

Survival in Patients With Malignant Pleural Effusions Who Developed Pleural Infection

A Retrospective Case Review From Six UK Centers

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OBJECTIVE: Malignant pleural effusion (MPE) incidence is increasing, and prognosis remains poor. Indwelling pleural catheters (IPCs) relieve symptoms but increase the risk of pleural infection. We reviewed cases of pleural infection in patients with IPCs for MPE from six UK centers between January 1, 2005, and January 31, 2014.

METHODS: Survival in patients with pleural infection was compared with 788 patients with MPE (known as the LENT [pleural fluid lactate dehydrogenase, Eastern Cooperative Oncology Group performance status, serum neutrophil to lymphocyte ratio, and tumor type] cohort) and with national statistics.

RESULTS: Of 672 IPCs inserted, 25 (3.7%) became infected. Most patients (20 of 25) had mesothelioma or lung cancer. Median survival in the pleural infection cohort appeared longer than in the LENT cohort, although this result did not achieve significance (386 days vs 132 days; hazard ratio, 0.67; $P = .07$). Median survival with mesothelioma and pleural infection was twice as long as national estimates for mesothelioma survival (753 days vs < 365 days) and double the median survival of patients with mesothelioma in the LENT cohort (339 days; 95% CI, nonoverlapping). Survival with lung and breast cancer did not differ significantly between the groups. Sixty-one percent of patients experienced early infection. There was no survival difference between patients with early and late infection ($P = .6$).

CONCLUSIONS: This small series of patients with IPCs for MPE suggests pleural infection may be associated with longer survival, particularly in patients with mesothelioma. Results did not achieve significance, and a larger study is needed to explore this relationship further and investigate whether the local immune response, triggered by infection, is able to modulate mesothelioma progression.

CHEST 2015; 148(1):235-241

Manuscript received September 5, 2014; revision accepted November 3, 2014; originally published Online First November 27, 2014.

ABBREVIATIONS: HR = hazard ratio; IPC = indwelling pleural catheter; LENT = pleural fluid lactate dehydrogenase, Eastern Cooperative Oncology Group performance status, serum neutrophil to lymphocyte ratio, and tumor type; MPE = malignant pleural effusion

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This research was presented in abstract form (S117) at the British Thoracic Society Winter Meeting, December 5, 2014, London, England.

FUNDING/SUPPORT: The authors have reported to CHEST that no funding was received for this study.

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DOI: 10.1378/chest.14-2199

Malignant pleural effusions (MPEs) are common, affecting up to 200,000 people in the United States and United Kingdom each year.¹ Their presence often signifies advanced or metastatic disease, and consequently they are associated with poor prognosis. Median survival ranges from 3 to 15 months, depending on underlying tumor type and stage. Lung cancer is the most common underlying pathology and is associated with the worst outcome.¹ Predicting prognosis with MPEs is difficult, but recently a prognostic scoring system, the LENT (pleural fluid lactate dehydrogenase, Eastern Cooperative Oncology Group performance status, serum neutrophil to lymphocyte ratio, and tumor type) score, has been developed and validated as a tool to stratify patients into prognostic groups and predict life expectancy.²

Indwelling pleural catheters (IPCs) are increasingly used to relieve symptoms of MPEs. They are as effective at relieving symptoms as tube drainage and talc pleurodesis, and they improve quality of life.³ IPCs can be inserted as a day case procedure, leading to shorter inpatient stays. However, IPCs are associated with a higher risk of pleural infection, particularly if they remain in situ for long periods of time.³

There has been anecdotal evidence for decades that patients with pleural malignancy who survive iatrogenic pleural infection tend to have slower progression of their malignancy in the subsequent months.^{4,5} We wanted to explore this hypothesis and, hence, undertook a retrospective review of MPE cases from six UK centers who developed pleural infection in conjunction with an IPC. The aim was to determine whether these patients' survival differed from their predicted life expectancy.

Materials and Methods

All IPCs inserted for MPE between January 1, 2005, and January 31, 2014, in six UK centers were reviewed and cases of pleural infection identified. Recruitment periods differed between centers according to when services were established. Details are shown in e-Table 1. Pleural infection was defined as clinical symptoms and signs consistent with pleural infection, necessitating antibiotic treatment, with or without positive pleural fluid microscopy or culture. Superficial wound infections at IPC insertion site were not included.

Baseline data on patient demographics, oncologic diagnosis and treatment, and details of pleural infection were gathered retrospectively. The data collection sheet is shown in e-Table 2.

Local ethics approval was obtained for the LENT cohort and individual consent obtained from participants (UK Research Ethics Committee reference 08/H0102/11, Central Bristol). Data for the pleural infection cohort was collected as a retrospective audit of practice, in keeping with local ethics committee guidance.

Basic descriptive statistics were used to summarize patient characteristics and factors relating to pleural infection. The primary outcome measure was survival time, calculated from date of diagnosis with MPE and censored at date of death or final follow-up. Survival times were compared with results from a database of 788 patients with MPE, prospectively collected from three international pleural centers (LENT cohort)² and to national US⁶ and UK⁷⁻⁹ statistics. Kaplan-Meier curves were drawn to visually compare the two cohorts and Cox proportional hazards model used to calculate the hazard ratio (HR). Individual LENT scores were calculated at diagnosis, and LENT-predicted median life expectancy compared with actual survival (see e-Table 3 for LENT score calculation).

Univariable Cox regression modeling was undertaken to establish whether there was any association of age, performance status, duration of antibiotic treatment, oncologic treatment received, or timing of pleural infection with survival. All analyses were undertaken using Stata version 11 (StataCorp LP).

Results

Six hundred seventy-two IPCs were inserted during the study period. Twenty-five patients (3.7%) were identified as having experienced pleural infection. Each patient had a single episode of pleural infection, affecting a unilateral IPC. One individual with pleural infection also appeared in the LENT cohort. This patient was removed from the LENT group prior to analysis. Baseline characteristics of patients with pleural infection are summarized in Table 1, and a patient flow diagram is shown in Figure 1. Baseline information on the LENT cohort is available in e-Table 4.

Factors Relating to Infection

Microbiologic culture was positive in 22 of 25 cases (88%). Organisms are shown in Figure 2.

The times between IPC insertion and pleural infection are shown in Figure 3. Sixteen of 25 patients (64%) developed early infection (within 90 days of IPC insertion). Thirteen of 25 patients (52%) received IV antibiotics, and ten of 13 (77%) received additional oral antibiotics. Mean antibiotic duration was 24 days (range, 3-70 days). Fifteen of 25 patients (60%) were treated as inpatients, with an average length of stay of 10.5 days (range, 2-34 days).

No patients required surgery. Three of 25 IPCs (12%) were removed because of pleural infection. Information on pleurodesis was available for 19 patients. Eleven of 19 (58%) achieved pleurodesis, including the three patients who had their IPCs removed.

Three of 25 (12%) died within 30 days of being diagnosed with pleural infection. Although specific cause of death

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