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Treatment of Malignant Pleural Effusion: A Cost-Effectiveness Analysis

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Abstract

Background—Patients with malignant pleural effusion (MPE) have varied expected survival and treatment options. We studied the relative cost-effectiveness of various interventions. **Methods:** Decision analysis was used to compare Repeated Thoracentesis (RT), Tunneled Pleural Catheter (TPC), Bedside Pleurodesis (BP) and Thoracoscopic Pleurodesis (TP). Outcomes and utility data were obtained from institutional data and review of literature. Medicare allowable charges were used to ensure uniformity. Base case analysis was performed for two scenarios; expected survival of 3 months and 12 months respectively. The incremental cost effectiveness ratio (ICER) was estimated as the cost per quality-adjusted life year (QALY) gained over the patient's remaining lifetime.

Results—Under base case analysis with 3-month survival, repeated thoracentesis was the least expensive treatment (\$4946) and provided the fewest utilities (0.112 QALYs). The cost of therapy for the other options was; TPC \$ 6,450, BP \$ 11,224 and TP \$ 18,604. Tunneled pleural catheter dominated both pleurodesis arms, i.e. TPC was less expensive and more effective. The ICER for tunneled pleural catheter over repeated thoracentesis was \$ 49,978. The ICER was sensitive to complications and ability to achieve pleural sclerosis with TPC.

For base case analysis with 12-month survival, bedside pleurodesis was the least expensive treatment (\$13,057) and provided 0.59 QALYs. The cost of treatment for the other options was: TPC \$ 13,224, TP \$ 19,074 and RT \$ 21,377. Bedside pleurodesis dominated tunneled pleural catheter and thoracentesis. Thoracoscopic pleurodesis was more effective than bedside pleurodesis but the ICER for thoracoscopic over bedside pleurodesis was greater than \$250,000.

Conclusions—Using decision analysis, tunneled pleural catheter is the preferred treatment for patients with malignant pleural effusion and limited survival; bedside pleurodesis is the most cost-effective treatment for those with more prolonged expected survival.

Keywords

pleura; cost analysis

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Introduction

Malignant pleural effusion (MPE) is a common clinical problem in thoracic surgery. Diagnosis is commonly established by initial thoracentesis. Conventional management of MPE has involved bedside or thorascopic chemical pleurodesis, often using talc as the therapeutic agent.(1-7) Long-term indwelling pleural catheters have been utilized for MPE for almost a decade with good outcomes.(8-11) The choice of treatment for MPE is determined by many factors; local expertise, patient preference, need for tissue diagnosis, presence of loculations in the pleural space, performance status of patient, and expected survival of the patient.

Since resources are limited, it is reasonable to compare the cost of various treatments options for common diseases, especially if treatments lead to similar clinical outcomes. Economic evaluation is a method to examine this trade-off between costs and effects of comparative treatments. (12) The effectiveness of treatments is evaluated in terms of survival (life-years) attributable to the treatment or quality adjusted life years (QALYs). To calculate QALYs, any state of health or disability is assigned a utility on a scale ranging from 0 (immediate death) to 1 (a state of perfect health). The outcome of any health intervention can then be calculated as the product of the increase in utility that it may cause and the time in years over which it may be enjoyed. Health economics analyses have been rarely performed to compare competing treatments for MPE.(13)

The objective of the current study is to study the relative cost-effectiveness of various treatment options for MPE; Repeated Thoracentesis, Tunneled Pleural Catheter, Bedside Pleurodesis, and Thorascopic Pleurodesis.

Material and Methods

A decision analysis model was constructed using Tree Age Pro 2010 software (TreeAge Software, Inc, Williamstown, MA). Criteria were chosen to define a population of patients which would be representative of common findings in patients with a malignant pleural effusion. This type of analysis is well described in the literature and the interested reader can find detailed explanations elsewhere.(14) Such analyses have been previously described in thoracic surgical problems (15, 16) and are structured to include a base strategy and alternative strategies. The results are reported as incremental cost-effectiveness: the ratio of additional costs imposed by the alternative strategy over the additional benefits gained. The incremental cost effectiveness ratio (ICER) was estimated as the cost per quality-adjusted life year gained over the patient's remaining lifetime using a decision model. When one strategy is shown to be both more effective and less expensive than the other strategy, it is said to "dominate" the more expensive and less effective alternative.

The data utilized for model inputs came from 2 sources. We performed a Pubmed literature search for the period from 1995-2010 using the terms "malignant pleural effusion" and "treatment" and the results were augmented with additional citations from the lists of references within the works chosen for closer scrutiny. The chosen references were used to create reasonable estimates for the results of therapeutic interventions, the benefits accrued to the patients, and the probabilities of certain key events that would occur to the patients. Additionally, with the approval of the Institutional Review Board, we assessed results of thorascopic pleurodesis at our institution for a 3-year period from 2008-10. Following the recommendation of the Panel on Cost-effectiveness in Health and Medicine we based costs on the Medicare allowable.(17)

A decision tree was constructed and loaded with the associated costs, benefits, and probabilities. Two decision trees are shown at <http://www.cardiothoracicsurgery.wustl.edu/PurietalIllustrations.asp>.

A decision tree reads from left to right and begins with a decision node (square) in which a treatment modality is selected. From there, a series of probability nodes (circles) capture the likelihood of chance events for patients subjected to any of the treatments. Finally, the terminal nodes (triangles) represent terminal states for the analysis and are labeled with the costs expended to reach that state as well as the estimated utilities for patients reaching that terminal state. Health state utility values were estimated from published literature. A health state of a resolved pleural effusion (e.g. successful pleurodesis) was assumed to have a utility value of 0.599; unresolved/persistent pleural effusion a utility value of 0.473; an indwelling pleural catheter a utility value of 0.58; and a complication, a utility value of 0.4. (13, 18, 19)

We chose to study the problem for two different patient profiles. Clinically, it is well recognized that patients presenting with malignant pleural effusion may have a relatively short expected survival or may have a protracted survival, often depending upon their disease burden, performance status, and co-morbidities. Thus we constructed two distinct decision models; one assuming a 3-month survival period and the second with a 12-month expected survival. We performed the analysis from a payer's perspective. The effect of uncertainty in the model was addressed by one- and two-way sensitivity analyses to determine the effect of our parameter assumptions on the outcome.

Results

Analysis of institutional data revealed that 93 patients had undergone thoracoscopic pleurodesis between 2008 and 2010. The 30-day mortality was 3/93 (3%) and the rate of complications was 8/93 (9%).

The incidence of pleural sclerosis, risk of complications or mortality, and cost data utilized in the model with expected survival of 3 months, is shown in table 1. We assumed that none of the therapies led to a longer survival, thus the differences in effectiveness were demonstrated by improved quality of life. Under base case analysis with 3-month survival, repeated thoracentesis was the least expensive treatment (\$4946) and provided the lowest utility for the 3-month survival (0.112 QALYs). The cost of therapy for the other options was; TPC \$ 6,450, BP \$ 11,224 and TP \$ 18,604. Tunneled pleural catheter dominated both pleurodesis arms (was more effective and less expensive). (Please see <http://www.cardiothoracicsurgery.wustl.edu/PurietalIllustrations.asp> for a decision tree depicting the decision analysis for various treatment options in malignant pleural effusion in a patient with an expected survival of 3 months.) The ICER for tunneled pleural catheter over repeated thoracentesis was \$ 49,978. The ICER was sensitive to complications and incidence of pleural sclerosis with TPC i.e. if the incidence of pleural sclerosis with TPC dropped below that assumed in the base case, or the incidence of complications with TPC rose above baseline, the strategy became less cost-effective (Table 2). If the incidence of pleural sclerosis with TPC dropped below 38%, the ICER went up to \$51,300, thus crossing a commonly accepted threshold of \$50,000/QALY. Again, if the risk of major complications with TPC rose even slightly above the base case assumption of 5%, this threshold was crossed (data not shown). Varying the effectiveness and morbidity among reasonable estimates for each parameter for either pleurodesis option did not change the outcomes in this short-term survival model. These options are far more expensive and the qualitative results do not merit the additional expenditure.

For base case analysis with 12-month survival, bedside pleurodesis was the least expensive treatment (\$13,057) and provided 0.59 QALYs (Table 3). The cost of treatment for the other options was: TPC \$ 13,224, TP \$ 19,074 and RT \$ 21,377. The results of the decision analysis are shown at <http://www.cardiothoracicsurgery.wustl.edu/PurietalIllustrations.asp>. Bedside pleurodesis dominated (was more effective and less expensive than) tunneled pleural catheter and repeated thoracentesis. Thoracoscopic pleurodesis was more effective than bedside pleurodesis but also more expensive in that the ICER for thoracoscopic over bedside pleurodesis was greater than \$250,000 per QALY (Table 3). In sensitivity analysis, varying the effectiveness and morbidity of both pleurodesis options across a clinically plausible range did not bring the ICER for thoracoscopic over bedside pleurodesis below \$50,000. The results of a 2-way sensitivity analysis between bedside pleurodesis and tunneled pleural catheter are shown in figure 1. We see that increasing rates of pleural symphysis with BP, and rising complication rate with TPC would favor BP as the appropriate cost-effective decision.

Comment

Our decision models evaluating alternative treatments for malignant pleural effusion focus on the palliation of symptoms rather than the more objective, yet likely less relevant end-point of pleural sclerosis. The cost-effectiveness analysis confirms that a less invasive strategy (TPC or thoracentesis) is preferable in patients with a very short expected survival; however spending more resources to create a pleurodesis may be the preferred option in patients with a longer expected survival. These results appear to be clinically logical and reflect the performance status of the patients and their likelihood of deriving benefit from a more “permanent” procedure. Only one other study has looked at relative cost-effectiveness of therapies for MPE. (13) Olden et al compared TPC and talc pleurodesis for patients with a 6-month expected survival, and found that pleurodesis dominated TPC, though the differences in both costs and utilities between the two options were small. Their study did not explicitly discriminate between thoracoscopic and bedside pleurodesis. We considered these two modalities of pleurodesis separately as their effectiveness, rate of complications, and costs are different. We also chose to include thoracentesis only as a treatment arm as it is more closely reflects a real-world situation.

Our model assumes that a diagnosis of MPE has been previously established, the pleural space is uncomplicated, the lung is not trapped, and that every patient is suitable for a procedure under sedation or anesthesia. Clearly, many patients encountered in clinical practice do not meet these criteria. Such anatomic and physiologic constraints may make one form of therapy preferable over another, regardless of the economic analysis.

Our clinical approach to patients with malignant pleural effusion is similar to the results of the current analysis. In patients with a poor performance status and very short life expectancy, we prefer to use TPCs. Pleurodesis is utilized when the lung is not trapped and the patient has an acceptable performance status. For patients with reasonable performance status who require tissue diagnosis, have loculated effusions, or have an intraoperative diagnosis of MPE, we employ thoracoscopic pleurodesis.

Our paper has certain limitations. The analysis is based upon a combination of prospective and retrospective reports from published literature and our institutional data. Thus our analysis is subject to the biases of a retrospective study, including selection bias in treatment allocation. The estimates of utilities for various disease states in the model are derived from published literature.

These estimates may not always be transferable to populations outside the original study setting. Additionally, there are only a few reports that specifically look at utilities for

baseline and post-treatment states for patients with malignant pleural effusions. The utilities provided by most treatment arms in the model (except repeated thoracentesis) are similar and thus the economic analysis is influenced by the cost of the therapy. We considered expected life-spans of 3- and 12- months respectively for our model. Since lung and breast cancer are responsible for more than 50% of MPEs, newer agents for lung cancer and improved survival in breast cancer patients may indicate the need to consider longer time frames in comparing therapies for malignant pleural effusions. We did not consider the ancillary costs associated with recurrence of effusions, like need for oxygen therapy and physician visits. Such costs are difficult to estimate, are likely to be similar in various treatment groups and are not expected to change the outcomes of the model. Additionally, based upon our clinical practice, we assumed that half of the patients are facile at draining their tunneled pleural catheters themselves, thus lowering the cost of the TPC arm. If this is not the case, the additional nursing costs of TPC may increase its cost in the 3-month survival model, and make it a less cost-effective option.

The cost-effectiveness analysis in the present study was performed from a payer's perspective. The payer is defined as an individual or organization that assumes financial responsibility for health-care services. Alternate approaches to economic analyses in medicine are to consider the societal perspective or a combined approach. (20, 21) The societal perspective includes all program costs, no matter who incurs them, and all program consequences, no matter who experiences them. In the societal perspective, the net cost of an intervention is calculated by deducting the cost of disease averted and the cost of productivity losses from the program cost. Thus an intervention that is more effective and also more costly from a payer's perspective is likely to look more attractive (lower ICER) from a societal perspective when external costs averted are deducted from the cost of the intervention. Such costs might include transportation costs and costs of work lost by caregivers and family members in some strategies but not in others.

For the purpose of this study, we utilized Medicare allowable charges as costs wherever possible. This approach ensures uniformity of cost data and makes the results as broadly applicable as possible and has been utilized by others.(22) Medicare allowable charges vary geographically but generally the direction and degree of change (increase or decrease) is expected to be similar for treatment arms. Alternate standardized sources of cost have been utilized in other studies. (17, 23, 24) While it is meaningful to use a standardized system of cost estimation for economic analyses in medicine, charges billed by individual institutions for the same service vary widely as does the amount reimbursed by private insurers. There is an understandable reluctance on the part of some institutions to share their actual cost and charge information thus explaining the lack of this information in published literature.

Local expertise and the type of medical practice may influence the interpretation and application of economic analyses in medicine. Our analysis has been conducted from a thoracic surgical perspective, with thoracoscopic procedures performed in the operating room under general anesthesia, and pleural catheters placed under mild sedation. Successful outpatient catheter based pleurodesis has been described (25) and such an approach would substantially lower the cost of pleurodesis as hospitalization is a major proportion of the costs. Similarly, patient-centered accelerated care pathways can decrease hospital stay after thoracic operations (26) and thus significantly lower the cost of thoracoscopic pleurodesis.

The ideal scenario for conducting cost-effectiveness analyses in medicine is when cost and utility data are collected prospectively in a controlled setting. While, to our knowledge, no such randomized trial is currently underway for MPE, we have initiated institutional efforts to prospectively collect utility data in patients with MPE and other related thoracic surgical

problems. Data collected from this and other similar population based studies will further clarify the relative cost-effectiveness of therapies for malignant pleural effusion.

Conclusions

Using decision analysis, tunneled pleural catheter is the preferred treatment for patients with malignant pleural effusion and limited survival while bedside pleurodesis is the most cost-effective treatment for those with prolonged expected survival. The therapies provide similar utilities and, based upon local expertise, the treatment decision may be tailored for individual patients.

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Figure 1.

Decision tree depicting the decision analysis for various treatment options in malignant pleural effusion in a patient with an expected survival of 3 months. The figure depicts the event probabilities, costs and outcomes associated with the treatment options. The symbols used in the diagram are described in the methods section of the text.

Table 1

Base case assumptions for a patient with malignant pleural effusion with expected survival of 3 months.

Treatment	Incidence of pleural sclerosis	Source of pleural sclerosis data	Risk of complications	Source of complications data	Total Cost (2010 US\$)	Source of cost data
Repeated thoracentesis	0%	References (6, 27, 28)	2%	Reference (29)	4946	CMS allowable, Institutional data
Tunneled pleural catheter	40%	References (8-11)	5%	Reference (8)	6450	CMS allowable, Institutional data
Bedside pleurodesis	73%	References (6, 7, 30, 31)	Complications 9% Mortality 1%	References (7, 30, 32, 33),	11224	CMS allowable, Institutional data
Thoracoscopic pleurodesis	87%	References (2-5, 7)	Complications 14%, Mortality 2%	References (2-5, 7), Institutional data	18604	CMS allowable, Institutional data

Table 2

Results of 1-way sensitivity analysis with variations in the rate of pleural sclerosis with tunneled pleural catheter. The table shows that as the assumed rate of pleural sclerosis with TPC increases from 15% to 75% (column 1), the strategy becomes more cost-effective, demonstrated by a decrease in the ICER from \$58,070 to \$32,510 as shown in column 8 of the table.

TPC sclerosis	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0.25	Repeated thoracentesis	\$4,946		0.1123 yrs		\$44,063	
	Tunneled pleural catheter	\$6,652	\$1,706	0.1416 yrs	0.0294 yrs	\$46,969	\$58,070
	Catheter pleurodesis	\$11,224		0.1362 yrs		\$82,391	(Dominated)
	Thoracoscopic pleurodesis	\$18,604		0.1365 yrs		\$136,285	(Dominated)
0.375	Repeated thoracentesis	\$4,946		0.1123 yrs		\$44,063	
	Tunneled pleural catheter	\$6,484	\$1,538	0.1422 yrs	0.0300 yrs	\$45,589	\$51,300
	Catheter pleurodesis	\$11,224		0.1362 yrs		\$82,391	(Dominated)
	Thoracoscopic pleurodesis	\$18,604		0.1365 yrs		\$136,285	(Dominated)
0.5	Repeated thoracentesis	\$4,946		0.1123 yrs		\$44,063	
	Tunneled pleural catheter	\$6,315	\$1,369	0.1428 yrs	0.0306 yrs	\$44,220	\$44,793
	Catheter pleurodesis	\$11,224		0.1362 yrs		\$82,391	(Dominated)
	Thoracoscopic pleurodesis	\$18,604		0.1365 yrs		\$136,285	(Dominated)
0.625	Repeated thoracentesis	\$4,946		0.1123 yrs		\$44,063	
	Tunneled pleural catheter	\$6,147	\$1,201	0.1434 yrs	0.0312 yrs	\$42,862	\$38,535
	Catheter pleurodesis	\$11,224		0.1362 yrs		\$82,391	(Dominated)
	Thoracoscopic pleurodesis	\$18,604		0.1365 yrs		\$136,285	(Dominated)
0.75	Repeated thoracentesis	\$4,946		0.1123 yrs		\$44,063	
	Tunneled pleural catheter	\$5,978	\$1,032	0.1440 yrs	0.0318 yrs	\$41,516	\$32,510
	Catheter pleurodesis	\$11,224		0.1362 yrs		\$82,391	(Dominated)
	Thoracoscopic pleurodesis	\$18,604		0.1365 yrs		\$136,285	(Dominated)

C/E – Cost effectiveness; Eff – effectiveness (in Quality-Adjusted Life Years); ICER – Incremental Cost-Effectiveness Ratio; Incr Cost – Incremental cost; Incr Eff – Incremental effectiveness (in Quality-Adjusted Life Years); TPC_sclerosis – Incidence of pleural sclerosis with TPC (shown as a fraction)

Table 3

Result of decision analysis base case with 12 month expected survival.

Strategy	Cost (\$)	Incremental Cost (\$)	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER
Bedside pleurodesis	13057		0.590		Base case
Tunneled pleural catheter	13224	167	0.589/	-0.001	Dominated
Thoracoscopic pleurodesis	19074	6017	0.592	0.002	>250,000
Repeated thoracentesis	21377	8320	0.450	-0.14	Dominated

ICER - Incremental cost-effectiveness ratio in dollars per additional quality adjusted life year; QALY - Quality adjusted life year