Optimal Management of Malignant Pleural Effusions (Results of CALGB 30102)

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Abstract

The optimal strategy to achieve palliation of malignant pleural effusions (MPEs) is unknown. This multi-institutional, prospective, randomized trial compares 2 established methods for controlling symptomatic unilateral MPEs. Patients with unilateral MPEs were randomized to either daily tunneled catheter drainage (TCD) or bedside talc pleurodesis (TP). This trial is patterned after a previous randomized trial that showed that bedside TP was equivalent to thoracoscopic TP (CALGB 9334). The primary end point of the current study was combined success: consistent/reliable drainage/pleurodesis, lung expansion, and 30-day survival. A secondary end point, survival with effusion control, was added retrospectively. This trial randomized 57 patients who were similar in terms of age (62 years), active chemotherapy (28%), and histologic diagnosis (lung, 63%; breast, 12%; other/unknown cancers, 25%) to either bedside TP or TCD. Combined success was higher with TCD (62%) than with TP (46%; odds ratio, 5.0; $P = .064$). Multivariate regression analysis revealed that patients treated with TCD had better 30-day activity without dyspnea scores (8.7 vs. 5.9; $P = .036$), especially in the subgroup with impaired expansion (9.1 vs. 4.6; $P = .042$). Patients who underwent TCD had better survival with effusion control at 30 days compared with those who underwent TP (82% vs. 52%, respectively; $P = .024$). In this prospective randomized trial, TCD achieved superior palliation of unilateral MPEs than TP, particularly in patients with trapped lungs. (*JNCCN* 2012;10:975–982)

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Approximately 100,000 new malignant pleural effusions (MPEs) occur annually in the United States, adversely affecting quality of life (QOL), often within months of death.[1,2] Optimal palliative management of these symptomatic patients is still not well understood, which has resulted in considerable practice variation in the United States largely due to physician preference, referral patterns, and payment options for these therapies. Accordingly, inpatient or operative management dominates in some regions.

Intermittent external drainage through an indwelling catheter is gaining popularity, because it has the advantage of avoiding hospitalization and inflammatory complications caused by talc pleurodesis.[3] Alternatively, pleurodesis is a well-accepted and relatively brief therapy, which, if successful, yields permanent control. Talc is used commonly, because it is equivalent to or better than the more expensive agents.[4–7] This study evaluated whether tunneled catheter drainage (TCD) was equivalent or superior to talc pleurodesis (TP) to determine whether wider use of less-invasive outpatient management can be justified.

Materials and Methods

A prospective, randomized phase III trial was initiated by the Cancer and Leukemia Group B (CALGB) and activated on May 15, 2002, across a broad group of cooperative institutions. Central Institutional Review Board (IRB) approval was granted on April 25, 2002, with subsequent local IRB approvals. From October 15, 2002, to December 14, 2004, 67 patients were registered and appropriately consented, and 57 were evaluable (Figure 1). The study was closed early because of slow accrual, which was attributed to randomization refusal because after its presentation subjects preferred in roughly equal proportions to have either the inpatient

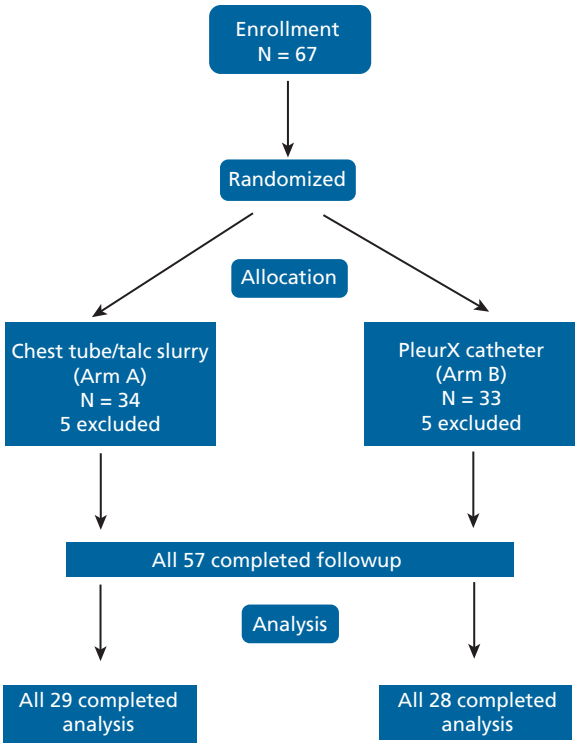

Figure 1 CONSORT patient flow diagram.

or the outpatient management. Seventeen patients were enrolled at one institution, and another 20 centers each enrolled between 1 and 7 cases.

Eligibility and Objectives

Symptomatic patients with malignancy proven by histology or cytology were eligible for this study if a chest roentgenogram (CXR) showed evidence of a previously untreated, unilateral pleural effusion requiring pleurodesis or ongoing drainage. Patients were ECOG performance status (PS) 0 to 2 with no active pleural infection, talc allergy, or other contraindication to talc use. Investigators avoided enrolling patients with likely trapped lungs, anticipated survival of fewer than 60 days, or severe comorbid medical conditions.

The primary objective was to compare the proportion of maintained successful treatments 30 days after intervention. A combined "success" achieved all predetermined criteria: 1) alive, 2) no effusion recurrence, 3) lung reexpansion of 90% or greater after effusion drainage, and 4) completion of the intervention by 2 weeks based on removal of the chest tube inserted for TP or proper function of the TCD.

An important secondary objective was to test for differences in QOL 7 and 30 days posttreatment, including patient acceptance and satisfaction, and level of symptoms and dyspnea (Condensed Memorial Symptom Assessment Scale, dyspnea index, and Karnofsky Self-Reported Performance Rating Scale).

TP: Chest Tube With Talc

For the TP procedure, a single dose of 4 to 5 g of sterile talc slurry within 100 mL of saline was infused into the pleural space using a chest catheter (≥ 24 French), with proper placement confirmed on CXR. Talc was given within 36 hours of chest tube placement, and the tube was clamped for 2 hours while patient position was changed to facilitate talc distribution. Pleurodesis was assumed when chest drainage decreased to 150 mL in 24 hours, leading to tube removal followed by CXR. Management of all patients in this arm was inpatient and replicated the talc slurry arm of the successful CALGB 9334, including chest tube size, and followed guidelines for use of sterile talc prepared locally or by pharmaceutical companies.[8]

TCD: PleurX Catheter

The placement technique for the PleurX catheter (Denver Biomedical, Denver, Colorado) has been described elsewhere.[2] The catheters were accessed under aseptic technique and drained daily using evacuated drainage bottles. Apart from the initial drainage at the time of insertion, no more than 1000 mL of fluid was drained at a single instance. A CXR was taken within 36 hours after the initial drainage of pleural fluid. Thereafter, the catheter was drained once daily by the patient, family member, or visiting nurse using aseptic technique, and the output recorded. When the drainage volume was less than 30 mL each time over 72 hours (3 consecutive days), the PleurX catheter was removed in the outpatient setting. TCD is generally an outpatient procedure because that is how payment is structured for its use, although a few patients may have had their catheters placed as inpatients and then been discharged.

Effusion Control Criteria

The local treating physician reviewed the CXR images and estimated the percent expansion of the lung beneath the effusion. Although CT estimates are more accurate, CXR monitoring is standard clinical practice and less intrusive to a frail population. Image sets were graded by the primary investigator when the local investigator was not available (5 cases) and as part of case quality review. Lung expansion was measured with CXR pretreatment, postdrainage, on the last inpatient day, at the first clinical visit, at 30 days, and at 60 days.

A complete response was defined as no pleural fluid accumulation greater than that seen on the CXR after completion of MPE drainage. Recurrence was defined as accumulation of pleural fluid greater than levels measured at the time that the catheter or chest tube was permanently removed.

Statistical Considerations

CALGB 30102 was designed as a 2-arm randomized phase III study to compare TP and TCD with respect to 1) the proportion of patients with successful effusion control at 30 days (see criteria described previously), and 2) the QOL scores reported by patients and physicians. The study was designed to randomize 530 patients in equal proportion to the 2 treatment arms via permuted block randomization scheme stratified according to inpatient status (yes, no), disease type (breast, lung, other), and whether they were receiving systemic chemotherapy concurrently (yes, no). For a 2-sided test conducted at the 0.10 level of significance, the study with 530 patients has approximately 90% power to detect an increase of the "success" rate from 53% in the TP arm to 66% in the TCD arm. Nine patients were excluded from analysis; 6 were ineligible because bilateral effusions were found, and 3 never started protocol treatment because of other disease complications (see Figure 1).

The 30- and 60-day "success" rates for effusion control were compared using Fisher's exact test, and baseline prognostic factors that might affect success were evaluated further using a stepwise approach in a logistic regression model. QOL score differences at 30 and 60 days were tested using the Wilcoxon rank sum test and analysis of linear regression. The Cochran-Mantel-Haenszel association test was used to analyze lung expansion effect on success. Complete case data were used to compute how the QOL scores changed over time, and imputation methods were used to investigate how the dropouts impacted the estimates.

CALGB statisticians performed statistical analyses on SAS 9.1 (SAS Institute Inc., Cary, NC). All *P* values are 2-sided. The CALGB Audit Committee and statistical staff performed regular central and onsite monitoring to insure safety, institutional protocol, and federal regulation compliance.

Post Hoc Analysis

Although greater than 90% expansion was used in CALGB 9334 (after which this study was patterned), achieving that value was not incorporated into its composite end point the same way. More importantly, CALGB 9334 investigators were not expressly required to quantify the percent expansion. The investigators of CALGB 30102 believed that investigator quantification would enhance this study, particularly because the central radiologist imaging review for CALGB 9334 only validated qualitative improvement, but not the local 90% expansion interpretation because of the inherent inaccuracy of plain films. Despite similar eligibility criteria, only 36% of patients in this study (compared with 68% in CALGB 9334) achieved greater than 90% expansion despite the same requirement of predicted full expansion. It became evident from CXR review that investigators from CALGB 9334 were inclined to classify a lung as expanded greater than 90% (so the patient could be analyzed) if it largely filled the chest cavity, even if thoracic volume was reduced 10% to 20% by pleural restriction caused by tumor or pleurodesis effects. Accordingly, the expansion value for success was reduced to 70% or greater from the original plan. With this cut point, 65% of the cases achieved "successful" expansion, normalizing the data with CALGB 9334. Furthermore, 70% or greater expansion was perceived by the study team as the lowest result acceptable to most clinicians.

The investigators also chose to analyze patients with the same end point as CALGB 9334—survival with maintenance of expansion—to reduce the effect of an arbitrary cut point. Final data analysis was delayed until late 2008 for multiple reasons, including the need to complete or confirm observations in a population of patients from multiple institutions who had died or were otherwise difficult to follow, and fluctuations in local research and central statistical resources for this project.

Results

Efficacy Analyses

Table 1 summarizes the balanced patient demographic and baseline clinical characteristics according to treatment arms; lung (62%) and breast cancer (12%) were the most common.

No statistical differences in reexpansion were seen between the treatment arms. The patients who underwent TP were somewhat more likely to achieve an expansion of 70% or greater postdrainage, (75% vs. 58%; $P = .250$), but maximal expan-

Table 1 Patient Demographic and Baseline Clinical Characteristics

Characteristics	TP (N = 29)	TCD (N = 28)	Overall (N = 57)
Age (y)			
Mean/median	60/62	64/67	62/62
Range	33–85	28–86	28–86
Gender, N (%)			
Male	16 (55)	17 (61)	33 (58)
Female	13 (45)	11 (39)	24 (42)
Race, N (%)			
White	24 (83)	21 (75)	45 (79)
Non-White	5 (17)	7 (25)	12 (21)
PS, N (%)			
0/1	16 (55)	17 (63)	33 (59)
2	13 (45)	10 (37)[a]	23 (41)
Type of Cancer, N (%)			
Lung	17 (59)	19 (68)	36 (63)
Breast	4 (14)	3 (11)	7 (12)
Other types[b]	8 (27)	6 (21)	14 (25)
Inpatient Status, N (%)[c]			
Inpatient	13 (45)	13 (46)	26 (46)
Outpatient	16 (55)	15 (54)	31 (54)
Concurrent Chemotherapy, N (%)			
Receiving	7 (24)	9 (32)	16 (28)
Not receiving	22 (76)	19 (68)	41 (72)
Initial Drainage (mL)			
Mean/median	1443/1000	1244/1150	1349/1100
Range	20–4000	192–2700	20–4000

Abbreviations: PS, performance status; TCD, tunneled catheter drainage; TP, talc pleurodesis.
[a]One patient's PS data are missing.
[b]No patients with mesothelioma were included in this study.
[c]At time of randomization, see text for location of procedure.

sions during the entire study were similar (79% vs. 73%; $P = .754$). Although not significant, the maximum expansion during treatment was higher than measured at pretreatment for 96% in the TP arm versus 88% in the TCD arm ($P = .340$). Similarly, slightly better maintenance (no lower-than-previous measurements) of this expansion was seen at 30 days (58% vs. 52%; $P = .761$) and 60 days (63% vs. 50%; $P = .510$).

Table 2 summarizes the outcomes of the treatment procedures. The original overall combined success rate (defined earlier) was higher for TCD (62%) than for TP (46%) but was not significant ($P = .290$). Using the end point from CALGB 9334, patients treated with TCD had significantly better survival without effusion recurrence within 30 days compared with those treated with TP (82% vs. 52%, respectively; $P = .0239$).

Logistic regression analysis modeled success rates based on arm, gender, admission status (inpatient vs. outpatient), PS (0/1 vs. 2), concurrent chemotherapy, good/poor expansion (defined in the next section), dyspnea score, and initial drainage. The odds ratio for TCD success was 5 times higher than for TP (95% CI, 1–23; 2-sided $P = .064$). Logistic regression also showed that patients with good expansion experienced better success (odds ratio, 5; 95% CI, 1–25; $P = .053$). All other covariates did not affect success significantly. This finding should be interpreted with caution because of the mere proximity to achieving significance, and only 15 patients in the TP arm and 18 in the TCD arm had the complete data set for the logistic regression analysis. It should be noted that the investigators originally analyzed and presented the preliminary data, which included 1 patient assigned to TP who received the chest tube but not the talc. Both of the P values presented earlier achieved statistical significance ($P < .05$) until this patient was removed.

Pleurodesis occurred in 86.2% of patients treated with TP compared with 68.0% of those treated with TCD ($P = .1883$, but data were missing on 3 patients treated with TCD). The assigned therapy could not be completed by the local investigator for TP and TCD cases, respectively, because of loculation (1 vs. 2), failed lung expansion (2 vs. 0), and chest tube/catheter occlusion (1 each). No patients died while the chest tube was in place, but in the TCD group 4 deaths occurred with the catheter in place before pleurodesis was achieved.

Therapy-attributable complications from 63 treated patients (including 6 ineligible patients) were low but somewhat more frequent for the TCD group. Recurrent dyspnea was only seen in TP cases. One acute respiratory distress syndrome (ARSD)–related death occurred in the TCD group. Life-threatening (grade 4) serious adverse events (SAE) were fatigue (n = 1) and dyspnea (n = 1) in the TP group and 1 myocardial infarction in the TCD cohort. One severe (grade 3) SAE occurred in the TP group (dyspnea) compared with 6 in the TCD group

Table 2 Frequencies of Clinical Outcomes

Clinical Outcomes	TP N/Total (%)	TCD N/Total (%)	*P* Value[a]
Overall success[b]	13/28 (46)	16/26 (62)	.2898
Alive within 30 d of the procedure	25/29 (86)	26/28 (93)	.6701
Effusion absent within 30 d	18/29 (62)	24/28 (86)	.0700
Alive without recurrence within 30 d	0015/29 (52)	23/28 (82)	.0239
Initial lung reexpansion ≥ 70%	1	19/26 (73)	.7540
Chest tube ≤ 14 d[c]	28/29 (97)	NA	NA
Effusion controlled within 60 d	17/29 (59)	22/28 (79)	.1550
Talc/PleurX procedure completed	24/30 (80)	25/ 6 (96)	.1080
Pleurodesis achieved	25/29 (86)	17/26 (65)	.1115
Total drainage			
Mean/median	1911/1480	5802/2484	.0721[d]
Range	300–6640	45–24,895	
Days drainage device in place			
Mean/median	5/4	49/31	< .0001[e]
Range	1–32	2–286	
Removal before death			
N (%)	29/29 (100)	24/28 (86)	.0518
Other survival			
Alive within 30 days	25/29 (86)	26/28 (93)	
Alive at 31–90 d	25/29 (86)	19/28 (68)	.2616
Alive beyond 90 d	21/29 (72)	17/28 (61)	
Median survival (Kaplan-Meier estimates)			
Median (d)	147	147	.5144[f]
95% CI	100–201	61–220	

Abbreviations: TCD, tunneled catheter drainage; TP, talc pleurodesis.
[a]*P* values were from Fisher's exact 2-sided tests otherwise specified.
[b]The definition of success is that a patient survived without effusion recurrence within 30 days, lung reexpansion ≥ 70% after desired effusion is drained, or chest tube removed before 14 days (TP only).
[c]Applied to TP only.
[d]*P* value = .0721 was from Wilcoxon rank sum 2-sided test. *P* value = .0219 from linear regression analysis after adjusting for initial drainage, inpatient status at baseline, gender, whether receiving chemotherapy concurrently when enrolling to the study, and disease type (lung, breast, or other cancers). *P* value = .0969 of the same linear regression only among patients with lung and breast cancer.
[e]Wilcoxon rank sum 2-sided test.
[f]Log-rank 2-sided test.

(3 pain and 1 each of leukocytosis, wound infection, and neutropenia).

QOL Analyses

The maximum lung expansion (best of postdrainage, last inpatient CXR, and first clinical visit measurements) was correlated with dyspnea scores calculated at baseline before randomization, at 7 days, and at 30 days posttreatment. No significant relationship was seen between baseline dyspnea score and percent lung expansion at any of the 3 time points; however, 30-day assessments of dyspnea-free exercise and CXR lung expansion correlated significantly (r = 0.322; *P* = .0486). This relationship implies that those with a better dyspnea-free score had better lung expansion. Similarly, a trend was seen toward better dyspnea scores for 29 patients whose maximal lung expansion at 30 days was 70% or greater compared with the 9 whose values were less (7.8 vs. 4.5; *P* = .02, Wilcoxon rank sum test).

Baseline measures of QOL were not predictors of baseline lung expansion or of 30-day CXR lung expansion. However, several QOL measures from the 30-day assessment were related to 30-day CXR expansion, including overall QOL from the Condensed Memorial Symptom Assessment Scale form, PS, dyspnea score, physical function, social life, and overall QOL from the changes in function form (Table 3). All of these are significant in a positive direction; that is, an increase in the QOL measure corresponds with an increased chance of greater than 70% expansion at 30-day CXR.

To test the importance of lung trapping, the median value of early reexpansion estimates (maximum value of postdrainage, last inpatient, and first clinical visit) in TP were set at 80%, and 88% in TCD. "Good" and "Poor" expansion were defined by expansion above and below these medians, respectively. Patients treated with TCD had better 30-day effusion control than those treated with TP after adjusting for good expansion cases (92% vs. 81%) and especially poor expansion (77% vs. 33%; $P = .026$, Cochran-Mantel-Haenszel association test). Reanalyzing the results using 70% expansion as the cut point produced a similar results.

Multivariate regression analysis revealed that TCD had better dyspnea scores than TP (8.5 vs. 6.1; $P = .047$) after adjusting for baseline dyspnea score, initial drainage, gender, inpatient status, and patient PS at baseline. Further analysis showed that this statistical difference was driven by scores from the poor expansion group (9.0 vs. 4.9; $P = .033$) but not by the good expansion group (8.6 vs. 8.5; $P = .949$), again noting the benefits of TCD, particularly for those with trapped lungs.

Discussion

Despite its limitations, this study supports TCD as an effective alternative to TP and suggests that it may be better in certain circumstances. The use of intrapleural talc has been a concern of investigators who noted problems with idiosyncratic immediate respiratory distress and based on autopsy findings that patients show systemic distribution of talc after pleural administration.[9–17] Although immediate ARDS was not associated with talc in this series, severe dyspnea was seen in 2 cases.

In CALGB 9334, 486 patients randomized to thoracoscopic poudrage or chest tube talc slurry experienced similar success (60% vs. 53%, respectively), but more respiratory complications occurred in those undergoing general anesthesia for thoracoscopy. Those patients also experienced significant 30-day mortality (17.1% vs. 10.3% current). This finding illustrates the investigators' difficulty in predicting longevity in these patients and the preterminal nature of MPEs. Similarly, many patients did not experience greater than 90% expansion (24% in CALGB 9334 vs. 64% current, although the latter is probably a semantic issue; see "Post Hoc Analysis"). Because predicting expansion is unreliable and does not influence overall relief of dyspnea and QOL, perhaps it should not be used for future studies until better predictors of lung expansion are developed.

In CALGB 9334 and other studies of pleurodesis agents, adverse events caused by sclerosant inflammation may be difficult to distinguish from the natural sequelae experienced by frail deteriorating patients. A pleurodesis alternative (TCD) has become popular only over the past decade. In fact, TCD commonly achieves pleurodesis through maintaining apposition of pleura inflamed by catheter or tumor effects.

Although one phase III randomized multicenter trial suggested equivalency between the PleurX catheter and chest tube drainage with doxycycline pleurodesis, no similar comparison trials between TCD and chest tube with talc pleurodesis have been reported.[3] A retrospective review of inpatient and outpatient use of a pleural catheter and inpatient chest tube showed reduced short-term cost in outpatient catheter use.[3] An approximately 19% incidence in complications related to use of pleural catheters were seen, mostly related to device failure, and a 4% incidence of infection. More recently, some early device occlusive failures have been addressed with instilling fibrinolytic agents. Hospital stay data were not collected in this current study because TCD is a proven outpatient procedure, but whether it speeded discharges for those randomized as inpatients may have been interesting to see.

The current study supports the findings of others that TCD is preferred for patients with complicated effusions, such as those where the lung may be trapped.[18–21] Furthermore, it should be noted that, although the use of TCD prolongs therapy, this added duration may maintain lung expansion and QOL improvement parameters better. It is reasonable to

Table 3 Quality of Life Results From Logistic Regression Analysis With Lung Expansion Single Predictor at 30 Days

Measure	CXR Percent Lung Expansion (Log OR [2-sided *P* value])	OR Odds Ratio (95% CI)
Distress score[a]	-0.4459 (0.3313)	N/A
Number of symptoms[a]	-0.0798 (0.4642)	N/A
Overall QOL (MSAS)[a]	0.0471 (0.0095)	1.048 (1.012, 1.086)
Performance status[a]	0.0772 (0.0058)	1.080 (1.023, 1.141)
Dyspnea score[a]	0.2678 (0.0212)	1.307 (1.041, 1.641)
Physical function	0.7566 (0.0687)	2.131 (1.057, 4.813)
Emotional dtate	0.7566 (0.0687)	2.131 (0.944, 4.813)
Social life	1.2188 (0.0150)	3.383 (1.268, 9.029)
Overall QOL (CiFF)	1.0778 (0.0121)	2.938 (1.267, 6.816)

Abbreviations: CiFF, changes in function form; CXR, chest roentgenogram; MSAS, Memorial Symptom Assessment Score; N/A, not applicable; OR, odds ratio; QOL, quality of life.

[a]Measure was also assessed at baseline and did not have a significant association with either baseline or 30-day CXR.

expect that protracted evacuation therapy generates better tissue coaptation through allowing time for tissue expansion, mediastinal/diaphragmatic shifts, and sealing of the pleural space, although this driving force was gone in several days once the chest tube was removed in the talc group. However, some patients opted not to undergo TCD, and when the lung is only partially trapped, it is reasonable to use talc, as in this study, because evidence shows that it is effective in up to half of cases. This leaves TCD as a fallback option.

This study was limited because patients often preferred inpatient (TP) or outpatient (TCD) management, making randomization difficult. This required changes in the statistical analyses (already cited), increased type I error, reduced statistical power to detect infrequent events, and yielded a sample that might not represent the overall population. Alternatively, the data in this study are valuable because randomization tends to solve problems with retrospective bias and whether another randomized investigation of these 2 popular approaches will be effectuated is unclear because of the inpatient/outpatient issue. This general problem of comparing newer, less invasive (or less toxic) standard therapies is a challenge for any traditional randomized design, and calls for the adoption of alternative trial designs. An entirely outpatient study with talc delivered through a small catheter might be more popular, but little experience exists delivering talc through PleurX catheters.

Although the distribution of patients over the participating centers was uneven, this probably did not affect the results, because the treatment methods are well established and any practice variation would be addressed through randomization. Concerns regarding less experience with the newer method of TCD at the low-volume centers might have been a bias against it, whereas the patients with trapped lungs may have biased the study in its favor. An objective method to detect trapped lungs, such as pleural compliance determination, could have addressed this limitation.[22] However, pleural compliance measurement techniques are not performed consistently in most hospitals, would have required additional invasive procedures, and never have proven feasible or uniform enough to be used in a prospective clinical trial. Similarly, prediction of survival or whether symptoms such as dyspnea are from the MPEs is very difficult to determine clinically before drainage. Accordingly, a better surrogate measurement than lung expansion may exist to assess the effectiveness of these procedures. Requiring additional procedures or objective testing for this frail population would have created additional challenges that would have prevented accrual. For instance, although the investigators would have preferred a more objective and blinded assessment of the effusion recurrence end point, they stayed with the CXR review by the treating physician, which was proven successful in CALGB 9334, because it is the clinical standard, it has low level of intrusiveness, and any institutional or investigator bias in interpretation would be addressed through the randomization process.

Wide practice variability exists regarding how patients at risk for malignant effusions are evaluated and treated. Patients who are uncomfortable often receive an expeditious chest tube, video-assisted thoracoscopic surgery (VATS) assessment, or small catheter drainage as the initial procedure based on local preferences or available resources rather than guidelines based on high-quality evidence. Furthermore, suspected histolo-

gies with better prognoses (or that require more tissue for pathologic review), such as breast cancer or mesothelioma, could trigger different approaches using VATS.

In conclusion, clinicians should consider TCD to treat MPEs because it not only avoids hospitalization and stress of pleurodesis but may more predictably relieve dyspnea. In particular, it deals better with the remarkably frequent occurrence of unsuspected trapped lung in practices that do not use objective tests such as pleural compliance. Given how common and morbid MPEs are, further study is warranted, perhaps with an alternative study design to improve acceptance by potential volunteers.

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