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Study protocol for DICE trial: Video-assisted thoracoscopic surgery decortication versus interventional radiology guided chest tube insertion for the management of empyema

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ABSTRACT

Background: Empyema is a common thoracic surgery presentation, defined as pus in the pleural space. Despite the commonality of empyema, consensus on initial management remains ambiguous. Two standard of care treatment options include inserting a chest tube (thoracostomy) and the administration of intrapleural fibrinolytics, or an initial surgical approach, surgical decortication. Due to the complexity of this pleural space infection, often repeat interventions are required after initial management in order to achieve source control and resolution of clinical symptoms. This study aims to identify the most effective initial management option for empyema.

Study design: We present a study protocol for a randomized control trial (RCT) comparing adult individuals with empyema to one of two standard of care initial management options. Participants will be randomized into either interventional radiology guided chest tube insertion with intrapleural fibrinolytics (Dornase 5 mg and Alteplase 10 mg intrapleural twice daily for three days) or video-assisted thoracoscopic surgery (VATS) decortication.

Methods: All adults with empyema meeting inclusion criteria will be invited to participate. They will be randomized into one of two intervention groups; interventional radiology guided chest tube insertion with fibrinolytics or initial VATS decortication. Each intervention will take place within 48 hours of randomization. The primary outcome will be the rate of re-intervention within 30 days. Re-intervention is defined as repeat chest tube insertion, VATS decortication, or decortication via thoracotomy. Secondary outcomes include a change in the size of empyema, length of stay, morbidity, as well as 30-day and 90-day mortality, as well as quality of life measurements.

Anticipated impact: This study is aimed at identifying the most effective initial management option for individuals with empyema.

1. Background

Empyema is a common thoracic surgery presentation with approximately 6.7 cases per 100,000 population occurring annually in Ontario, Canada [1]. Traditional treatment methods first included chest tube insertion or thoracostomy to penetrate its thick fibrous peel and obtain source control. The addition of intrapleural fibrinolytics has been incorporated into empyema management based on the multi-centre intra-pleural sepsis trial (MIST 2). This was a randomized control trial (RCT) examining four separate treatment arms; double placebo, placebo combined with intrapleural DNAse (5 mg), intrapleural t-PA (10 mg) with placebo, and intrapleural t-PA (10 mg) combined with DNase (5

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mg) for six doses over three days [2]. This study demonstrated a statistically significant difference in the reduction of pleural empyema in the t-PA and DNase combined arm ($P = 0.005$) when compared with all the other arms [2]. This RCT has established the combination of t-PA and DNase as the gold standard therapy for fibrinolytics in those presenting with empyema.

MIST 2 trial was revolutionary in standardizing fibrinolytic agents, their dosing and length of treatment to improve empyema resolution compared to thoracostomy alone. There are limitations, however, in extrapolating information from this trial and applying it to clinical use. For example, the method of chest tube insertion was not clarified (e.g. percutaneous, bedside, under image guidance), nor whether the insertion was standardized across all investigators [2]. Literature overwhelmingly suggests that image guided thoracostomy with ultrasound decreases the complication rate (pneumothorax, infection, procedure failure, intercostal bleeding), compared with a blind chest tube insertion [3–5]. Therefore, if such benefits genuinely exist, it would be advantageous to consider it the standard of care to have Interventional Radiologists, experts in image-guided procedures, perform thoracostomy for empyema to improve patient outcomes.

Surgical decortication is another commonly accepted standard of practice. This includes the removal of the thick fibrous peel of an empyema, suctioning of pus, wash out of the pleural space, and drain (chest tube) placement. Typically, this can be accomplished with a minimally invasive approach using small incisions through the rib spaces, called Video-Assisted Thoracoscopic Surgery (VATS). A review of the literature reveals few randomized controlled trials (RCTs) that compare thoracostomy combined with MIST 2 trial fibrinolytics to VATS decortication. A search of databases in OVID MedLine, PubMed, and Cochrane Systematic Reviews revealed only one adult RCT that compared VATS decortication to thoracostomy with fibrinolytics. Wait et al., in 1997 used a small study population of twenty patients in each arm, randomizing participants to either bedside thoracostomy with streptokinase or VATS decortication [6]. This study demonstrated that in adults with a fibrinopurulent effusion, VATS decortication was associated with an increased rate of empyema resolution and a shorter length of stay [6]. The trial does not use the updated MIST 2 trial recommendations to add Dornase to the fibrinolytic regime. With advances in radiological imaging, ultrasound and fluoroscopic guidance to aid chest tube insertion would have been beneficial. This study suggested a benefit via a surgical approach, but the practical limitations in the study's non-surgical arm suggest that further investigations are required.

2. Rationale and background of study aims

As we examine the treatment options for empyema, emerging evidence may suggest VATS decortication is superior to non-operative alternatives. A Cochrane Systematic Review of eight trials (6 pediatric and 2 adult) examining treatment methods for empyema provided evidence suggesting there were similar complication rates between VATS decortication and chest tube drainage (although this does not specify with or without fibrinolytics). At the same time, those receiving VATS had a decreased length of hospital stay [7]. In addition, a recent study from the United States using the New York State Inpatient Database examined 4095 patients with a diagnosis of empyema. It evaluated their treatment with respect to chest tube insertion, VATS decortication, or decortication via thoracotomy [8]. Patients who received a chest tube compared with those who underwent a surgical approach had higher mortality during their initial hospital stay (chest tube:15.4%, VATS:4.7%, open: 6.0%, $p < 0.001$) [8]. Patients' readmission rate within thirty days was also significantly higher for the chest tube group (6.1%) compared with the surgical group (VATS 1.9% and open: 2.1%, $p < 0.001$), lending support that an initial surgical approach for empyema may be warranted [8]. A study from Ontario, Canada, examined the current state of empyema management in the province [9]. This was a retrospective review of 9014 adults who were discharged from hospital with a diagnosis of empyema between 1996 and 2015. They were stratified into either non-operative management (chest tube with or without fibrinolytics) or operative (VATS or open decortication) [8]. In calculating adjusted risk ratios, those treated non-operatively had a higher mortality risk as an inpatient (17.2% vs. 10.6%; RR_{adj} 1.32–1.54) at 30 days compared with an operative approach, lending support to potentially increased mortality as well [9].

To examine routine practise at our own institution, a retrospective chart review of a single thoracic surgeon experience was conducted. All individuals referred for empyema between 2017 and 2019 were evaluated, which totalled 46 patients. Of these, 74% (34) underwent initial chest tube insertion, 21.7% (10) underwent initial surgical management and 4.3% (2) underwent no intervention. Of those whom the primary intervention was a chest tube insertion, 23.5% (8) required repeat or additional chest tube insertion, 35.3% (12) required surgical intervention and 41.2% (14) required no additional intervention. Of the 10 individuals who underwent initial surgical management, none required repeat interventions. Both procedures were associated with a low mortality rate of 2.2% (3) in this cohort, where two individuals passed away from significant co-morbidities opting for palliation, and one as a consequence of complications from bedside chest tube insertion.

3. Hypothesis and aim of the study

We speculate that initial surgical management with VATS decortication will result in a decreased number of repeat interventions in treating empyema within 30 days, an important quality of life measurement.

3.1. Primary objective

- To identify the initial management option, either IR guided chest tube insertion with MIST 2 Trial fibrinolytics or VATS decortication, that will provide the fewest repeat interventions within 30 days. Repeat intervention is defined as repeat chest tube insertion or surgical intervention (VATS decortication or thoracotomy) after the initial intervention.

3.2. Secondary objective

- To identify the initial management option that is associated with the largest change in size of empyema (measured by the volume change calculated by the region of interest on Osirix®), the lowest number of complications (myocardial infarction, pulmonary embolus, deep vein thrombosis, respiratory failure, etc.), the lowest 30-day and 90-day mortality, as well as the shortest length of hospital stay. Osirix is an image processing application specifically designed to navigate, visualize and measure multimodal and multi-dimensional images with capabilities from 2D-5D.

4. Methods and analysis

4.1. Settings and participants

The study design will be a single centre RCT occurring at the Kingston Health Sciences Centre (KHSC). All adults with empyema that meet all inclusion criteria will be invited to participate (See Fig. 1).

4.1.1. Inclusion criteria

- Clinical evidence of infection including a fever or elevated serum levels of inflammatory markers such as an elevated white-cell count or C-reactive protein
- CT Chest suggesting the presence of empyema

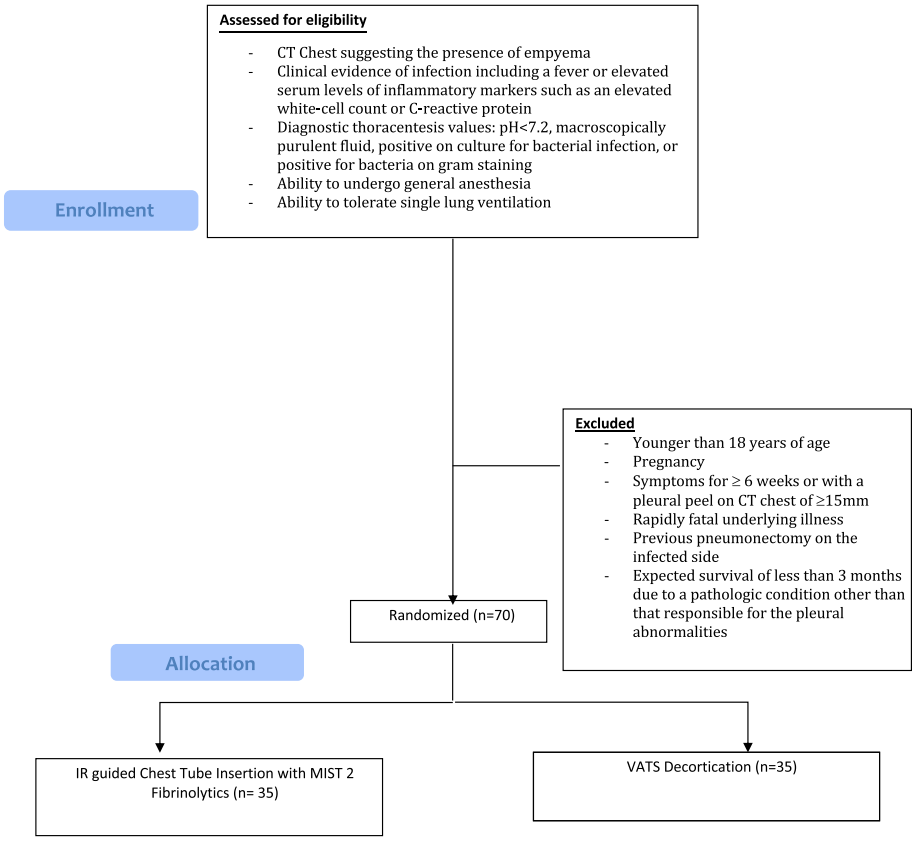

Fig. 1. Participant selection and randomization.

- Diagnostic thoracentesis values: pH < 7.2, macroscopically purulent fluid, positive on culture for bacterial infection, or positive for bacteria on gram staining
- Ability to undergo general anesthesia
- Ability to tolerate single lung ventilation

4.1.2. Exclusion criteria

- Younger than 18 years of age
- Previous treatment with intrapleural fibrinolytic agents, Dornase, or both for empyema
- Known sensitivity to intrapleural fibrinolytic agent or DNase
- Pregnancy
- Symptoms for ≥6 weeks or with a pleural peel on CT chest of ≥15 mm
- Rapidly fatal underlying illness: e.g. sepsis, rapid deterioration requiring intubation, requiring vasopressors for hemodynamic support etc.
- Previous pneumonectomy on the infected side
- Expected survival of less than 3 months due to a pathologic condition other than that responsible for the pleural abnormalities

4.2. Enrollment

Patients suspected of an empyema will undergo a CT Chest as well as a diagnostic thoracentesis to confirm an exudative effusion. Fluid analysis must meet the above inclusion criteria. All participants will undergo a repeat CT chest before chest tube removal or in the absence of clinical improvement. Reassessment for residual empyema with a repeat CT chest is the standard of practice at our institution. It provides an objective measurement of any residual empyema and determines if any further interventions are warranted. This is combined with the participants' clinical presentation to determine the overall clinical improvement.

4.3. Randomization

Participants will be randomized using block randomization in groups of ten using an online calculator. The study team will not be blinded as the participants will be allocated to one of two intervention groups, IR guided chest tube insertion with intrapleural fibrinolytics (Dornase 5 mg and Alteplase 10 mg twice daily for three days) or VATS decortication. Each intervention will occur within 48 h of randomization.

4.4. Study outcomes

The primary outcome will be the rate of repeat intervention within 30 days, an important quality of life measurement for patients with empyema. Repeat intervention is defined as repeat chest tube insertion, surgical intervention in the form of either VATS decortication or thoracotomy after chest tube insertion with fibrinolytics, or repeat surgical intervention. To measure this outcome, participants will be monitored daily by the study team while in hospital and up to 6 weeks post intervention. Once discharged, the electronic medical record will be used to access patient information to obtain information on new radiographic interventions, visitations to the hospital, or re-admission. A 30-day follow up phone conversation from initial intervention will be completed by the study team to obtain any additional information from the participants. Patients will also be interviewed by the study team at their 6-week thoracic surgery follow up clinic appointment. Health related quality of life will be measured by applying the World Health Organization Disability Assessment Schedule (WHODAS), to assess for differences in six domains of functioning. This will be administered at the time of randomization, discharge and at the 6-week follow up appointment (Appendix 2).

The change of the size of empyema will be calculated by a chest

radiologist. The size and location of the empyema will be measured in three planes on CT imaging, comparing the initial empyema size on admission to the empyema size on discharge using Osirix®.

All data on patient complications will be collected. The length of hospital stay will be measured by calculating the days and minutes using the electronic medical record to obtain the date and time of admission or transfer and discharge. Mortality data will be collected from the online electronic medical record.

Follow up data will be collected. This includes any patient concerns captured on thoracic surgery assessment forms, vital signs in outpatient surgery follow up, mortality within 30 and 90 days as well as the cause of death. Patient satisfaction with the study will also be determined by a telephone interview 30 days post-initial intervention. Additional follow up will be conducted up to 6 weeks to allow for the time for patients to complete their six-week course of antibiotics and to be seen in thoracic surgery clinic. If patients do not present for the follow up visit, they will be contacted via telephone to ensure they are recovering favorably.

All adverse events and mortalities will be reported to the Health Sciences Affiliated Teaching Hospitals Research Ethics Board (HSREB).

4.5. Sample size and calculation

The most recent study from North America examining the association between initial empyema treatment modality and rate of re-intervention was by Semenkovich et al. They outlined that out of 4095 patients in New York State undergoing admission for empyema, those who received thoracostomy for treatment of empyema had a 44% failure rate requiring either VATS or open decortication after the initial intervention. In contrast, only 15% of patients who received VATS as the initial intervention required re-intervention in the form of an open decortication [8]. Currently, there is no Canadian data that addresses this issue, and data from our own institution correlates closely with our neighboring state of New York. Thus, we calculate a sample size of 70 patients (35 per arm) is required to detect a statistically significant difference at a power of 80% and an alpha of 0.05. We do not anticipate any difficulty recruiting this number of patients given the population data we have presented for our own institution earlier.

4.6. Recruitment

All adults diagnosed with empyema and meeting inclusion criteria will be invited to participate in the trial. Referrals from other services such as respirology, internal medicine, or peripheral centres being transferred for thoracic surgery care will also be invited to participate. Informed consent will be obtained in person by a research nurse not directly participating in the care of the patient, in order to prevent undue coercion. All patients will be provided with a copy of the informed consent form, and a patient information sheet. A copy of the consent form will be kept in their research portfolio.

4.7. Data collection, confidentiality and archiving of documents

All data collection will be performed by members of the research team. A document will be placed on the participant's chart identifying them as a study participant. A signed hard copy of the consent form will be securely stored in a locked filing cabinet in the Department of Surgery at the Kingston Health Sciences Centre (KHSC).

All data collected will be stored in electronic form in an excel spreadsheet. This will be kept on a hospital network computer and will be both encrypted and password protected and kept locked in the Department of Surgery at KHSC.

A separate electronic excel sheet linking participant hospital healthcare number with a study number will be stored on a hospital network computer and will also be both encrypted and password protected. This will be kept on a hospital computer, encrypted and password protected that will be locked in the Department of Surgery at KHSC.

Data will be securely kept for 10 years and then destroyed by the study team.

4.8. Statistical analysis plans

Data will initially be analyzed descriptively, including means, standard deviations and range checks for continuous data, and frequencies and percentages for the categorical data. The continuous data will also be assessed for the normality of the underlying distribution using the Shapiro-Wilk test. Comparisons between the two treatment groups will be made with the two-tailed Student's *t*-test for continuous data, or the Mann-Whitney *U* test in the event of non-normal distributions. The Pearson Chi-square test or Fisher's Exact Test will be used to compare categorical data between the two groups.

5. Ethics

This clinical trial was approved by the Health Sciences and Affiliated Teaching Hospitals Research Ethics Board (HSREB) on June 30, 2020. This trial is registered through ClinicalTrials.gov; Clinical Trials ID NCT03584113.

6. Discussion

Empyema is a common thoracic surgery presentation, yet its optimal initial management remains unknown. Traditionally, two initial interventions have been commonly accepted and include chest tube insertion with intrapleural fibrinolytics, or VATS decortication. The initial treatment is often largely dependent upon the service managing the patient and centre-specific practices. Data from New York, our neighboring state, as well as our own hospital would suggest that initial intervention with chest tube insertion and fibrinolytics often leads to multiple repeat interventions and potential increased morbidity compared with initial VATS decortication [8]. Additionally, population-based data from Ontario also lends support that a non-operative approach to empyema is associated with an increased risk of 30-day mortality compared with initial operative intervention [9]. While retrospective population-based studies have highlighted the importance of considering an initial operative approach to empyema, there have been no randomized control trials which have compared the interventions thus far.

This study is unique in that not only does it compare two acceptable intervention strategies, but also standardizes each group ensuring that regardless of allocation, each participant is receiving optimal care within 48 hours. We propose a modern and precise approach to chest tube insertion with intrapleural fibrinolytics involving IR image-guided chest tube placement. This method of chest tube insertion differs from a blind bedside insertion technique and aims to reduce technical variability and limits this potentially confounding variable between the two groups. The insertion technique has been standardized between all interventional radiologists (Appendix 1).

Similarly, VATS decortication surgery will be standardized amongst thoracic surgeons at our institution (Appendix 1). Each intervention will be ensured to occur within 48 hours of randomization, preventing any delays in definitive treatment. Since our patient population is similar to that of Semenkovich et al. (2018), we anticipate that participants randomized into the VATS decortication arm may experience fewer repeat interventions, decreased morbidity, and a reduction in overall mortality compared to the non-surgical arm.

Empyema can have a major impact on the quality of life of patients. Multiple interventions, lack of empyema resolution, poor clinical improvement and prolonged hospitalizations can negatively affect the domains of functioning outlined by the WHO (cognition, mobility, self-care, getting along, life activities, & participation) [10]. We specifically chose the number of repeat interventions as the primary outcome to

highlight its importance as an objective quality of life measurement for patients suffering from empyema. While other secondary outcomes will also be examined including change in size of empyema, length of stay, morbidity and mortality; emphasis is placed on identifying the treatment option that improves patient experience. Using the WHODAS questionnaire at the time of randomization, at discharge, and at 6-week follow up will also provide an in-depth longitudinal overview of patient quality of life outcomes and allows for comparison of the two intervention groups throughout treatment. Study participants will be followed for a total of 6 weeks to assess for any immediate complications. Long-term follow up will be determined at the discretion of their attending thoracic surgeon.

Interventions for the treatment of empyema, like any procedure, is associated with some risk. Chest tube insertion involves the risk of bleeding, infection, and iatrogenic injury to surrounding structures including lung and even liver, spleen, and hollow viscus organs if the tube inadvertently enters the intra-abdominal cavity. On the other hand, surgical risks include general anesthetic risk and procedural risk. General anesthetic risk includes myocardial infarction, stroke, deep vein thrombosis, pulmonary embolism, and respiratory failure. Procedural risk includes bleeding, infection, and iatrogenic injury to surrounding structures. In contrast to patients undergoing elective thoracic surgery where lung function tests are obtained pre-operatively, this is not feasible in the acute setting with empyema management which contributes to uncertainty regarding the patient's post-operative recovery and respiratory status. Although the surgical risks may seem more significant compared to non-operative management, it is anticipated that the morbidity associated with increased hospital stay and repeat interventions in the non-operative arm will likely surpass those in the surgical group. A recent prospective study examined sixty-six patients with early-stage empyema who were followed and divided into two groups. Group A (28 participants) were stage I (exudative) managed conservatively by respirologists. Group B consisted of 38 participants of both stage I (exudative) and stage II (fibrinopurulent) empyema that were managed by thoracic surgery [11]. Group A patients were treated with non-surgical modalities including thoracostomy and fibrinolytics [11]. Group B was treated with VATS decortication [9]. Mean hospital stay for group A was 22 days, with 10.7% major morbidity (pulmonary embolism, renal failure and CVA), along with a 7.1% mortality rate [11]. In Group B the mean hospital stay was 4.1 days, there were no mortalities and no major morbidities [11]. While it is difficult to make definitive conclusions on outcomes since interventions were stratified based on complexity of pleural collections, we hypothesise that initial VATS decortication will produce similar results decreasing overall morbidity. This study may potentially present the basis for recommendations to treat empyema with early surgical intervention.

6.1. Limitations

The main limitation to this RCT is that it is a single-centred study. Therefore, our results may not be generalizable to other centres, particularly if thoracic surgery or interventaional radiology is not readily available. Additionally, we recognize that institutions hold varying practices where not all image-guided chest tubes are placed by IR. We feel that any image-guided chest tube placement is likely more accurate than blind insertion, hence this study is still generalizable to other centres. We believe that the results obtained from this RCT may guide future clinicians managing empyema, providing a valuable future reference.

7. Conclusion

Empyema is a common disease where there is a dichotomy in the optimal initial management. We seek to determine the primary intervention, either IR guided thoracostomy with fibrinolytics or VATS decortication, that will result in the fewest repeat interventions within 30-days, and improve the quality of life for patients with empyema. We hypothesise that initial VATS decortication for empyema will be superior to IR guided chest tube insertion group with intrapleural fibrinolytics, presenting a shift in paradigm in empyema management.

CRediT Author Statement

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Declaration of competing interest

The authors declare no competing interests. This clinical trial did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Appendix 1. Outline of Procedural Steps for Each Arm

Both Treatment Arms

Bedside Thoracentesis: The patient will be positioned with arms and head resting supported on a bedside adjustable table or if unable to sit, lying at the edge of the bed with the ipsilateral arm over the head and the midaxillary line accessible for the insertion of the needle. The level of the effusion will be confirmed using either ultrasound guidance or percussion of dullness to confirm fluid/pus between the rib spaces. Once the level of fluid/pus has been confirmed, the thoracentesis site can be identified below this level at either the mid-posterior line (for posterior insertion) or midaxillary line (lateral insertion). The skin will be anesthetized with lidocaine (1% or 2% with or without epinephrine) on the superior aspect of the rib, down to the pleura. An 18G needle is then inserted over the superior aspect of the rib aspirating back until pleural fluid is obtained. Pleural fluid will then be sent to the lab for analysis. Approximately 30–50 mLs of pleural fluid is required.

Interventional radiology image guided chest tube insertion with MIST 2 trial fibrinolytics arm

Chest Tube Insertion (Thoracostomy): Participants randomized to this group will be transported to the Interventional Radiology Department. This procedure will be performed by one of four interventional radiologists involved in the study. If either of these four individuals are not on call and the study members require intervention, one will be called in to perform the procedure. The patient will be positioned appropriately and provided with sedation and/or local anesthetic under the discretion of the interventional radiologist. Using sterile and Seldinger technique under ultrasound guidance, a 12-24Fr chest tube will be inserted superior to the rib in the intercostal space directed at the empyema collection. The default chest tube selection will be a 16 Fr ThalQuick chest tube. The chest tube will be sutured in place and the position again confirmed with fluoroscopy. Throughout the procedure the patient's hemodynamic status (heart rate, blood pressure and oxygen saturation) will be monitored by the nursing staff. Once the patient recovers, they will be transferred to an inpatient unit (thoracic surgery ward, internal medicine ward, or a critical care bed) to receive their fibrinolytics.

Adverse Effects: Risks of IR inserted tube thoracostomy include: risk of pneumothorax, bleeding, infection and small risk of diaphragm injury with the insertion of chest tube although significantly diminished when performed under direct visualization.

VATS Decortication Arm

VATS decortication surgery: Participants randomized to this group will be transported to the operating room. The patient will be positioned supine. Peripheral IV lines and an arterial line will be established. General anesthesia will be obtained and a dual-lumen endobronchial tube will be placed. Heparin 5000 units S.C. will be administered for deep vein thrombosis prophylaxis. Flexible bronchoscopy will be performed. The left and right mainstem bronchi, lobar bronchi, and segmental bronchial orifices will be examined. The patient will be repositioned in the lateral decubitus position with the affected side up. All safety straps will be placed. All pressure points will be covered. The patient will then be prepped and draped in the usual sterile fashion.

A planned 5 mm skin incision will be made in the 7th intercostal space. Anesthesia will deflate the lung on the operating side prior to entering the pleural space. A mosquito instrument will be used to traverse the latissimus dorsi, serratus anterior, and intercostal muscles above the rib until the parietal pleura is breached. A 5 mm camera port will be placed. A 5 mm 30-degree thoracoscope will be inserted into the camera port to confirm chest entry and the pleura will be inspected for adhesions. Adhesions will be taken down with electrocautery. Two additional 10 mm ports will be placed. One in the mid-axillary line in the 5th interspace and one posteriorly. A 5 mm suction-irrigator system will drain the fluid collections which will be sent to pathology and microbiology for cytology/gram stain/culture-aerobic, anaerobic, mycobacterial and fungal. The lung will be mobilized by detaching pleural adhesions, and the inferior pulmonary ligament will be divided. Gelatinous/fibrinous deposits and blood clots will be removed. The chest wall and diaphragm will be decorticated. A plane will be carefully developed between the lung and the visceral pleural rind. The visceral pleural peel will undergo circumferential decortication, thereby freeing the entire lung and allowing it to fully expand. Traction is applied to the peel with countertraction applied to the lung. Necrotic tissue will be resected. The pleural rind will be sent to pathology (to rule out malignancy) and to microbiology. The hemithorax will be irrigated with sterile saline. The pleural space will be widely drained with a 28 french anterior-basal chest tube and a 28 french posterior-apical chest tube. The chest tubes will be secured with a #1 silk twice. A horizontal U-stich will be placed with #2 ethibond. The skin wound will be closed with an interrupted #1 monocryl. The duration of the procedure should be about 90 min.

Adverse Effects: Risks of VATS Decortication include normal general thoracic surgery post-operative risks such as: risk of general anesthetic, myocardial infarction, DVT, pulmonary embolism, pneumonia, and respiratory failure. Other risks include bleeding, infection, and iatrogenic injury to surrounding structures (e.g. lung parenchyma causing a prolonged airleak, vessel injury requiring repair, phrenic nerve injury, and thoracic duct injury).

Appendix 2. WHODAS 36- Item Version Self-administered

This questionnaire asks about difficulties due to health conditions. Health conditions include diseases or illnesses, other health problems that may be short or long lasting, injuries, mental or emotional problems, and problems with alcohol or drugs.

Think back over the past 30 days and answer these questions, thinking about how much difficulty you had doing the following activities. For each question, please circle only one response.

In the past 30 days, how much difficulty did you have in:						
Understanding and communicating						
D1.1	Concentrating on doing something for 10 min?	None	Mild	Moderate	Severe	Extreme or cannot do
D1.2	Remembering to do important things?	None	Mild	Moderate	Severe	Extreme or cannot do
D1.3	Analysing and finding solutions to problems in day-to-day life?	None	Mild	Moderate	Severe	Extreme or cannot do
D1.4	Learning a new task, for example, learning how to get to a new place?	None	Mild	Moderate	Severe	Extreme or cannot do
D1.5	Generally understanding what people say?	None	Mild	Moderate	Severe	Extreme or cannot do
D1.6	Starting and maintaining a conversation?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting around						
D2.1	Standing for long periods such as 30 min?	None	Mild	Moderate	Severe	Extreme or cannot do
D2.2	Standing up from sitting down?	None	Mild	Moderate	Severe	Extreme or cannot do
D2.3	Moving around inside your home?	None	Mild	Moderate	Severe	Extreme or cannot do
D2.4	Getting out of your home?	None	Mild	Moderate	Severe	Extreme or cannot do
D2.5	Walking a long distance such as a kilometre [or equivalent]?	None	Mild	Moderate	Severe	Extreme or cannot do

In the past 30 days, how much difficulty did you have in:						
Self-care						
D3.1	Washing your whole body?	None	Mild	Moderate	Severe	Extreme or cannot do
D3.2	Getting dressed?	None	Mild	Moderate	Severe	Extreme or cannot do
D3.3	Eating?	None	Mild	Moderate	Severe	Extreme or cannot do
D3.4	Staying by yourself for a few days?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting along with people						
D4.1	Dealing with people you do not know?	None	Mild	Moderate	Severe	Extreme or cannot do
D4.2	Maintaining a friendship?	None	Mild	Moderate	Severe	Extreme or cannot do
D4.3	Getting along with people who are close to you?	None	Mild	Moderate	Severe	Extreme or cannot do
D4.4	Making new friends?	None	Mild	Moderate	Severe	Extreme or cannot do
D4.5	Sexual activities?	None	Mild	Moderate	Severe	Extreme or cannot do
Life activities						
D5.1	Taking care of your household responsibilities?	None	Mild	Moderate	Severe	Extreme or cannot do
D5.2	Doing most important household tasks well?	None	Mild	Moderate	Severe	Extreme or cannot do
D5.3	Getting all the household work done that you needed to do?	None	Mild	Moderate	Severe	Extreme or cannot do
D5.4	Getting your household work done as quickly as needed?	None	Mild	Moderate	Severe	Extreme or cannot do

If you work (paid, non-paid, self-employed) or go to school, complete questions D5.5–D5.8, below. Oth-erwise, skip to D6.1.

Because of your health condition, in the past 30 days, how much difficulty did you have in:						
D5.5	Your day-to-day work/school?	None	Mild	Moderate	Severe	Extreme or cannot do
D5.6	Doing your most important work/school tasks well?	None	Mild	Moderate	Severe	Extreme or cannot do
D5.7	Getting all the work done that you need to do?	None	Mild	Moderate	Severe	Extreme or cannot do
D5.8	Getting your work done as quickly as needed?	None	Mild	Moderate	Severe	Extreme or cannot do
Participation in society						
In the past 30 days:						
D6.1	How much of a problem did you have in joining in community activities (for example, festivities, religious or other activities) in the same way as anyone else can?	None	Mild	Moderate	Severe	Extreme or cannot do
D6.2	How much of a problem did you have because of barriers or hindrances in the world around you?	None	Mild	Moderate	Severe	Extreme or cannot do
D6.3	How much of a problem did you have living with dignity because of the attitudes and actions of others?	None	Mild	Moderate	Severe	Extreme or cannot do
D6.4	How much time did you spend on your health condition, or its consequences?	None	Mild	Moderate	Severe	Extreme or cannot do
D6.5	How much have you been emotionally affected by your health condition?	None	Mild	Moderate	Severe	Extreme or cannot do
D6.6	How much has your health been a drain on the financial resources of you or your family?	None	Mild	Moderate	Severe	Extreme or cannot do
D6.7	How much of a problem did your family have because of your health problems?	None	Mild	Moderate	Severe	Extreme or cannot do
D6.8	How much of a problem did you have in doing things by yourself for relaxation or pleasure?	None	Mild	Moderate	Severe	Extreme or cannot do

H1	Overall, in the past 30 days, how many days were these difficulties present?	*Record number of days*
H2	In the past 30 days, for how many days were you totally unable to carry out your usual activities or work because of any health condition?	***Record number of days***
H3	In the past 30 days, not counting the days that you were totally unable, for how many days did you cut back or reduce your usual activities or work because of any health condition?	***Record number of days***

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