

Comparative Effectiveness of Pleural Drainage Procedures for the Treatment of Complicated Pneumonia in Childhood

Samir S. Shah, MD, MSCE¹
 Matthew Hall, PhD²
 Jason G. Newland, MD³
 Thomas V. Brogan, MD⁴
 Reid W. D. Farris, MD⁴
 Derek J. Williams, MD, MPH⁵
 Gitte Larsen, MD, MPH⁶
 Bryan R. Fine, MD, MPH⁷
 James E. Levin, MD, PhD⁸
 Jeffrey S. Wagener, MD⁹
 Patrick H. Conway, MD, MSCE¹⁰
 Angela L. Myers, MD, MPH³

¹ Division of Infectious Diseases, The Children's Hospital of Philadelphia and the Departments of Pediatrics and Biostatistics and Epidemiology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania.

² Child Health Corporation of America, Shawnee Mission, Kansas.

³ Section of Infectious Diseases, Children's Mercy Hospital and Clinics, University of Missouri-Kansas City, Kansas City, Missouri.

⁴ Division of Critical Care, Seattle Children's Hospital and the Department of Pediatrics, University of Washington School of Medicine, Seattle, Washington.

⁵ Division of Pediatric Hospital Medicine, Vanderbilt University School of Medicine and the Monroe Carell, Jr. Children's Hospital at Vanderbilt, Nashville, Tennessee.

⁶ Division of Pediatric Critical Care, Primary Children's Medical Center, and the Department of Pediatrics, University of Utah, Salt Lake City, Utah.

⁷ Division of Pediatric Hospital Medicine, Children's Hospital of The King's Daughters and the Department of Pediatrics, Eastern Virginia Medical School, Norfolk, Virginia.

⁸ Department of Pediatrics, Children's Hospital of Pittsburgh of UPMC, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania.

⁹ Section of Pulmonary Medicine, Department of Pediatrics, University of Colorado School of Medicine and The Children's Hospital, Aurora, Colorado.

¹⁰ Division of General Pediatrics, Hospital Medicine and Anderson Center for Health Systems Excellence Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio.

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OBJECTIVE: To determine the comparative effectiveness of common pleural drainage procedures for treatment of pneumonia complicated by parapneumonic effusion (ie, complicated pneumonia).

DESIGN: Multicenter retrospective cohort study.

SETTING: Forty children's hospitals contributing data to the Pediatric Health Information System.

PARTICIPANTS: Children with complicated pneumonia requiring pleural drainage.

MAIN EXPOSURES: Initial drainage procedures were categorized as chest tube without fibrinolysis, chest tube with fibrinolysis, video-assisted thoracoscopic surgery (VATS), and thoracotomy.

MAIN OUTCOME MEASURES: Length of stay (LOS), additional drainage procedures, readmission within 14 days of discharge, and hospital costs.

RESULTS: Initial procedures among 3500 patients included chest tube without fibrinolysis (n = 1762), chest tube with fibrinolysis (n = 623), VATS (n = 408), and thoracotomy (n = 797). Median age was 4.1 years. Overall, 716 (20.5%) patients received an additional drainage procedure (range, 6.8–44.8% across individual hospitals). The median LOS was 10 days (range, 7–14 days across individual hospitals). The median readmission rate was 3.8% (range, 0.8%–33.3%). In multivariable analysis, differences in LOS by initial procedure type were not significant. Patients undergoing initial chest tube placement with or without fibrinolysis were more likely to require additional drainage procedures. However, initial chest tube without fibrinolysis was the least costly strategy.

CONCLUSION: There is variability in the treatment and outcomes of children with complicated pneumonia. Outcomes were similar in patients undergoing initial chest tube placement with or without fibrinolysis. Those undergoing VATS received fewer additional drainage procedures but had no differences in LOS compared with other strategies. *Journal of Hospital Medicine* 2011;6:256–263. © 2011 Society of Hospital Medicine

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Additional Supporting Information may be found in the online version of this article.

Community-acquired pneumonia, the most common serious bacterial infection in childhood, may be complicated by parapneumonic effusion (ie, complicated pneumonia).¹ Children with complicated pneumonia require prolonged hospitalization and frequently undergo multiple pleural fluid drainage procedures.² Additionally, the incidence of complicated pneumonia has increased,^{3–7} making the need to define appropriate therapy even more pressing. Defining appropriate therapy is challenging for the individual physician as a result of inconsistent and insufficient evidence, and wide variation in treatment practices.^{2,8}

Historically, thoracotomy was performed only if initial chest tube placement did not lead to clinical improvement.^{9,10} Several authors, noting the rapid resolution of symptoms in children undergoing earlier thoracotomy, advocated for the use of thoracotomy as initial therapy rather than as a procedure of last resort.^{11–4} The advent of less invasive techniques such as video-assisted thoracoscopic surgery (VATS) has served as an additional impetus to consider surgical drainage as the initial treatment strategy.^{15–18} Few well-designed studies have examined the relative efficacy of these interventions.^{2,19–22} Published randomized trials were single center, enrolled few patients, and arrived at different conclusions.^{19,21,22} In addition, these trials did not examine other important outcomes such as requirement for additional pleural fluid drainage procedures and hospital readmission. Two large retrospective multicenter studies found modest reductions in length of stay (LOS) and substantial decreases in the requirement for additional pleural fluid drainage procedures in children undergoing initial VATS compared with initial chest tube placement.^{2,20} However, Shah et al² included relatively few patients undergoing VATS. Li et al²⁰ combined patients undergoing initial thoracentesis, initial chest tube placement, late pleural fluid drainage (by any method), and no pleural fluid drainage into a single “non-operative management” category, precluding conclusions about the relative benefits of chest tube placement compared with VATS. Neither study^{2,20} examined the role of chemical fibrinolysis, a therapy which has been associated with outcomes comparable to VATS in two small randomized trials.^{21,22}

The objectives of this multicenter study were to describe the variation in the initial management strategy along with associated outcomes of complicated pneumonia in childhood and to determine the comparative effectiveness of different pleural fluid drainage procedures.

Methods

Data Source

The Pediatric Health Information System (PHIS), which contains resource utilization data from 40 freestanding children's hospitals, provided data for this multicenter retrospective cohort study. Participating hospitals are located in noncompeting markets of 27 states plus the District of Columbia. The PHIS database includes patient demographics,

diagnoses, and procedures as well as data for all drugs, radiologic studies, laboratory tests, and supplies charged to each patient. Data are de-identified, however encrypted medical record numbers allow for tracking individual patients across admissions. The Child Health Corporation of America (Shawnee Mission, KS) and participating hospitals jointly assure data quality and reliability as described previously.^{23,24} The Children's Hospital of Philadelphia Institutional Review Board reviewed and approved this study.

Patients

Children ≤ 18 years of age receiving a pleural drainage procedure for complicated pneumonia were eligible if they were discharged from participating hospitals between January 1, 2004 and June 30, 2009. Study participants met the following criteria: 1) discharge diagnosis of pneumonia (International Classification of Diseases, 9th revision [ICD-9] discharge diagnosis codes 480.x-483.x, 485.x-487.x), 2) discharge diagnosis of pleural effusion (ICD-9 codes 510.0, 510.9, 511.0, 511.1, or 511.9), and 3) billing charge for antibiotics on the first day of hospitalization. Additionally, the primary discharge diagnosis had to be either pneumonia or pleural effusion. Patients were excluded if they did not undergo pleural fluid drainage or if their initial pleural fluid drainage procedure was thoracentesis.

Study Definitions

Pleural drainage procedures were identified using ICD-9 procedure codes for thoracentesis (34.91), chest tube placement (34.04), VATS (34.21), and thoracotomy (34.02 or 34.09). Fibrinolysis was defined as receipt of urokinase, streptokinase, or alteplase within two days of initial chest tube placement.

Acute conditions or complications included influenza (487, 487.0, 487.1, 487.8, 488, or V04.81) and hemolytic-uremic syndrome (283.11). Chronic comorbid conditions (CCCs) (eg, malignancy) were identified using a previously reported classification scheme.²⁵ Billing data were used to classify receipt of mechanical ventilation and medications on the first day of hospitalization.

Measured Outcomes

The primary outcomes were hospital LOS (both overall and post-initial procedure), requirement for additional pleural drainage procedures, total cost for index hospitalization, all-cause readmission within 14 days after index hospital discharge, and total cost of the episode (accounting for the cost of readmissions).

Measured Exposures

The primary exposure of interest was the initial pleural fluid drainage procedure, classified as chest tube placement without fibrinolysis, chest tube placement with fibrinolysis, VATS, or thoracotomy.

Statistical Analysis

Variables were summarized using frequencies and percentages for categorical variables, and median, interquartile range (IQR), and range for continuous variables. Outcomes by initial pleural drainage procedure were compared using chi-squared tests for categorical variables and Kruskal-Wallis tests for continuous variables.

Multivariable analysis was performed to account for potential confounding by observed baseline variables. For dichotomous outcome variables, modeling consisted of logistic regression using generalized estimating equations to account for hospital clustering. For continuous variables, a mixed model approach was used, treating hospital as a random effect. Log transformation was applied to the right-skewed outcome variables (LOS and cost). Cost outcomes remained skewed following log transformation, thus gamma mixed models were applied.^{26–29} Odds ratios and 95% confidence intervals (CIs) were reported for comparison of dichotomous outcomes and the adjusted means and 95% CIs were reported for continuous outcomes after appropriate back transformation.

Additional analyses addressed the potential impact of confounding by indication inherent in any observational study. First, patients with an underlying CCC were excluded to ensure that our results would be generalizable to otherwise healthy children with community-acquired pneumonia. Second, patients undergoing pleural drainage >2 days after hospitalization were excluded to minimize the effect of residual confounding related to differences in timing of the initial drainage procedure. Third, the analysis was repeated using a generalized propensity score as an additional method to account for confounding by indication for the initial drainage procedure.³⁰ Propensity scores, constructed using a multivariable generalized logit model, included all variables listed in Table 1. The inverse of the propensity score was included as a weight in each multivariable model described previously. Only the primary multivariable analyses are presented as the results of the propensity score analysis were nearly identical to the primary analyses.

Medical records of a randomly selected subset of subjects from 6 hospitals were reviewed to determine the accuracy of our algorithm in identifying patients with complicated pneumonia; these subjects represented $\approx 1\%$ of the study population. For the purposes of medical record review, complicated pneumonia was defined by the following: 1) radiologically-confirmed lung infiltrate; 2) moderate or large pleural effusion; and 3) signs and symptoms of lower respiratory tract infection. Complicated pneumonia was identified in 118 of 120 reviewed subjects for a positive predictive value of 98.3%.

All analyses were clustered by hospital. Analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC). A two-tailed $P < 0.05$ was considered statistically significant.

Results

Patient Characteristics

During the study period, 9,680 subjects had complicated pneumonia. Subjects were excluded if they did not have a pleural drainage procedure ($n = 5798$), or if thoracentesis was the first pleural fluid drainage procedure performed ($n = 382$). The remaining 3500 patients were included. Demographic characteristics are summarized in Table 1. The median patient age was 4.1 years (IQR: 2.1–7.2 years). An underlying CCC was present in 424 (12.1%) patients. There was no association between type of drainage procedure and mechanical ventilation. However, factors associated with more severe systemic illness, such as blood product transfusion, were more common among those undergoing initial chest tube placement with or without fibrinolysis (Table 1).

Initial Pleural Fluid Drainage Procedures

The primary procedures included chest tube without fibrinolysis (47.8%); chest tube with fibrinolysis (17.8%); thoracotomy (22.8%); and VATS (11.7%) (Table 1). The proportion of patients undergoing primary chest tube placement with fibrinolysis increased over time from 14.2% in 2004 to 30.0% in 2009 ($P < 0.001$; chi-squared test for trend). The initial procedure varied by hospital with the greatest proportion of patients undergoing primary chest tube placement without fibrinolysis at 28 (70.0%) hospitals, chest tube placement with fibrinolysis at 5 (12.5%) hospitals, thoracotomy at 5 (12.5%) hospitals, and VATS at 2 (5.0%) hospitals (Figure 1). The median proportion of patients undergoing primary VATS across all hospitals was 11.5% (IQR: 3.9%–26.5%) (Figure 1). The median time to first procedure was 1 day (IQR: 0–3 days).

Outcome Measures

Variation in outcomes occurred across hospitals. Additional pleural drainage procedures were performed in a median of 20.9% of patients with a range of 6.8% to 44.8% (IQR: 14.5%–25.3%) of patients across all hospitals. Median LOS was 10 days with a range of 7–14 days (IQR: 8.5–11 days) and the median LOS following the initial pleural fluid drainage procedure was 8 days with a range of 6 to 13 days (IQR: 7–8 days). Variation in timing of the initial pleural fluid drainage procedure explained 9.6% of the variability in LOS (Spearman rho, 0.31; $P < 0.001$).

Overall, 118 (3.4%) patients were readmitted within 14 days of index discharge; the median readmission rate was 3.8% with a range of 0.8% to 33.3% (IQR: 2.1%–5.8%) across hospitals. The median total cost of the index hospitalization was \$19,574 (IQR: \$13,791–\$31,063). The total cost for the index hospitalization exceeded \$54,215 for 10% of patients and the total cost of the episode exceeded \$55,208 for 10% of patients. Unadjusted outcomes, stratified by primary pleural fluid drainage procedure, are summarized in Table 2.

In multivariable analysis, differences in total LOS and post-procedure LOS were not significant (Table 3). The odds

TABLE 1. Characteristics of Patients With Complicated Pneumonia Requiring Pleural Fluid Drainage, Stratified by Initial Pleural Fluid Drainage Procedure^a

	Overall	Chest Tube Without Fibrinolysis	Chest Tube With Fibrinolysis	Thoracotomy	VATS	P Value
N	3500	1672 (47.8)	623 (17.8)	797 (22.8)	408 (11.7)	
Age						
<1 year	335 (9.6)	176 (10.5)	56 (9.0)	78 (9.8)	25 (6.1)	
1 year	475 (13.6)	238 (14.2)	98 (15.7)	92 (11.5)	47 (11.5)	0.003
2–4 years	1230 (35.1)	548 (32.8)	203 (32.6)	310 (38.9)	169 (41.4)	
5–9 years	897 (25.6)	412 (24.6)	170 (27.3)	199 (25.0)	116 (28.4)	
10–14 years	324 (9.3)	167 (10.0)	61 (9.8)	65 (8.2)	31 (7.6)	
15–18 years	193 (5.5)	106 (6.3)	29 (4.6)	40 (5.0)	18 (4.4)	
>18 years	46 (1.3)	25 (1.5)	6 (0.96)	13 (1.6)	2 (0.5)	
Comorbid Conditions						
Cardiac	69 (2.0)	43 (2.6)	14 (2.3)	12 (1.5)	0 (0.0)	0.006
Malignancy	81 (2.3)	31 (1.9)	18 (2.9)	21 (2.6)	11 (2.7)	0.375
Neurological	138 (3.9)	73 (4.4)	20 (3.2)	34 (4.3)	11 (2.7)	0.313
Any Other Condition	202 (5.8)	96 (5.7)	40 (6.4)	47 (5.9)	19 (4.7)	0.696
Payer						
Government	1240 (35.6)	630 (37.8)	224 (36.0)	259 (32.7)	127 (31.3)	<0.001
Private	1383 (39.7)	607 (36.4)	283 (45.4)	310 (39.2)	183 (45.07)	
Other	864 (24.8)	430 (25.8)	116 (18.6)	222 (28.1)	96 (23.65)	
Race						
Non-Hispanic White	1746 (51.9)	838 (51.6)	358 (59.7)	361 (47.8)	189 (48.7)	<0.001
Non-Hispanic Black	601 (17.9)	318 (19.6)	90 (15.0)	128 (17.0)	65 (16.8)	
Hispanic	588 (17.5)	280 (17.3)	73 (12.2)	155 (20.5)	80 (20.6)	
Asian	117 (3.5)	47 (2.9)	20 (3.3)	37 (4.9)	13 (3.4)	
Other	314 (9.3)	140 (8.6)	59 (9.8)	74 (9.8)	41 (10.6)	
Male Sex	1912 (54.6)	923 (55.2)	336 (53.9)	439 (55.1)	214 (52.5)	0.755
Radiology						
CT, no US	1200 (34.3)	600 (35.9)	184 (29.5)	280 (35.1)	136 (33.3)	<0.001
CT and US	221 (6.3)	84 (5.0)	53 (8.5)	61 (7.7)	23 (5.6)	
US, no CT	799 (22.8)	324 (19.4)	178 (28.6)	200 (25.1)	97 (23.8)	
No US, no CT	1280 (36.6)	664 (39.7)	208 (33.4)	256 (32.1)	152 (37.3)	
Empiric Antibiotic Regimen						
Cephalosporins alone	448 (12.8)	181 (10.83)	126 (20.2)	73 (9.2)	68 (16.7)	<0.001
Cephalosporin and clindamycin	797 (22.8)	359 (21.5)	145 (23.3)	184 (23.1)	109 (26.7)	
Other antibiotic combination	167 (4.8)	82 (4.9)	30 (4.8)	38 (4.8)	17 (4.2)	
Cephalosporin and vancomycin	2088 (59.7)	1050 (62.8)	322 (51.7)	502 (63.0)	214 (52.5)	
Mechanical ventilation	494 (14.1)	251 (15.0)	75 (12.0)	114 (14.3)	54 (13.2)	0.307
Corticosteroids	520 (14.9)	291 (17.4)	72 (11.6)	114 (14.3)	43 (10.5)	<0.001
Blood product transfusions ^b	761 (21.7)	387 (23.2)	145 (23.3)	161 (20.2)	68 (16.7)	0.018
Vasoactive infusions ^c	381 (10.9)	223 (13.3)	63 (10.1)	72 (9.0)	23 (5.6)	<0.001
Admission to intensive care	1397 (39.9)	731 (43.7)	234 (37.6)	296 (37.1)	136 (33.3)	<0.001
Extracorporeal membranous oxygenation	18 (0.5)	13 (0.8)	2 (0.3)	3 (0.4)	0 (0.0)	0.163
Hemolytic-uremic syndrome	31 (0.9)	15 (0.9)	6 (1.0)	7 (0.9)	3 (0.7)	0.985
Influenza	108 (3.1)	53 (3.2)	27 (4.3)	23 (2.9)	5 (1.2)	0.044
Arterial blood gas measurements	0 (0,1)	0 (0, 2)	0 (0,1)	0 (0, 1)	0 (0, 1)	<0.001
Days to first procedure	1 (0, 3)	1 (0, 2)	1 (1, 3)	1 (1, 3)	1 (1, 3)	<0.001

Abbreviations: CT, computed tomography; US, ultrasound; VATS, video-assisted thoracoscopic surgery.

^aValues listed as number (percent) or median (interquartile range).

^bBlood product transfusions included administration of packed red blood cells, cryoprecipitate, fresh frozen plasma, or platelets.

^cVasoactive infusions included dobutamine, dopamine, epinephrine, norepinephrine, vasopressin, and milrinone.

of additional drainage procedures were higher for all drainage procedures compared with initial VATS (Table 3). Patients undergoing initial chest tube placement with fibrinolysis were less likely to require readmission compared with patients undergoing initial VATS (Table 3). The total cost for the episode of illness (including the cost of readmis-

sion) was significantly less for those undergoing primary chest tube placement without fibrinolysis compared with primary VATS. The results of subanalyses excluding patients with an underlying CCC (Supporting Appendix online, Table 4) and restricting the cohort to patients undergoing pleural drainage within two days of admission (Supporting

Appendix online, Table 5) were similar to the results of our primary analysis with one exception; in the latter subanalysis, children undergoing initial chest tube placement without fibrinolysis were also less likely to require readmission compared with patients undergoing initial VATS.

Discussion

This multicenter study is the largest to evaluate the management of children hospitalized with complicated pneumonia. We found considerable variation in initial management and outcomes across hospitals. Differences in timing of the initial drainage procedure explained only a small amount of the variability in outcomes. Children undergoing initial VATS less commonly required additional drainage procedures while children undergoing initial chest tube placement with fibrinolysis less commonly required readmission. Differences in total and post-procedure LOS were not statis-

tically significant. Differences in cost, while statistically significant, were of marginal relevance.

Previous studies have also shown significant variation in treatment and outcomes of children with complicated pneumonia across hospitals.^{2,8} Our study provides data from additional hospitals, includes a substantially larger number of patients undergoing initial VATS, distinguishes between fibrinolysis recipients and nonrecipients, and is the first to compare outcomes between four different initial drainage strategies. The creation of national consensus guidelines might reduce variability in initial management strategies, although the variability in outcomes across hospitals in the current study could not be explained simply by differences in the type or timing of the initial drainage procedure. Thus, future studies examining hospital-level factors may play an important role in improving quality of care for children with complicated pneumonia.

Patients with initial thoracotomy or chest tube placement with or without fibrinolysis more commonly received additional drainage procedures than patients with initial VATS. This difference remained when patients with CCCs were excluded from the analysis and when the analysis was limited to patients undergoing pleural fluid drainage within 2 days of hospitalization. Several small, randomized trials demonstrated conflicting results when comparing initial chest tube placement with fibrinolysis and VATS. St. Peter et al²² reported that 3 (17%) of 18 patients undergoing initial chest tube placement with fibrinolysis and none of the 18 patients undergoing initial VATS received additional pleural drainage procedures. Sonnappa et al²¹ found no differences between the two groups. Kurt et al¹⁹ did not state the proportion of patients receiving additional procedures. However, the mean number of drainage procedures was 2.25 among the 8 patients undergoing initial chest tube placement while none of the 10 patients with VATS received additional drainage.¹⁹

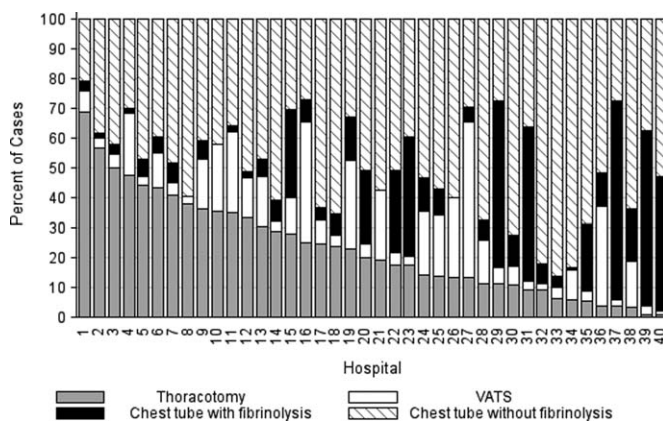


FIGURE 1. Distribution of initial procedure type by hospital. The y-axis shows the percentage of patients undergoing specific pleural fluid drainage procedures. Each number on the x-axis represents data from one hospital.

TABLE 2. Unadjusted Outcomes of Patients With Complicated Pneumonia Undergoing Pleural Fluid Drainage, Stratified by Initial Pleural Fluid Drainage Procedure^a

	Overall	Chest Tube Without Fibrinolysis	Chest Tube With Fibrinolysis	Thoracotomy	VATS	P Value ^b
Additional Procedure	716 (20.5)	331 (19.8)	144 (23.1)	197 (24.7)	44 (10.8)	<0.001
Readmission within 14 days	118 (3.4)	54 (3.3)	13 (2.1)	32 (4.0)	19 (4.7)	0.096
Total LOS (days)	10 (7, 14)	10 (7, 14)	9 (7, 13)	10 (7, 14)	9 (7, 12)	<.001
Post-initial Procedure LOS (days)	8 (5, 12)	8 (6, 12)	7 (5, 10)	8 (5, 12)	7 (5, 10)	<0.001
Total Cost, Index Hospitalization (\$) ^c	19319 (13358, 30955)	19951 (13576, 32018) ^c	19565 (13209, 32778) ^d	20352 (14351, 31343)	17918 (13531, 25166)	0.016
Total Cost, Episode of Illness (\$) ^e	19831 (13927, 31749)	20151 (13764, 32653)	19593 (13210, 32861)	20573 (14419, 31753)	18344 (13835, 25462)	0.029

Abbreviations: VATS, video-assisted thoracoscopic surgery.

^a Values listed as number (percent) or median (interquartile range); *P* < 0.05 considered statistically significant

^b Chi-squared test for categorical variables and Kruskal-Wallis test for continuous variables

^c *P* = 0.008 compared with VATS (pairwise comparison)

^d *P* = 0.057 compared with VATS (pairwise comparison)

^e Hospital charges were adjusted for hospital location using the Centers for Medicare and Medicaid price/wage index and converted to costs using hospital-level cost-to-charge ratios.

TABLE 3. Multivariable Analysis of The Association Between Initial Pleural Fluid Drainage Procedure and Outcomes for Children With Complicated Pneumonia

	Adjusted OR (95% CI) ^a	P Value
Additional pleural drainage procedure		
Chest tube without fibrinolysis	1.82 (1.10–3.00)	.019
Chest tube with fibrinolysis	2.31 (1.44–3.72)	<0.001
Thoracotomy	2.59 (1.62–4.14)	<0.001
VATS	Reference	–
Readmission within 14 days		
Chest tube without fibrinolysis	0.61 (0.36–1.05)	.077
Chest tube with fibrinolysis	0.45 (0.23–0.86)	.015
Thoracotomy	0.85 (0.52–1.39)	.521
VATS	Reference	–
	Adjusted Mean (95% CI) ^a	P Value
Total LOS (days)		
Chest tube without fibrinolysis	8.0 (7.8–8.2)	.339
Chest tube with fibrinolysis	8.1 (7.9–8.3)	.812
Thoracotomy	8.1 (7.9–8.3)	.632
VATS	8.1 (7.9–8.3)	Ref
Post-initial procedure LOS (days)		
Chest tube without fibrinolysis	7.3 (7.0–7.5)	.512
Chest tube with fibrinolysis	7.5 (7.2–7.8)	.239
Thoracotomy	7.3 (7.0–7.6)	.841
VATS	7.3 (7.1–7.6)	Reference
Total cost, index hospitalization (\$)		
Chest tube without fibrinolysis	22928 (22000–23895)	.012
Chest tube with fibrinolysis	23621 (22631–24655)	.657
Thoracotomy	23386 (22419–24395)	.262
VATS	23820 (22808–24878)	Reference
Total cost, episode of illness (\$)		
Chest tube without fibrinolysis	23218 (22278–24199)	.004
Chest tube with fibrinolysis	23749 (22752–24790)	.253
Thoracotomy	23673 (22693–24696)	.131
VATS	24280 (23244–25362)	Reference

Abbreviations: CI, confidence interval; LOS, length of stay; OR, odds ratio; VATS, video-assisted thoracoscopic surgery.

^aAll models adjusted for age, sex, race, month of admission, primary payer, radiologic imaging performed, empiric antibiotic therapy, concurrent diagnosis of influenza or hemolytic uremic syndrome, presence of underlying chronic comorbid conditions, timing of primary pleural fluid drainage procedure, and receipt of corticosteroids and requirement for mechanical ventilation, blood product transfusions, vasoactive infusions, intensive care unit hospitalization, extracorporeal membranous oxygenation, and arterial blood gas measurements within the first two days of hospitalization and clustered on hospital.

Thoracotomy is often perceived as a “definitive” procedure for treatment of complicated pneumonia. However, several possibilities exist to explain why additional procedures were performed less frequently in patients undergoing initial VATS compared with initial thoracotomy. The limited visual field in thoracotomy may lead to greater residual disease post-operatively in those receiving thoracotomy compared with VATS.³¹ Additionally, thoracotomy substantially disrupts the integrity of the chest wall and is consequently associated with complications such as bleeding and air leak into the pleural cavity more often than VATS.^{31,32} It is thus possible that some of the additional procedures in patients receiving initial thoracotomy were necessary for manage-

ment of thoracotomy-associated complications rather than for failure of the initial drainage procedure.

Similar to the randomized trials by Sonnappa et al²¹ and St. Peter et al,²² differences in the overall and post-procedure LOS were not significant among patients undergoing initial VATS compared with initial chest tube placement with fibrinolysis. However, chest tube placement *without* fibrinolysis did not result in significant differences in LOS compared with initial VATS. In the only pediatric randomized trial, the 29 intrapleural urokinase recipients had a 2 day shorter LOS compared with the 29 intrapleural saline recipients.³³ Several small, randomized controlled trials of adults with complicated pneumonia reported improved pleural fluid drainage among intrapleural fibrinolysis recipients compared with non-recipients.^{34–36} However, a large multicenter randomized trial in adults found no differences in mortality, requirement for surgical drainage, or LOS between intrapleural streptokinase and placebo recipients.³⁷ Subsequent meta-analyses of randomized trials in adults also demonstrated no benefit to fibrinolysis.^{38,39} In the context of the increasing use of intrapleural fibrinolysis in children with complicated pneumonia, our results highlight the need for a large, multicenter randomized controlled trial to determine whether chest tube with fibrinolysis is superior to chest tube alone.

Two small randomized trials^{21,22} and a decision analysis⁴⁰ identified chest tube with fibrinolysis as the most economical approach to children with complicated pneumonia. However, the costs did not differ significantly between patients undergoing initial VATS or initial chest tube placement with fibrinolysis in our study. The least costly approach was initial chest tube placement without fibrinolysis. Unlike the randomized controlled trials, we considered costs associated with readmissions in determining the total costs. Shah et al⁴¹ found no difference in total charges for patients undergoing initial VATS compared with initial chest tube placement; however, patients undergoing initial VATS were concentrated in a few centers, making it difficult to determine the relative importance of procedural and hospital factors.

This multicenter observational study has several limitations. First, discharge diagnosis coding may be unreliable for specific diseases. However, our rigorous definition of complicated pneumonia, supported by the high positive predictive value as verified by medical record review, minimizes the likelihood of misclassification.

Second, unmeasured confounding or residual confounding by indication for the method of pleural drainage may occur, potentially influencing our results in two disparate ways. If patients with more severe systemic illness were too unstable for operative interventions, then our results would be biased towards worse outcomes for children undergoing initial chest tube placement. We adjusted for several variables associated with a greater systemic severity of illness, including intensive care unit admission, making this possibility less likely. We also could not account for some factors associated with more severe local disease such as the size

and character of the effusion. We suspect that patients with more extensive local disease (ie, loculated effusions) would have worse outcomes than other patients, regardless of initial procedure, and that these patients would also be more likely to undergo primary surgical drainage. Thus, this study may have underestimated the benefit of initial surgical drainage (eg, VATS) compared with nonsurgical drainage (ie, chest tube placement).

Third, misclassification of the method of initial pleural drainage may have occurred. Patients transferred from another institution following chest tube placement could either be classified as not receiving pleural drainage and thus excluded from the study or classified as having initial VATS or thoracotomy if the reason for transfer was chest tube treatment failure. Additionally, we could not distinguish routine use of fibrinolysis from fibrinolysis to maintain chest tube patency. Whether such misclassification would falsely minimize or maximize differences in outcomes between the various groups remains uncertain. Fourth, because this study only included tertiary care children's hospitals, these data are not generalizable to community settings. VATS requires specialized surgical training that may be unavailable in some areas. Finally, this study demonstrates the relative efficacy of various pleural fluid drainage procedures on short-term clinical outcomes and resource utilization. However, long-term functional outcomes should be measured in future prospective studies.

Conclusions

In conclusion, emphasis on evidence driven treatment to optimize care has led to an increasing examination of unwarranted practice variation.⁴² The lack of evidence for best practice makes it difficult to define "unwarranted" variation in the treatment of complicated pneumonia. Our study demonstrates the large variability in practice and raises additional questions regarding the optimal drainage strategies. Published randomized trials have focused on comparisons between chest tube placement with fibrinolysis and VATS. However, our data suggest that future randomized trials should include chest tube placement without fibrinolysis as a treatment strategy. In determining the current best treatment for patients with complicated pneumonia, a clinician must weigh the impact of needing an additional procedure in approximately one-quarter of patients undergoing initial chest tube placement (with or without fibrinolysis) with the risks of general anesthesia and readmission in patients undergoing initial VATS.

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Address for correspondence and reprint requests:

Dr. Samir S. Shah, MD, MSCE, Division of Infectious Diseases, Room 1526 (North Campus), The Children's Hospital of Philadelphia, 34th Street and Civic Center Boulevard, Philadelphia,

PA, 19104; Telephone: 215-590-4378; Fax: 267-426-0380; E-mail: shahs@email.chop.edu Received 15 September 2010; revision received 4 October 2010; accepted 18 October 2010.

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