Original Research Article

Etiology and prognostic evaluation of malignant pleural effusion

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ABSTRACT

Background: Malignant pleural effusion is a common medical problem in patients with cancer. The survival of patients with malignant pleural effusion is generally poor. The objectives of our study were to reveal possible prognostic factors of malignant pleural effusion.
Methods: Fifty-three consecutive patients, 34 male and 19 female patients of malignant pleural effusion diagnosed by pleural fluid positive for malignant cytology and/or pleural tissue positive for malignancy by thoracoscopy biopsy. Performance status by the Eastern Cooperative Oncology Group (ECOG) score and LENT score was calculated at the time of diagnosis. Median survival time was calculated using Kaplan-Meier analysis curve. Survival time was defined as the time from diagnosis to death or the last follow-up.
Results: Most common cause of malignant pleural effusion was lung carcinoma 46 (86.79%). Adenocarcinoma was the most common 31 (58.5%) followed by NSCLC 10 (18.0%). Low, moderate and high-risk LENT score was found in 3 (5.7%), 35 (66%) and 15 (28.3%) respectively. The median survival time of pleural fluid sugar less than 20 were 3 months. The median survival time of LENT low, medium and high risk was 12 months, 5.2 months and 2.5 months respectively. The median survival time of patients with ECOG score of 1 and 4 was 6.5 months and 1 month respectively. Patients with bilateral pleural fluid had a mean survival time of 2 months.
Conclusions: Adenocarcinoma lung is the most common etiology of malignant pleural effusion. The median overall survival time was 4 months. Higher ECOG score and LENT score are associated with shorter survival time.

Keywords: Malignant pleural effusion, Median survival, Thoracoscopy, Malignant cytology

INTRODUCTION

Malignant pleural effusion (MPE) is defined as the accumulation of a significant number of exudates in the pleural space, accompanied by the presence of malignant cells or tumor tissue. Epidemiological information is limited, but an estimated 50,000 new diagnoses are made in UK each year.

The majority is due to metastatic disease most commonly lung cancer in men and breast cancer in women. These two cancers combined account for 50-60% of all malignant pleural effusion.[2] Hodgkin and non-hodgkin lymphoma is the third most common cause of MPE and also the most common cause in young adults.[3] Mesothelioma is the most common type of primary pleural tumor which is associated with malignant pleural effusion in more than 90% of cases.[4] No primary tumor is identified in 5% to 10% of malignant pleural effusion.[5]

A malignant tumor can cause a pleural effusion both directly and indirectly. Breech in the integrity of lymphatic system between the parietal pleura and mediastinal lymph nodes can result in pleural fluid formation.[6] Direct tumor invasion of pleura may also contribute to the formation of pleural effusion.[7]

Despite the progress in cancer treatment, the management of MPE remains palliative, with median survival ranging from 3 to 12 months.[8] A number of factors may help to predict survival of patients including tumor characteristics, extent of disease, co morbidities and the composition of effusion.[9-11] To this, LENT score (pleural fluid LDH, Eastern Cooperative Oncology Group (ECOG) performance score, neutrophil to lymphocyte ratio and tumor type) was proposed as a tool for accurate prediction of survival. LENT prognostic score is the first validated prognostic score in MPE, which predicts survival with significantly better accuracy than ECOG. Performance status alone can be used to guide decision making in the treatment of MPE.[12]

With the heterogeneity in the group of patients with MPE, there is a challenge to predict prognosis and survival. With improved techniques in the management of pleural effusion and better oncological options, there is an increasing need for good prognostication to tailor the most appropriate treatment. The goal of this study was to identify the prognostic factors and overall survival in patients with MPE.

METHODS

It is a hospital based prospective study done in department of pulmonary medicine, Guwahati medical college, Assam for the period of one year from August 2018 to 2019. Fifty-three patients of any age group with malignant pleural effusion and or thoracoscopic biopsy specimen positive for malignancy were included in the study. Informed consent was obtained from every participant before any intervention. Patients who denied consent and those with non aspirable pleural fluid were excluded from this study. Ethical committee clearance has been obtained for this study. Pleural fluid sugar, LDH, total count, differential count, malignant cytology of pleural fluid and thoracoscopy biopsy of pleura were evaluated. Performance status by ECOG score and LENT score was calculated at the time of diagnosis. Survival time was defined as the time from diagnosis to death or the last follow-up. Median survival time was calculated using Kaplan-Meier analysis curve.

Statistical analysis

Kaplan-Meier curves were computed for the study participants according to various parameters. Log rank (Mantel-cox) test was used to statistically determine the significant difference in survival time between the patients grouped according to the parameters, p value of less than 0.001 was taken to be significant.

RESULTS

Out of 53 patients in this study 34 patients were male and 19 patients were female. Age of male patients was from 24 to 75 years (56.03±12.08 years) and female age was

from 22 to 82 years (50.84±15.55 years). Patients' characteristics are presented in (Table 1).

Table 1: Characteristics of the study population (n=53).

Characteristics	N	%
Gender		
Male	33	62.2
Female	20	37.7
Diagnosis		
Adenocarcinoma lung	31	58.5
Breast cancer	1	1.9
Mesothelioma	3	5.7
Non-hodgkin lymphoma	2	3.8
Non-small cell lung carcinoma lung	10	18.9
Ovarian cancer	1	1.9
Squamous cell carcinoma lung	5	9.4
LENT score		
Low risk	3	5.7
Moderate risk	35	66
High risk	15	28.3
ECOG score		
0	1	1.9
1	27	50.9
2	13	24.5
3	8	15.1
4	4	7.5
PF side		
Right	28	52.8
Left	22	41.5
Bilateral	3	5.7
PF malignant cytology		
Positive	36	67.9
Negative	17	32.1
Survival status		
Alive	11	20.8
Dead	42	79.2
PF sugar category		
<20	9	17
>20	44	83

Most common cause of malignant pleural effusion was lung carcinoma 46 (86.79%), among which adenocarcinoma was the most common 31 (58.5%) followed by NSCLC 10 (18.0%) and squamous carcinoma in 5 (9.4%) of cases. MPE due to mesothelioma, ovarian carcinoma, breast carcinoma and non-hodgkin lymphoma was 3, 1, 1 and 2 cases respectively (Table 2).

LENT score was done in this study. Low risk, moderate risk and high risk was found in 3 (5.7%), 35 (66%) and 15 (28.3%) respectively (Figure 1). ECOG score was done and found highest in score-1, 27 (50.9%) followed by score-2, 13 (24.5%) (Figure 2). Out of 53 patients with MPE 28 (52.8%) of patients were having right side, 22

(41.5%) left side and 3 (5.7%) had bilateral pleural effusion.

Malignant cytology of pleural fluid was positive in 36 (67.9%) of patients and thoracoscopy biopsy positive in 17 (32.1%) patients. Pleural fluid sugar was estimated in all patients with effusion, pleural fluid sugar >20 mg/dl found in 44 (83%) and <20 mg/dl found in 9 (17%) patients. Out of 53 patients with malignant pleural effusion 42 (79.2%) died within one year of follow up.

Kaplan-Meier curves were computed for the study participants according to various parameters. Log rank (Mantel-cox) test was used to statistically determine the significant difference in survival time between the patients grouped according to the parameters.

The median survival time of patients with pleural fluid sugar less than or equal to 20 was found to be 3 months, while those with >20 was having a higher median survival time of 4.5 months. However, this difference in survival time was not statistically significant (p=0.108) (Figure 3).

Table 2: Types of carcinoma causing MPE.

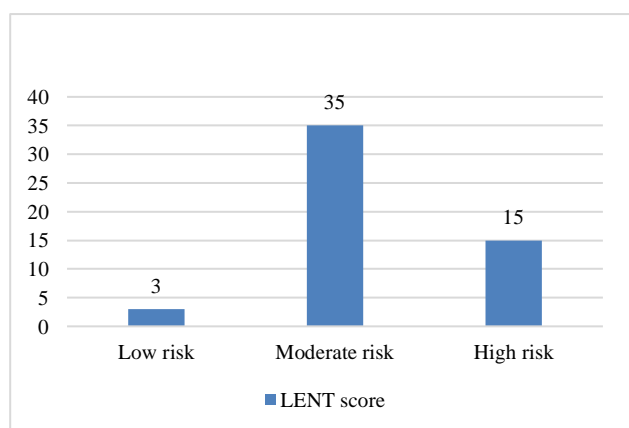| MPE	Type of cancer	Number	%
Lung carcinoma	Adenocarcinoma	31	58.5
	Non-small cell lung carcinoma	10	18.9
	Squamous cell carcinoma	5	9.4
Outside lung	Non-hodgkin lymphoma	2	3.8
	Breast cancer	1	1.9
	Ovarian cancer	1	1.9
	Mesothelioma	3	5.7

Figure 1: Distribution of study participants according to LENT score.
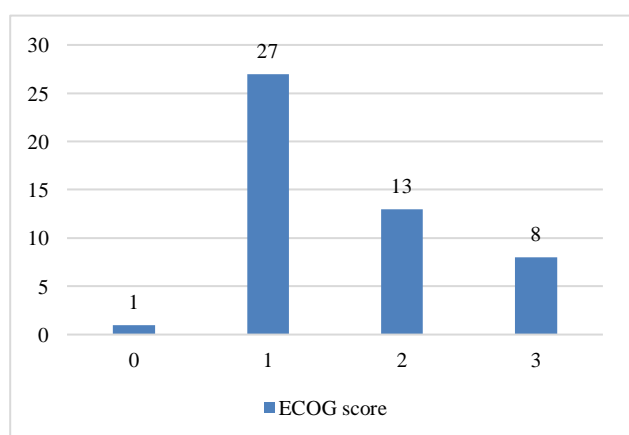

Figure 2: Distribution of study participants according to ECOG score.

The median survival time of low risk LENT score patients was found to be 12 months, while medium risk LENT score patients were having a median survival time of 5.2 months and those with high risk LENT score had a median survival time of 2.5 months. This difference in survival time between the groups was statistically significant (p<0.001) i.e., as the risk increases with LENT score, the median survival time decreased (Figure 4).
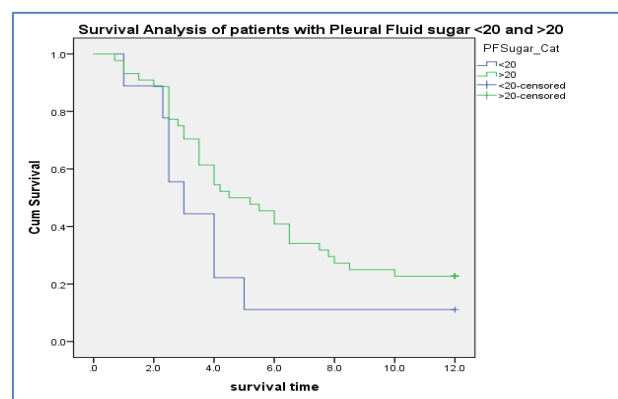

Figure 3: Survival analysis of patients with pleural fluid sugar.

The median survival time of patients with ECOG score of 1 was found to be 6.5 months, score of 2 had a median survival time of 4 months, score 3 had a median survival time of 2.5 months and score 4 had a median survival time of 1 month. The survival time gradually decreased as the ECOG score increased and this decrease was statistically significant (p<0.001) i.e., the patients with higher ECOG scores were found to be having lesser survival time (Figure 5).
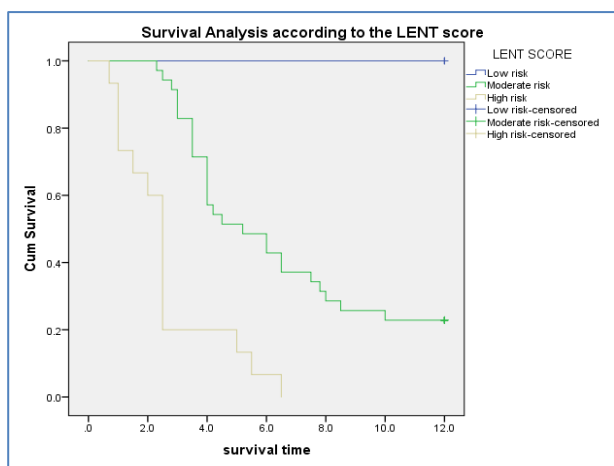
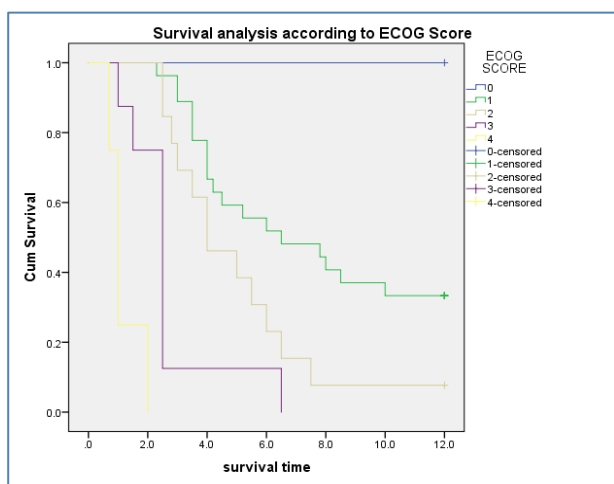**Figure 4: Survival analysis according to the LENT score.**

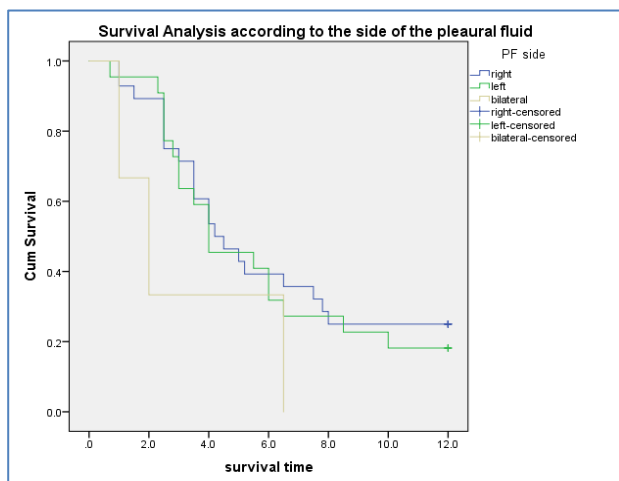**Figure 5: Survival analysis according to ECOG score.**

Figure 6: Survival analysis according to the side of the pleural effusion.

The median survival time of patients with left side pleural fluid was found to be 4 months, while those with right side pleural fluid were having a higher median survival time of 4.2 months and those with bilateral pleural fluid had a mean survival time of 2 months. This difference in survival time between the sides was not statistically significant (p=0.286) (Figure 6).

DISCUSSION

In this study it was found that lung carcinoma was the most common cause of malignant pleural effusion 46 (86.79%), and among the lung carcinoma, adenocarcinoma 31 (58.5%) was the most common cause of malignant pleural effusion followed by NSCLC 10 (18.0%). According to study conducted by Saha et al, in eastern India most common etiology was lung cancer (88.9%) among which most common etiology was adenocarcinoma (52.8%), followed by squamous cell carcinoma (13). Another study by Chatterjee et al, revealed that most common etiology of MPE is lung carcinoma (44%) followed by breast carcinoma (19.8%).[14]

In our study it was shown that pleural fluid sugar does not effects on survival of the patient. In contrast to our study Martinez-Moragon et al, showed that patients with low pleural fluid glucose (<60 mg/dl) and high LDH (>600 U/l) had poor survival and failure of pleurodesis.[15] Zulkifli et al, conducted a study on 30 day survival of patients with MPE which showed pleural fluid sugar <60mg/dl was 22 days.[16]

In our study LENT low risk score the median survival was 12 months and higher risk LENT score was 2.5 months. A study done by Ari et al, showed that the median survival in high risk LENT score group was 44 days.[17] Similar to our study, a study conducted by Jenifer et al, at south India showed that median survival time of moderate and high LENT scores are 6 months and 3 months respectively.[18]

In this study it was shown that the median survival time of patients with ECOG score of 1 was found to be 6.5 months and score 4 had a median survival time of 1 month. Similar study done by Zambani et al showed that ECOG grade o the median survival was 55 months and ECOG grade 4 the median survival was 1 month.[19]

In this study it was shown that the median survival time of left sided pleural, right sided and bilateral effusion was 4 months, 4.2 months and 2 months respectively. Similar study done by Jenifer et al, showed that survival time of bilateral pleural effusion was 30 days.[18] Biasi et al, in their analysis of a cohort of patients who underwent thoracocentesis, also reported higher mortality at 30 days in patients with bilateral MPE.[20]

CONCLUSION

From the study it has been concluded that adenocarcinoma lung is the most common etiology of malignant pleural effusion. The median overall survival

time is 4 months. Higher ECOG score and LENT scores are associated with shorter survival time.

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