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Declining frequency of thoracoscopic decortication for empyema — redefining failure after fibrinolysis

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ABSTRACT

Background: Primary fibrinolysis for pediatric empyema has become standard of care at our institution. Early study of our protocol revealed a 16% thoracoscopic decortication rate after primary fibrinolysis. We now report the frequency with which children progress to operation with maturation of the protocol.
Methods: A database of patients diagnosed with empyema between September 2014 and March 2019 was examined. Patients who underwent tissue plasminogen activator (tPA) therapy with or without subsequent video-assisted thoracoscopic (VATS) decortication were included. Patients with additional indications for tube thoracostomy or VATS were excluded.
Results: Forty-eight patients were included. Median age was 4.5 years [IQR 2–9.3]. Median length of stay (LOS) was 8 days [IQR 6–11]. No patients underwent primary VATS. Median days with a chest tube was 5 [IQR 5–6] and median number of doses of tPA was 3 [IQR 3–3]. Seven patients (14.6%) had a chest tube replaced without undergoing VATS. The VATS rate was 4.2% in the first half of this study but 0% in the last 33 months.
Conclusion: Thoracoscopic decortication is rarely necessary in children with empyema. Raising the threshold for surgical intervention and utilizing further nonoperative measures can avoid an operation in most children without increasing in-hospital length of stay.
Level of evidence: IV

A major sequela of pneumonia is the formation of a parapneumonic effusion which can progress to empyema, with several studies reporting an increasing incidence of empyema in children over the last two decades [1–3]. In addition to systemic antibiotics, treatment of empyema can include chemical fibrinolysis via chest tube and/or mechanical debridement with video-assisted thoracoscopic surgery (VATS). Chemical fibrinolysis has been shown to be as equally effective as mechanical debridement for the treatment of empyema in multiple randomized trials [4–7]. While early studies reported high failure rates of 30%–50% for primary fibrinolysis [2,5], more recent prospective studies and trials have shown that less than a fifth of patients treated with primary fibrinolysis will require operative intervention [4,6,8,9]. Furthermore, primary surgical debridement is associated with higher costs despite a similar failure rate when compared to chemical fibrinolysis [4,8].

In a previously conducted prospective randomized trial comparing primary fibrinolysis versus VATS in children with empyema at our institution, there was no difference in length of hospital stay (LOS) or days of oxygen therapy requirements between the two arms. However, the VATS group accrued significantly more hospital charges [4]. Based on the findings from this trial, we developed a protocol using chemical fibrinolysis as the primary intervention for children diagnosed with empyema, and initial results revealed an 84% success rate of nonoperative management [8]. With the progressive maturation of our experience, the typical triggers for surgical intervention have been reconsidered and were made less stringent. The aim of this study was to determine the frequency with which children with empyema fail fibrinolytic therapy and require operative intervention with this modified approach.

1. Materials and methods

Following IRB approval (#14100421), a retrospective review of a prospectively maintained database of children diagnosed with empyema between September 2014 and March 2019 was performed. Empyema was defined as either: 1) septations or loculations in the pleural

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space visualized on computed tomography (CT) scan or ultrasound (US) OR 2) pleural fluid containing a white blood cell (WBC) count greater than 10,000 cells/μL or with bacteria seen on gram stain or culture. Patients less than 19 years of age who underwent either primary fibrinolysis therapy (ipsilateral chest tube placement with at least one instillation of tissue plasminogen activator with or without subsequent VATS decortication) or primary VATS were included. The following were the exclusion criteria: immunocompromised patients, those with empyema in association with another disease process, other indications for thoracostomy tube placement (ipsilateral pneumothorax, bronchopleural fistula or need for lung/pleural biopsy) and contraindications to VATS (ipsilateral necrotizing pneumonia or lung abscess) (Fig. 1).

1.1. Protocol

Patients were treated based on a modified protocol from the initial study (Fig. 2). In brief, a chest tube was placed with sedation at the bedside or in a procedure room, and then placed to −20 cm H_2O. Fibrinolysis was performed with 4 mg of tissue plasminogen activator (tPA) dissolved in 40 mL of saline solution injected into the chest tube. The chest tube was then clamped for a dwell time of one hour before being placed on suction. This was performed once daily for three days, injecting a total of three doses of tPA. Criteria for chest tube removal included the absence of an air leak and a drainage output of less than 1 cc/kg/day. Patients with persistent symptoms (prolonged oxygen requirement or fevers following completion of the three doses) were reimaged using either US or CT

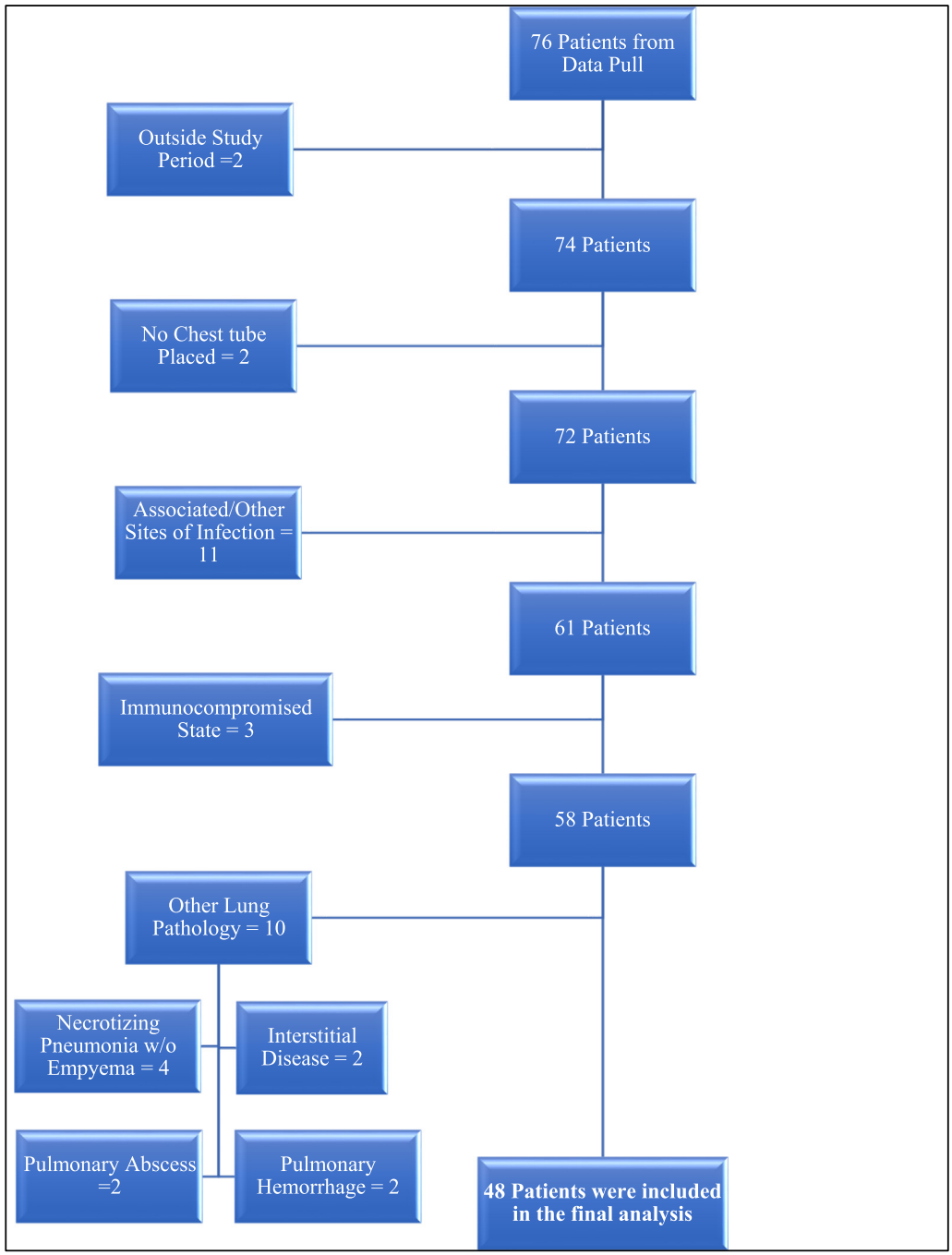

Fig. 1. Patient selection criteria.

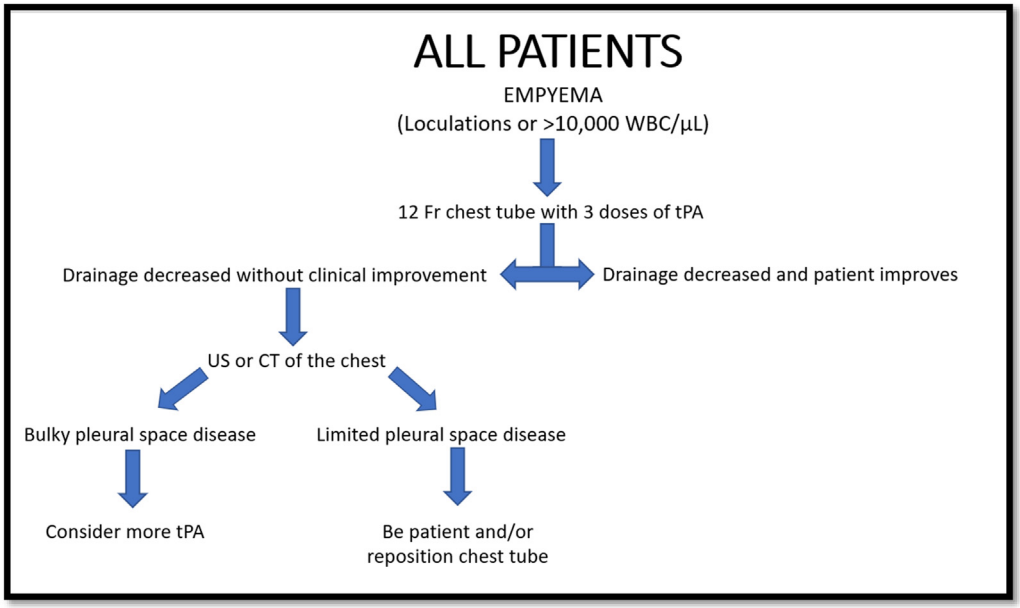

Fig. 2. Modified protocol for the management of empyema.

scan. If a persistent loculated effusion is seen and the tube is remotely located away from the collection, the chest tube was repositioned or replaced by interventional radiology (IR) under US guidance. If the preexisting chest tube was in the appropriate location, an additional course of fibrinolytic therapy was considered. Patients who remained symptomatic with poor oral intake or persistent oxygen requirements despite the second round of tPA underwent VATS.

1.2. Outcome measures

Demographic characteristics, including age, weight, gender and past medical history were obtained. The outcome of interest was rate of progression to VATS. Secondary measures included duration of chest tube placement, number of doses of tPA given, VATS as a primary or secondary therapy, and total and post-chest tube LOS. Readmissions or Emergency Room (ER) visits within 30 days of discharge were also recorded.

1.3. Statistical analysis

Descriptive statistics were calculated with continuous data reported as median with interquartile ranges (IQR) and categorical data reported as proportions. Analysis was performed in STATA® (StataCorp, College Station, TX) with a p-value of < 0.05 considered significant.

2. Results

A total of 48 patients met inclusion criteria (Fig. 1). The median age was 4.5 years [IQR 2–9.5] and 56% were male. The median weight at the time of admission was 17 kg [IQR 12.2–30.2]. Fibrinolytic therapy was the first line of treatment in all patients and no patient underwent primary VATS. Forty-five patients (94%) were admitted to the pediatric service, while three patients were admitted to the surgical service. Thirty patients had their thoracostomy tube placed by IR, 9 patients had a thoracostomy tube placed by the surgical team, 7 patients had their thoracostomy tube placed by the pediatric intensive care team, and 2 patients were transferred from an outside institution with preexisting thoracostomy tube.

The median number of tPA doses per patient was 3 [IQR 3–3], with three patients (6%) requiring a total of 6 doses. The median in-dwell duration for a thoracostomy tube was 5 days [IQR 5–6]. IR was consulted in 73% of patients, either for initial placement, adjustment, or replacement of the chest tube. Seven patients (14.6%) had their thoracostomy tube adjusted or replaced by IR without undergoing VATS. Two patients underwent VATS (4.2%), both occurring in the first two years of this study. These patients were discharged 10 and 11 days after fibrinolytic treatment (4 and 3 days post-VATS) respectively. No patient underwent VATS in the last 33 months of the study.

The overall median total LOS was 8 days [IQR 6–11]. There was no statistically significant difference in LOS among those who did not require tube adjustment/replacement versus those who did versus those who underwent VATS (6 days [IQR 5–7] vs 9 days, [IQR 5.5–11.5] vs 10.5 days, $p = 0.09$). Three patients returned to the ER and four patients were readmitted to the hospital for recurrent/persistent symptoms. None of them required surgical intervention. There were no mortalities through the hospital course and 30 days postdischarge in the cohort.

3. Discussion

A decade after the initial randomized trial demonstrating the efficacy and effectiveness of primary fibrinolysis for empyema at our institution, thoracoscopic decortication has become a rare event. In the last 5 years included in this analysis, only two patients underwent VATS during the initial part of the study period and no patient underwent VATS in the last 33 months of the study. Postthoracostomy tube LOS did not differ by need for tube adjustment/replacement, suggesting that a repeated course of fibrinolytic therapy can lead to successful nonoperative treatment of empyema without increasing hospital stay. Taking into account the six patients who had repositioning or replacement of their existing tube and the patient who received an additional 3 doses of tPA without tube adjustment, the failure rate of *initial* fibrinolysis is 20%, essentially similar to our initial study and other previous series [4,6–8]. However, with the current modified protocol, the failure rate of primary fibrinolysis, now defined as progression to VATS, is currently at 4% over the entire study period and 0% among the 24 patients managed over the last 33 months of the study.

The success of this protocol can be attributed to some developments with the maturation of the protocol. The primary medical teams, including the infectious disease (ID) services, have a better understanding of the expected clinical course and the role of chemical fibrinolysis. They now appreciate that once the pleural space has cleared or attenuated,

persistent clinical symptoms (fevers and continued oxygen requirements) can safely be attributed to parenchymal disease which will resolve with systemic treatment using antibiotics. This has resulted in less pressure to intervene early after fibrinolysis, as well as after removal of the thoracostomy tube despite persistent clinical symptoms or chest x-ray showing the inevitable tiny residual effusion or lung consolidation. Not surprisingly, nearly half of patients with an empyema at our institution were treated by the medical team, in conjunction with radiology, with little or no involvement of the surgery service. Since interventional radiologists place thoracostomy tubes under image-guidance, it has been the natural inclination to involve IR early in the management to better direct the initial placement or subsequent repositioning of the thoracostomy tube. In addition, we have been able to institute a protocol, in concert with our ID colleagues, to limit the duration of antibiotic therapy based on completion of fibrinolytic therapy and resolution of symptoms. This reflects the growing confidence that a treated pleural space is no longer a meaningful contributor of illness despite persistent symptoms.

As an institution, we have also become more proactive about addressing poorly functioning thoracostomy tubes after fibrinolysis. If the drainage output decreases and an effusion is found to be persistent on chest x-ray, a flush is attempted to clear a potentially clogged tube. If this fails, patients are now most commonly referred to radiology for imaging and potential intervention. In the interventional suite, a US is performed and the tube can be repositioned or replaced if located away from the undrained loculated collections with consideration for a second course of tPA, or removed if the effusion proves to be trivial or the opacity on x-ray proves to be consolidated lung. In our series, seven patients underwent chest tube adjustment, only two of whom received additional fibrinolysis with 3 doses of tPA, and none of whom underwent VATS or a second chest tube adjustment. Notably, none of the patients who had a radiology consultation underwent VATS, while two (15%) of those without a radiology consultation did. This was in the initial stage of the protocol. In both patients, the thoracostomy tube had been removed, and the patients redeveloped symptoms and imaging showed reaccumulation of the empyema. Since our last VATS decortication in 2016, only two patients had thoracostomy tubes placed by the surgical team. Likewise, the consultation to radiology increased from 54% to 89% in the first and second half of patients, which suggests more reliance on imaging to determine clearance of disease from the pleural space and on our IR colleagues to perform image-guided placement of the thoracostomy tube or need for additional intervention. The choice of IR is simply because of the availability of image guided placement and the ability to confirm the need for repositioning. The same result can be achieved in the hands of surgeons who are skilled and comfortable with US imaging of the chest. Ideally for this process, US should be employed during the initial placement or during repositioning. The current management highlights the strong need for in-depth US training for surgeons, especially as these tools become readily available for point-of-care use. This can eliminate the visit to the IR suite in facilities without such capabilities or where the IR services are not readily available around the clock.

This study corroborates the guidelines provided by the American Pediatric Surgical Association (APSA) which suggested, as a Grade A recommendation, that chemical fibrinolysis should be first line therapy for the treatment of empyema [10]. The guidelines also recommend considering VATS for patients who "fail" chemical fibrinolysis, with failure defined as those who have persistent pleural space disease and systemic symptoms after primary fibrinolysis. Interestingly, this was a Grade D recommendation with no comparative literature to support this practice. This is corroborates the findings in a multidisciplinary survey of physicians primarily caring for pediatric patients where 80% of respondents stated that there was no written institutional guideline or policy regarding the treatment of empyema [11]. Among surgeons who responded to this survey, 37% thought that first-line treatment should be thoracostomy tube with chemical fibrinolysis, while 37% thought it should be tube and VATS [11]. As our modified protocol for the treatment of empyema has matured over time, this current study provides additional clarity and conclusive evidence on what should be defined as failure of fibrinolytic therapy. Based on our current practice, persistent clinical symptoms after fibrinolytic therapy with demonstrable clearance of pleural space disease should not be considered a failure.

This study is not without limitations. This was a retrospective study design from a single institution with a small sample size. However, this study utilized a standardized treatment protocol devised from a randomized clinical trial with prospectively collected data, reinforcing the validity of the treatment method. The small sample size was a result of stringent selection criteria designed to identify patients with isolated empyema in order to properly identify the best treatment modality without influence from comorbidities. This conforms with the design of the initial randomized trial to truly identify patients that this protocol will benefit. We were unable to make any clinically significant comparisons between those that underwent VATS and those who did not owing to the low VATS rate. However, this reflects the success of primary fibrinolytic therapy and further validates the protocol over a 5-year period.

4. Conclusions

Thoracoscopic decortication is rarely necessary in children with empyema. Raising the threshold for surgical intervention and utilizing further nonoperative measures can avoid an operation in most children without increasing in-hospital length of stay.

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Disclosures

Declarations of interest: none

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