



## RESEARCH ARTICLE

## Efficacy of Initial Large-Volume Thoracentesis for Malignant Pleural Effusions

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### Abstract

**Introduction:** Large malignant pleural effusions (MPE) are common and can cause respiratory distress. Large-volume thoracentesis (LVT) is the most readily available initial procedure, but its efficacy for large MPE with acute respiratory symptoms is unknown.

**Methods:** We reviewed LVT for MPE causing  $\geq 50\%$  opacification of the hemithorax who presented with acute respiratory symptoms. LVT was defined as draining  $\geq 1.5$  liters (L). We catalogued volume removed and percent opacification of the hemithorax after LVT in order to correlate with outcomes, including need for repeat thoracentesis and definitive pleural procedures, i.e., Tunneled pleural catheters (TPCs), chest tubes, or pleurodesis.

**Results:** 76 LVT were identified. The most common cause was lung cancer (35.5%). Median opacification of the hemithorax prior to LVT was 66% (IQR 55%-88%), and median volume drained was 1.6 L (IQR 1.5-2.0). Only 15.8% had  $\geq 50\%$  decrease in opacification, and 10.5% had complete drainage. The majority of patients (56.6%) required repeat thoracentesis. Definitive pleural procedures were performed in 46.7%. No characteristics were associated with repeat thoracentesis, but lung cancer (OR 6.74, 95CI 1.93-23.46,  $p = 0.003$ ) and requiring  $\geq 2$  repeat thoracentesis (OR 9.88, 95CI 2.10-46.49,  $p = 0.004$ ) were associated with definitive pleural procedures. TPC was the most common definitive procedure (62.9% of definitive procedures; 46.1% of all cases). No variables were associated with length-of-stay or adverse outcomes.

**Conclusion:** LVT is not effective for definitive pleural drainage for large MPE. LVT may avoid respiratory failure, but most patients required repeat thoracentesis, and almost half required definitive pleural procedures.

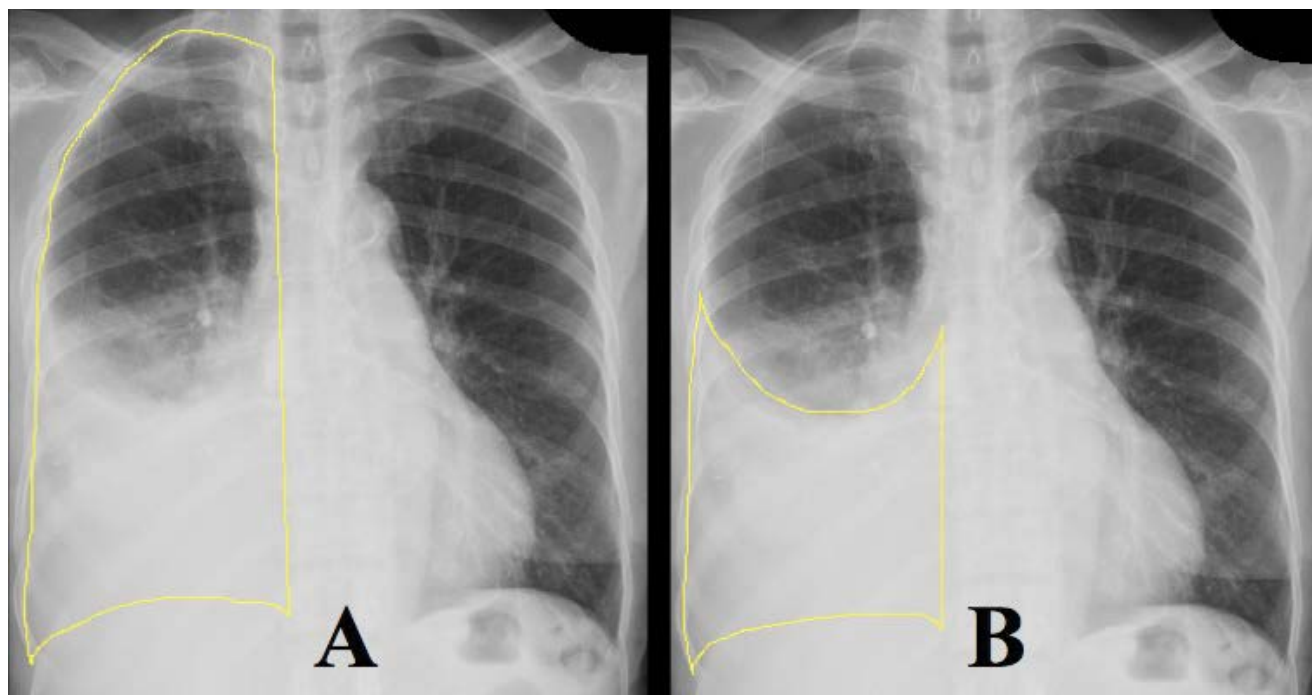
### Keywords

Large-volume thoracentesis, Malignant pleural effusion, Re-expansion pulmonary edema, Pleural drainage, Bedside procedures

### Introduction

Management of malignant pleural effusions (MPEs) is a common challenge to acute care providers in various settings [1]. Uncertainty exists regarding the most appropriate and effective initial therapy [2-4]. MPEs often recur, requiring frequent thoracentesis-prompting providers to consider more definitive and invasive pleural interventions [4-6]. Guidelines recommend a multi-disciplinary approach incorporating clinical, patient and logistical factors in decision-making for general management [1,3,7].

MPE volume and symptoms vary, with some progressing to acute respiratory distress or failure. In such cases, providers must urgently select appropriate initial pleural interventions to palliate symptoms, while simultaneously considering optimal long-term drainage. Tra-



**Figure 1:** Quantifying Opacification of Hemithorax. Image J software was used to determine the percentage of the hemithorax that was opacified by pleural effusion. Panel A demonstrates the first measurement of the entire hemithorax; Panel B demonstrates the second measurement of the effusion. Percent opacification was calculated by dividing the second measurement by the first.

ditional workflows are based on limited available data to guide decision making for the initial management of large effusions, with the majority of data centered on smaller volume thoracentesis (< 1.5 L). We reviewed patients with large MPEs who were admitted with acute respiratory symptoms to determine the long-term efficacy of an initial Large-volume thoracentesis (LVT).

## Materials and Methods

We reviewed all LVT at an urban safety-net tertiary-care teaching hospital from 2008-2019. LVT was defined as drainage of  $\geq 1.5$  L of pleural fluid. Patients included met the following criteria: 1) > 18 years of age; 2) Presence of respiratory symptoms (dyspnea, hypoxia, new/increased oxygen use) and 3) Large MPE (defined as  $\geq 50\%$  opacification on chest X-ray (CXR)). ImageJ® software was used to calculate the percent of hemithorax opacification on CXR pre- and post-LVT (Figure 1). MPEs without pre- and post-procedural chest imaging were excluded. All effusions were drained under sonographic guidance at bedside.

Complete drainage of an effusion was defined as < 10% residual opacification after LVT. Pneumothorax ex vacuo was defined as dependent or basilar air in the pleural space after LVT accompanied by thickening of the visceral pleura. We collected the number of pleural procedures required after an initial LVT, including repeat thoracentesis and definitive pleural procedures-defined as chest tube placement, pleurodesis or Tunneled pleural catheter (TPC). Patient demographics, comorbidities and outcomes were reviewed. Hospital length-of-stay, and a composite outcome of adverse events was stud-

ied. The composite outcome of adverse events included any of the following: ICU admission, shock requiring vasopressors, non-invasive ventilation, mechanical ventilation or all-cause hospital mortality.

Statistical analyses were performed with Stata 11.2 (College Station, TX). Not all continuous data were normally distributed, and so median values with Interquartile ranges (IQR) were calculated. Non-parametric analyses were performed with Wilcoxon rank sum and Spearman correlation testing for categorical and continuous variables, respectively. Regression modeling was used to identify characteristics associated with the need for repeat thoracentesis or definitive pleural procedures; Univariate were included in multivariate analysis if univariate  $p < 0.1$ .

## Results

We identified 76 LVT that met inclusion criteria (Table 1). Median age was 55 (IQR 47-64) years. The most common etiologies of MPE were lung (35.5%), lymphoma (18.4%), and gastrointestinal (10.5%).

Median known duration of the MPE was 4 (IQR 2-8) weeks. Median opacification of the hemithorax prior to LVT was 66% (IQR 55%-88%).

A median volume of 1.6 L (IQR 1.5-2.0) was drained, corresponding to a 30% (IQR 18%-45%) decrease in opacification. Only 15.8% had  $\geq 50\%$  decrease in opacification, with 10.5% resulting incomplete drainage. The majority of patients (55.2%) required at least one repeat thoracentesis after initial LVT (IQR 1-3). There was a 9.2% incidence of pneumothorax ex vacuo. All-cause

**Table 1:** Patient & effusion characteristics.

Characteristic	N = 76 (%)
<b>Patient</b>	
Age (years), median (IQR)	55 (47-64)
Female	22 (28.9)
Smoking history	45 (59.2)
Anemia (Hgb < 10 g/dL)	18 (23.7)
Atrial fibrillation	8 (10.5)
Chronic renal disease	7 (9.2)
Cirrhosis	2 (2.6)
Coronary disease	7 (9.2)
Diabetes	13 (17.1)
Heart failure	7 (9.2)
Hypertension	37 (48.7)
Obesity (BMI ≥ 30)	18 (23.7)
<b>Effusion</b>	
<b>Etiology</b>	
Lung cancer	27 (35.5)
Lymphoma	14 (18.4)
Gastrointestinal	8 (10.5)
Breast	3 (3.9)
Other	24 (31.6)
Massive	24 (31.6)
Right-sided	50 (65.8)
Initial diagnosis	24 (31.6)
Duration (weeks)	4 (2-8)
Duration > 4 weeks	50 (65.8)
Volume drained (L), median (IQR)	1.6 (1.5-2.0)

**Abbreviations:** Hgb: Hemoglobin; L: Liters; BMI: Body Mass Index; IQR: Interquartile Range

in-hospital mortality was 5.3%, and the composite adverse outcome occurred in 7.9% of cases (Table 2).

Definitive pleural procedures were performed in 46.7% of MPEs, and the median time to such intervention was 13 (IQR 6-35) days. Patients who eventually required definitive pleural procedures received more repeat thoracentesis after the initial LVT (median 1, IQR 0-1) as compared to patients who did not have ultimately undergo a definitive procedure (median 0, IQR 0-1,  $p = 0.004$ ). In multivariate analysis, lung cancer (OR 6.74, 95% CI 1.93-23.46,  $p = 0.003$ ) and requiring  $\geq 2$  repeat thoracentesis (OR 9.88, 95% CI 2.10-46.49,  $p = 0.004$ ) were associated with need for definitive pleural procedures. TPC was the most common definitive pleural procedure (62.9%), followed by chest tube (37.1%) and pleurodesis (8.6%).

## Discussion

This study is the first to consider the efficacy of initial LVT for large MPE in the setting of acute respiratory symptoms. After LVT, only a minority of patients had significant pleural drainage, with few attaining complete

**Table 2:** Patient & effusion outcomes.

Outcomes	N = 76 (%)
<b>Radiographic</b>	
Pre-procedure opacification (%), median (IQR)	66 (55-88)
Post-procedure opacification (%), median (IQR)	35 (21-54)
Percent drainage (%), median (IQR)	30 (18-45)
Drained > 50%	12 (15.8)
Complete drainage	8 (10.5)
<i>Pneumothorax ex vacuo</i>	7 (9.2)
<b>Overall</b>	
Repeat thoracentesis needed	42 (55.2)
Definitive intervention	
Chest tube	10 (27)
TPC	20 (54)
Pleurodesis	7 (19)
<b>Number of repeat thoracentesis</b>	
0	34 (44.7)
1	23 (30.3)
2	8 (10.5)
3	6 (7.9)
$\geq 4$	5 (6.6)
Hospital length-of-stay (days), median (IQR)	5 (4-12)
Time to definitive intervention (days), median (IQR)	13 (6-35)
Composite adverse outcome	6 (7.9)
Shock	3 (3.9)
ICU admission	4 (5.3)
Non-invasive ventilation	2 (2.6)
Mechanical ventilation	1 (1.3)
Hospital mortality	4 (5.3)

**Abbreviations:** IQR: Interquartile Range; TPC: Tunneled Pleural Catheter; ICU: Intensive Care Unit

drainage. The majority of patients required at least one further thoracentesis, with nearly half needing a more definitive invasive pleural procedure.

All LVT were defined a priori as having drained  $\geq 1.5$  L, but the median total drainage was only 1.6 L. Volume removed was not associated with need for repeat thoracentesis or definitive pleural procedures. We suspect that volume removed was limited by previously established guidance recommending limiting drainage to 1.5 L. We suspect that operators may have limited drainage volume to avoid Re-expansion pulmonary edema (REPE), despite data to suggest its safety [8,9]. Nevertheless, even draining > 50% of the opacified hemithorax in our cohort was not associated with fewer repeat procedures.

While a single initial LVT appears to have been ineffective at accomplishing drainage for large MPE, the incidence of respiratory failure and other adverse out-

comes was low. One goal of managing MPE is to palliate symptoms; therefore, even incomplete drainage may be beneficial. Nearly half of patients underwent definitive pleural drainage within two weeks of presentation. While generally lower risk, repeated procedures in patients with advanced malignancies can decrease quality of life and prolong hospitalization [4,10]. With nearly half of cases requiring a TPC, it could be considered as the initial procedure of choice upon admission for a known or highly suspected MPE with acute respiratory distress, provided infection has been reasonably excluded.

## Conclusion

A single initial LVT for large MPE with acute respiratory symptoms may palliate symptoms but is not often effective at accomplishing definitive pleural drainage. An initial multidisciplinary consideration of the appropriate short and long-term drainage options should be employed in order to reduce the number of procedures and potential complications. Further study might consider prospective clinical and radiographic outcomes of patients with large MPE who receive early tube thoracostomy or TPC placement as the initial intervention.

## Disclosures

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SAP, VEP & SBS developed the study design. VEP, SXC & SS contributed in the data collection. SBS & VEP provided statistical analysis. SAP, VEP, SBS, & SS contributed to the manuscript writing. All authors have seen and approved the final manuscript for submission.

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