



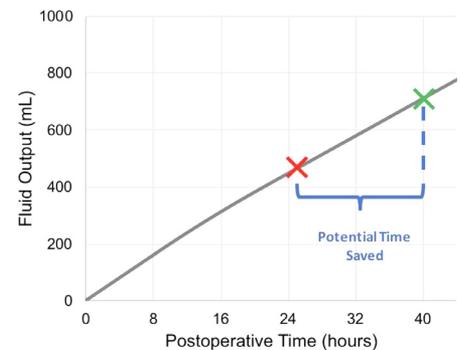
Early Identification of Patients Who Will Meet 24-Hour Fluid Output Threshold for Chest Tube Removal After Lung Resection

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Improving evidence-based chest tube removal may reduce the length of stay following surgery. Presently, most chest tube removal protocols include a fluid output threshold based on a 24-hour observation period. The purpose of this study was to evaluate if, within a 24-hour time period, fluid output measurements at 6, 8, and 12 hours could predict if the total 24-hour fluid output would comply with a predetermined volume threshold considered acceptable for safe chest tube removal. Following lung resection, pleural fluid output data were prospectively recorded by a digital drainage system and analyzed retrospectively. Twenty-four-hour fluid output was calculated from every available 6-, 8-, and 12-hour measurement and compared to set 24-hour output criteria for chest tube removal (ie, 400 mL, 250 mL, and 20% of whole-body lymphatic flow). Performance of interim fluid outputs in predicting whether 24-hour fluid output criteria were satisfied was measured. From 2015 to 2018, 150 patients had digital pleural fluid drainage data suitable for analysis. Performance of interim fluid output data in identifying which patients would satisfy 24-hour output criteria ranged from 85% (95% confidence interval [CI] = 83–86) to 94% (95% CI = 93–94) for specificity, 75% (95% CI = 73–76) to 92% (95% CI = 90–93) for positive predictive value, and 6% (95% CI = 6–7) to 15% (95% CI = 14–17) for false-positive rate. Potential time saved in duration of drainage using interim fluid output data ranged from 10 to 16 hours. Pleural fluid output measured for 6-, 8-, and 12-hour durations can accurately identify patients who will meet 24-hour fluid output threshold for safe chest tube removal.

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Time saved using 6-hour prorated threshold (red X) vs 24-hour threshold criteria (green X).

Central Message

A prorated threshold (red X) based on 6, 8, or 12 hours of pleural fluid output can be used to identify patients who will meet the 24-hour fluid output threshold (green X) for safe chest tube removal.

Perspective Statement

There may be an opportunity to gain clinical efficiency without compromising safety by using shorter fluid drainage periods to determine if chest tubes can be removed following lung surgery. This may in turn help reduce the length of postoperative stay.

Abbreviations: CI, confidence interval; CXR, chest x-ray; FPR, false-positive rate; IQR, interquartile range; PPV, positive predictive value; $T_{\text{fluid threshold}}$, time until 24-hour fluid output volume criteria attainment; VATS, video-assisted thoracoscopic surgery; WBLF, whole-body lymphatic flow

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INTRODUCTION

Intercostal drains remain an unavoidable reality for patients who undergo lung resection. They can be a source of significant discomfort to the patient and ongoing pleural drainage is often a rate-limiting step in discharge from the hospital.^{1,2} It can be a challenge to ensure that chest tubes are not removed prematurely while attempting to minimize the duration of pleural drainage. Even when chest tubes are managed under the supervision of experienced thoracic surgeons using digital drainage devices, inefficiencies can result in unnecessarily prolonged chest tube drainage.³

The cumulative pleural fluid volume output over 24 hours is typically used as a clinical parameter in the management of chest tubes. The goal of our study was to determine whether or not the cumulative pleural fluid output at shorter intervals (ie, 6, 8, and 12 hours) could accurately predict whether or not the fluid output for that given 24-hour period was equal to or less than a prescribed volume threshold considered safe for chest tube removal. We hypothesized that pleural fluid output data measured over durations shorter than 24 hours would safely identify patients who are candidates for chest tube removal based on predetermined 24-hour fluid output criteria.

MATERIALS AND METHODS

Data were collected retrospectively from patients who underwent lung resection surgery between September 2015 and February 2018. Data collection approval was granted from our Institutional Research Ethics Board. Data extracted included demographic information, diagnosis, type of procedure, and recorded digital pleural fluid output data. Exclusion criteria were pneumonectomy, age less than 18 years, or digital data record incomplete or unavailable for analysis. Digital data were not available for every consecutive lung resection performed during the study period for various reasons including the restriction of device use to lobectomy cases, the limited number of devices available for use earlier on in our experience, overwritten digital data, and loss of data during digital device maintenance. The system has a limited data storage capacity of approximately 40 patient-days. The data cannot be retrieved while the device is connected to a patient. It must be manually downloaded from the digital device via USB connection using proprietary software. When the maximum storage capacity has been reached, the device overwrites previously saved data. Chest tubes were managed according to our institutional protocol which uses a pleural fluid output less than or equal to 20% of whole-body lymphatic flow (WBLF) as a safe threshold for chest tube removal.³ There is a wide range of fixed 24-hour fluid output considered safe for chest tube removal (eg, 100–500 mL/24 h).^{1,3–9} Two of these 24-hour fixed thresholds were selected based on review of the literature (400 mL/24 h, 250 mL/24 h).

Digital Data Collection and Preprocessing

Pleural fluid output was prospectively recorded by a digital drainage system (Thopaz, Medela, Baar, Switzerland) at 10-minute intervals during the postoperative period. Due to

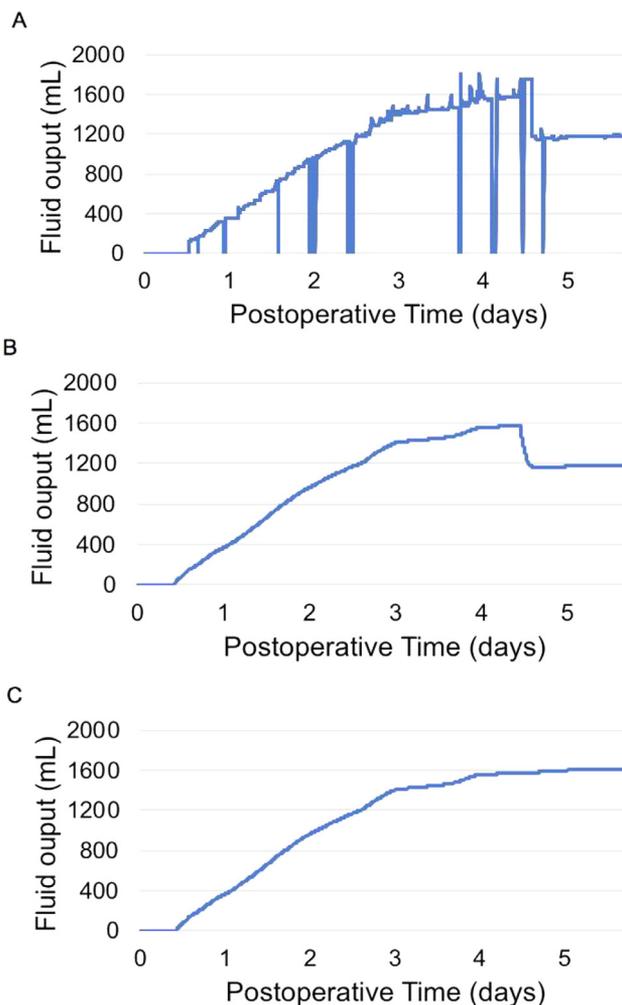


Figure 1. Demonstration of the steps required to process the Thopaz digital drainage data for a single patient. (A) Raw data (pleural fluid output recorded from a digital drainage device), (B) smoothed data using a Locally Weighed Scatterplot Smoothing algorithm, and (C) smoothed data with negative fluid output values removed.

limitations of the sensor apparatus in detecting the amount of fluid in the collection chamber of the digital drainage device, we noted that some recorded 10-minute fluid output values were negative (ie, <0 mL). We addressed this through implementation of a high-pass filter which assigned a value of 0 mL to all recorded fluid outputs that were negative. We also observed that a recorded cumulative fluid output value could sometimes be less than the previously recorded cumulative fluid output. To resolve this issue, the recorded digital data were smoothed using Locally Weighed Scatterplot Smoothing algorithm (LOWESS) as implemented in the R software (Lucent Technologies, New Jersey) with 5 iterations of smoothing at a span of 5% (Fig 1).^{10,11}

Statistical Analysis

The time interval in hours between the end of surgery and the first time point at which the 24-hour fluid output volume

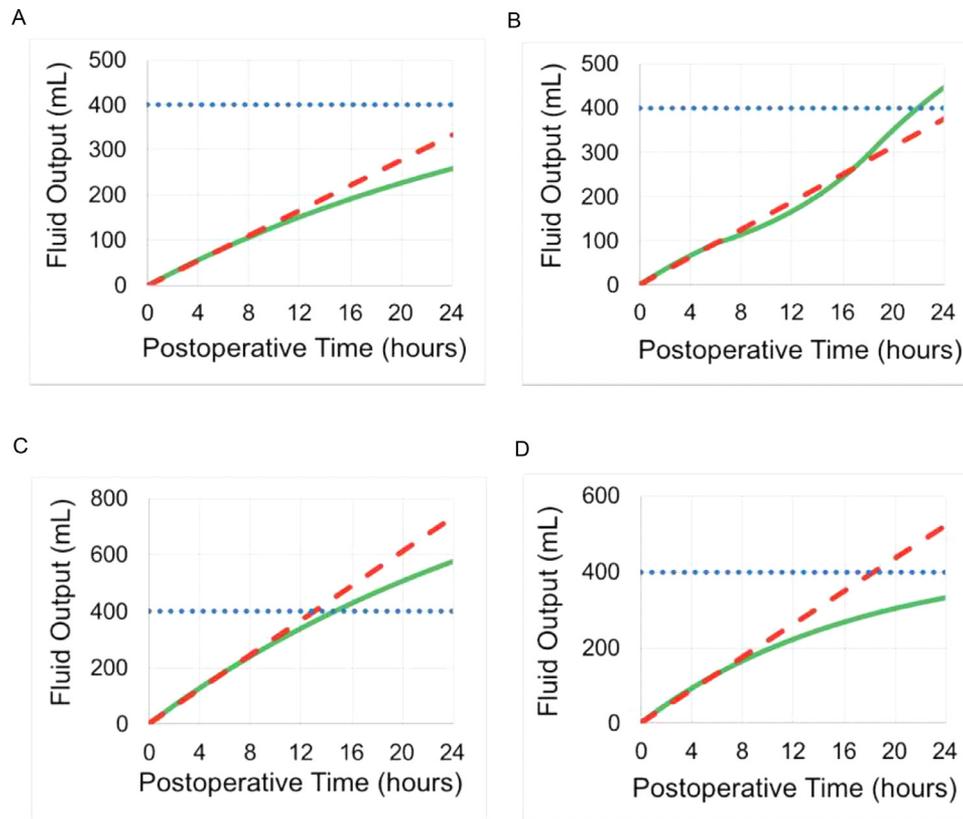


Figure 2. Pleural fluid output of a patient in order to demonstrate an example of how a single analysis of a 6-hour prorated interim output (red broken line) was interpreted as a (A) true-negative, (B) false-negative, (C) true-positive, and (D) false-positive when compared to the 24-hour pleural fluid output (green line) of a patient with a 24-hour threshold criteria of 400 mL/24 h (blue dotted line). (Color version of figure is available online at <http://www.semthorcardiovascsurg.com>.)

criteria were met ($T_{\text{fluid threshold}}$) was used to calculate sensitivity and specificity. For each postoperative hour within this time period, the 6-, 8-, and 12-hour interim fluid outputs were calculated starting at postoperative hour 6, 8, and 12, respectively. The number of time points evaluated varied depending on the prorated threshold being used as the longer the duration of the prorated threshold, the more hours of observation are required to begin the analysis (ie, it takes 12 hours of postoperative pleural fluid collection to begin analysis of a 12-hour prorated threshold, whereas it only takes 6 hours of observation for a 6-hour prorated threshold). The number of time points analyzed also varied based on the 24-hour threshold criteria used to determine when chest tubes could be removed from the standpoint of fluid drainage (ie, a 400 mL criteria will be met sooner than a 250 mL criteria). The 6, 8, and 12-hour interim fluid outputs were prorated to 24 hours (eg, the 6-hour total was multiplied by 4) and compared to the total fluid output 18, 16, and 12 hours later, respectively. If both the prorated interim output and the 24-hour fluid drainage did not meet the predetermined threshold for removal, the interim prorated fluid output was classified as a true-negative (Fig. 2A). If the prorated interim output met the criterion for removal but the 24-hour drainage did not, the interim prorated output was classified as a false-positive (Fig. 2D). False-negatives and true-positives were

determined accordingly. The potential time saved in the duration of chest tube drainage when using prorated thresholds to guide chest tube removal was calculated as the interval of time between the first instance these prorated thresholds were met and $T_{\text{fluid threshold}}$ (Fig. 3). Whether these first instances were true- or false-positives was then determined in order to calculate performance parameters. This efficiency analysis was confined to the subset of patients where fluid output, as opposed to air leak, was the rate-limiting factor for chest tube removal. This same analysis was then repeated while limiting chest tube removals to the hours of 6 AM to 6 PM in order to simulate clinical efficiency and time saved in a realistic setting where time of day is also a limiting factor to chest tube management.

Numerical continuous data were expressed as a median value with a 25th–75th percentile interquartile range (IQR). Statistical analysis of ordinal variables was conducted. Categorical variables were compared using Fisher's exact test while numerical variables were compared using two-sided Student's *t*-test or the Wilcoxon rank sum test wherever appropriate. Performance characteristics (eg, specificity, positive predictive value, false-positive rate) were compared using the chi-squared test. A *P* value <0.05 was considered statistically significant. Calculations were carried out using R (Lucent Technologies, New Jersey), SPSS 24 (IBM, Armonk, NY), and Excel 2010 (Microsoft, Redmond, WA).

THORACIC — CHEST TUBE REMOVAL AFTER LUNG RESECTION

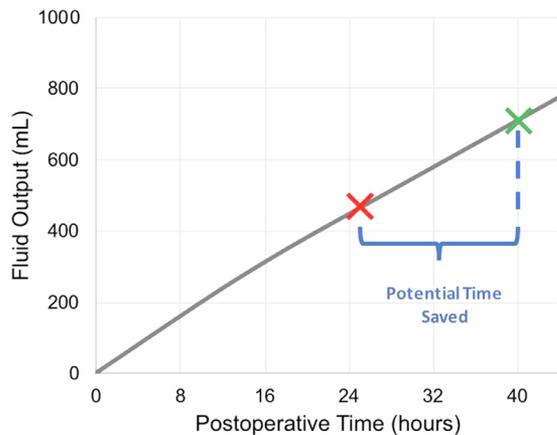


Figure 3. Example of the potential time saved in the duration of chest tube drainage of a patient with the implementation of this protocol by measuring the time between the first time the prorated threshold is met (Red X) to the first time the 24-hour threshold criteria are met (Green X). (Color version of figure is available online at <http://www.semthorcardiovascsurg.com>.)

RESULTS

From September 2015 to February 2018, digitally recorded pleural fluid output data were available for analysis in 150 lung resection patients. As shown in Table 1, 62% were female patients (93/150), the median age was 66 (IQR = 61–72) years, and non–small cell lung cancer was the most common indication for surgery (81%; 121/150). Most procedures were completed using a VATS approach (68%; 102/150). Surgical procedures included lobectomies (77%; 116/150) and sublobar resections (segmentectomy = 12%; [18/150]; wedge = 11%; [16/150]). Upper lobe resections were performed in 54% of the cases (81/150). The median $T_{\text{fluid threshold}}$ was significantly shorter after sublobar resections with all three 24-hour output criteria evaluated (Table 2).

The performance characteristics of the prorated interim fluid outputs in predicting whether or not the corresponding 24-hour fluid output threshold would be met are detailed in Table 3. The number of time points available to perform the sensitivity analysis varied with each of the three 24-hour fluid output criteria for chest tube removal used (400 mL = 4082; 20% WBLF = 4850; 250 mL = 6289). The number of hourly data points ranged from 3782 to 5989 for the 8-hour prorated threshold analysis and 3182 to 5389 for the 12-hour prorated threshold analysis. As shown in Table 3, when a 6-hour prorated drainage volume was used, specificity, positive predictive value (PPV), and false-positive rate (FPR) ranged from 85% to 88%, 75% to 91%, and 12% to 15%, respectively. When an 8-hour threshold was used, specificity, PPV, and FPR ranged from 88% to 90%, 76% to 91%, and 10% to 12%, respectively. When a 12-hour threshold was used, specificity, PPV, and FPR ranged from 91% to 94%, 80% to 92%, and 6% to 9%, respectively. Specificity and PPV increased with an increasing duration of interim fluid output threshold and were highest with the 12-hour duration of measurement. The false-positive rate

Table 1. Baseline Characteristics of Patients

Characteristic	n = 150
Average age, years \pm SD*	65.7 \pm 9.9
Female gender, n (%)	93 (62%)
Average BMI [†] , kg/m ² \pm SD	27.1 \pm 5.2
Smoker, n (%)	94 (63%)
Preoperative diagnosis, n (%)	
Nonsquamous cell lung cancer	121 (81%)
Metastatic cancer	16 (11%)
Carcinoid	5 (3%)
Squamous cell lung cancer	1 (0%)
Interstitial lung disease	2 (1%)
Undetermined nodule	5 (3%)
Primary procedure	
Lobectomy	109 (73%)
Segmentectomy	18 (12%)
Wedge	16 (11%)
Bilobectomy	7 (5%)
Secondary procedure	
Wedge	67 (45%)
Other	7 (5%)
VATS [‡] approach, n (%)	102 (68%)
VATS converted to thoracotomy, n (%)	21 (14%)
Lung lobe, n (%) [§]	
Right upper lobe	46 (31%)
Right middle lobe	17 (11%)
Right lower lobe	29 (19%)
Left upper lobe	35 (23%)
Left lower lobe	30 (20%)

*Standard deviation.

[†]Body mass index.

[‡]Video-assisted thoracoscopic surgery.

[§]Total amount of lung lobes operated is 157 despite N = 150 due to 7 bilobectomies.

decreased with increasing duration of fluid output measurements and was lowest for a 12-hour prorated threshold. There was no statistically significant difference between performance characteristics of the 6-, 8-, and 12-hour interim volume outputs for each of the 24-hour drainage criteria for chest tube removal. The subset of 66 patients (66/150; 44%) where fluid output was the limiting factor for all three 24-hour criteria

Table 2. Comparison of Time Until Fluid Threshold Is Met Following Sublobar Resection and Lobar Resection Using a 250 mL Threshold, a 400 mL Threshold, and a 20% of Whole-Body Lymphatic Flow Threshold [Median (Interquartile Range)]

24-Hour Threshold Criteria	Median Time Until Criteria Is Met (h)	
	Sublobar Resection	Lobar Resection
20% WBLF*	24.3 (24.0–31.0)	24.5 (24.1–50.3)
250 mL	24.6 (24.2–49.7)	31.4 (24.2–66.3)
400 mL	24.2 (24.0–24.5)	24.3 (24.0–45.6)

*Whole-body lymphatic flow.

Table 3. Comparison of Performance Parameters of Short-Term Fluid Output Between 6, 8, and 12 Hours Using a 250 mL Threshold, a 400 mL Threshold, and a 20% Whole-Body Lymphatic Flow Threshold in Correctly Identifying Patients Whose Pleural Fluid Output Will Satisfy 24-Hour Threshold Criteria for Chest Tube Removal

Performance Parameter	Duration of Prorated Threshold (h)	24-Hour Threshold			P Value		
		20% WBLF*	400 mL	250 mL	A [‡]	B [§]	C
Specificity (95% CI) [†]	6	85% (83–86)	86% (84–88)	88% (87–89)	0.3484	0.0001	0.0210
	8	88% (86–89)	88% (86–89)	90% (89–91)	0.9635	0.0020	0.0093
	12	92% (91–93)	91% (90–93)	94% (93–94)	0.2197	0.0333	0.0012
Positive predictive value (95% CI)	6	83% (81–84)	91% (89–92)	75% (73–76)	<0.0001	<0.0001	<0.0001
	8	85% (83–86)	91% (90–92)	76% (75–78)	<0.0001	<0.0001	<0.0001
	12	88% (86–89)	92% (90–93)	80% (78–83)	0.0002	<0.0001	<0.0001
False-positive rate (95% CI)	6	15% (14–17)	14% (12–16)	12% (11–13)	0.3484	0.0001	0.0210
	8	12% (11–14)	12% (11–14)	10% (9–11)	0.9635	0.0020	0.0093
	12	8% (7–9)	9% (7–10)	6% (6–7)	0.2197	0.0333	0.0012

*Whole-body lymphatic flow.

[†]Data calculated with a 95% confidence interval shown as upper and lower value.

[‡]P value represents significance level of comparison between the 20% WBLF and 400 mL 24-hour thresholds.

[§]P value represents significance level of comparison between the 400 mL and the 250 mL 24-hour thresholds.

^{||}P value represents significance level of comparison between the 250 mL and the 20% WBLF 24-hour thresholds.

chosen for chest tube removal was identified. The potential improvement in chest tube duration associated with the use of prorated 6, 8, and 12-hour interim fluid output data instead of 24-hour output values is summarized in Table 4. There was a statistically significant difference in potential time saved for each of the prorated interim outputs for all three 24-hour output thresholds except for when the 12-hour prorated threshold was compared to the 250 mL 24-hour criteria. The potential improvement in chest tube duration ranged from 10 to 16 hours and was best with the 6-hour prorated threshold with an average improvement of 16 hours. There is a slight decrease when limiting chest tube removal between the hours of 6 AM and 6 PM whereby the potential improvement in chest

tube duration drops to 7–12 hours. The 6-hour prorated threshold still showed the greatest improvement in chest tube duration with an average of 12 hours (Table 5).

DISCUSSION

Unnecessary delays in removing pleural drains can often be uncovered when this component of surgical care is examined with scrutiny. In-dwelling chest tubes can be a rate-limiting step for hospital discharge. Efforts to drive early recovery after pulmonary resection should focus on optimizing all aspects of perioperative surgical care including the duration of chest tube drainage. Early prediction of successful chest tube removal presents an opportunity to decrease pain and suffering and gain efficiency

Table 4. Duration of Drainage Time Saved: 24-Hour Threshold Criteria vs Prorated Threshold in All Patients (N = 66) for Whom Fluid Criteria Was the Rate-Limiting Factor

24-Hour Threshold Criteria	Average Time Until Criteria Is Met [h (95% CI)]*		Average Potential Time Saved [h (95% CI)]*	P Value
	24-Hour Threshold	Prorated Threshold		
6-hour prorated threshold				
20% WBLF [†]	39.3 (33.6–44.2)	23.5 (17.5–29.5)	15.8 (14.9–16.6)	0.0006
250 mL	45.2 (38.3–52.1)	30.3 (23.1–37.4)	14.9 (14.0–15.9)	0.0038
400 mL	33.6 (29.0–38.1)	17.5 (12.5–22.4)	16.1 (15.2–16.9)	<0.0001
8-hour prorated threshold				
20% WBLF	39.3 (33.6–44.2)	25.3 (19.2–31.3)	14.0 (13.2–14.9)	0.0012
250 mL	45.2 (38.3–52.1)	31.7 (24.5–38.8)	13.5 (12.7–14.4)	0.0084
400 mL	33.6 (29.0–38.1)	19.6 (14.5–24.6)	14.0 (13.1–14.9)	0.0001
12-hour prorated threshold				
20% WBLF	39.3 (33.6–44.2)	28.5 (22.4–34.6)	10.8 (9.7–11.9)	0.0119
250 mL	45.2 (38.3–52.1)	35.5 (28.3–42.7)	9.6 (8.8–10.5)	0.0600
400 mL	33.6 (29.0–38.1)	22.1 (17.3–27.0)	11.4 (10.0–12.9)	0.0010

*Data calculated with a 95% confidence interval shown as upper and lower values.

[†]Whole-body lymphatic flow.

Table 5. Average Potential Time Until Chest Tube Is Removed (*N* = 66) for Whom Fluid Criteria Was the Rate-Limiting Factor and While Limiting Chest Tube Removal to the Hours Between 6 AM and 6 PM

24-Hour Threshold Criteria	Average Potential Time Until Chest Tube Is Removed [Hours (95% CI)]*		Average Potential Time Saved [Hours (95% CI)]*	<i>P</i> Value
	24-Hour Threshold	Prorated Threshold		
6-hour prorated threshold				
20% WBLF [†]	40.4 (34.3–46.6)	28.9 (22.9–34.9)	11.5 (9.9–13.1)	0.0085
250 mL	46.7 (39.6–53.8)	35.0 (27.5–42.4)	11.7 (10.1–13.4)	0.0245
400 mL	34.5 (29.6–39.5)	22.8 (17.7–27.8)	11.7 (10.3–12)	0.0012
8-hour prorated threshold				
20% WBLF	40.4 (34.3–46.6)	32.3 (26.4–38.3)	8.1 (6.7–9.4)	0.0598
250 mL	46.7 (39.6–53.8)	37.8 (30.6–44.9)	8.9 (7.4–10.5)	0.0804
400 mL	34.5 (29.6–39.5)	26.7 (21.8–31.6)	7.8 (6.7–9.0)	0.0265
12-hour prorated threshold				
20% WBLF	40.4 (34.3–46.6)	33.5 (27.2–39.8)	6.9 (5.5–8.4)	0.1192
250 mL	46.7 (39.6–53.8)	39.8 (32.4–47.2)	6.9 (5.5–8.2)	0.1802
400 mL	34.5 (29.6–39.5)	27.8 (22.8–32.8)	6.7 (5.7–7.8)	0.0598

*Data calculated with a 95% confidence interval shown as upper and lower values.

[†]Whole-body lymphatic flow.

without compromising patient safety. There has been interest in extending the upper limit of what is considered a safe fluid output threshold for the removal of pleural drains after lung resection (eg, up to 500 mL/24 h).^{1,4–9} When taking into account suction level, surgical approach, and resected lobe, some investigators have had success with even higher thresholds of up to 875 mL per day.¹² Despite the seemingly ever-increasing fluid output threshold considered safe for chest tube removal, this approach to reducing the duration of pleural drainage still requires patients to be monitored for minimum intervals of 24 hours.

This research study was not aimed at resolving the controversy in the literature as to what constitutes the optimal fluid output threshold for drain removal. This study was also not meant to attempt to evaluate or predict total pleural drainage volume. Instead, the focus was set on examining the trend in pleural fluid output irrespective of procedure (ie, lobar vs sublobar resection) or approach (ie, open vs VATS) and transform this data into relevant information to assist the clinical team in safely removing drains earlier.¹³ We demonstrated that our methodology produced consistent results across at least 3 different 24-hour fluid output thresholds considered safe for chest tube removal. We demonstrated that the use of fluid output data over shorter time intervals (ie, 6, 8, and 12 hours) can reliably predict whether or not the total output for the corresponding 24-hour period will meet criteria for safe removal. In the subgroup of patients for whom fluid output was the rate-limiting step for chest tube removal, the use of prorated thresholds was associated with a reduction in the duration of drainage that could translate into a shorter length of stay. When chest tube removal is limited to the hours between 6 AM and 6 PM, there is a loss of efficiency in reducing the duration of chest tube drainage. However, there is still a significant advantage, especially if the 6- or 8-hour prorated thresholds are used. If patients were to be managed in the most efficient way possible,

then chest tubes should be removed at any time of the day or night. This approach would lead to even greater potential for decreased length of stay. While there is no indication that overnight chest tube removal would compromise safety, we are not aware of any survey data on whether patients would prefer having their chest drain out as early as possible even if it means that this occurs at night. Further research into the relationship between efficiency and patient satisfaction is required.

The use of digital sensors to continuously monitor pleural fluid output remains in its infancy and improvements in precision are needed. Limitations of the current technology will likely be overcome in future technological upgrades. Meanwhile, we have successfully minimized the impact of sensor-related noise in the data by applying a simple filtering algorithm. This is a widely used engineering approach to improve the signal to noise ratio in digitally recorded data.¹⁰ We think that aberrant fluid output measurements probably have little impact in the clinical setting since they are relatively easy to identify in the graphical representation of the fluid output data provided by the digital drainage devices used in this study. We implemented a smoothing algorithm to facilitate automated statistical analysis of fluid drainage data. Another limitation of this study is the relatively small sample size of patients where fluid output was the rate limiting factor for chest tube removal. We acknowledge that this undermines our ability to detect statistically significant differences. We also acknowledge that our model has yet to be tested in a prospective validation cohort. However, we believe the tens of thousands of data points that were available for analysis provided results that are robust with a low potential for systemic bias. We recognize that using fluid output data over shorter time intervals (ie, 6–12 hours) to make decisions regarding chest tube management may not be appropriate for all clinical situations. For instance, chronic obstructive pulmonary disease in patients over the age of 70 who underwent lower

lobectomy may be more prone to rapid development of a significant pleural effusion on the second postoperative day.^{13,14} In this highly selective group of patients, pre-emptive drain removal based on a shorter interval drainage data could possibly be associated with a higher probability of chest tube reinsertion for fluid reaccumulation. It should be noted that in this cohort of 150 patients, none of them satisfied all 3 of these criteria. Lastly, we think it is important to state that this protocol is not suitable in patients with bloody chest tube drainage. Close monitoring and clinical judgment should be exercised in cases where postoperative bleeding is suspected.

In summary, pleural fluid drainage data collected with a digital pleural drainage device over 6, 8, or 12 hours can reliably predict if the corresponding 24-hour fluid output will fall under a threshold that is considered safe for chest tube removal. This approach represents an opportunity to gain clinical efficiency and improve patient experience by shortening the duration of chest tube drainage without compromising safety. More research is needed to explore innovative ways to capitalize on the new stream of digitally captured pleural space data that is now available to the surgical team.

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