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Michael H. Livingston
Western University

Sara Colozza
Schulich School of Medicine & Dentistry

Kelly N. Vogt
Western University

Neil Merritt
Western University

Andreana Bütter
Western University, andreana.butter@lhsc.on.ca

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Making the transition from video-assisted thoracoscopic surgery to chest tube with fibrinolytics for empyema in children: Any change in outcomes?

Michael H. Livingston, MD, MSc
Sara Colozza
Kelly N. Vogt, MD, MSc
Neil Merritt, MD
Andreana Bütter, MD, MSc

Correspondence to:
A. Bütter
Department of Pediatric Surgery
London Health Sciences Centre
Children's Hospital
800 Commissioners Rd East
London ON N6A 4G5
andreana.butter@lhsc.on.ca

Background: There is ongoing variation in the use of video-assisted thoracoscopic surgery (VATS) and chest tube with fibrinolytics (CTWF) for empyema in children. Our objective was to report outcomes from a centre that recently made the transition from VATS to CTWF as the primary treatment modality.

Methods: We conducted a historical cohort study of children with empyema treated with either primary VATS (between 2005 and 2009) or CTWF (between 2009 and 2013).

Results: Sixty-seven children underwent pleural drainage for empyema during the study period: 28 (42%) were treated with primary VATS, and 39 (58%) underwent CTWF. There were no significant differences between the VATS and CTWF groups for length of stay (8 v. 9 d, p = 0.61) or need for additional procedures (4% v. 13%, p = 0.19). Length of stay varied widely for both VATS (4–53 d) and CTWF (5–46 d). Primary VATS failed in 1 (4%) patient, who required an additional chest tube, and CTWF failed in 5 (13%) patients. Additional procedures included 3 rescue VATS, 2 additional chest tubes and 1 thoracotomy. All patients recovered and were discharged home.

Conclusion: Primary VATS and CTWF were associated with similar outcomes in children with empyema. There appears to be a subset of children at risk for treatment failure with CTWF. Further research is needed to determine if these patients would benefit from primary VATS.

Contexte : Il existe une certaine variation dans le choix de l'intervention chirurgicale thoracoscopique assistée par vidéo (CTAV) ou de l'installation d'un drain thoracique accompagné de fibrinolytiques (DTIF) pour traiter la pleurésie purulente chez les enfants. L'objectif de cette étude était de décrire les résultats observés dans un centre ayant récemment remplacé la CTAV par le DTIF comme traitement de première intention.

Méthodes : Nous avons mené une étude de cohorte rétrospective auprès d'enfants atteints de pleurésie purulente, qui ont été traités soit par CTAV (entre 2005 et 2009), soit par l'installation d'un DTIF (entre 2009 et 2013).

Résultats : Pendant la période à l'étude, 67 enfants ont subi un drainage pleural. De ce nombre, 28 (42 %) ont été traités par CTAV, et 39 (58 %) par DTIF. Aucune différence significative n'a été observée entre ces 2 groupes sur le plan de la durée du séjour (8 j. [CTAV] contre 9 j. [DTIF], p = 0,61) et du recours à des interventions supplémentaires (4 % [CTAV] contre 13 % [DTIF], p = 0,19). La durée du séjour était toutefois très variable dans les 2 cas : entre 4 et 53 jours dans le groupe de la CTAV, et entre 5 et 46 jours dans celui du DTIF. La CTAV a échoué dans un cas (4 %), et un drain thoracique supplémentaire a dû être installé. La pose d'un DTIF s'est soldée par un échec dans 5 cas (13 %), qui ont nécessité 3 CTAV d'urgence, l'installation de 2 drains thoraciques additionnels et une thoracotomie. Tous les patients se sont rétablis et ont obtenu leur congé.

Conclusion : La CTAV et le DTIF employés comme traitements de première intention sont associés à des résultats semblables chez les enfants atteints de pleurésie purulente, mais l'installation d'un DTIF semble être plus susceptible d'échouer chez un sous-ensemble d'enfants. D'autres recherches seront nécessaires pour déterminer s'il serait préférable d'avoir recours à la CTAV comme traitement de première intention.

A recent survey of pediatric hospitals in the United States demonstrated that the incidence of empyema in children nearly doubled from 3.1 to 6.0 per 100 000 between 1997 and 2009.[1] Changes during this time period also demonstrated increased use of pleural drainage procedures. Prior to the advent of minimally invasive surgery, pleural drainage could be accomplished only via thoracentesis, chest tube insertion, or thoracotomy.[2,3] The emergence of video-assisted throracoscopic surgery (VATS) in the 1990s provided clinicians with a new approach that permitted mechanical débridement and drainage of the pleural space without the need for a thoracotomy.[4] With primary VATS, the majority of patients experience a complete recovery and do not require additional interventions.[5] In fact, a systematic review from 2005 indicated that primary VATS was associated with better outcomes than nonoperative management.[5] This included decreased chest tube duration, duration of antibiotics, need for repeat procedures, length of stay in hospital and mortality.

Over the past decade, the popularity of primary VATS has been challenged by the increasing use of chest tube with fibrinolytics (CTWF).[6–9] With this technique, children undergo chest tube insertion in the operating room (or in the interventional radiology suite) under general anesthesia (or conscious sedation). These patients then receive intrapleural fibrinolytics administered through the chest tube for 3 days to break down fibrin adhesions and facilitate pleural drainage. A systematic review from 2010 of 3 small, randomized controlled trials (RCTs) comparing VATS and CTWF revealed no significant differences in outcomes.[7,10–12] Both approaches were associated with similar length of stay in hospital and rates of treatment failure, defined as the need for additional chest tubes or surgery. Since then, a fourth single-centre RCT comparing VATS and CTWF was published.[13] That study found that VATS was associated with earlier chest tube removal, shorter length of stay and faster resolution of symptoms.[13] While hospital costs were higher with VATS in 3 of these 4 trials, an economic analysis demonstrated that primary VATS was more cost-effective when length of stay was longer than 10 days.[14]

In 2012, the American Pediatric Surgical Association (APSA) Outcomes and Clinical Trials Committee performed an extensive review on the management of empyema in children.[6] They concluded that the best available evidence suggests that VATS is neither superior nor inferior to CTWF and that both treatment modalities remain clinically equivalent.[6,15] Since primary VATS appears to be more expensive, the committee recommended that CTWF be used as first-line therapy and that VATS should be reserved as a rescue treatment for the subset of patients in whom CTWF fails.

Recommendations from APSA were further strengthened by results from the first multicentre RCT published in 2014.[16] This study once again demonstrated no statistically significant differences in clinical outcomes between children treated with primary VATS (n = 50) and those treated with primary CTWF (n = 53), including median length of stay (14 v. 13 d), median postoperative stay (10 v. 9 d), days of fever after treatment (4 v. 6 d), or need for a second drainage procedure (15% v. 10%, p = 0.47). There was a statistically significant difference in terms of chest tube duration (p < 0.001), but the magnitude was small (median 5 d for CTWF v. 4 d for VATS).

The best available evidence suggests that although primary VATS and CTWF are clinically equivalent, CTWF is less expensive, less invasive (since it involves 1 small incision for chest tube insertion rather than the 2 or 3 incisions required for primary VATS), and can often be performed with conscious sedation rather than a general anesthetic. Despite these advantages, many centres continue to use VATS as their primary treatment modality.

The purpose of this study was to determine if switching from VATS to CTWF within a single institution was associated with improved outcomes among children with empyema. While systematic reviews of RCTs represent the highest level of evidence, the trials reported to date for VATS and CTWF have not included all subgroups of patients, such as those with certain pre-existing comorbidities. Our centre switched from using primary VATS to CTWF in 2009. As such, we decided to review our experience and report the clinical outcomes associated with each treatment strategy.

METHODS

After obtaining ethics approval (REB#16987), we identified all pediatric patients (age < 18 yr) who presented to the Children's Hospital at London Health Sciences Centre with a diagnosis of pleural empyema between November 2005 and April 2013. Our hospital is the sole pediatric referral centre for a catchment area of 1.7 million people, with approximately 10–20 cases of empyema per year. Participants in this study were sequentially identified using a prospective database as well as a retrospective review of diagnostic codes from our centre's medical records. We excluded those who underwent chest tube insertion alone (and did not receive intrapleural fibrinolytics) or primary thoracotomy performed by a thoracic surgeon who primarily treated adults. All children in this study had stage II empyema, confirmed by the presence of septations and loculated fluid on ultrasound.[17]

Baseline variables included demographic data, the type of initial treatment, oxygen requirements, admission to the intensive care unit upon presentation to our centre, initial ultrasound findings and presence of necrosis on any imaging before pleural drainage. Outcomes included timing of pleural drainage, length of stay in hospital, readmission to hospital and need for additional procedures.

All VATS procedures were performed by a single pediatric surgeon (A.B.) and typically involved 2 incisions of 5 mm

(and occasionally a third incision of 5 mm if there were severe loculations). A chest tube was inserted through 1 of these incisions at the end of the procedure, ranging in size from 12-Fr to 24-Fr (depending on the size of the child). In August 2009, after review of the literature and discussion with other pediatric surgeons, we changed our treatment strategy for empyema in children from primary VATS to CTWF. This formed the basis of our study groups: all children who underwent primary VATS were treated between September 2005 and July 2009, while those who underwent CTWF were treated between August 2009 and April 2013.

Patients treated with CTWF underwent chest tube insertion with conscious sedation or general anesthesia. This procedure was typically performed in the interventional radiology suite under ultrasound and fluoroscopic guidance. After insertion, pleural fluid was allowed to drain, and tissue plasminogen activator (tPA) was administered within 12 hours. Typically, 4 mg of tPA was dissolved in 40 mL of normal saline and inserted directly through the chest tube. After administration, the chest tube was clamped for 1 hour, and the patient was placed in 3 different positions for 20 minutes each (left lateral decubitus, right lateral decubitus and supine). Patients received tPA once daily for 3 days, and chest tube drainage was monitored closely. The chest tube was left in place until completion of the 3-day course, pleural drainage was less than 50 mL in a 24-hour period and the patient was asymptomatic. A chest radiograph was obtained to confirm radiologic improvement before chest tube removal. Patients who had ongoing symptoms underwent placement of a second chest tube or rescue VATS (at the discretion of the treating surgeon).

Statistical analysis

We analyzed the data using the Statistical Package for the Social Sciences version 21. Descriptive statistics included median, range and frequency. Analytical statistics included *t* tests for independent means for continuous data and χ^2 tests for categorical data. We used Yates correction when applying the χ^2 test to all 2 × 2 contingency tables with cells containing expected values of less than 5.

Results

We identified 67 infants, children and adolescents who underwent pleural drainage between November 2005 and April 2013. Twenty-eight (42%) were treated with primary VATS between November 2005 and July 2009 by a single pediatric surgeon. Thirty-nine (58%) underwent CTWF between August 2009 and April 2013. We excluded children who were treated with chest tube insertion alone and did not receive intrapleural fibrinolytics (*n* = 9) or who underwent primary thoracotomy performed by a thoracic surgeon who primarily treated adults (*n* = 8).

Baseline demographic and clinical characteristics are summarized in Table 1. Mean age was similar between the groups: 5.2 years (range 2 mo to 16 yr) for VATS versus 6.1 years (range 6 mo to 17 yr) for CTWF (*p* = 0.39). The groups were also similar in terms of sex (46% v. 38% boys, *p* = 0.62), need for supplemental oxygen (7% v. 15%, *p* = 0.52), immediate admission to the intensive care unit (18% v. 28%, *p* = 0.49), and ultrasound findings and presence of lung necrosis on initial imaging (21% v. 10%, *p* = 0.36).

The timing of the procedure was slightly earlier for CTWF than primary VATS (median 1 d v. 2 d after admission), but this trend did not achieve statistical significance (*p* = 0.07). Similarly, more patients appeared to undergo drainage within 48 hours of admission with CTWF than VATS (79% v. 57%, *p* = 0.06). There were no significant differences between VATS and CTWF for overall length of stay (median 8 d v. 9 d, *p* = 0.61), length of stay postprocedure (6 d v. 8 d, *p* = 0.28) and frequency of hospital stay longer than 10 days (29% v. 44%, *p* = 0.21). Furthermore, overall length of stay varied widely for both VATS (4–53 d) and CTWF (5–46 d).

Outcomes associated with each treatment modality are summarized in Table 2. There were no significant differences between the 2 treatment modalities in terms of treatment failure, as defined by the need for additional procedures (4% v. 13%, *p* = 0.19). There were also no conversions to thoracotomy with primary VATS, but 1 (4%) patient required an additional chest tube postoperatively. Primary CTWF failed in 5 (13%) patients: 2 (5%) required a second chest tube and 3 (8%) underwent rescue VATS. One of the patients who required a second chest tube eventually proceeded to thoracotomy and open decortication performed by a thoracic surgeon who primarily treated adults.

One child treated with primary VATS and 1 who underwent CTWF experienced symptomatic anemia and required transfusion of packed red blood cells. In both patients, there was no hemodynamic instability, and no additional procedures were required. All children in both treatment groups recovered and were discharged home. There was 1 readmission to hospital in each group.

Discussion

The purpose of this study was to explore how changing from primary VATS to CTWF affects clinical outcomes among children with empyema treated at a single institution. Our centre experienced similar length of stay, rates of treatment failure and complications with each approach. Primary VATS and CTWF were used to treat children of all ages, ranging from infants to fully grown adolescents. Complications were rare for both strategies, with postprocedural bleeding requiring transfusion occurring in less than 5% of patients and not resulting in the need for additional interventions. Furthermore, while

most children were discharged home within 10 days, both treatment modalities were associated with some children having a length of stay beyond 1 month.

None of the outcomes assessed demonstrated statistically significant differences between VATS and CTWF. There was a trend toward earlier pleural drainage with CTWF (by 1 d) and shorter length of stay postprocedure with VATS (by approximately 2 d). There are several possible reasons for this finding. First, competition for operating room time may have meant that pleural drainage was achieved slightly earlier with CTWF (which was performed in the interventional radiology suite) than with primary VATS. Second, clinicians and parents may have been more willing to proceed with early pleural drainage via CTWF because it is less invasive and may not require a general anesthetic. Finally, the 3-day course of intrapleural fibrinolytics after chest tube insertion may explain why length of stay postprocedure was slightly higher with CTWF. Despite these trends, the overall length of stay

was not significantly different between the approaches. This finding is similar to that reported by the systematic review of 3 RCTs[7] and the recent multicentre RCT.[16]

Limitations

There are several limitations to this study. First, there were a small number of participants, and as such, most statistical comparisons were underpowered. Second, this study used historical rather than contemporary groups, and so the results may have been biased by factors other than the 2 treatment modalities. For example, there may have been baseline differences between the treatment groups that were not captured in the data reported here (e.g., increased duration of symptoms before presentation in 1 group compared with the other). There may also have been important changes over time in terms of disease itself (e.g., increased virulence of micro-organisms in the more recent cohort treated with CTWF) or clinical management (e.g.,

Table 1. Baseline characteristics of patients who underwent pleural drainage via video-assisted thoracoscopic surgery versus chest tube with fibrinolytics

	Group; no. (%)*		
Characteristic	VATS, *n* = 28	CTWF, *n* = 39	*p* value
Time period	2005–2009	2009–2013	—
Age, mean [range], yr	5.2 [2 mo–17 yr]	6.1[6 mo–17 yr]	0.39
Male sex	13 (46)	15 (38)	0.62
Female sex	15 (54)	24 (62)	
Supplemental oxygen on admission to hospital	2 (7)	6 (15)	0.52
Immediate admission to ICU	5 (18)	11 (28)	0.49
Ultrasound findings			
Simple septations	5 (18)	10 (26)	0.59
Complex septations	22 (79)	24 (74)	—
Pleural thickening	5 (18)	5 (13)	—
Ultrasound not performed	3 (11)	2 (5)	—
Necrosis on imaging	6 (21)	4 (10)	0.36

CTWF = chest tube with fibrinolytics; ICU = intensive care unit; VATS = video-assisted thoracoscopic surgery.
*Unless indicated otherwise.

Table 2. Outcomes of patients who underwent pleural drainage via video-assisted thoracoscopic surgery versus chest tube with fibrinolytics

	Group; no. (%)*		
Outcome	VATS, *n* = 28	CTWF, *n* = 39	*p* value
Days to procedure, median [range]	2 [0–10]	1 [0–13]	0.07
Procedure within 48 h of admission	16 (57)	31 (79)	0.06
LOS postprocedure, median [range], d	6 [3–48]	8 [3–45]	0.28
LOS, median [range], d	8 [4–53]	9 [5–46]	0.61
Participants with LOS > 10 d	8 (29)	17 (44)	0.21
Total additional procedures	1 (4)	5 (13)	0.19
Additional chest tube	1 (4)	2 (5)	—
Rescue thoracoscopic surgery	0 (0)	3 (8)	—
Rescue thoracotomy	0 (0)	1 (3)	—
Transfusion for bleeding postprocedure	1 (4)	1 (3)	—
Readmission to hospital	1 (4)	1 (3)	—

CTWF = chest tube with fibrinolytics; LOS = length of stay; VATS = video-assisted thoracoscopic surgery.
*Unless indicated otherwise.

increased recognition of the need for early pleural drainage in more recent years).

Finally, this study relied partly on retrospective data, and as such, we were unable to assess the experiences of patients and their families in a prospective fashion. Randomized controlled trials in this area have similar limitations, with the primary focus being on objective outcomes, such as length of stay, cost and need for additional procedures. Three of the single-centre trials reported the use of pain medication after each procedure, but none assessed patient-reported pain using validated questionnaires or other assessments.[11–13] One of the trials noted decreased duration of narcotic use with VATS compared with CTWF (2.2 d v. 7.6 d, $p = 0.043$),[12] but 2 others did not report any differences.[11,13] Outcomes related to pain were not reported in the recent multicentre RCT.[16]

CONCLUSION

Clinicians, parents, and hospital administrators should bear in mind that the only consistent benefits of CTWF over VATS are related to the procedure itself: CTWF costs less, results in fewer scars and may be performed under conscious sedation rather than general anesthesia. While these advantages are not insignificant, they do not appear to consistently translate into decreased use of pain medication or length of stay in hospital. Furthermore, there appears to be a subset of children with empyema who are at risk for treatment failure with CTWF. In the present study, the frequency of additional procedures following CTWF was 13% compared with 4% with VATS.

The current recommendation from the APSA Clinical Trials and Outcomes Committee is that all patients be offered a trial of CTWF followed by rescue VATS in cases of failure of nonoperative management. A superior approach might be to offer primary VATS to children who are identified as being at high risk for treatment failure with CTWF. Using primary VATS in a targeted fashion would necessitate the development of a prognostic score based on a large sample of children treated with CTWF. This strategy is currently being explored in adults through the development of the "RAPID" score.[18] This tool identifies high-risk adult patients with empyema using the following baseline characteristics: renal impairment (R), age older than 70 years (A), purulent pleural fluid on thoracentesis (P), hospital-acquired infection (I) and poor diet as measured by low albumin (D).

We are in the process of developing a similar score for children by pooling data from 3 children's hospitals from the past decade. In doing so, our hope is to identify baseline characteristics (including clinical, demographic, radiologic and laboratory variables) that predict treatment failure with CTWF. This may lead to the development of a combined treatment strategy where low-risk patients are given a trial of CTWF, whereas those identified as high-risk are treated with primary VATS.

References

1. Kelly MM, Shadman KA, Edmonson MB. Treatment trends and outcomes in US hospital stays of children with empyema. *Pediatr Infect Dis J* 2014;33:431-6.
2. Stiles QR, Lindesmith GG, Tucker BL, et al. Pleural empyema in children. *Ann Thorac Surg* 1970;10:37-44.
3. Kosloske AM, Cartwright KC. The controversial role of decortication in the management of pediatric empyema. *J Thorac Cardiovasc Surg* 1988;96:166-70.
4. Kern JA, Rodgers BM. Thoracoscopy in the management of empyema in children. *J Pediatr Surg* 1993;28:1128-32.
5. Avansino JR, Goldman B, Sawin RS, et al. Primary operative versus nonoperative therapy for pediatric empyema: a meta-analysis. *Pediatrics* 2005;115:1652-9.
6. Islam S, Calkins CM, Goldin AB, et al. APSA Outcomes and Clinical Trials Committee. 2011-2012. The diagnosis and management of empyema in children: a comprehensive review from the APSA Outcomes and Clinical Trials Committee. *J Pediatr Surg* 2012;47:2101-10.
7. Mahant S, Cohen E, Weinstein M, et al. Video-assisted thorascopic surgery vs chest drain with fibrinolytics for the treatment of pleural empyema in children: a systematic review of randomized controlled trials. *Arch Pediatr Adolesc Med* 2010;164:201-3.
8. Walker W, Wheeler R, Legg J. Update on the causes, investigation and management of empyema in childhood. *Arch Dis Child* 2011;96:482-8.
9. Shah SS, Hall M, Newland JG, et al. Comparative effectiveness of pleural drainage procedures for the treatment of complicated pneumonia in childhood. *J Hosp Med* 2011;6:256-63.
10. Sonnappa S, Cohen G, Owens CM, et al. Comparison of urokinase and video-assisted thoracoscopic surgery for treatment of childhood empyema. *Am J Respir Crit Care Med* 2006;174:221-7.
11. St Peter SD, Tsao K, Spilde TL, et al. Thoracoscopic decortication vs tube thoracostomy with fibrinolysis for empyema in children: a prospective, randomized trial. *J Pediatr Surg* 2009;44:106-11.
12. Kurt BA, Winterhalter KM, Connors RH, et al. Therapy of parapneumonic effusions in children: video-assisted thoracoscopic surgery versus conventional thoracostomy drainage. *Pediatrics* 2006;118:e547.
13. Cobanoglu U, Sayir F, Bilici S, et al. Comparison of the methods of fibrinolysis by tube thoracostomy and thoracoscopic decortication in children with stage II and III empyema: a prospective randomized study. *Pediatr Rep* 2011;3:e29.
14. Cohen E, Weinstein M, Fisman DN. Cost-effectiveness of competing strategies for the treatment of pediatric empyema. *Pediatrics* 2008;121:e1250-7.
15. Gasior AC, Knott EM, Sharp SW, et al. Experience with an evidence-based protocol using fibrinolysis as first line treatment for empyema in children. *J Pediatr Surg* 2013;48:1312-5.
16. Marhuenda C, Barceló C, Fuentes I, et al. Urokinase versus VATS for treatment of empyema: a randomized multicenter clinical trial. *Pediatrics* 2014;134:e1301-7.
17. The American Thoracic Society Subcommittee on Surgery. Management of nontuberculous empyema. *Am Rev Respir Dis* 1962;85:935-6.
18. Rahman NM, Kahan BC, Miller RF, et al. A clinical score (RAPID) to identify those at risk for poor outcome at presentation in patients with pleural infection. *Chest* 2014;145:848-55.