

Impact of a dedicated malignant pleural effusion clinic on the management of malignant pleural effusion

Abstract

Background: Malignant pleural effusions (MPE) are common complications of advanced malignancy. The treatment of MPE is generally focused on palliation of respiratory symptoms. The main drawback of the traditional method of pleurodesis is the requirement for hospitalization.

Objectives: To examine the safety, efficacy and economy of management of a dedicated MPE clinic.

Methods and analysis: A retrospective cohort study was designed to compare complication rates, pleural effusion control, length of hospital stay, type of interventions, estimated hospital days saved between two three-year non-contemporary periods – before the implementation of MPE clinic and after.

Results: Pre MPE clinic and MPE clinic group comprised of 115 and 161 patients respectively. The number of hospital admissions was lower in the MPE clinic period (42.4% vs 73.9%; $p < 0.0001$) and the pleural effusion control was higher in the same group (65.2% versus 51.3%; $p = 0.02$). The estimated hospital days saved was 1001 days over 3 years.

Conclusion: A dedicated malignant pleural effusion (MPE) clinic is a strategy of malignant effusion management that reduces hospital admission days and, will allow patients to spend more time outside hospital, reduce costs and save healthcare resources. Outpatient MPE clinic is of particular importance in the setting of the health care system and the overcrowded hospitals. The ability to avoid a one week hospitalization for a palliative intervention and replace it with a simple and effective outpatient procedure should appeal to patients and administrators alike.

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Introduction

Malignant pleural effusions (MPE) are common complications of advanced malignancies and are commonly associated with advanced cancers of the lung, breast and colon.¹ It has been estimated that 150,000 patients develop MPE every year in the United States.² The median survival varies according to the primary cancer site and is from 3 to 6 months for non-small cell lung cancers to 6 to 24 months for breast cancers.^{3,4} Subacute dyspnoea is the most common symptom associated with MPE,^{5,6} progressing over days or weeks. This symptom can be associated with chest discomfort or cough. Symptomatic MPE frequently require invasive pleural drainage procedures for relief of symptoms. Traditionally, patients with MPE are admitted to hospitals with associated inpatient cost that is estimated to exceed \$12 million per year.⁷

The treatment goals of patients with MPE have been focused on rapid and complete palliation of associated pulmonary symptoms. The conventional approach of achieving these goals in patients with MPE usually requires 4 to 6 days of hospitalization. While in-hospital, these patients often undergo interventions such as Talc Pleurodesis.^{8,9} More recently, it has been suggested that perhaps these patients could be managed on an out-patient basis. Such a strategy could lead to better quality of life for patients and their families, less hospitalizations and may have positive implications on healthcare costs and resources.¹⁰⁻¹²

Putnam et al.¹³ suggested that outpatient management of MPE can be effective and is associated with reduced costs to healthcare; overall length of stay was higher for inpatients compared to outpatient management (7 days versus 0). There are several studies¹³⁻¹⁵ that

showed the safety and efficacy of outpatient treatment of malignant pleural effusion; however, to our knowledge no study has examined the functionality or resource saving implications of a clinic whose sole purpose is to service patients with MPE. Therefore, the objective of this study was to examine the safety, efficacy, and economy of management of a dedicated MPE clinic.

Methods

Study Design: This is a single centred retrospective study investigating the efficacy of a MPE clinic with respect to clinical outcomes. The study was approved by the Institutional Research Ethics Board of Trillium Health Partners.

Population: Patients greater than 18 years of age, with initial presentation of MPE between 2008 and 2014 at our institution were included either through inpatient hospital discharge records or through the thoracic surgical oncology clinic records. Admissions for causes other than pleural effusion were excluded.

Group stratification: Patients were stratified into 2 groups based on the time of presentation. Patient who presented with MPE between April 1, 2008 to March 31, 2011 were categorized as pre-MPE clinic group (Pre-MPE clinic); these patients were managed for a malignant pleural effusion either as an inpatient or an outpatient in the general thoracic oncology clinic before the creation of a formalized MPE clinic. Patients who presented with an initial malignant pleural effusion between April 1, 2011 to March 31, 2014 were categorized into the MPE clinic group (MPE clinic); these patients were predominantly managed in a formalized bi-weekly malignant pleural effusion clinic.

The aim of the MPE clinic is to provide comprehensive outpatient palliative management of MPE negating the need for invasive procedures and hospitalization. During two half day clinics per week, outpatient referrals are received from both the community and within the hospital. In order to be assessed in the MPE clinic, referred patients should have a diagnosis of cancer, either clinically or pathologically, and have a pleural effusion on a chest radiograph. Patients are generally referred by oncologists, medical internists, palliative or family physicians. In the clinic, each patient is assessed by a thoracic surgeon, a trained oncology nurse and a palliative care nurse. Diagnostic thoracentesis or pleural catheter insertions are performed at the bedside during the clinic using local anaesthesia depending on patient's clinical status and symptoms.

Post procedure imaging is obtained the same day and close follow up is ensured through the clinic, the community care access centres, and the palliative care team in order to minimize emergency rooms visits and inpatient hospitalizations. To ensure proper care of the Tunneled pleural catheter (TPC) and successful home drainage, all patients are provided with homecare services. Homecare nurses receive special training in the management of the catheters which they drain typically three times per week. These nurses are provided with a troubleshooting algorithm to manage the drains and are supported by the MPE clinic nurse during the week and the thoracic surgeon on-call during off hours. The accessibility of clinic personnel is a central feature of the outpatient MPE management that addresses catheter related issues on continued basis.

Patients are seen in follow up two weeks following catheter insertion and then every six weeks or as required until catheter removal or death. Catheters are routinely removed when pleural drainage is less than 50 ml on three separate occasions and no change in the chest x-ray is observed. During clinic visits, symptom control is assessed using the Edmonton Symptom Assessment System (ESAS).¹⁶

Outcomes: The primary outcome was efficacy of the MPE clinic assessed by comparing the following variables between Pre-MPE and MPE clinic patient cohorts; 1) the proportion of patients with malignant pleural effusion presenting as an outpatient compared to in-hospital presentation; 2) the proportion of none or small pleural effusion control versus moderate or large at 90 days on chest radiograph defined by radiology reports; 3) intervention type - the proportion of tunneled pleural catheters (TPC), chemical pleurodesis or other interventions; 4) length of stay in hospital for those that required admission; and 5) overall survival. The secondary outcome was to compare safety measures with respect to the 2 cohorts. This included proportion of; symptomatic loculations; cellulitis; dislodged catheters; blocked catheters, moderate or large pneumothorax; subcutaneous emphysema; pain; fluid leakage; fever; re-interventions; re-admissions; and empyema. The third outcome was economy

of management of pleural effusions by MPE clinic defined by the estimated hospital days saved in each of the cohorts.

Statistics: Baseline covariates along with outcomes were compared between Pre-MPE and Post-MPE clinic cohorts. Categorical variables were compared using the chi-square test. For continuous variables, normality was tested using the Shapiro-Wilk test; parametric covariates were compared using the Student's t-test and non-parametric covariates using the Wilcoxon Signed Rank test. Time to event analyses was generated using Kaplan Meier Curves and compared using the log-rank test.

All dichotomous variables are reported as frequency and percentage while continuous variables are reported using mean $\pm$ standard deviation (SD). All analyses were performed using SAS version 9.4.¹⁷

Results

Between April 1, 2008, to March 31, 2014, 285 patients were diagnosed with MPE. Of these, 115 (41.7%) were diagnosed with MPE in the Pre-MPE clinic period and 161 (58.3%) in the MPE clinic. The patients in this study were relatively young (65.0 $\pm$ 12.8 years), predominantly female (168, 60.9%) with the primary tumor source being lung (149, 53.9%). Clinically relevant baseline demographics between the Pre and MPE clinic cohorts were similar (Table 1).

With regards to the primary outcome of efficacy, the proportion of patients presenting with first episode of MPE as an in-patient was significantly less in the MPE clinic cohort compared to Pre-MPE clinic (Pre-MPE clinic: 73.9% vs MPE clinic: 42.4%, $p < 0.0001$); however for patients that were admitted, the median length of stay was statistically similar for both groups ($p = 0.09$). The predominant procedure of choice in the Pre-MPE clinic cohort was chemical pleurodesis (67.8%); in contrast, the use of tunneled pleural catheter (TPC) was the most common procedure performed in the MPE clinic cohort (72.1%), $p < 0.0001$ (Table 2).

Safety was assessed by assessing rates of complications of each cohort. Complications were similar between the 2 cohorts with the exception of a higher proportion of empyema (Pre-MPE clinic: 0%, MPE clinic: 5.6%, $p = 0.01$) and higher re-hospitalization rate (Pre-MPE clinic: 0.9%, MPE clinic: 5.6%, $p = 0.05$) present in the MPE cohort. Majority of the re-hospitalization in the MPE group was due to empyema (3/9). For the most part, patients were treated in the hospital with intravenous antibiotics and continuous pleural drainage via TPC, with thrombolysis and additional chest drains for loculated fluid collections. While similar, the most common complication in both groups was symptomatic loculation (25-30%) and the least common was empyema and fever (0%) in the Pre-MPE cohort and fluid leak (1.2%) and cellulitis (1.2%) in the MPE cohort (Table 3).

Table 1 Baseline demographics of patients initially presenting with malignant pleural effusion

Baseline Demographics	Pre MPE Clinic (n=115)	MPE Clinic (n=161)	P value
Age	63 (54-75)	66 (57-75)	0.15
Male	45 (39.1)	63 (39.1)	1.00
Primary Tumour Type			0.20
Lung	66 (57.4)	83 (51.6)	
Breast	24 (20.9)	37 (23.0)	
Ovary	2 (1.7)	12 (7.5)	
Gentourinary	5 (4.4)	3 (1.9)	
Mesothelioma	1 (0.9)	4 (2.5)	
Others	17 (14.8)	22 (13.7)	

Table 1 Continued...

Baseline Demographics	Pre MPE Clinic (n=115)	MPE Clinic (n=161)	P value
Malignant pleural fluid cytology	80 (69.6)	127 (78.9)	0.08
Intervention Side			0.002
Right	55 (47.8)	76 (47.2)	
Left	44 (38.3)	80 (49.7)	
Bilateral	16 (13.9)	5 (3.1)	

Table 2 Comparison of efficacy outcomes between cohorts of patients in pre-malignant pleural effusion (MPE) clinic and after establishment of the MPE clinic

Efficacy Outcomes	Pre-MPE Clinic (n=115)	MPE Clinic (n=161)	P value
In-patient at First Presentation	85 (73.9%)	68 (42.4%)	<0.001
Pleural effusion control	59 (51.3%)	105 (65.2%)	0.02
Length of stay (median, (interquartile range), in days)	13 (7-21)	9 (5-21)	0.09
Intervention			<.0001
Tunneled pleural catheter	23 (20.0%)	116 (72.1%)	
Chemical Pleurodesis	78 (67.8%)	35 (21.7%)	
Other Intervention	14 (12.2%)	10 (6.2%)	

Table 3 Comparison of safety outcomes between cohorts

Complications	Pre MPE Clinic (n=115)	MPE Clinic (n=161)	P value
Symptomatic Loculation	29 (25.2%)	49 (30.4%)	0.34
Cellulitis	2 (1.7%)	2 (1.2%)	1.00
Dislodged Catheter	8 (7.0%)	9 (5.6%)	0.64
Blocked Catheter	3 (2.6%)	7 (4.4%)	0.53
Moderate or large Pneumothorax	3 (2.6%)	5 (3.1%)	1.00
Subcutaneous Emphysema	0 (0.0%)	4 (2.5%)	0.14
Pain	1 (0.9%)	7 (4.4%)	0.15
Fluid leak	2 (1.7%)	2 (1.2%)	1.00
Fever	0 (0.0%)	5 (3.1%)	0.08
Reintervention	22 (19.1)	27 (16.8)	0.61
Empyema	0 (0.0%)	9 (5.6%)	0.01
Readmission	1 (0.9%)	9 (5.6%)	0.05

Finally, based on a 26.9% decrease in total hospitalizations (adjusted for re-admission) and 40% increase in referrals for new malignant pleural effusions from Pre-MPE clinic to MPE clinic time period, the estimated hospital days saved was 1001 days over this study period of 3 years.

Discussion

The presence of MPE portends a poor prognosis for cancer patients. Predominantly, patients with MPE are managed as in-patients.^{9,18} However, this in-patient management has implications on patients' quality of life and healthcare systems resources. As such, certain centres have started to manage these patients as out-patients in ad-hoc MPE clinics whose functionality with respect to efficacy, safety and costs have not been widely reported. In this study, we reported data from our newly established MPE clinic, which showed significant reduction of in-patient admissions for MPE management, safety of out-patient MPE clinics—measured in terms of complication rates and effective use of TPC compared to traditional chemical pleurodesis.

Given the dismal overall prognosis of patients with MPE, the outpatient nature of treatment may be of particular importance. Management of symptoms as an outpatient allows patients to maintain control over their lives and minimizes time spent in the hospital. A 2-week hospital stay, which was the median hospital stay in our study, for these patients, may represent 10% of their remaining life span away from the comfort of their own homes, families and friends.

Data on the use of TPCs in the treatment of MPE have been accumulating over the past 15 years.¹⁸⁻²¹ Their use in dedicated MPE clinics may offer several key benefits over previous approaches such as; more liberal patient selection which can include patients with trapped lung;²² outpatient placement without sedation or general anesthesia;^{13,23-27} a rapid and persistent symptomatic improvement;⁹ cost effectiveness;¹³ and low complication rates.^{9,13-16,28} These observed benefits as well as superior MPE control rate could explain the higher utilization of TPC in our MPE cohorts.

In addition, the MPE clinic can expedite patient referrals to supportive programs such as the Dyspnea Management Clinic, the Palliative Rehabilitation Program, Supportive and Palliative Care Outpatients Clinics and the Psychological Oncology Program. This seamless accessibility to other resources may also have significant impact on quality of patients' end of life.

In our study, complications were generally infrequent. In our MPE clinic cohort, the most frequent complication (5.6%) was empyema related to TPC infection. Our empyema rate was in line with the rates of 1-5% in other studies published.^{14,15} However, not all these empyema patients required hospitalization.

There are several studies that have attempted to address the question of cost effectiveness of various ways of managing MPE. A recent study based on the (TIME-2 trial)²⁹ demonstrated overall mean costs over a 1 year follow up of \$4,993 for TPC vs. \$4,581 for pleurodesis. The incremental mean cost difference of \$401 (95% CI: -1,387 to

2,261) was statistically not significant, but if patients survived less than 14 weeks TPC became significantly less costly (\$-1,719, 95% CI: -3,376 to -85). Another recent study by Olden and Holloway³⁰ using an estimated survival time of 6 months concluded that the TPC to be slightly more expensive than talc pleurodesis (\$9,012 versus \$8,171 USD) with similar effectiveness. However, sensitivity analysis suggested that TPC may be cost effective for patients with a prognosis of 6 weeks or less. Puri and colleagues³¹ compared four pleural interventions for MPE management in their cost-effective analysis: repeated thoracentesis, TPC, bedside pleurodesis and thorascopic pleurodesis. Based on projected figures the paper concluded that TPC is most cost-effective in providing Quality Adjusted Life Years (QALYs) for patients with limited survival. Michaud and his colleagues³² study published as an abstract and presented at the American Thoracic Society (ATS) international conference in 2011 compared the cost benefit of talc pleurodesis by video-assisted thorascopic surgery (VATS), medical thorascopy (MT), and talc slurry (TS) with that of TPCs. TPCs were the most cost-effective at \$1958/quality-adjusted life month (QALM) and dominated the other 3 options: \$19,149 per QALM for VATS, \$9844/ QALM for MT, and \$8737/QALM for TS. In our study, approximately 333 hospital days were saved by outpatient MPE management per year. Although we did not compare the cost of running a MPE clinic to inpatient care of patients with MPE, Our findings demonstrated that the cost saving of having an MPE clinic is significant.

There are several potential limitations to our study mainly arising from its retrospective cohort design and short overall survival of the patients. Although important, we were not able to measure the quality of life of the patients, their dyspnea score, or patients' satisfaction in real time. The quantification of cost savings could not be performed as the expenses associated with outpatient management of these patients are unknown.

In conclusion, our data suggest that MPE management in a dedicated outpatient clinic; is safe and effective; can significantly reduce the need for hospitalization; and may minimize healthcare resource consumption. Further studies to examine cost effectiveness of an MPE clinic as well as outpatient quality of life assessment are highly suggested.

Acknowledgments

None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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