectively maintained thoracic trauma database. The primary outcome is need for secondary intervention, defined as additional TT placement, VATS, tPA, or thoracotomy for the management of retained hemothorax. Secondary interventions will be screened according to indication. Only secondary interventions directed at management of retained collection will be considered in the analysis for our primary outcome. Secondary intervention aimed at persistent air leaks or post-pull pneumothorax will be considered separately in any analysis. Data abstraction will occur from FMLH medical records program (EPIC). We will also request data from our Froedtert Trauma Registry Program.

The Froedtert Hospital Trauma Program Trauma Registry will be accessed for the purpose of data collection. The following variables will be pulled: All possible variables from "DCF – Multi-Center TT Irrigation Data Sheet_AME21315 tracked changes".

Sample Size

This prospective comparative study will include participants from multiple Trauma Centers around the country. Nationally, approximately 10-30% of patients who undergo standard TT placement for the management of traumatic hemothorax require secondary intervention.[6] Both our pilot study & single institution prospective study demonstrated a 5% intervention rate for retained hemothorax among patients who underwent thoracic irrigation at the time of TT placement.[21] Collaboration with the biostatistics department at MCW suggests that a propensity matched analysis to a separate group of patients who did not undergo irrigation is the best study design.

To power the experimental cohort, a sample size calculation was performed utilizing a two-sample z-test with an alpha of 0.05 and 80% power. A power analysis utilizing 10% and 20% secondary intervention rates for the irrigation and standard cohorts, respectively, demonstrates that 108 patients are needed for analysis within the irrigation cohort. To appropriately perform a propensity score matched analysis, enrollment of patients into the standard thoracostomy tube cohort in a 3:1 fashion requires approximately 324 patients within the control cohort. A power analysis using 5% and 20% secondary intervention rates for the irrigation and standard cohorts, respectively, requires 52 patients within the irrigation cohort and 156 in the control cohort. A power analysis using 5% and 10% secondary intervention rates for the irrigation and standard cohorts, respectively, requires 239 patients in the irrigation cohort and 717 in the control cohort. A complete power analysis with variation in treatment proportions is attached.

We will start this study using 20% as the approximate national intervention rate, based on current literature, with the goal of detecting a 50% reduction in the experimental arm (i.e. 10% secondary intervention rate after thoracic irrigation). Therefore, we will plan to enroll 108 patients in the irrigation cohort and 324 patients in the control cohort. An interim analysis will be conducted once 50% patients have been enrolled in the irrigation cohort. The secondary intervention rate in the irrigation cohort and the standard cohort will be determined, and any adjustments to sample size will be made at that time.

Thoracostomy Tube Protocol

Indications for TT insertion have been well established.[22] At MCW, thoracostomy tube insertion will be performed according to Division of Trauma Policy (TPP.0027), using 28-36 French TT. Irrigation will be performed according to the attached protocol, at the discretion of the attending Trauma surgeon. The tube will then be managed in accordance with Division of Trauma Policy (TPP.0028), with secondary interventions performed as deemed necessary according to the Trauma faculty.

Each participating site will insert thoracostomy tubes according their divisional policies. Thoracic irrigation will be performed at the discretion of the attending Trauma surgeon, according to standard of care at each institution. Each site will follow the attached protocol for TT irrigation.

Procedure / Data Analysis:

This is an observational prospective data collection study. We will not alter our standard of care practice at MCW in any way during the study duration. Each participating site will also practice according to their standard of care. If a site chooses to implement a TT irrigation protocol, approval should be obtained from their local divisional & IRB committees. If a participating site already performs thoracic irrigation, efforts should be made to follow the TT irrigation protocol provided with this study.

Eligible trauma patients will be admitted with a hemothorax or hemopneumothorax and have a TT placed, with or without irrigation. At MCW, education will be provided monthly to the residents, APPs, and faculty on the Trauma service to notify study staff when eligible patients are admitted. We will also review the Trauma inpatient list for eligible patients. Each participating site will develop a method to screen for patients based on the resources available at their institution; this method should be included in the proposal submitted to their IRB. The attached data sheet includes all the variables that will be collected. The data at each site will be collected by a member of the study team and entered into the secure REDCap database specifically created for

this project. At MCW, our institution's data will also be entered into a secure password protected electronic excel spreadsheet, with all electronic data stored on the secure MCW Box platform.

Once REDCap data entry from each site has been completed, data analysis will take place at MCW in conjunction with MCW biostatisticians. All patients who underwent thoracic irrigation will be analyzed with an intent-to-treat model. Data will be analyzed using a logistic regression model for the categorical outcome (secondary intervention) and a linear regression model for the log-transformed numeric outcomes (TT duration, ventilator days, ICU LOS, hospital LOS, etc.). Propensity score methods will be used to isolate the effect of thoracic irrigation on a patient's outcomes, and adjust for potential selection bias in this comparative study. Propensity scores will be estimated using a logistic regression model with age, sex, mechanism of injury, abbreviated injury score - chest, and TT size as predictors. The predicted probabilities will then used to obtain the weights as the inverse probability of treatment. Corresponding estimates (odds ratio & mean differences) and p-values will be reported. Continuous variables will be reported as mean (standard error of the mean) if normally distributed and median (interquartile range) if not normally distributed. Categorical variables will be reported as counts and percentages.

Inclusion Criteria:

- Trauma patients admitted with initial indication for thoracostomy tube placement of hemothorax or hemopneumothorax
  (Once all participating sites have been established, a complete listing of hospitals will be provided)
- Patients must present to Froedtert Hospital (or participating site hospitals) within 24 hours of the traumatic event, either blunt or penetrating injury
- Follow up data available including radiologic studies performed within 24 hours of tube placement and hospital records to determine if any additional intervention(s) was performed
- 18 years of age or older

Exclusion Criteria:

- Less than 18 years of age
- Patients who had the thoracostomy tube removed (intentionally or unintentionally dislodged) prior to 24 hours TT duration
- Patients requiring operative exploration of the thoracic cavity within 6 hours following thoracostomy tube placement
- Patients with Thoracotomy or Video Assisted Thoracoscopic surgery as initial treatment for hemothorax and/or hemopneumothorax
- Patients with TT placed for isolated pneumothorax
- Patients who have a TT placed for hemothorax or hemopneumothorax more than 24 hours after presentation, or more than 24 hours after their trauma

Primary Outcome:

Our primary outcome is secondary intervention, defined as additional TT placement, Video Assisted Thoracoscopic Surgery (VATS), or thoracotomy for the management of retained hemothorax.

Ethics:

IRB approval will be obtained from the Medical College of Wisconsin Institutional Review Board. Ethical considerations are discussed below.

Risks to Subjects:

Potential loss of patient privacy / confidentiality is the risk of this study.

Protection Against Risk:

Only approved study staff will have access to the data in question and to patient PHI, which will be used to determine eligibility. All collected PHI will be kept in a locked filing cabinet in the locked office of study staff when not in use. MCW institution data will be entered into a secure password protected electronic excel spreadsheet, will all electronic data stored on the secure MCW Box platform. Each participating site will store their data according to their institutional security protocols. Deidentified data from all participating sites will eventually be entered into a REDCap database created for this project.

The MCW Box platform is a secure data storage system provided through the Medical College of Wisconsin. The MCW Box platform provides data encryption utilizing 256-bit SSL, SSAE 16 Type II, and maintains a safe-harbor certification for security. Box sync's encrypted authorization token technology keeps user data secure and work seamlessly with existing MCW desktop encryption systems.

MCW Box is licensed for storage of PHI data as it provides maximum security and allows users to assign different levels of security based on individuals' roles within a project. All files stored on MCW Box are stored within a secure server on the MCW campus and can be synced to MCW owned computers kept in locked offices within Froedtert Hospital.

Content from Box is available remotely through their encrypted website which requires two step verification and login each time the site is accessed. Users have access only to files in which they have been granted access, increasing the security of data storage.

Potential Benefits of the Proposed Research to Subject and Society:

There is no direct benefit to participants of the study. We do hope to benefit science and / or society with the results, as it relates to irrigation of a thoracostomy tube placed for hemothorax or hemopneumothorax decreasing the secondary intervention rate.

Importance of Knowledge to be Gained:

This study will describe current statistics, and may give some insight to optimal care; resulting in fewer complications, and improved morbidity / mortality in thoracic trauma patients.

Informed Consent Forms:

This is an observational prospective study that involves minimal risk to participants. The risks of this study include loss of confidentiality or privacy, and precautions are taken to minimize those risks.

This research involves review of the medical record and is considered minimal risk. We will not alter in any way the standard of care for those patients who are eligible. Eligible patients will be identified through faculty reporting or by review of the daily trauma patient list. Thus, patients will not be contacted specifically for the purposes of research. As such, we are requesting a waiver of informed consent from the IRB at MCW. There are no informed consent forms for this study. Each participating site will also conduct this study in accordance with their divisional standard of care. If a site chooses to implement a TT irrigation protocol, that will need to be reviewed by local divisional and IRB committees.

We are not recording data that would affect the rights, welfare, employability, or insurability of a person. The privacy and confidentiality of the participant will be protected in that we will only record the essential information needed for this study. Access to medical records that contain patients' personal information will be limited to research study personnel. This study is observational only and will record information that is normally collected as a part of the standard of clinical care.

It is not practical to conduct this research without waiver of consent, to avoid selection bias in patients who sustain hemothorax or hemopneumothorax. The act of obtaining consent could create significant bias; only those who are able and willing will provide consent, but those who die early or cannot provide consent following injury would be unavailable for study participation. These high-risk patients are critical to the study. Without waiver of consent, the study could be compromised due to the inability to collect data on all eligible patients. This could lead to misinterpretation of our practices and results.

References

1. Benns MV, Egger ME, Harbrecht BG, Franklin GA, Smith JW, Miller KR, Nash NA, Richardson JD. Does chest tube location matter? An analysis of chest tube position and the need for secondary interventions. J Trauma Acute Care Surg. 2015;78(2):386-90.
2. Helling TS, Gyles NR, 3rd, Eisenstein CL, Soracco CA. Complications following blunt and penetrating injuries in 216 victims of chest trauma requiring tube thoracostomy. J Trauma. 1989;29(10):1367-70.
3. Chou YP, Kuo LC, Soo KM, Tarng YW, Chiang HI, Huang FD, Lin HL. The role of repairing lung lacerations during video-assisted thoracoscopic surgery evacuations for retained haemothorax caused by blunt chest trauma. Eur J Cardiothorac Surg. 2014;46(1):107-11.
4. McManus K, McGuigan J. Minimally invasive therapy in thoracic injury. Injury. 1994;25(9):609-14.
5. Richardson JD, Carrillo E. Thoracic infection after trauma. Chest Surg Clin N Am. 1997;7(2):401-27.
6. DuBose J, Inaba K, Demetriades D, Scalea TM, O'Connor J, Menaker J, Morales C, Konstantinidis A, Shiflett A, Copwood B, et al. Management of post-traumatic retained hemothorax: a prospective, observational, multicenter AAST study. J Trauma Acute Care Surg. 2012;72(1):11-22; discussion -4; quiz 316.
7. Eddy AC, Luna GK, Copass M. Empyema thoracis in patients undergoing emergent closed tube thoracostomy for thoracic trauma. Am J Surg. 1989;157(5):494-7.
8. Etoch SW, Bar-Natan MF, Miller FB, Richardson JD. Tube thoracostomy. Factors related to complications. Arch Surg. 1995;130(5):521-5; discussion 5-6.
9. Morales Uribe CH, Villegas Lanau MI, Petro Sanchez RD. Best timing for thoracoscopic evacuation of retained post-traumatic hemothorax. Surg Endosc. 2008;22(1):91-5.
10. Meyer DM, Jessen ME, Wait MA, Estrera AS. Early evacuation of traumatic retained hemothoraces using thoracoscopy: a prospective, randomized trial. Ann Thorac Surg. 1997;64(5):1396-400; discussion 400-1.
11. Smith JW, Franklin GA, Harbrecht BG, Richardson JD. Early VATS for blunt chest trauma: a management technique underutilized by acute care surgeons. J Trauma. 2011;71(1):102-5; discussion 5-7.
12. Coselli JS, Mattox KL, Beall AC, Jr. Reevaluation of early evacuation of clotted hemothorax. Am J Surg. 1984;148(6):786-90.
13. Heniford BT, Carrillo EH, Spain DA, Sosa JL, Fulton RL, Richardson JD. The role of thoracoscopy in the management of retained thoracic collections after trauma. Ann Thorac Surg. 1997;63(4):940-3.
14. Lang-Lazdunski L, Mouroux J, Pons F, Grosdidier G, Martinod E, Elkaim D, Azorin J, Jancovici R. Role of videothoracoscopy in chest trauma. Ann Thorac Surg. 1997;63(2):327-33.
15. Landreneau RJ, Keenan RJ, Hazelrigg SR, Mack MJ, Naunheim KS. Thoracoscopy for empyema and hemothorax. Chest. 1996;109(1):18-24.
16. Liu DW, Liu HP, Lin PJ, Chang CH. Video-assisted thoracic surgery in treatment of chest trauma. J Trauma. 1997;42(4):670-4.
17. Mackenzie JW. Video-assisted thoracoscopy. Treatment for empyema and hemothorax. Chest. 1996;109(1):2-3.
18. Durham RM, Olson S, Weigelt JA. Penetrating injuries to the stomach. Surg Gynecol Obstet. 1991;172:298e302.
19. Ramanathan R, Wolfe LG, Duane TM. Initial suction evacuation of traumatic hemothoraces: a novel approach to decreasing chest tube duration and complications. Am Surg. 2012;78(8):883-7.
20. Savage SA, Cibulas GA, 2nd, Ward TA, Davis CA, Croce MA, Zarzaur BL. Suction evacuation of hemothorax: A prospective study. J Trauma Acute Care Surg. 2016;81(1):58-62.
21. Kugler NW, Carver TW, Paul JS. Thoracic irrigation prevents retained hemothorax: a pilot study. J Surg Res. 2016;202(2):443-8.
22. Dev , S. P., Nascimiento , B. J., Simone , C., & Chien , V. (2007). Chest-Tube Insertion. New England Journal of Medicine, 357(15), e15.