Study Protocol

Title of study: A cohort study of prognostic factors for predicting clinical outcomes in patients with malignant pleural effusion

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Background

Malignant pleural effusion (MPE) is common, and is estimated to affect up to a half of patients with malignancy, either at the time or during subsequent clinical course after the diagnosis of malignancy. Lung cancer is the most common cause of MPE, followed by breast cancer, lymphoma, unknown primary genitourinary and gastrointestinal carcinoma. Pleural involvement indicates dissemination of malignancy and suggests a poorer prognosis and the median survival rate ranges from 3 to 12 months, with lung cancer showing the shortest survival among Caucasian cohorts. Patients with MPE frequently suffer from effusion related symptoms requiring therapeutic drainage. Conventionally, the options of therapeutic drainage of MPE include needle aspiration, and intercostal drain insertion with or without chemical pleurodesis. Needle aspiration allows quick relief of effusion and symptoms, though the volume of pleural effusion being aspirated with each attempt of needle puncture is limited to 1-1.5 litres, and repeated puncture involves risks of complications. Intercostal drain insertion will allow gradual drainage of large pleural effusion over days, but the shortcomings being the long hospitalization of at least a week, and the presence of trapped lung would preclude chemical pleurodesis for definitive fluid control. Up to 40% of MPE patients still require repeated pleural drainage procedure, even after Talc chemical pleurodesis. The much longer hospitalization period is considered unfavourable for patients with limited lifespan in terms of weeks or a few months, who would spend more time with their family. In recent few years, indwelling pleural catheter (IPC) has provided a relatively novel option of palliative MPE drainage, on an ambulatory out-patient setting. IPC has been reported to be cost-effective, in particular for patients with survival of less than 14 weeks. With the limited time span, it is important to balance between the aim of symptomatic relief and maintaining patient's quality of life. Invasive procedures and prolonged hospitalisation can cause great distress to patients. Predicted survival of patients with MPE would be important in informing the most suitable method for relieving MPE. Previous studies have identified relevant factors on prediction of survival in patients with malignant pleural effusion but so far, there is no data for Chinese patients. The LENT scoring system (pleural fluid lactate dehydrogenase, Eastern Cooperative Oncology Group performance score, neutrophil -to-lymphocyte ratio and tumour type) is a new validated prognostic score in malignant pleural effusion.

This study aims to identify prognostic factors and evaluate the use of LENT score in Chinese patients with malignant pleural effusion that can subsequently shed light on the treatment approach.

Objectives

To investigate the prognostic factors predicting survivals and need of repeated pleural drainage in patients with malignant pleural effusion

Trial Design:

Longitudinal cohort study, observational

Study investigations:
Patients are retrospectively identified from Hospital Authority Clinical Management System. Clinical Data Analysis and Reporting System (CDARS) will be used to retrieve the list of adult subjects (age 18 or above) having been investigated at Queen Mary Hospital, with the diagnosis of malignant pleural effusion from 2010 and onwards. Upon commencement of the current study, patients newly diagnosed to have malignant pleural effusion, who are under the care of Department of Medicine, will also be prospectively recruited and informed consent will be obtained for use of their data. Their baseline demographic data, blood test results and pleural fluid results will be retrieved/ collected, and data on their subsequent clinical course will also be collected for study purpose. The blood tests and pleural fluid workups are all clinical routine investigations, and study only involves data utilization. The study does not involve any additional interventions for the subjects.

The study does not involve retrieval of sensitive data, nor any active interventions on study subjects. Data will be anonymous and the individuals will not be identifiable. Any database collected will be encrypted. Therefore, for retrospectively found subjects, irrespective of their status at the study time (alive or dead), informed consent will not be actively pursued.

The following data will be collected:
1. Baseline characteristics:
   Patient variables including age, performance status and other co-morbidities will be collected at the start of study, and at the time of diagnosis of MPE.

2. Blood tests data:
   Variables at initial diagnosis will be collected including complete blood count, inflammatory variable such as C-reactive protein, lactic dehydrogenase, protein and albumin levels.

3. Pleural fluid data:
   Variables including pH, glucose, lactic dehydrogenase and protein level will be collected.

Outcomes:
1. Primary outcome/endpoints:
   Rate of fluid recurrence requiring invasive pleural interventions

2. Secondary endpoints:
   Survival
   Need of definitive fluid control measure
   Complications of pleural interventions

Statistical analysis
Multivariable Cox model and linear regression will be undertaken to identify factors predictive of survival and need of pleural tapping. A modified LENT score (pleural fluid lactate dehydrogenase, Eastern Cooperative Oncology Group performance score, neutrophil -to-lymphocyte ratio and tumour type) will be investigated for risk stratification using the Kaplan Meier survival curve and Receiver Operating Characteristic curve analysis.