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Effect of an Indwelling Pleural Catheter vs Chest Tube and Talc Pleurodesis for Relieving Dyspnea in Patients With Malignant Pleural Effusion

The TIME2 Randomized Controlled Trial

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MALIGNANT PLEURAL EFFUSION causes disabling dyspnea in more than 1 million people worldwide annually and prevalence is increasing.¹⁻⁴ Patients have a mean life expectancy of 4 months.⁵ The aim of treatment is symptom palliation while minimizing adverse events.

Guidelines recommend chest tube insertion and pleurodesis as a first-line treatment,¹ with talc being the most effective pleurodesis agent.⁶ Median hospitalization is 7 days and the 30-day failure rate for talc pleurodesis, defined as recurrent pleural fluid requiring further intervention, is approximately 30%.⁷

For editorial comment see p 2432.

Context Malignant pleural effusion causes disabling dyspnea in patients with a short life expectancy. Palliation is achieved by fluid drainage, but the most effective first-line method has not been determined.

Objective To determine whether indwelling pleural catheters (IPCs) are more effective than chest tube and talc slurry pleurodesis (talc) at relieving dyspnea.

Design Unblinded randomized controlled trial (Second Therapeutic Intervention in Malignant Effusion Trial [TIME2]) comparing IPC and talc (1:1) for which 106 patients with malignant pleural effusion who had not previously undergone pleurodesis were recruited from 143 patients who were treated at 7 UK hospitals. Patients were screened from April 2007-February 2011 and were followed up for a year.

Intervention Indwelling pleural catheters were inserted on an outpatient basis, followed by initial large volume drainage, education, and subsequent home drainage. The talc group were admitted for chest tube insertion and talc for slurry pleurodesis.

Main Outcome Measure Patients completed daily 100-mm line visual analog scale (VAS) of dyspnea over 42 days after undergoing the intervention (0 mm represents no dyspnea and 100 mm represents maximum dyspnea; 10 mm represents minimum clinically significant difference). Mean difference was analyzed using a mixed-effects linear regression model adjusted for minimization variables.

Results Dyspnea improved in both groups, with no significant difference in the first 42 days with a mean VAS dyspnea score of 24.7 in the IPC group (95% CI, 19.3-30.1 mm) and 24.4 mm (95% CI, 19.4-29.4 mm) in the talc group, with a difference of 0.16 mm (95% CI, -6.82 to 7.15; $P=.96$). There was a statistically significant improvement in dyspnea in the IPC group at 6 months, with a mean difference in VAS score between the IPC group and the talc group of -14.0 mm (95% CI, -25.2 to -2.8 mm; $P=.01$). Length of initial hospitalization was significantly shorter in the IPC group with a median of 0 days (interquartile range [IQR], 0-1 day) and 4 days (IQR, 2-6 days) for the talc group, with a difference of -3.5 days (95% CI, -4.8 to -1.5 days; $P<.001$). There was no significant difference in quality of life. Twelve patients (22%) in the talc group required further pleural procedures compared with 3 (6%) in the IPC group (odds ratio [OR], 0.21; 95% CI, 0.04-0.86; $P=.03$). Twenty-one of the 52 patients in the catheter group experienced adverse events vs 7 of 54 in the talc group (OR, 4.70; 95% CI, 1.75-12.60; $P=.002$).

Conclusion Among patients with malignant pleural effusion and no previous pleurodesis, there was no significant difference between IPCs and talc pleurodesis at relieving patient-reported dyspnea.

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Indwelling pleural catheters (IPCs) are increasingly used as an alternative treatment to talc pleurodesis.¹ Indwelling

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pleural catheters are inserted as day-case procedures and permit domiciliary drainage; offering advantages of outpatient management, patient control over symptoms, and spontaneous pleurodesis in 46%.⁸ However, complications include pleural infection, displacement, catheter tract metastases, and tube blockage.^{9,10}

There are no robust clinical data to address which of these treatments is more effective at palliating symptoms and improving quality of life.¹¹ Large case series exist,¹² but, to our knowledge, only 1 randomized trial has compared doxycycline pleurodesis with IPC use.¹³

The objective of this trial was to compare the efficacy of IPCs with chest tube and talc slurry pleurodesis at relieving dyspnea in the first-line management of malignant pleural effusions, with secondary objectives including assessment of quality of life, hospital stay, and adverse events.

METHODS

Study Design

The Second Therapeutic Intervention in Malignant Effusion Trial (TIME2) was an open-label randomized controlled trial. Recruitment occurred at 7 UK centers between April 2007 and February 2011. Ethical and regulatory approval for the study was obtained from the Milton Keynes research ethics committee before recruitment commenced. After written informed consent, patients were randomized to receive either talc (chest tube and talc slurry pleurodesis) or IPC (Rocket Medical).

Participants Enrolled

Adults with a clinically confident diagnosis of symptomatic malignant pleural effusion requiring pleurodesis were enrolled. The diagnosis was established by either histocytological proof of pleural malignancy or the presence of a recurrent large pleural effusion in the context of histologically proven cancer outside the pleural space.

Exclusion criteria were age younger than 18 years, expected survival of less than 3 months, chylothorax, previous lobectomy or pneumonectomy on the

side of the effusion, previous attempted pleurodesis, pleural infection, total white blood cell count of less than 1000/ μ L, hypercapnic ventilatory failure, pregnancy, lactating mothers, irreversible bleeding diathesis, and irreversible visual impairment.

Randomization

Patients were randomized in a 1:1 ratio to either IPC or talc using minimization, with a random component of 80%. Minimization assigns patients to the group that minimizes the between-group differences in the specified baseline covariates. Group assignments were carried out by the central telephone randomization service of the Medical Research Council. Minimization criteria were histological tissue type (mesothelioma vs nonmesothelioma) and World Health Organization (WHO) performance status (0/1 vs 2/3).¹⁴

Trial Interventions

Indwelling pleural catheters were inserted using a standard technique as an outpatient procedure unless the patient was an inpatient.¹⁵ Initial large volume drainage was performed and patients, relatives, or community nurses were trained in IPC management. Drainage was advised for 3 times weekly or as required for relief of dyspnea. The IPC was removed once significant drainage ceased for at least 4 weeks and there was no radiological evidence of significant fluid reaccumulation.

Patients randomized to the talc group were admitted to hospital and managed with a 12F guidewire percutaneous chest tube insertion and talc slurry pleurodesis with 4 g of sterile high-grade talc (Novatech) following British Thoracic Society treatment guidelines.¹ Participants with extensive trapped lung based on chest radiograph (<50% of lung surface in apposition to the chest wall) did not undergo pleurodesis but remained in the trial follow-up.

All participants received treatment of the primary tumor in accordance with standard care guidelines and oncological advice.

Trial Assessments

Patients were followed up for 12 months after randomization. Patients completed 100 mm visual analog scale (VAS) scores assessing dyspnea and chest pain over the preceding 24 hours at approximately the same time each day for 42 days; at 10, 14, 18, 22, and 26 weeks; and at 9- and 12-month assessments. The VAS was a 100-mm line anchored with no breathlessness or chest pain at 0 mm and maximum possible breathlessness or chest pain at 100 mm.¹⁶ Patients were asked to make a mark along the line at a point representing their level of dyspnea or chest pain.

The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-30) assessment of complications and health care use were measured at 1, 2, 4, 6, 10, 18, 22, and 26 weeks and at 9 and 12 months.

Trial Outcomes

The primary outcome was the mean daily dyspnea over the first 42 days after enrollment as measured by a 100 mm VAS, all of which were measured by 2 independent researchers. The scores were averaged. If the 2 measurements differed by more than 3 mm, both measurements were repeated by the same researchers.

Secondary outcomes were (1) the proportion of patients achieving clinically significant decrease in mean VAS dyspnea over first 42 days (10 mm)¹⁷; (2) mean VAS dyspnea at 6 weeks, 3 months, and 6 months; (3) mean daily chest pain over the first 42 days as measured by a 100 mm VAS; (4) mean VAS chest pain at 6 weeks, 3 months, and 6 months; (5) nights spent in hospital from randomization to discharge; (6) all-cause mortality up to 1 year; (7) self-reported global quality of life assessed by EORTC-QLQ 30 as a percentage (a higher number means better quality of life, minimal clinically meaningful improvement¹⁸); and (8) frequency of serious and nonserious adverse events as assessed by a blinded independent reviewer.

Pleurodesis failure rate in the talc group (defined as the need for further ipsilateral pleural intervention), the spontaneous pleurodesis rate in the IPC group (defined as removal of IPC following spontaneous cessation of drainage with no significant fluid recurrence on chest radiograph or thoracic ultrasound and no further ipsilateral pleural intervention), and IPC drainage frequency and number of 600 mL drainage bottles used were recorded.

Statistical Methods

Data were analyzed on an intention-to-treat basis and all randomized patients in whom an outcome was available were included in the analysis. All analyses were predetermined prior to any data analysis, unless specifically stated. Analyses were adjusted for the minimization variables (performance status and mesothelioma).¹⁹ Stata version 12.1 (StataCorp LP) statistical software was used for all analyses.

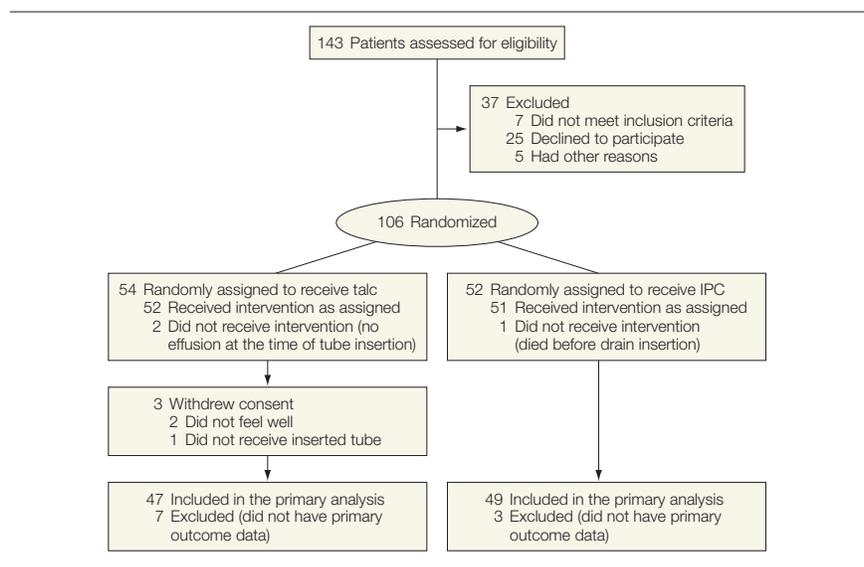
The difference between treatment groups in mean daily dyspnea and chest pain VAS score over 42 days was calculated using a mixed-effects linear regression model. This approach was used to account for days with missing VAS scores (the analysis did not differentiate between scores missing due to patient death and those missing because the patient did not complete their VAS score on that day). Study day was modeled as a continuous variable using fractional polynomials and was included in the model as a random effect. The model adjusted for the baseline VAS score and mean imputation was used for patients from whom a baseline score was unavailable.²⁰ A number of sensitivity analyses were performed using multiple imputation under a variety of missing-at-random and missing-not-at-random scenarios.

Full details of all statistical analyses can be found in the statistical analysis plan (eSupplement available at <http://www.jama.com>).

Power Calculation

Power calculations were based on pilot data (10 patients who received talc

Figure 1. Patient Flowchart



Talc indicates chest tube and talc slurry pleurodesis; IPC, indwelling pleural catheter.

and 10 patients who received IPC) demonstrating a mean (SD) decrease VAS dyspnea score of 7 mm (14 mm). Patients in the IPC group experienced a mean [SD] decrease of 14 mm (11 mm) vs 21 mm (10 mm) of those in the talc group. To detect a mean difference of 7 mm between the treatment groups (5% significance, 90% power) assuming a common between-group standard deviation of 10 mm and a loss to follow-up of 25%, 114 patients were required. The trial management group met following the recruitment of 106 patients and blinded assessment of data quality demonstrated total loss to follow-up of less than 10%, providing a greater than 90% power with the 106 recruited patients; the study recruitment was terminated at this point.

RESULTS

Patients

The trial flowchart is presented in FIGURE 1. One hundred six patients were randomized at 7 UK hospitals between April 2007 and February 2011—54 to the talc treatment group and 52 to the IPC treatment group—and were followed up until February 2012. Baseline demographic variables were well matched (TABLE 1). There were small differences in dyspnea with

a mean VAS score of 62 mm in the IPC group vs 55 mm in the talc group and in chest pain with a mean VAS score of 29 mm in the IPC group vs 22 mm in the talc group. The types of malignancies were also slightly different with 31% having breast cancer in the IPC group vs 20% in the talc group and 17% having lung cancer in the IPC group vs 30% in the talc group.

Primary End Point

Three patients in the IPC group and 7 in the talc group had no recorded VAS scores so were excluded from the VAS score analyses. The 5 patients in the IPC group and the 15 in the talc group who died during the first 42 days were included in the analysis. The median number of days with observed VAS scores was 41 in both groups (interquartile range [IQR], 15-42 days for the talc group; IQR, 33-42 days for the IPC group).

There was no significant difference in dyspnea during the first 42 days between groups. The IPC group had a mean VAS of 24.7 mm (95% CI, 19.3-30.1 mm) vs 24.4 mm (95% CI, 19.4-29.4 mm) for the talc group, for a difference of 0.16 mm (95% CI, -6.82 to 7.15 mm; *P* = .96). Dyspnea improved in both groups from baseline for a mean

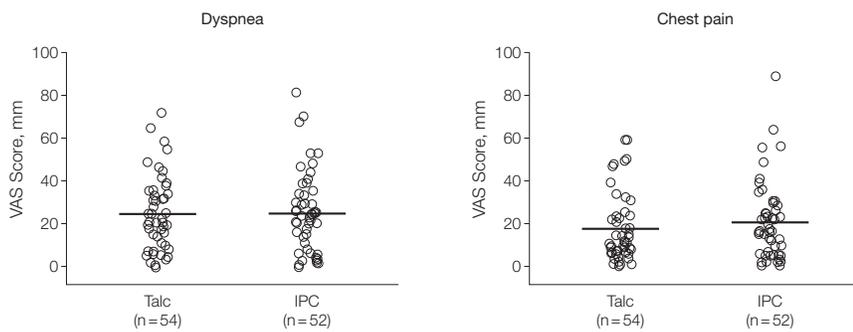
Table 1. Baseline Demographic Data for 106 Patients With Malignant Pleural Effusion

	IPC	Talc
Patients, No. (%)	52	54
Age, mean (SD), y	67 (11)	67 (12)
Male:female (% men)	23:29 (44)	23:31 (43)
Type of malignancy ^a		
Breast	16	11
Lung	9	16
Mesothelioma	6	5
Other	21	21
VAS dyspnea, mean (SD), mm	62 (22)	55 (26)
VAS chest pain, mean (SD), mm	29 (30)	22 (29)
Size of effusion on chest radiograph, % hemithorax (SD)	51 (23)	49 (25)
EORTC QLQ-30: global health status, % (SD)	37 (23)	37 (20)
Inpatient:outpatient at enrollment (% inpatient)	19:33 (35)	22:31 (42)

Abbreviations: EORTC QLQ-30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (higher % means better quality of life); IPC, indwelling pleural catheter; talc, chest tube and talc slurry pleurodesis; VAS, visual analog scale.

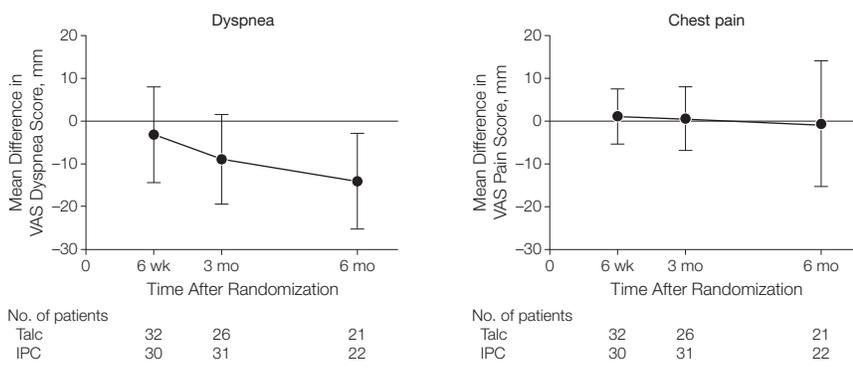
^aOther malignancies were colorectal (4 IPC, 3 talc), ovarian (2 IPC, 5 talc), adenocarcinoma of unknown primary (4 IPC, 2 talc); renal (3 IPC, 2 talc); sarcoma (1 IPC, 2 talc); thymoma (1 IPC, 1 talc); esophageal (2 IPC); peritoneal (1 IPC, 1 talc); prostate (1 IPC); ampullary (1 IPC); leiomyosarcoma (1 IPC); melanoma (1 talc); myeloma (1 talc); nasopharyngeal (1 talc), and unknown (1 IPC, 1 talc). One patient in the talc group died before enrollment, so no demographic data were available.

Figure 2. Comparison of Dyspnea and Chest Pain Among Patients Treated With Indwelling Pleural Catheters (IPCs) vs Patients Treated With Chest Tube and Talc Slurry Pleurodesis (Talc) at 42 Days



The bars represent the mean visual analog scale (VAS) score for dyspnea and pain.

Figure 3. Mean Difference in Visual Analog Scale (VAS) Score for Dyspnea and Chest Pain



The error bars represent 95% confidence intervals.

decrease of 37.0 mm (95% CI, 29.2-44.8 mm) for the IPC group and 30.2 mm (95% CI, 22.0-38.4) for the talc group. Sensitivity analyses, which included patients with no recorded VAS scores, confirmed no significant difference between treatment groups for an under-extreme-missing not-at-random difference of -2.8 (95% CI, -12.4 to 6.8; $P = .56$).

Secondary End Points

Proportion of Patients Achieving Clinically Significant Decrease in Mean VAS Dyspnea Over 42 Days. A clinically significant decrease in mean VAS dyspnea (10 mm)¹⁷ was observed in 42 of 49 patients (86%) in the IPC group and in 35 of 47 patients (74%) in the talc group. This difference was not statistically significant (OR, 0.90; 95% CI, 0.18-4.43; $P = .90$).

Dyspnea After 6 Weeks. During the follow-up, 86 patients were alive at 6 weeks, 69 at 3 months, and 54 at 6 months. Sixty-two patients had VAS scores at 6 weeks, 57 at 3 months, and 43 at 6 months.

There was no significant difference in dyspnea between the groups until 6 months, at which point there was a clinically and statistically significant decrease in dyspnea in the IPC group compared with the talc group. The mean VAS difference was -8.9 mm (95% CI, 1.7 to -19.4 mm; $P = .10$) at 3 months and -14.0 mm (95% CI, -25.2 to -2.8; $P = .01$) at 6 months (FIGURE 2 and FIGURE 3).

Chest Pain. Data completeness for chest pain was similar to that of the primary outcome. A reduction in chest pain from baseline was observed in both study groups with a mean decrease VAS over 42 days of 8.2 mm (95% CI, 0.3-16.2 mm) in the IPC group and 4.4 mm (95% CI, 3.8 to 12.6 mm) in the talc group. There was no significant difference in chest pain between treatment groups for the duration of the trial (Figure 2 and Figure 3).

Length of Hospital Stay. Overall, 51 patients (98%) in the IPC group and 48 (89%) in the talc group were included in the length-of-stay analysis. One pa-

tient in the IPC group and 3 in the talc group were excluded for lack of follow-up information, and 3 patients in the talc group were excluded because they died of underlying malignancy while they were in the hospital (2 at 9 days and 1 at 13 days).

The time from randomization to discharge was a median of 0 days (IQR, 0-1 day) in the IPC group vs a median of 4 days (IQR, 2-6 days) in the talc group: a difference of -3.5 days (95% CI, -4.8 to -1.5; $P < .001$).

Post hoc analysis showed that 23% in the IPC group and 16% in the talc group were readmitted to the hospital for repeat drainage or drain-related complications, for an odds ratio (OR) of 1.59 (95% CI, 0.52-5.08; $P = .51$). Over 12 months, the IPC group spent a median of 1 day (IQR, 0-3 days) in the hospital for drainage or drain-related complications, whereas the talc group spent a median of 4.5 days (IQR, 2.5-7.5 days; $P < .001$).

Mortality. Mortality data were available for all patients. During the study, 91 patients (86%) died with a median duration of follow-up of 6.1 months (IQR, 2.0-11.2 months). Median survival time was 200 days (IQR, 39-392 days) in the talc group and 153 days (IQR, 73-288 days) in the IPC group. The Kaplan-Meier plot demonstrated crossing hazards (FIGURE 4), and there was strong evidence against the proportional hazards assumption ($P = .008$). Post hoc analysis using restricted mean survival time,²¹ adjusting for underlying malignancy type (breast vs lung vs other) showed a small but statistically significant increase in survival time in the IPC group of up to 6 weeks compared with the talc group, with a difference of 0.1 months (95% CI, 0.01-0.2 months; $P = .04$). There was no significant difference in survival time up to 1 year for a difference of -0.8 months (95% CI, -2.4 to 0.8 months; $P = .32$).

Quality of Life. Sixty-nine patients at 6 weeks, 56 at 3 months, and 41 at 6 months had observed quality-of-life data.

Global quality of life measured by the QLQ-30 improved in both groups at 6

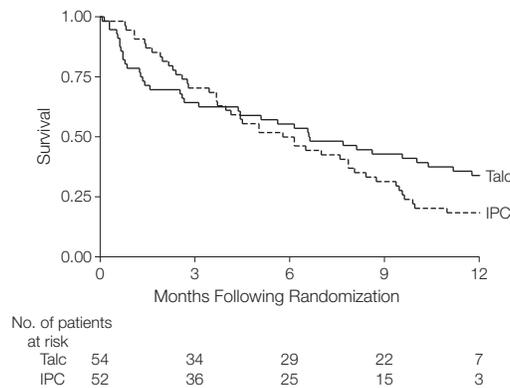
weeks with an increase of 18.3 in the IPC group and 7.1 in the talc group. There was no significant difference in quality of life at any time point. The mean score at 6 weeks was 59.0 (95% CI, 51.8 to 66.3) in the IPC group and 48.3 (95% CI, 50.1 to 56.5) in the talc group, with a difference of 4.8 (95% CI, -1.6 to 11.2; $P = .14$).

Adverse Events. The frequencies of serious and nonserious adverse events are summarized in TABLE 2. Twenty-one of 52 patients (40%) in the IPC group vs 7 of 54 patients (13%) in the talc group experienced adverse events (OR, 4.70; 95% CI, 1.75-12.60; $P = .002$). There were no significant differences between groups, 9 patients (17%) in the IPC group vs 5 (9%) in the talc group experienced serious ad-

verse events (OR, 2.1; 95% CI, 0.57-7.71; $P = .26$).

Two patients reported as having nonserious pleural infections were both asymptomatic and treated with oral antibiotics. Five other patients with pleural infection required admission for intravenous antibiotic treatment. One pleural infection was considered to have contributed to the patient's death. All serious pleural infections occurred late (50, 63, 102, 114, and 206 days after IPC insertion). One patient was taking sunitinib at the time of infection, but no other patients were undergoing chemotherapy. None of the IPCs were removed because of the infection. Three patients went on to have a spontaneous pleurodesis.

Figure 4. Survival Estimates Between Patients Treated With Indwelling Pleural Catheters (IPCs) vs Patients Treated With Chest Tube and Talc Slurry Pleurodesis (Talc)



The difference in mean survival time up to 1 year between IPC and talc is -0.8 (95% CI, -2.4 to 0.8).

Table 2. Summary of Adverse Events by Treatment Group^a

Type of Adverse Event	IPC		Talc	
	Serious	Nonserious	Serious	Nonserious
Pleural infection	5	2	1	0
Cellulitis	1	5	0	1
Symptomatic fluid loculation requiring fibrinolytics	1	2	1	0
Catheter site metastases	0	1	0	0
Catheter blockage	1	9	1	0
Other ^b	1	0	2	3
Total	9	19	5	4

Abbreviations: IPC, indwelling pleural catheter; talc, chest tube and talc slurry pleurodesis.

^aThis table represents the total number of adverse events. A single patient may have had more than 1 adverse event.

^bThe serious adverse events included in the "Other" category were chest pain requiring readmission (1 IPC), surgical emphysema (1 talc), persistent air leak (1 talc). The 3 nonserious adverse events in the talc group were all chest tube displacement prior to pleurodesis. The complications of symptomatic fluid loculation requiring fibrinolytics, cellulitis, and blocked catheter in the talc group were observed in 2 patients who had IPCs inserted following failure of pleurodesis.

IPC Drainage, Pleurodesis Success, and Spontaneous Pleurodesis Rate. Mean number of 600-mL drainage bottles used during initial IPC drainage was 3 (range, 1-7). The mean IPC drainage frequency in the first 42 days was twice weekly. Twenty-nine of 51 patients (57%) had their IPCs removed; however 3 patients (6%) subsequently required further pleural intervention (1 therapeutic aspiration, 2 chest tube insertions), giving an overall spontaneous pleurodesis rate of 51%.

In the talc group, 6 patients had not undergone pleurodesis, 3 due to trapped lung and 3 due to chest tube displacement. Twelve talc patients (22%) had further pleural procedures compared with 3 (6%) in the IPC group (OR, 0.21; 95% CI, 0.04-0.86; $P = .03$).

COMMENT

To our knowledge, this is the first randomized trial to directly compare IPCs with chest tube and talc slurry pleurodesis for initial treatment of symptomatic malignant pleural effusion and to assess the key outcome of dyspnea. Our results demonstrate that both strategies are highly effective treatments for relieving dyspnea with more than 75% achieving a clinically significant improvement and demonstrated that there was no significant difference in the clinically important outcome measures of chest pain and quality of life between these treatments. As such, IPCs cannot be advocated as a superior treatment to talc pleurodesis for palliation of symptoms. However, other factors such as length of hospital stay, adverse events, and the inconvenience of on-going drainage may be important factors in patient and physician choice of initial treatment modality in malignant pleural effusion, and this study provides initial data on which to base some of these choices.

Current guidelines¹ advocate talc slurry pleurodesis as first-line therapy for malignant pleural effusion, with IPCs reserved for second-line treatment or for those without complete

lung reexpansion. The results of this study suggest that both talc pleurodesis and indwelling catheters are effective initial treatments for symptom relief in malignant pleural effusion. Alternative first-line treatments include surgical pleurodesis with decortication or medical thoracoscopy and talc poudrage. A previous study has shown no significant difference in pleurodesis failure rate between talc poudrage and talc slurry. However, the relative dyspnea relief associated with these treatments has not been assessed⁷ and this should be the subject of further study.

The secondary outcomes in this study suggest that there may be advantages to the use of IPCs. These include a significantly shorter initial and total duration of hospital stay for drainage and drain related complications, congruent with published nonrandomized series,²² a clinically significant improvement in dyspnea in the IPC group at 6 months, and a 16% absolute reduction in the proportion of patients requiring further pleural interventions over 12 months. These secondary results are encouraging but should be interpreted with caution because this study was not powered to definitively address these outcomes.

The potential advantages of IPCs are, however, associated with an increase in observed adverse events (OR, 4.7) compared with talc pleurodesis, including 5 patients (9.6%) with pleural infection, meeting regulatory criteria for seriousness, compared with 1 (1.9%) in the talc group. The 2 nonserious pleural infections reported may have represented catheter colonization rather than infection because both patients were asymptomatic.

Overall cost of these treatments will be an important factor in determining which treatments are offered in the future. Previous studies comparing talc with IPC treatment have suggested reduced initial costs for IPC treatment but potential increased community care costs.^{23,24} Cost analysis was not the primary purpose of this study; however, cost economic analysis of our data, in-

cluding assessment of both in-hospital and primary care use, is currently in progress.

There are several limitations to this study. The nature of the interventions under investigation meant that blinding was not possible, and the primary outcome measure was subjective (dyspnea VAS). Although these factors may have permitted bias in self-reported dyspnea measurement, the treatment intent in malignant pleural effusion drainage is palliative; a subjective, patient-reported measure is therefore a necessary and relevant outcome in a trial assessing such treatments. This trial demonstrates that both talc pleurodesis and IPCs are effective treatments for relieving dyspnea and improving patients' quality of life but that indwelling catheters are not superior to talc pleurodesis for these outcomes. Although there may be other advantages to the use of IPCs—reduced hospital stay and decreased requirement for further pleural procedures—these potential benefits have not been definitively proven and require further investigation. The results from this study provide evidence on which discussion of relative risks and benefits of each treatment can be based—treatment choice is likely to depend on individual patients' attitude toward hospital stay, home drainage, and relative adverse effects.

CONCLUSION

Among patients with malignant pleural effusion and no previous pleurodesis, there was no significant difference between IPCs and talc pleurodesis in relieving patient-reported dyspnea. Indwelling pleural catheters reduce time in hospital but are associated with an excess of adverse events.

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Author Contributions: Dr Rahman had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs Mishra and Davies were joint first authors.

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Study supervision: R.J.O. Davies, Rahman.

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