

type is slightly superior to ECOG PS in predicting survival. The score is clinically relevant, prognosis being easily calculated, thus aiding in explaining the prognosis to patients and also in guiding the selection of appropriate treatment strategies.^[18] Moreover, the LENT scoring system is more objective than ECOG PS alone. The present study was undertaken to evaluate the role of the LENT score in predicting survival in MPE.

MATERIALS AND METHODS

This was a single-center prospective observational study conducted on 30 patients with MPEs who presented to the department of pulmonary medicine.

Inclusion criteria

All patients aged 18 years and above with proved MPEs were included in the study.

Exclusion criteria

1. Patients who have HIV-positive serology
2. Patients with comorbid diseases such as end-stage renal disease, left ventricular failure, and idiopathic pulmonary fibrosis which is likely to influence survival
3. Patients not willing to participate in the study.

Patients with suspected MPEs were admitted to the hospital for further workup. The patient's demographic data were collected and noted. Detailed present and relevant history was taken. Thorough general physical examination was done.

The diagnosis of pleural effusion was done based on chest X-ray and ultrasound chest. All patients were subjected to routine baseline investigations such as complete blood count and metabolic profile and PF analysis. The PF analysis included total count, differential count, acid-fast staining, adenosine deaminase (ADA) levels, LDH levels, protein, sugar, cytology, and cellblock. Repeat cytology was done after 2 weeks if the initial report was negative for malignant cells. Contrast-enhanced computed tomography (CECT) was done in all cases after draining of the PF. Wherever indicated, histological diagnosis of the mass or nodular lesion found on CECT, ultrasound, computed tomography (CT)-guided fine-needle aspiration cytology (FNAC), or biopsy was done. A pleural biopsy was done in one case. In patients where both PF cytology and cell block were negative for malignancy, diagnosis is made based on the PF characteristics such as the color (hemorrhagic), low ADA, and lymphocyte-predominant effusions with a histologically proven malignancy in other organs. In eight cases, the primary malignancy was other than lungs. LENT score was calculated based on PF LDH, ECOG prognostic scale, peripheral blood NLR, and primary tumor. Based on the LENT score, patients were divided into high, moderate, and low risk and were followed up at 1, 3, 6 months or until death whichever was earlier. Survival is defined as the time from the diagnosis of effusion to death.

Ethical consent

Institutional ethical committee approval was taken, and written informed consent was taken from the study group before enrolling in the study.

Statistics

Statistical analysis was performed using SPSS Version 17 (IBM, Chicago Illinois, USA). Receiver operating characteristic (ROC) analysis comparing survival at 1, 3, 6 months using LENT and ECOG scores was done. Kaplan–Meier survival analysis with log-rank test was done for LENT score.

RESULTS

Thirty cases were taken for further study analysis. The mean age of the patients was 59.5 years (18–75). The majority of the patients were in the age group of 50–70 years (66.66%). The male-to-female ratio was 8:7. Pleural effusions were more common on the right side. The number of right, left, and bilateral effusions was 17, 12, and 1, respectively. In patients with carcinoma lung, the side of the effusion was on the side of the lesion. PF cytology was positive for malignant cells in 21 cases, and pleural biopsy was done in one case. In 8 cases, unexplained pleural effusions with histologically proven malignancies were found in organs other than the lung. Of the 30 patients, carcinoma lung was diagnosed in 22 and 8 had primary outside the lung. Two patients had a history of carcinoma cervix, one patient had a history of carcinoma breast, one case had malignant mesothelioma, one patient had a history of thymoma, one patient had a history of carcinoma thyroid, one patient had a history of carcinoma esophagus, and one case had a history of osteogenic sarcoma [Table 1]. Histopathology of the lung cancer was obtained using either FNAC or biopsy of the lung mass under image guidance of U/S or CT chest scanning. Adenocarcinoma was observed in 12 cases, squamous cell pathology in 7, and undifferentiated malignancy in 3. Seven patients had PF LDH levels >1500 IU, but a majority of the patients had their LDH levels between 500 and 1000 IU. The majority of the patients (24/30–80%) had an ECOG PS score of 2 or more. In patients with ECOG PS 0–2, the survival rates at 1, 3, and 6 months were 93%, 33%, and 26%, respectively, and in patients with ECOG PS 3 and 4, the survival rates at 1, 3, and 6, months were 39%, 6.6%, and 6.6%, respectively [Table 2]. In the present study, 14 patients were in a high-risk group (LENT score of 5–7) of which 7 were male and 7 were female, and 15 in a moderate-risk group (LENT score of 2–4) of which 8 were male and 7 were female, and only one patient in the low-risk group (LENT score of 0 and 1) [Table 3]. The median survival in the LENT

Table 1: Primary tumor type

Primary tumor	Number of patients
Carcinoma lung	22
Carcinoma cervix	2
Malignant mesothelioma	1
Carcinoma breast	1
Thymoma	1
Carcinoma thyroid	1
Carcinoma oesophagus	1
Osteogenic sarcoma	1

high-risk group ($n = 14$) was 30 days (16–73 days) and the moderate-risk group ($n = 15$) was 75 days (18–270 days). Overall median survival was 45 days. One-month survival for high-risk category was only 42%. The rest died in <1 month. In the moderate-risk group, the survival rates at 1, 3, and 6 months were 93%, 33%, and 26%, respectively [Table 4].

Receiver operative curve curves for survival at 1, 3, and 6 months using Eastern Cooperative Oncology Group Performance Status

ROC for survival at 1 month using ECOG PS: Area under curve (AUC) is 0.855, associated criterion is ECOG PS >2, sensitivity is 90%, specificity is 75%, and $P = 0.0001$; ROC for survival at 3 months: AUC 0.938, associated criterion ECOG PS >1, sensitivity 91.6%, specificity 83.3%, and $P = 0.0001$; ROC for survival at 6 months: AUC 0.976, associated criterion ECOG PS >1, sensitivity 92%, specificity 100%, and $P = 0.0001$ [Figure 1].

Receiver operative curve for survival at 1, 3, 6 months by using LENT score

ROC for survival at 1 month: AUC is 0.763, associated criterion is LENT score >4, $P = 0.0044$, sensitivity 80%, specificity 70%.^[6] ROC for survival at 3 months: AUC is 0.889, associated criterion is LENT >4, sensitivity 58.33% specificity 100%, $P \leq 0.0001$. ROC for survival at 6 months: AUC is 0.920, associated criterion is LENT >4, sensitivity 58.33%, specificity 100%, $P \leq 0.0001$ [Figure 2].

Receiver operative curve for survival at 1, 3, and 6 months by using the LENT score and Eastern Cooperative Oncology Group Performance Status

ROC for survival at 1 month using LENT score and ECOG PS: AUC for LENT and ECOG is 0.760 and 0.855, respectively, and $P = 0.1252$. ROC for survival at 3 months: AUC for LENT and ECOG PS is 0.889 and 0.938, respectively ($P = 0.2424$). ROC for survival at 6 months: AUC for LENT and ECOG PS is 0.920 and 0.976, respectively ($P = 0.2645$) [Figure 3].

Kaplan–Mier Survival Analysis

Table 5 shows Mean and median survival with 95% confidence interval (CI) based on LENT score (high, moderate, and low). The hazard ratio (HR) for high and moderate risk was 6.2728 (95% CI 1.4062–27.9808) and 1.6995 (95% CI 0.4580–6.3056), respectively. The Kaplan–Meier analysis showed a significant change in survival among different risk categories of LENT score Chi-squared 20.546, $P \leq 0.0001$ [Figure 4].

Table 2: Survival at 1,3,6 months based on eastern co-operative oncology group performance status

ECOG PS	Survival at 1 month, n (%)	Survival at 3 months, n (%)	Survival at 6 months, n (%)
1-2 (n=15)	93	33	26
3-4 (n=15)	39.9	6.6	6.6

ECOG: Eastern Cooperative Oncology Group, PS: Performance status

Table 3: LENT score risk groups

Sex	High risk (5-7)	Moderate risk (2-4)	Low risk (0-1)
Male	7	8	1
Female	7	7	0

LENT: Pleural fluid lactate dehydrogenase, Eastern Cooperative Oncology Group (ECOG), performance score (PS), neutrophil-to-lymphocyte ratio and tumour type

Table 4: Survival rates at 1,3,6 months based on LENT scoring (n=30)

Risk group	Survival at 1 month, n (%)	Survival at 3 months, n (%)	Survival at 6 months, n (%)
High (14/30)	6/30 (42)	0/30 (0)	0/30 (0)
Moderate (15/30)	14/30 (93)	5/30 (33)	4/30 (26)
Low (1/30)	1/30 (100)	1/30 (100)	1/30 (100)

LENT: pleural fluid lactate dehydrogenase, Eastern Cooperative Oncology Group (ECOG), performance score (PS), neutrophil-to-lymphocyte ratio and tumour type

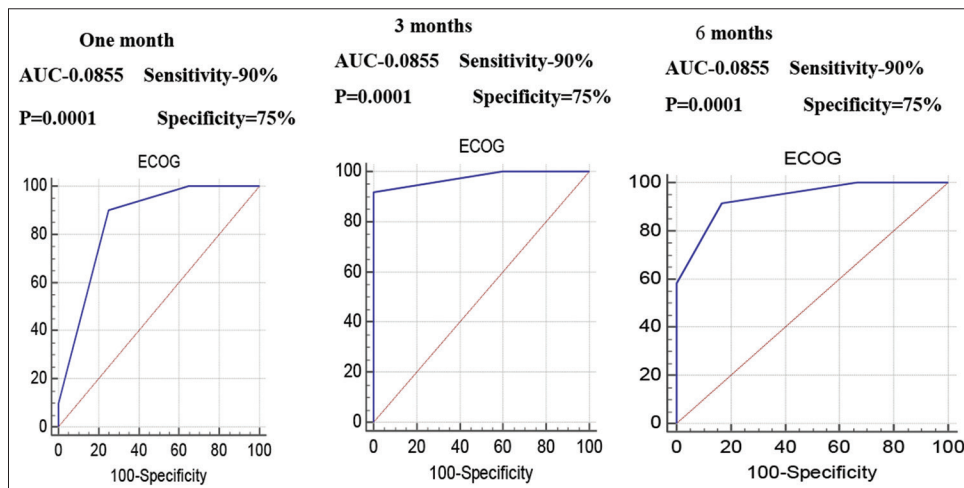


Figure 1: Receiver operating characteristic curves for survival at 1, 3, and 6 months using Eastern Cooperative Oncology Group Performance Status

Table 5: Kaplan Meier analysis: Mean, median survival in days with 95% confidence interval

LENT score risk category	Mean	SE	95% CI of mean	Median	95% CI of median
High	32.286	3.722	24.991-39.580	28.000	27.000-35.000
Moderate	104.133	19.861	65.205-143.061	75.000	62.000-90.000
Low	210.000	0.00	210.000-210.000	210.0	-
Overall	74.133	12.768	49.107-99.159	45.000	32.000-73.000

SE: Standard error, CI: Confidence interval, LENT: pleural fluid lactate dehydrogenase, Eastern Cooperative Oncology Group (ECOG), performance score (PS), neutrophil-to-lymphocyte ratio and tumour type

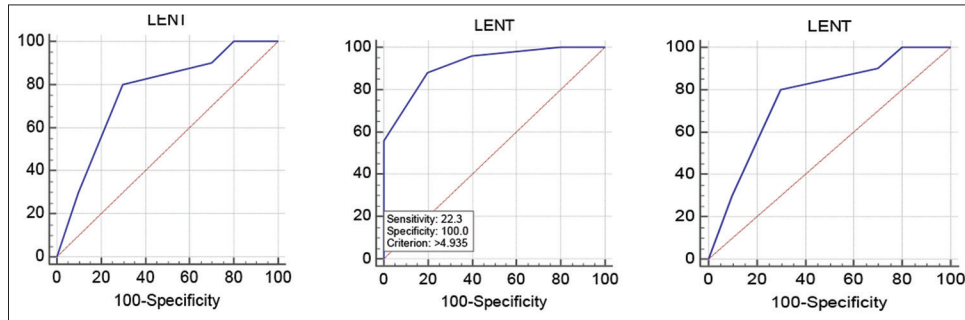


Figure 2: Receiver operative curve for survival at 1, 3, and 6 months using LENT score

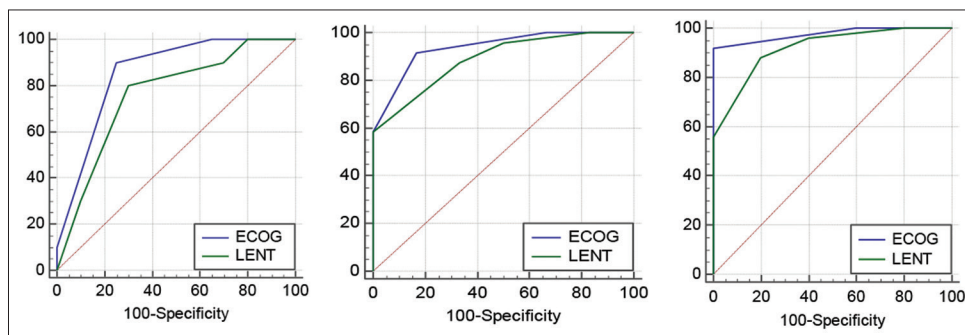


Figure 3: Receiver operating characteristic for survival at 1, 3, and 6 months using LENT score and Eastern Cooperative Oncology Group Performance Status

DISCUSSION

Malignant cells in PF and/or parietal pleura signifies disseminated or advanced disease and a reduced life expectancy in patients with cancer.^[19] Recently to predict the survival of patients with MPE, several efforts have been made.^[18,20-22]

Formation of risk categorization using LENT score and early validation based on international cohorts of MPE patients was the most important among them.^[18] This LENT scoring system divides patients into low-, moderate-, and high-risk groups based on PF LDH, COG performance status, serum NLR, and tumor type. Low-, moderate-, and high-risk groups are based on PF LDH, ECOG PS, serum NLR, and tumor type. The above scoring system also has the benefit of providing information on prognosis for both patients and doctors. The score has better interpretation than ECOG PS. As the LENT scoring system has more clinical relevance, it helps in deciding the treatment options tailoring to individual's predicted survival.^[23]

The current study was a prospective observational study conducted in patients with MPE, to evaluate the role of LENT

score. The median age in our study group was 60 years with a majority between 50 and 70 years of age group. Of the 30 subjects, 16 7 were male and 14 were female. These findings were similar to other studies.^[14,17,20] Lung malignancy was the most common tumor in our study ($n = 22$) and adenocarcinoma was the most common histological tumor type ($n = 12/22$), which was in concordance with other studies. Many studies evaluated the primary site of malignancy as a prognostic indicator in MPEs, with bronchogenic carcinoma having poor and breast and gynecological tumors having the best prognosis. The median survival among the lung cancer group in the present study was 37 days and 44 days in a study by O'clive *et al.*^[18] The concentration of LDH in PF was known to be associated with the prognosis of the patients. Higher LDH levels were associated with worsened survival of patients. In the present study, an LDH level of >1500 (which is allowed a score 1) was seen in only seven patients. Moreover, the majority of the patients had levels between 500 and 1000 IU. In a study by Martínez-Moragón *et al.*, LDH concentration of >600 U/L was a significant predictor of poor survival (6 vs. 10 months, $P < 0.01$).^[24] However, in a

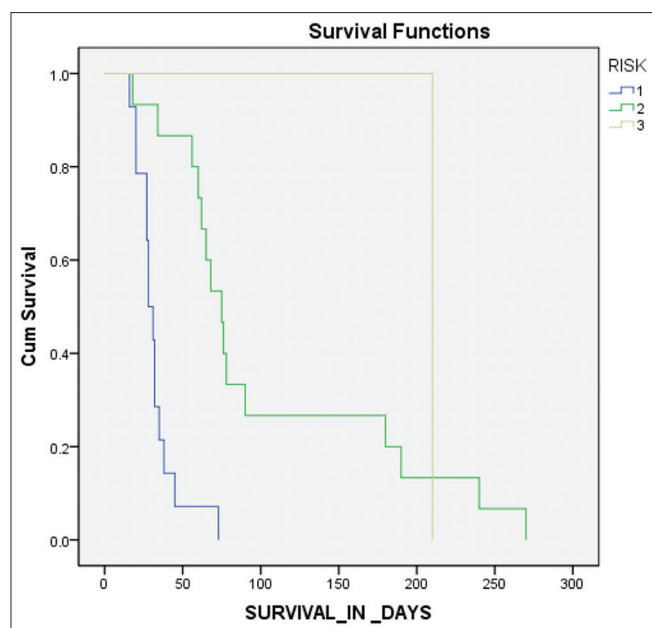


Figure 4: Kaplan–Meier survival analysis

multivariate study by Amiz Z *et al.*,^[25] high LDH concentration insignificantly corresponded to the 30-day survival of the patients. The present study showed that with PF LDH alone, there was no significant association with survival which was similar to other studies.^[17,25] The mechanisms for poor outcomes of malignancy with high NLR are poorly understood. In a systemic review and meta-analysis on the prognostic role of NLR in solid tumors by Templeton *et al.*, the median cutoff for NLR was 4.^[26] The prognostic effect of NLR was highest in mesothelioma, followed by pancreatic cancer, renal cell carcinoma, colorectal carcinoma, gastroesophageal cancer, and nonsmall-cell lung cancer. NLR cutoff in LENT score is 9; in our study, only one patient had an NLR of >9, although 16 patients had neutrophilia, they did not reach the cutoff value. ECOG scale evaluates disease progression and quantifies the extent to which the disease affects the daily living abilities of the patient. Chemotherapy trials of bronchogenic carcinoma had a cutoff of PS of 1 because patients with PS of 2 or more have been shown to have a particularly poor outcome in clinical trials after treatment.^[27]

In our study, the AUC in ROC analysis of survival at 1, 3, and 6 months using ECOG PS was 0.855, 0.938, and 0.976 ($P \leq 0.0001$). These values suggest that ECOG PS is a good predictor of prognosis in MPE, which was similar to the findings of studies by Zamboni *et al.* and Anevlavis *et al.*^[17,20] However, there are some limitations in prognostication by using the ECOG PS system.^[28] The median survival periods for high-, moderate-, and low-risk groups by the LENT scoring system and the overall median survival were low in the present study compared to studies by O’Clive and Psallidas.^[5,18] The possible explanation for the low survival was because of small study group and more importantly due to the significant number of lung cancer cases (22/30) which is a high-risk tumor with a poor survival in the present study compared to other studies.

ROC analysis for survival at 1, 3, and 6 months for LENT score showed AUC of 0.760 (0.570–0.896, $P = 0.0044$), 0.889 (0.720–0.974, $P \leq 0.0001$), and 0.920 (0.761–0.987, $P \leq 0.0001$), respectively. This is in agreement with other studies by Amelia *et al.* and Psallidas *et al.*^[5,18] Kaplan–Meier survival analysis with log rank test showed that there is a significant difference in survival between the risk groups based on LENT score (Chi-square 20.5469, $P \leq 0.0001$). The Kaplan–Meier survival analysis and ROC indicate that the LENT score was a significant prognostic score and can be used for predicting survival and risk stratifying of patients with MPE, in accordance with other studies. The AUC in ROC analysis of survival at 1, 3, and 6 months using LENT was 0.760, 0.889, and 0.920 ($P \leq 0.0001$), respectively, and for ECOG PS was 0.855, 0.938, and 0.976 ($P \leq 0.0001$). These values suggest that ECOG PS was slightly better than LENT scoring as prognostic variable though it was not a significant difference. Similar results were shown by Kato *et al.*, who evaluated the role of LENT score in patients of nonsmall cell lung cancer and concluded that both LENT and ECOG PS are good prognostic predictors for survival at 1, 3, and 6 months and there is no difference between the two in predicting the survival. These results are in contrary to the study by O’clive *et al.*

CONCLUSION

1. Both the LENT score and ECOG PS are good at predicting the survival rates in MPEs, and there is no statistically significant difference between ECOG PS and LENT scoring system in predicting prognosis
2. Although the findings from our study suggest that ECOG PS is a statistically significant prognostic factor, its subjective nature and the possibility of improvement in performance after PF drainage/ICT, might alter the prediction. Hence, depending only on ECOG PS may lead to misclassification of the patient risk
3. The LENT prognostic score is potent, easy to compute clinically relevant score on prognosis, which may aid in explaining the patients about prognosis and thereby guiding in the selection of proper treatment pathways.

Limitations

1. Small sample size
2. Less number of extrapulmonary malignancies or low-risk tumors.

Future studies are required which employ larger sample size with both high- and low-risk malignancies.

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Conflicts of interest

There are no conflicts of interest.

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