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Hemothorax: A Review of the Literature

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Abstract

Hemothorax is a collection of blood in the pleural cavity usually from traumatic injury. Chest X-ray has historically been the imaging modality of choice upon arrival to the hospital. The sensitivity and specificity of point-of-care ultrasound, specifically through the Extended Focal Assessment with Sonography in Trauma (eFAST) protocol has been significant enough to warrant inclusion in most Level 1 trauma centers as an adjunct to radiographs.[1,2] If the size or severity of a hemothorax warrants intervention, tube thoracostomy has been and still remains the treatment of choice. Most cases of hemothorax will resolve with tube thoracostomy. If residual blood remains within the pleural cavity after tube thoracostomy, it is then considered to be a retained hemothorax, with significant risks for developing late complications such as empyema and fibrothorax. Once late complications occur, morbidity and mortality increase dramatically and the only definitive treatment is surgery. In order to avoid surgery, research has been focused on removing a retained hemothorax before it progresses pathologically. The most promising therapy consists of fibrinolytics which are infused into the pleural space, disrupting the hemothorax, allowing for further drainage. While significant progress has been made, additional trials are needed to further define the dosing and pharmacokinetics of fibrinolytics in this setting. If medical therapy and early procedures fail to resolve the retained hemothorax, surgery is usually indicated. Surgery historically consisted solely of thoracotomy, but has been largely replaced in non-emergent situations by video-assisted thoracoscopy (VATS), a minimally invasive technique that

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Steven Idell, MD, PhD serves as a Founder and Chief Scientific Officer of LTI and a member of the Board of Directors of LTI, which provided funding for preparation of the drug product and for the trial. He has an equity position (first-tier conflict of interest) in the company, as does the University of Texas Horizon Fund and the UTHSCT. He has a conflict-of-interest plan acknowledging and managing these declared conflicts of interest through the UTHSCT and the UT System. He is an inventor on a patent (USPTO 7332469) held by the UT Board of Regents and licensed to LTI.
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shows considerable improvement in the patients' recovery and pain post-operatively. Should all prior attempts to resolve the hemothorax fail, then open thoracotomy may be indicated.

Introduction

Hemothorax has been consistently defined as a collection of blood in the pleural space or a pleural fluid hematocrit of greater than 50%.[3,4] It is estimated that 300,000 cases of hemothorax occur annually in the United States[5], the majority of which are due to thoracic trauma.[4] Although more infrequent, spontaneous and iatrogenic or vascular causes of hemothorax may also occur. Hemorrhage leading to a hemothorax can originate from the chest wall, intercostal vasculature, internal mammary arteries, great vessels, mediastinum, myocardium, lung parenchyma, diaphragm, or abdomen.[4,6-9] Management options range from observation to percutaneous drainage [tube thoracostomy, thoracentesis] and/or surgery [Video-Assisted Thoracic Surgery (VATS) or open thoracotomy]. There has been increasing use and reported success with instillation of intrapleural fibrinolytic therapy (IPTF) for retained hemothorax to degrade clotted blood and expedite percutaneous drainage in order to avoid more invasive surgical procedures.

A hematocrit value of pleural fluid below 50% does not necessarily rule out hemothorax. It has been reported that a hemothorax may become diluted with pleural fluid in as little as 3-4 days, mimicking a hemorrhagic effusion with a hematocrit between 25-50%.[3,10] Additionally, pleural fluid appears to be clinically indistinguishable from blood at a hematocrit greater than 5%.[10] Therefore, it may be prudent to examine a patient more closely for a source of hemorrhage, even when the hematocrit is below 50%.

The severity of a hemothorax is classified according to the amount of blood present within the pleural cavity. Intrapleural blood less than 400 ml is classified as a minimal hemothorax, while 400 ml to 1000 ml is a medium hemothorax. Anything greater than 1000 ml is considered a massive hemothorax.[11,12] The clinical consequences may reflect the acuity of the bleeding or exacerbate underlying comorbidities including anemia or coronary artery disease. Most patients who receive appropriate and timely care for hemothorax will have good outcomes with no long term disabilities.

Epidemiology and Etiology

There are three major etiologic categories of hemothorax: spontaneous, iatrogenic, and traumatic. Thoracic trauma is the most common cause[4,13-15] contributing to approximately 16,000–30,000 deaths per year[16,17] This is followed by iatrogenic, and least commonly, spontaneous.[18] In elderly patients the reported incidence is: blunt trauma 73.3%, iatrogenic trauma 25.0%, and spontaneous 1.7%.[19] All three origins of hemothorax can potentially involve major arteries such as the aorta, intercostal arteries, and internal mammary arteries leading to tension hemothorax, exsanguination and death.

Spontaneous Hemothorax

Due to the infrequency and variety of causes of spontaneous hemothorax, prior reviews have had to focus on case reports and small series within the literature.[3,10,18,20] The most common cause of spontaneous hemothorax is spontaneous pneumothorax.[10,21,22] A review of 29 articles by Patrini, et al.[3] organized the etiology of spontaneous hemothorax into four main categories: coagulopathic, vascular, neoplastic, and miscellaneous.

Coagulopathic etiologies consist of congenital diseases such as hemophilia or thrombocytopenia, or occur with therapeutic anticoagulation. Most cases of spontaneous hemothorax related to anticoagulation occur following treatment of pulmonary emboli, usually with heparin or warfarin.[10,18] Cases in which enoxaparin and tissue plasminogen activator (tPA) were administered have also occurred.[23,24]

Vascular origins are due to rupture or dissection of the descending thoracic aorta in patients with atherosclerosis or uncontrolled hypertension.[25] Genetic diseases such as Ehlers-Danlos Syndrome and Rendu-Osler-Weber Syndrome are associated with spontaneous hemothorax due to physiological alterations of the vasculature.[3,10]

Various neoplasias are associated with spontaneous hemothorax through various mechanisms including spontaneous rupture of a tumor or direct invasion of vasculature in or near the pleural cavity. Janik, et al.,[25] reviewed 145 publications and found 54 cases of spontaneous hemothorax caused by neoplasia, with the largest subset of those related to Von Recklinghausen Disease (neurofibromatosis). Other reported causes include costal exostoses, endometriosis, pulmonary sequestration, infections, pulmonary infarction, pancreatitis, tubal pregnancies, and extramedullary hematopoiesis.[3,10,18]

Iatrogenic Hemothorax

Iatrogenic hemothorax occurs during surgery or procedures when the lung parenchyma, surrounding vessels, or organs are inadvertently damaged. Thoracentesis, central venous catheterization, tube thoracostomy, and thoracotomy may all result in iatrogenic hemothorax. Some of these procedures are also used in the process to treat hemothorax. Central venous catheterization, specifically subclavian venous catheterization, and placement of chest tubes are among the most common iatrogenic causes of hemothorax,[26-30] with a reported incidence of approximately 1%.[31] The rate of complications from central venous catheterization is directly related to the experience of the operator,[32-36] the anatomic location of insertion,[32,37,38] and the use of ultrasound guidance.[35,39] Thoracentesis has a reported incidence of hemothorax from 0.1%−0.4%.[40,41] The incidence of hemothorax in the elderly is increased secondary to a higher incidence of intercostal artery tortuosity.[40]

Traumatic Hemothorax

Traumatic hemothorax can be due to either blunt or penetrating injury. Thoracic injuries occur in approximately 60%[4,14] of all polytrauma cases and are responsible for 15–30%[16,42] of all trauma mortalities.[14,43] Hemothorax, hemopneumothorax, and pneumothorax are the most common complications of either penetrating or blunt thoracic trauma, with a frequency ranging from 10–37%.[14-16,42,44-47] Hemothorax from blunt thoracic trauma has an overall mortality of 9.4% and is the leading cause of death in the fourth decade of life.[48,49] Gunshots and stabbings are the primary means of penetrating thoracic trauma,[11,45,50] whereas 70–80% of blunt thoracic trauma is caused by motor vehicle crashes.[14,15,42] While blunt thoracic trauma typically occurs far more frequently, mortality is significantly higher in penetrating chest trauma, with up to 90% not surviving transport to the hospital.[51] Should penetrating trauma also involve the heart, survival is less than 1%.[51] The mortality of penetrating chest trauma can also depend upon the means of injury. Gunshot wounds have a higher mortality than stab wounds.[52,53] Additionally, the severity of injuries sustained in trauma correlate with increased complications from hemothorax, as well as mortality.[54,55]

The distribution of trauma etiology can change rapidly in countries with conflict. At one hospital in Maiduguri, Nigeria 61.5% of all thoracic trauma was penetrating in origin.[56] During the Bosnia-Herzegovina conflict 94.9% of thoracic trauma in one hospital was penetrating in origin.[57] Most recently, Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) have several reports listing penetrating origins in thoracic trauma to be between 88–91%.[58-62] The mechanisms of penetrating thoracic injuries have also changed with time, with over 90% of penetrating thoracic injuries being due to gunshots during the civil war, whereas explosions were responsible for 81% of penetrating thoracic trauma in OEF/OIF.[61]

Detection of Hemothorax

Chest radiography (CXR) has traditionally been the initial tool in the emergency room for rapid evaluation of thoracic injury.[14,63-65] Upright CXR is preferred, because in the supine position the blood will be distributed along the entire posterior aspect of the affected pleural space rather than the diaphragmatic surface. This causes the hemothorax to be less apparent, as there is no blunting of the costophrenic angle. In upright radiography, blunting of the costophrenic angle is the most common sign of hemothorax and pleural effusions. The collection of fluid can be altered significantly if there are any intrapleural adhesions, which will cause any blood or fluid to occupy any space available.[14]

CXR has well known limitations. 300–500 mls of blood is required to blunt the costophrenic angle. This is especially true if the patient is in the supine position, because blood up to 1000 mls can be overlooked.[66] Since most severely injured patients arrive in the supine position, and upright CXRs cannot be safely performed, the amount of blood in the chest is often underestimated, and occasionally missed completely. Upright CXR cannot be used to accurately quantify the volume of hemothorax. (See Figures 1 and 2).

Ultrasound/Fast/eFAST

The Focused Assessment with Sonography in Trauma (FAST) is a bedside test developed in the mid 1990's for use in acute trauma patients to rapidly assess for intra-abdominal hemorrhage and to rule out clinically significant pericardial tamponade. It is performed by imaging in the sagittal plane the right and left upper quadrants of the abdomen, the suprapubic region in both sagittal and coronal planes, and a subxyphoid or parasternal view of the pericardium. The Extended Focused Assessment with Sonography in Trauma (eFast) adds additional views of the hemithoraces to look for signs of pneumothorax and hemothorax. These include the right and left pleural spaces (anterior axillary line between 6th and 9th intercostal spaces), and left and right anterior pleural spaces (midclavicular line between 2nd and 3rd intercostal spaces).[1,2] Multiple investigators report the utility of chest ultrasonography in diagnosing traumatic thoracic injuries.[67-74] Ultrasound can quantify volume, detecting 100 ml of pleural fluid with 100% accuracy,[67] and as little as 20 ml.[75] Specifically related to hemothorax, a recent meta analaysis[71] indicates ultrasound has an overall sensitivity of 67% and specificity of 99%, with multiple studies indicating a sensitivity over 90%.[68,76] Ultrasound has consistently been shown to be more sensitive than chest radiography for the detection of hemothorax.[67,68,74,77,78] Additional benefits to the use of ultrasound include the ability to be used in a pre-hospital setting, portability, reproducibility, non-invasiveness, and employs no contrast or radiation.

Despite the increasing use of ultrasound for diagnosis of traumatic injuries, there are some limitations. The sensitivity of ultrasound is influenced by the experience of the operator and the frequency of the transducer.[71,73] While ultrasound typically has a higher sensitivity than chest radiography for detecting hemothoraces, it is not as sensitive as computed tomography[2,72,74] and can miss other findings such as mediastinal hematomas.[79] (See Figure 3.)

Computed Tomography

Chest computed tomography (CT) is commonly used to detect additional injuries following chest radiograph and bedside sonography.[80-82] The patient may initially be studied using CXR and possibly ultrasound to quickly evaluate the extent of injuries, especially in cases of hemodynamic instability.[50] Once stability is achieved, a chest CT, preferably with intravenous contrast, can be performed to evaluate further pathology in detail.[65,83-86] CT will identify additional injuries in 20–30% of patients with an initial abnormal CXR. In cases of hemothorax, CT can reveal a collection of blood missed by the chest radiograph.[87,88] (See Figure 4 and Figure 5).

Acute Hemothorax: Early Management

Early identification of patients at risk for hemothorax following trauma significantly decreases morbidity and mortality.[89-91] Life threatening injuries require prompt attention either by thoracostomy or in severe cases, thoracotomy. Appropriate management of any patient with suspected hemothorax depends on their hemodynamic status. The Advanced Trauma Life Support Course, sponsored and updated by the American College of Surgeons,[92] provides practitioners with guidelines for the appropriate management of chest trauma, including hemothorax. Detailed management of hemothorax is beyond the scope of this review.

Delayed Hemothorax: Recognition and Management

The definition of delayed hemothorax has been described in two different ways. The first definition is any hemothorax that occurs 24h after initial imaging is negative.[42] The second definition proposed by Ritter et al.[7] states that a delayed hemothorax is any hemothorax that occurs after negative initial imaging regardless of elapsed time.[7] Delayed hemothorax has been reported to occur anywhere from 2 hours to 44 days after initial presentation.[7,93] Rib fractures are the most common cause of delayed hemothorax and are reported to occur in 30–80%[94-96] of patients with thoracic trauma. [94,96-99] Since rib fractures have been found to be associated with both acute and delayed hemothorax, some investigators advocate surgical fixation to improve outcomes in terms of respiratory failure and delayed complications such as recurrent and retained hemothorax, and chronic pain.[100-103] Rib fixation remains incompletely studied and controversial. [104]

CURRENT TREATMENT OPTIONS:

Expectant Management

Conservative (no intervention) management is determined by the overall severity of the chest injury and/or the acuity of blood loss. If the patient is hemodynamically stable, and the hemothorax is confirmed to be less than 300 ml, conservative management with observation, aggressive respiratory care and pain control can be attempted. [17,105-111] In several studies volumes greater than 260–300 ml were up to 4x more likely to require drainage. [105,106,109,111] Patients with hemothorax volumes less than 260–300cc were 72%−92% likely to resolve without significant complication and with no intervention. Patients that eventually required drainage were more likely to experience an increase in size of the hemothorax, hemodynamic instability or increasing respiratory distress.[105,109] In some reports, the only patients with occult hemothorax that developed an empyema were those treated with tube thoracostomy.[106,110] If observation is elected, it is suggested that early and frequent imaging (CXR) be repeated during the first 24 hours to ensure stability of the hemothorax and to detect any other potential pathologies. [17,107,108]

Needle Thoracentesis

Needle thoracentesis (also called thoracocentesis) has historically been used to evacuate hemothoraces, and is still often used to diagnose new onset pleural effusions suspicious for malignancy or infection.[112,113] Thoracentesis is still a common therapeutic method used for the removal of symptomatic pleural effusions.[114,115] At present, needle aspiration for the treatment of hemothorax is considered obsolete,[17] though small, clinically insignificant collections may still be treated with needle thoracocentesis at the discretion of the physician. [116]

Tube Thoracostomy

Tube Thoracostomy is the primary intervention for hemothorax. According to international practice management guidelines, all hemothoraces regardless of size should be considered for tube thoracostomy. [117] Small (occult) hemothoraces and pneumothoraces identified only by CT scan are frequently treated expectantly, though a chest tube may be used at the discretion of the physician. Most moderate sized and all massive hemothoraces should be treated with tube thoracostomy. [45,47,118-120] If treated early with adequate drainage, the need for additional surgery for retained or recurrent hemothoraces should be relatively low (10–15%).[47,51,118-124] Typically, bloody effusions that remain after tube thoracostomy are reabsorbed in 4–5 weeks without complication. [123]

It has been recommended that large bore tubes (28–40 Fr) be used for hemothorax evacuation to better quantify blood loss, and provide a conduit that will remain open and less likely to obstruct from clotting.[125,126] However, tube size is based more on surgeon preference and personal experience than rigorous scientific evidence.[127,128] Multiple reports have suggested that smaller bore tubes may be just as effective as larger bore tubes. Bore tube sizes as small 14 Fr have been compared to 28 Fr tubes and found to have similar performance.[129-131] Interestingly, there is invitro data suggesting that the viscosity of the pleural fluid should be a factor in determining the choice of tube size.[132]

Once placed, it is very important to continually re-examine the patient and follow the output of the chest tube for signs of ongoing bleeding.[133] The initial amount of suction applied to the chest tube remains a matter of debate, but most practitioners apply at least 20 to 40 cm of water negative pressure to the tube using various commercially available devices for collection and fluid measurement. Recent studies suggest that initially placing the chest tube to suction rather than water seal may be associated with improved outcome regarding duration of chest tube therapy, length of hospital stay, persistent air leak,[134] and risk of emyema[135] Savage et al.[136] believe that the benefits of initial suction evacuation are not significant with the exception being significant protection from recurrent pneumothorax. A chest X-ray should be repeated after tube insertion to confirm the proper position.[4] Reevaluation of the patient and monitoring of chest tube output should be done every hour for the first 24 hours after installation.

Complication rates from thoracostomy have been reported to be between 6–37%.[26,137,138] Proper training is required to perform tube thoracostomy correctly and safely.[51,139] Malpositioning is the most common complication following tube thoracostomy, especially during an emergency.[27,28,138] Dislodgement, infection, and laceration/perforation of organs may also occur.[51] Bleeding can be very serious, and may be due to laceration of an intercostal vein or artery.[40,140] Intrapulmonary placement is also a potential adverse event, occurring in up to 38% of thoracostomy complications when caregivers with minimal experience perform the procedure.[141]

Drainage from the hemithorax should in general be less than 100 ml in 24 hours before removal of the chest tube. Conversely, it has been reported that chest tubes can be removed with output as high as 2 ml/kg without additional intervention required.[142] A repeat chest radiograph should be performed prior and after removal to ensure complete lung re-expansion with no residual or recurrent pneumothorax.[143] Once discharged it is prudent to re-examine the patient in 1–2 weeks. Some reports suggest that repeat CXR may not be necessary due to low recurrence of hemothorax or pneumothorax.[144]

Video-Assisted Thoracic Surgery (VATS)

VATS as a means to perform surgery for multiple thoracic complications was developed during the 1990s, and is now accepted and widely applied by trauma surgeons.[145-147] This was in no small part due to the improving technology in endoscopes. VATS was initially developed to treat post operative hemothorax, but quickly was adapted to use for major lung resections.[148,149] In early trials, VATS conferred lower morbidity, better visualization, and a higher yield of detecting small injuries with less post-operative pain compared to thoracotomy. Improved lung function and the ability to evacuate and decorticate a lung following empyema were added benefits. Most patients also recovered quicker from surgery.[13,89,145,149-151] Single lung anesthesia is required for VATS and takes added time to implement. Thus, a major limiting factor of VATS is that the patient must be hemodynamically stable.[48,89,123,124,145,150,152-154] The patient can be actively bleeding during VATS as long as they remain hemodynamically stable.[10]

The timing of VATS is also very important when evacuating a hemothorax. Within 48–72 hours, VATS is usually successful for hemothorax evacuation and allows for early re-expansion of the lung with reduction in short and long term morbidity and mortality.[123,152,153] Performing VATS on the sixth post-trauma day or later is associated with a 15.8% possibility of conversion to an open thoracotomy. This delay results in development of pleural thickening and dense adhesions.[13,145] Some report that even up to the seventh day there remains significant benefit in performing VATS over thoracotomy,[107,155-157] but after seven days complications rise significantly.[152,158-160]

Uniportal VATS is a relatively new option in thoracic surgery and was originally proposed by two teams desiring to develop a minimally invasive thoracic surgical technique involving only a single incision.[161,162] One of the major benefits of Uniportal VATS is less pain secondary to rib retraction for multiple trocars.[163-165] Uniportal VATS retains many of the benefits of multiportal VATS for hemothorax evacuation including excellent visibility, decreased hospital length of stay, and avoidance of excess bleeding.[166] Placement of the incision is very important in uniportal VATS in order to have the best access for intrathoracic procedures and inspection. Several different approaches have been reported based on the indication.[167-171] In multiple studies, there has been no significant difference found between multiport VATS and uniportal VATS with respect to morbidity, mortality, cardiopulmonary complications, and wound infection. These findings support the idea that this procedure is a suitable and safe option for evacuating a hemothorax.[163,172-174]

Thoracotomy

Thoracotomy is a surgical procedure where the chest wall is incised, and a self-retaining retractor is used to gain access to the thoracic cavity. If the patient is actively bleeding into the thoracic cavity and remains hemodynamically unstable despite initial attempts at resuscitation, thoracotomy is the procedure of choice.[175] If the patient can be stabilized, VATS may be considered first.[4] Thoracotomy has a reported incidence of 2.6%−6% in all chest trauma cases.[47,176] In chest trauma cases involving hemothorax, thoracotomy has been reported to be performed 10% of the time, especially in patients with penetrating chest trauma.[11,177]

In contrast to the traditional lateral approach in elective surgery, the anterior thoracotomy approach has several indications for emergent hemorrhage control. The first indications for thoracotomy occur during the primary survey. If the patient presents in shock, has a chest wall defect, airway obstruction, tension pneumothorax, pericardial tamponade, or flail chest emergency thoracotomy should be performed. Significant output from a chest tube is also an indication for thoracotomy and is defined as 1000–1500 mls total in 24 hours or 200–500 mls/hour for 2 to 3 consecutive hours.[117,124] Specific internal injuries may also be indication for immediate thoracotomy including esophageal injury, diaphragmatic injury, cardiac injury, massive hemothorax and great vessel injury. Thoracotomy is also indicated if the patient develops fibrothorax or high-stage empyema.[10,11,46,50,107,154,177,178]

The standard approach in emergent thoracotomy is the anterolateral approach which provides an excellent view of the thoracic cavity.[47] In some types of injuries, the anterolateral approach may not be sufficient. In this case, either the clamshell or hemiclamshell approach may be used.[179] The hemiclamshell approach is also named the cervico-sterno-thoracotomy and involves an arch-shaped incision that begins at the manubrium of the sternum, extends down the midline of the sternum and then curves laterally along the posterior border of the pectoralis major, ending in the midaxiallary region.[180] The clamshell approach repeats the process on the opposite side of the chest, exposing the entire thoracic cavity.

There are times when a patient with severe trauma should not receive emergency thoracotomy. It has been found that patients with severe blunt trauma, emergency thoracotomy rarely results in successful resuscitation.[181-186] Of those patients in shock upon arrival to the ED, neurologically intact survival ranging from 1.5%−5%, and survival is less than 1% if there are no vital signs. Of those that receive cardiopulmonary resuscitation, 1.5% or less of patients survive neurologically intact with CPR lasting greater than 5–15 minutes.[184] Therefore, it has been recommended that emergent thoracotomy not be performed in patients with no signs of life upon arrival to the hospital.[187-191]

Prophylactic Antibiotics

Prophylactic antibiotics remain a contested issue in virtually every area of medicine, especially with the recent push for antimicrobial stewardship. This situation remains the same when treating hemothorax.[192-196] The previous consensus is that a dose of antibiotics is better than none.[193] Multiple publications have shown some benefit by using prophylactic antibiotics in patients with hemothoraces. It has been shown that the use of antibiotics at least 24 hours after the start of chest tube drainage for hemothorax can reduce en incidence of pneumonia from 14.8% to 4.1%, and the incidence of empyema from 8.7% to 0.8%.[192,193,195,197-199] In contrast, there have been reports that do not show significant reduction in pneumonia or empyema in traumatic hemopenumothorax.[192] Other reports have determined there is no significant difference in rates of empyema if the patient were receiving antibiotics for the entirety of chest tube duration, or for only the first 48 hours.[179]

The duration of antibiotic treatment and recommendations vary from 24 hours after chest tube removal to the point of chest tube removal. Twenty four hours of antibiotic treatment, typically first generation cephalosporins, is advised in traumatic hemothorax within the first

24 hours following chest tube placement.[193] Antibiotics should be directed towards *Staphyloccus aureus* and *Streptococcus* species which have been shown to grow from empyema cultures with some regularity.[179,193] A guideline in 2012 published by Moore. et al[200] was not able to make a recommendation on presumptive antibiotics with the evidence to that date. Most recently, a large multi-center study involving 1887 patients determined that there were no significant differences in the primary complications of empyema or pneumonia, as well as no significant difference in secondary measures including length of stay, mortality, *Clostridium difficile* colitis, or days requiring mechanical ventilation.[201]

The Life Cycle of Hemothorax: Resolution, Retained Hemothorax, Empyema, and Fibrothorax

There are two different physiologic stages of hemothorax resolution: early and late.[17] Some have speculated that an early defibrination of the hemothorax may occur with an increased pleural fluid protein concentration and a corresponding increase in intrapleural hyperosmotic pressure. This promotes the development of a pleural effusion.[202,203] As a hemothorax remains within the pleural cavity, it will typically complete spontaneous reabsorption within several weeks, especially if the volume is under 300mls.[19,147,204,205] If it does not reabsorb, it will become a retained hemothorax (RH). RH has been defined as blood occupying at least one-third of the pleural space which cannot be drained by thoracostomy after 72 hours or clots of at least 500 mls volume.[123,124] RH can begin to form as early as 24 hours after chest tube placement.[205] The incidence of retained hemothorax is estimated between 5–30%, based on the results of multiple studies, of which a large percentage requires surgical evacuation.[145,202,206] In a level I large trauma service in East Texas that is affiliated with the University of Texas Center of Tyler, the experience has been similar. As there were 1154 trauma centers in the US as of 2002[207], the annual incidence of traumatic RH in the US could approach 14,000 cases per year. The incidence of RH in malignant pleural effusions (MPE) is unknown, but with 150,000 cases of MPE annually in the US[125], additional cases of RH may occur in a population in which hemostasis is often impaired and for which chest surgery is often contraindicated.

The consequences of RH include fibrothorax, trapped lung or high rates of the development of subsequent empyema; 26.8 percent and pneumonia; 19.5 percent[208]. Predictors of the development of empyema after RH in trauma patients include an Injury Severity Score of 25 or greater, rib fractures and use of multiple interventions to alleviate the RH[209]

While the pathogenesis of organizing RH has not been well-delineated in the literature appears to involve derangements of local coagulation and fibrinolysis, as occurs in other forms of pleural organization[210,211]. The organization of blood in the pleural space involves initial coagulation, which may be due to procoagulants including tissue factor that is expressed by mesothelial and other cells within the pleural compartment[212,213]. These cells also express plasminogen activators and their inhibitors, including plasminogen activator inhibitor-1, which is strongly implicated in the pathogenesis of pleural organization[211,213,214]. Intrapleural organization and fibrosis is favored by suppression of local fibrinolysis that occurs concurrently with increased expression of procoagulant activity[211]. These derangement of pathways of fibrin turnover favor extravascular fibrin deposition within the pleural space and provide a rationale for the use of intrapleural fibrinolytic therapy (IPFT) to lyse RH and thereby avoid its complications.

Evacuating RH early is critical due to the complications that can occur within the late phase of physiological resolution. This has been reported multiple times when VATS was used to evacuate the retained hemothorax, resulting in favorable clinical outcomes.[154,178,205,215-217] It has been reported that as many as 25% of patients with a retained hemothorax will require multiple evacuation attempts.[208] But if it is managed appropriately, prognosis is usually excellent.

RH can undergo progressive organization over several days to become an empyema or fibrothorax. The overall incidence of empyema and fibrothorax in cases of retained hemothorax have been estimated at 5% and 1%, respectively.[66] Hemothoraces that fail to drain after initial tube thoracostomy may occur in about 20% of cases, 15–30% of those remaining will develop subsequent empyema or fibrothorax.[151,209,218] Failure to evacuate the hemothorax in these cases may be due to malposition or poor drainage of the chest tubes, which can influenced by the experience of the clinician.[51,139,219] Surgical exploration is an indicated treatment option when either empyema or fibrothorax are diagnosed.[46,154,178,215] Development of empyema and fibrothorax can lead to lung entrapment or collapse, potentially leading to respiratory failure.[123,135,202]

Empyema can occur as a complication of RH due to primary or secondary bacterial contamination of a hemothorax and can originate from broncho-tracheal lesions, esophageal injuries, penetrating missiles, long-standing clotted thoracostomy tube, and post-surgical exposure.[17,187] Independent risk factors for empyema are elevated injury score or failure to administer periprocedural antibiotics during tube placement.[198,220]

Fibrothorax results from organization of the fibrinous neomatrix that coats both the parietal and visceral pleural surfaces.[221] Adhesion of these surfaces; pleurodesis, traps the lung in position and prevents full expansion leading to persistent atelectasis and restricted pulmonary function. Fibrothorax often requires surgery, with decortication of the visceral pleura being the therapy of choice to provide lung re-expansion.[175,179,221,222]

Intrapleural Fibrinolytic Therapy (IPFT) for retained hemothorax

A recent meta-analysis of randomized and nonrandomized controlled trials in the literature suggests that IPFT, now commonly used for non-draining loculated parapneumonic pleural effusions of empyema[211], may be effective and well-tolerated for RH, leading to calls for more advanced clinical trial testing[223]. The use of any fibrinolytic; plasminogen activator agent was found to obviate the need for surgery in 87 percent of patients in this meta-analysis. The use of intrapleural tPA resulted in avoidance of surgery in 83 percent of patients, while the use of other agents was slightly better at 87 percent. As is the case in loculated empyema and complicated parapneumonic pleural effusions with failure to drain[224], no agent that has been approved for IPFT for the treatment of RH. The issue is potentially important as the rigors of approval by the Food and Drug Administration and other regulatory agencies includes robust assessment of patient safety. While none of the regimens used to date have undergone rigorous evaluation of patient safety, the weight of clinical evidence to date now suggests that IPFT is generally well-tolerated in patients with RH[223]. While a pharmacologic approach to treatment of RH is inherently desirable, efficacy and tolerability will need to be tested in future randomized, controlled clinical trials. Dose ranging studies will also be needed to define best practices in terms of selection of the agent to be used in IPFT for RH, as well as the doses and schedules that yield optimal outcomes.

Experimental Techniques for the Management of Hemothorax and its Complications

Several unique techniques have been used to treat hemothorax and its related complications. In one report of 20 patients, intrathoracic lavage was performed at the time of thoracostomy tube placement and resulted in improved secondary intervention rates[225,226] In another study involving 110 patients with thoracoabdominal trauma and subsequent billiary-gastroenteric contamination, thoracic irrigation was performed through lesions in the diaphragm resulting in decreased rates of intrathoracic complications.[227] Pulsed lavage has been used to assist with the extraction of retained hemothorax and empyema.[228,229] Intrapleural epinephrine has been used to control bleeding in cases of massive hemothorax.[230]

Discussion

The acute management of hemothorax has remained relatively stable over the course of decades. The chest tube has been the crux of management for hemothorax nearly since its discovery, and remains so to this day. Current guidelines support attempted drainage of any sized hemothorax, there is significant evidence that small hemothoraces may be managed expectantly and will likely have good outcomes. Thoracentesis has fallen out of favor for drainage of hemothorax, but is still used for diagnostic purposes and drainage of pleural effusions. For severe or complicated hemothoraces thoracotomy was often the procedure of last resort, and still is for patients who are hemodynamically unstable or with significant comorbidities. In those patients who are hemodynamically stable, VATS has steadily become the preferred procedure when surgery is indicated. VATS offers several benefits over thoracotomy including reduction of post operative pain, improved cosmetic results, and fewer post-operative complications. These benefits seemingly have been improved upon with the advent of Uniportal VATS, which uses a solitary access point to perform surgical procedures which can be as complicated as lobectomies.

The major focus of research and innovation in hemothorax management is the prevention and evacuation of retained hemothoraces. By preventing retained hemothoraces, the incidence of late complications such as empyema and fibrothorax are reduced, improving overall morbidity and mortality. The introduction of intrapleural fibrinolytics has been a major area of focus for both retained hemothorax and empyema, and has been used as early as the 1950s. A major benefit of fibrinolytics in addition to the reduction of late complications is the reduction in invasive surgical procedures to evacuate a retained hemothorax. While there are no major guidelines published recommending the use of intrapleural fibrinolytics, a recent meta-analysis by Hendrickson, et al., shows promise. Additional clinical trials and research into the pathophysiology of fibrinolytics will be needed to gain Food and Drug Administration approval for this indication, but the majority of evidence favors the inclusion of this procedure in the algorithm for hemothorax management.

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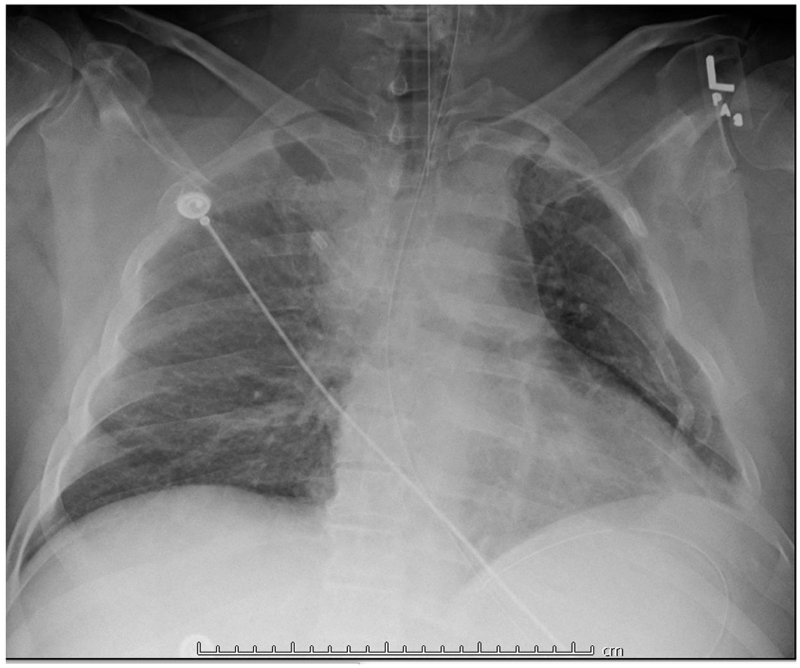

Figure 1.

Patient # 1. Chest X-ray showing multiple L rib fractures. Patient is lying supine, intubated, on mechanical ventilation. The X-ray does not conclusively show a hemothorax.

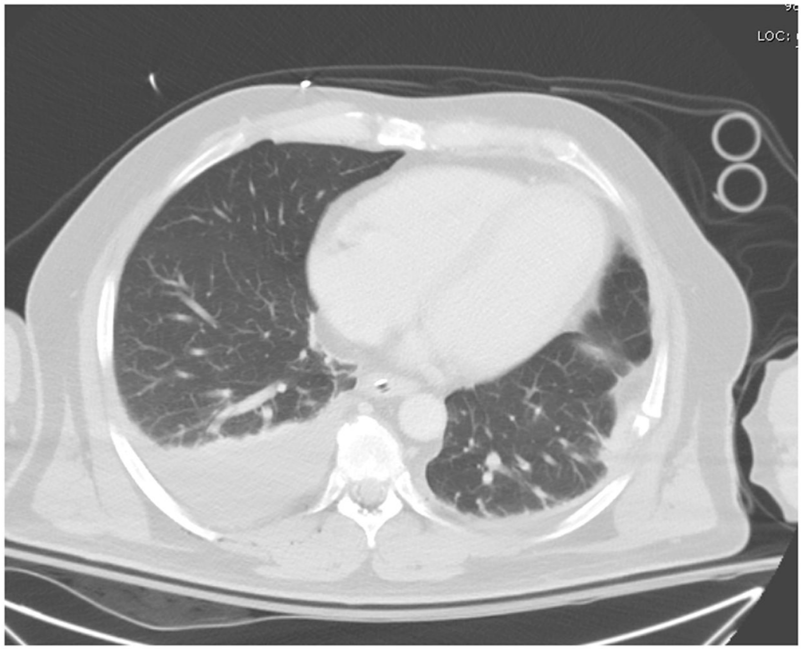

Figure 2.
Thoracic CT scan, Patient # 1. Patient surprisingly had no significant blood in the left hemithorax, but 800 ml of blood from a right hemothorax was drained via tube thoracostomy.

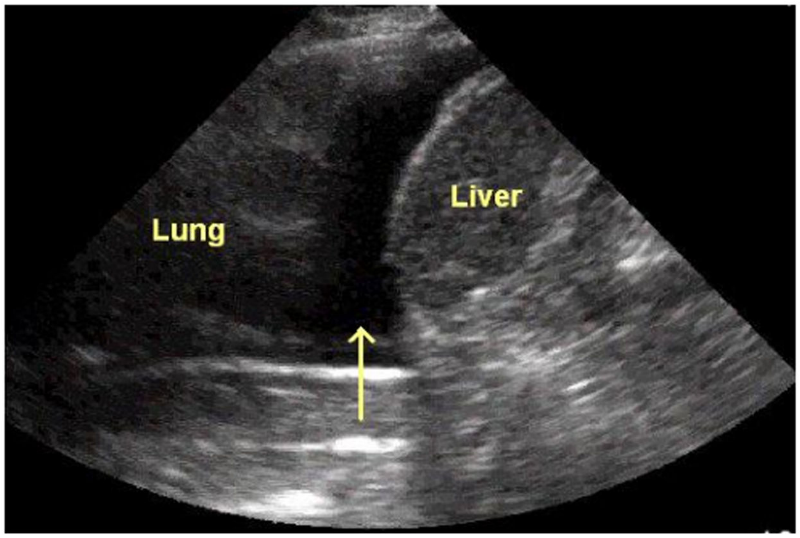

Figure 3.

Sagittal view of the right upper quadrant and lower right hemithorax. The dark area depicted By the arrow is diagnostic for either fluid or blood in the right hemithorax.

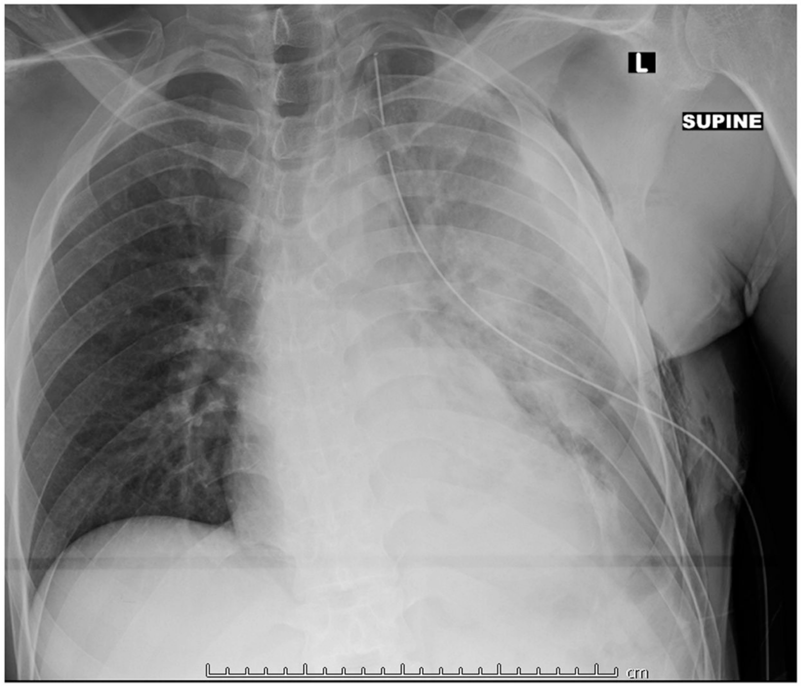

Figure 4.

Chest X-ray showing a massive L hemothorax following blunt trauma from a motor vehicle crash. A tube thoracostomy has already been performed, but the hemothorax is incompletely evacuated.

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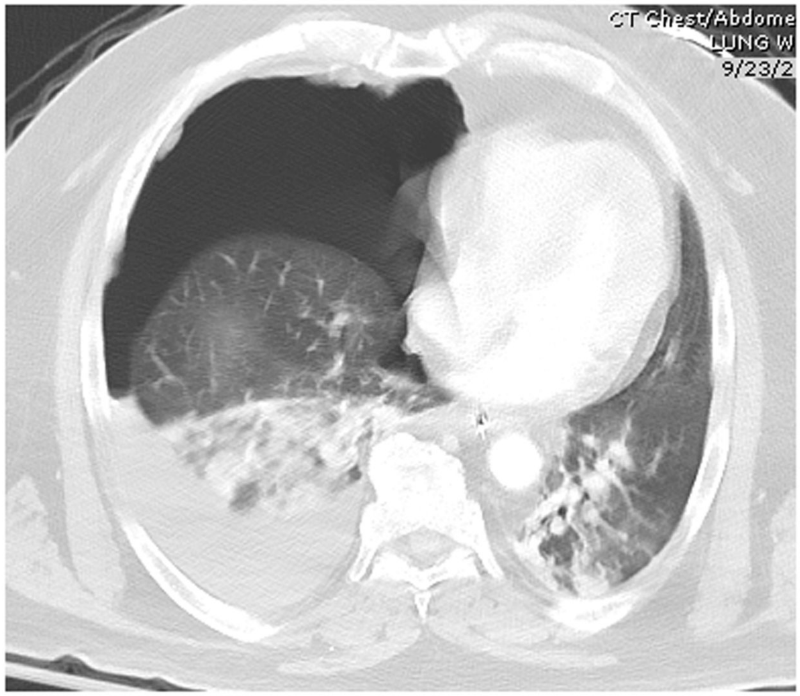

Figure 5.

CT scan of the chest demonstrating large right hemopneumothorax. Note motion artifact blurring right heart border and thoracic contents