Title:
Prospective comparison of a short versus long chest tube water seal trial for traumatic pneumothorax ("CT Pro Study")

Primary Investigator:
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Background
Chest tube placement is a common intervention in trauma patients, yet there is little scientific evidence to guide management after placement. As a result practices vary considerably, as demonstrated by a survey of 734 members of the Eastern Association for the Surgery of Trauma (1). The optimal duration of a water seal trial prior to tube removal is unknown. Use of water seal trials is thought to be beneficial, (2) and retrospective data suggests that shorter trials are safe and as effective as longer trials (3). EAST members varied in their preference for water seal duration in patients with pneumothorax, using 4 hours (20%), 6 hours (21.3%), 12 hours (12.8%), and 24 hours (43%).

Primary aim
To compare a shorter versus a longer water seal trial regimen prior to chest tube removal in patients with a chest tube placed for traumatic pneumothorax.

Secondary aim
To inform the practices of trauma providers for water seal duration.

Inclusion criteria
Trauma patients
Traumatic pneumothorax with chest tube placed (concomitant hemothorax or pleural effusion acceptable)
Age 18 years or older
Blunt or penetrating mechanism
All sizes of chest tube, including "pigtail" catheters
Chest tubes placed at the bedside or in a radiology suite
Either spontaneous or positive pressure ventilation
Presence of a single chest tube in one or both pleural cavities (single unilateral or bilateral tubes)
Use of water seal trial of at least 1 hour prior to chest tube removal
First episode of water seal trial

Exclusion criteria
Those not meeting inclusion criteria
Iatrogenic or procedure-related pneumothorax, such as from central line placement
Patients with chest tubes placed as part of, or present during, a thoracic operation
Patients with prior history of surgery involving the pleural cavity ipsilateral to the study chest tube
Patients with severe acute respiratory distress syndrome (ARDS)
Patients with bronchopleural fistula or other condition causing continuous air leak for over 24 hours
Patients with bronchial injury
Patients with empyema
Patients with chylothorax
Patients with bullous emphysema

Patients with more than one chest tube on the same side at any time prior to the study chest tube removal
Patients who have had a previous chest tube after the same traumatic injury episode, on the same side as the tube in the study
Chest tubes that were withdrawn or removed unintentionally
Chest tubes that were physically clamped or occluded as part of the removal process (i.e. a "clamping trial")
Water seal trials other than the first trial for any one chest tube

Therapeutic interventions
None. Patients will have chest tubes placed as part of routine practice at the discretion of their own medical team. A standard chest radiograph (CXR) will be required before and after chest tube removal.

Study methodology
- Trauma centers will be enrolled that already use a water seal trial prior to chest tube removal with duration of either 6 hours (Short) or 24 hours (Long), +/- 2 hours. That is, the Short group may include durations from a minimum of 4 to a maximum of 8 hours, and the Long group from minimum 22 to maximum 26 hours. Patients with trial durations outside of these parameters will still be included for an intent-to-treat analysis.
****Centers must enroll as a Short trial center or Long trial center, as defined above.**

- Centers will be included if they use one of the two water seal regimens as part of their current chest tube management.
- Patients must have some degree of traumatic pneumothorax prior to chest tube placement, but may also have concomitant hemothorax or pleural effusion.
- Chest tubes must be placed directly to suction after insertion, with a minimum of 24 hours continuous suction prior to water seal
- Chest tubes must remain on suction from insertion until the water seal trial is initiated (with the exception of short periods of patient in-hospital transportation or ambulation). There is no upper time limit for the duration of suction.
- Only the first water seal trial for each chest tube will be included in the study
- Patients with bilateral chest tubes may have water seal trials for each tube either simultaneously or sequentially, at the study center's discretion.
- Chest tubes must be removed at the end of the water seal trial if study criteria are met* to be eligible for inclusion, or placed back to suction for clinical indications. However, clinician judgment regarding management will supersede study requirements at all times.
- Patients must have a CXR at the end of the water seal trial prior to chest tube removal, and between 4 and 8 hours after chest tube removal

* Criteria for study chest tube removal:
1. Minimum 24 hours continuous suction prior to water seal trial
2. Air leak absent or resolved
3. Pneumothorax resolved or judged to be small and/or of minimal significance
4. Pneumothorax has not enlarged significantly (at study center's discretion) while on water seal
5. Chest tube fluid output of < 200 ml in the 24 hours prior to the water seal trial
6. Study center agrees with removal based on their usual standards of practice

Primary outcomes
Incidence of recurrent or worsening pneumothorax after chest tube removal
Incidence of water seal trial failure (i.e. tube not removed or put back to suction)

Secondary outcomes
Incidence of additional intervention for ipsilateral pneumothorax after chest tube removal (i.e. another chest tube, drain, or surgical intervention)
Duration of chest tube presence
Number of CXRs performed after chest tube removal during the hospital stay
Hospital length of stay

Variables to be collected
***If patient has 2 eligible chest tubes (i.e. 1 on each side), data should be completed on two separate forms**

PATIENT DATA:
1. Age in years
2. Sex
    - male, female, other
3. Mechanism of injury
    - blunt
    - penetrating
4. Injury Severity Score (ISS)
5. Abbreviated Injury Scale (AIS) head
6. Abbreviated Injury Scale (AIS chest
7. Abbreviated Injury Scale (AIS abdomen
8. Number of rib fractures on the side of the chest tube
9. Breathing during water seal trial
    - spontaneous
    - positive pressure
    - both
10. Hospital length of stay (# calendar days)
11. In-hospital mortality
    - alive
    - dead

CHEST TUBE DATA:
12. Location of chest tube placement
    - Emergency Department
    - Operating room
    - ICU
    - Patient care ward (non-ICU)
    - Radiology suite
13. Duration of chest tube (# calendar days)
14. Side of chest tube

- left
- right

15. Breathing at time of tube removal
    - spontaneous
    - positive pressure
16. Indication for placement
    - pneumothorax
    - pneumothorax with hemothorax/effusion
17. Size of chest tube in French units
18. Method of tube placement
    - over a wire/percutaneous (e.g. pigtail)
    - direct pleural entry/open
19. Duration of suction prior to water seal trial (# calendar days)
20. Actual duration of water seal trial (# hours)
21. Water seal trial outcome
    - chest tube removed
    - chest tube placed back to suction
    - chest tube continued on water seal, removal criteria NOT met (free text reason)
    - chest tube continued on water seal, removal criteria MET (free text reason)

RADIOLOGY DATA:

22. Size of pneumothorax* at end of water seal trial prior to chest tube removal
    (*see data dictionary for measurement instructions)
23. Size of pneumothorax* after chest tube removal
    (*see data dictionary for measurement instructions)
24. Number of CXRs taken after chest tube removal during hospital stay

COMPLICATIONS:

25. Chest tube or pleural drain reinsertion (ipsilateral to study chest tube)
    - during index hospital stay, Yes/No
    - within 30 days of discharge, Yes/No
26. Thoracic surgical intervention (ipsilateral to study chest tube) after chest tube removal (VATS or thoracotomy)
    - during index hospital stay, Yes/No
    - within 30 days of discharge, Yes/No
27. Readmission within 30 days for recurrent pneumothorax (ipsilateral to study chest tube)
    - Yes/No

Data collection and statistical analysis plan

The study was designed to demonstrate the non-inferiority of 6-hour water seal trial compared with 24-hour water seal trial prior to chest tube removal in terms of 1) incidence of water seal trial failure and 2) recurrent or worsening pneumothorax after chest tube removal. Data will be analyzed on an intent-to-treat basis and a per-protocol basis. Patient demographic and clinical factors will be summarized and compared between the two cohorts using appropriate descriptive statistics and hypothesis testing procedures. Primary and secondary outcomes will be compared between the two

cohorts using Pearson's chi-square test (or Fisher's exact test in case of small numbers) and Wilcoxon rank sum test (or Student t-test if normality assumption is satisfied). Univariable logistic regressions will be used first to examine how each individual demographic and clinical factor is related to the primary outcomes. Then a multivariable model will be estimated including all confounding factors. Depending on the results, a variable selection may be applied to select a subset of factors to fit a reduced model. We may also explore to include random effects in the regression models to account for the intra-correlation among patients from the same trauma center due to other latent or uncontrollable factors. Unadjusted and adjusted odds ratios (ORs) along with 95% confidence intervals (CIs) will be reported. Statistical significance will be assessed at 0.05 level.

Power analysis was conducted for the main primary outcome, the incidence of recurrent or worsening pneumothorax after chest tube removal (Table 1). The final required sample size estimates were calculated using a range of incidences for this outcome, due to the variability found in the literature from 6% to 25% (3 – 6). An additional 5% of patients will be required to account for loss of follow-up or missing data. Using the middle range estimated incidence of 15% for this outcome, with a 5% non-inferiority margin plus 5% attrition rate, we estimate that 1, 325 patients will be needed to achieve power. If the incidence of this outcome in our study is actually lower than estimated based on interim analysis and is closer to 10%, then 937 total patients will be needed.

Table 1 – Required sample sizes per group to conclude non-inferiority between the two groups in terms of recurrence of pneumothorax, assuming incidence rates = 10%, 15%, or 20% with a non-inferiority margin = 3%, 5% or 7% (before accounting for 5% attrition)

	10%	15%	20%
3%	1237	1752	2199
5%	446	631	792
7%	228	322	404

Consent procedures

IRB approval with waiver of informed consent is anticipated, since participating centers will provide patient care according to their current and usual practice

Risk/Benefit analysis

No more than minimal risk is expected as a result of study participation, since participating centers will provide patient care to study patients according to their current and usual practice.
Potential benefits are that if non-inferiority is demonstrated, using the shorter water seal trial may decrease length of stay, improve efficiency of care, and potentially decrease costs.

References

1. Parker MP, Newcomb AB, Liu C, Michetti CP. Chest Tube Management Practices by Trauma Surgeons. *J Surg Res*. 2019 Dec;(244):225-230.
2. Martino K, Merrit S, Boyakye K, et al. Prospective randomized trial of thoracostomy removal algorithms. *J Trauma.* 1999;46(3):369-371.
3. Bridges LC, Torrent DJ, Mosquera C, Bard MR. Chest Tube Removal in Simple Pneumothorax: Does Water-Seal Duration Matter? *Am Surg.* 2017;83(8):901-905.

4. Tawil I, Gonda JM, King RD, Marinaro JL, Crandall CS. Impact of positive pressure ventilation on thoacostomy tube removal. *J Trauma.* 2010;68(4):818-821.
5. Bell RL, Ovadia P, Abdullah F, Spector S, Rabinovici R. Chest tube removal: end-inspiration or end-expiration? *J. Trauma.* 2001;50:674-677.
6. Thitivaraporn P, Samoon P, Prichayudh S, Pak-Art R, Sriussadaporn S, Kritayakirana K. A randomized controlled trial in removing tube thoracostomy using party balloon valsalva. J Am Coll Surg. 2015;221(4);Suppl 2:e139.