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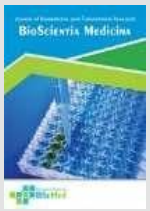

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LENT Score as a Prognosis Factor for Overall Survival and Progression-Free Survival in Malignant Pleural Effusion Patients at Tertiary Hospitals in West Sumatera, Indonesia

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A B S T R A C T

Background: Malignant pleural effusion (MPE) has a variable survival rate and prognosis. The LENT score is one method for assessing survival rates in patients with MPE. This study aimed to investigate the LENT score as a prognostic factor for overall survival (OS) and progression-free survival (PFS) of patients with MPE at a tertiary hospital in West Sumatera. **Methods:** This study was an observational analytic study involving several tertiary hospitals in West Sumatera with a minimum observation period of 2 years. Data were collected from medical records. We used Kaplan Meier analysis to assess OS and PFS. **Results:** A total of 198 subjects met the inclusion criteria. Most MPE patients in this study were aged ≥60 years, male, smokers, pleural fluid lactate dehydrogenase value <1500, ECOG 1, serum NLR value <9, and high-risk cancer, namely lung cancer. The distribution of LENT scores for MPE patients was evenly distributed among the low, medium, and high-risk groups. Kaplan Meier analysis showed that the median OS based on LENT scores were 804 days, 275 days, and 161 days, respectively (log-rank test p = 0.000). The median PFS based on LENT scores were 715 days, 202 days, and 106 days, respectively (log-rank test p=0.000). The OS and PFS findings are longer than previous studies. **Conclusion:** Based on LENT scores, overall survival and progression-free survival MPE patients at tertiary hospitals in West Sumatera have a better prognosis compared to previous studies.

1. Introduction

The incidence of malignancy complicated by pleural effusion is currently increasing. As many as 76% of malignancies cause pleural effusion. Malignant pleural effusion (MPE) is proven by the presence of primary cancer and/or by finding malignant cells on anatomical pathology examination. The incidence of MPE in the United States is reported to be 150,000 per year, while in China, in 2021, a 23.7% incidence of MPE was found. Data on MPE cases in Indonesia currently reaches 64.3% of cases. Malignant pleural effusion causes high morbidity and mortality with variable patient survival and is associated with prognosis. Patients with malignant pleural effusion generally have a poor prognosis with an average overall survival (OS) of 30 days to 1 year. Overall survival in patients after diagnosis of MPE is an average of 1-12 months. A low survival rate will lead to a high mortality rate in patients with MPE. Studies report a reported prevalence of death from MPE of 4.5 to 7.9% of cases in the United States. The mortality rate of patients

with MPE was reported to be 11.6% of cases, with an average hospital stay of 5.5 days.[1-7]

Various studies indicate various methods that can be used to assess the survival rate of patients with MPE, including the PROMISE Score and the LENT Score. The PROMISE score is used to predict the probability of survival of MPE patients within 3 months. This score is divided into 2 clinical and biological assessments by TIMP-1 (Tissue inhibitor of metalloproteinase-1) examination. This examination is not available in all hospitals, so this score is impractical to use in contrast to the LENT score, which is widely used in clinical practice and research because it is a simple indicator in predicting patient survival and guiding the choice of management for the patient. The LENT score consists of four values, namely lactate dehydrogenase (LDH), Eastern Cooperative Oncology Group (ECOG), neutrophil-lymphocyte ratio (NLR), and primary tumor type. Prediction of survival time in MPE patients is very important to determine the right treatment options in order to minimize discomfort at the end of the patient's life. The use of LENT scores can be used to find out the overall survival and progression-free survival of malignant pleural effusion patients.[8-15] This study aimed to explore the LENT score as a prognostic factor for overall survival and progression-free survival in patients with malignant pleural effusion in a tertiary hospital in West Sumatera, Indonesia.

2. Methods

This study was an observational study with a cross-sectional approach and used secondary data obtained from the medical records installation of Dr. M. Djamil General Hospital, Padang, Achmad Muchtar Bukittinggi General Hospital, and M. Natsir Solok General Hospital. A total of 198 research subjects participated in this study, where the research subjects met the inclusion criteria. The inclusion criteria in this study were patients with malignant pleural effusion at Dr. M. Djamil General Hospital Padang, Achmad Muchtar General Hospital Bukittinggi, and M. Natsir Solok General Hospital and had complete medical record data. Patients with other diseases that can cause pleural effusion, such as pleural effusion due to infectious disease, cardiovascular disease, and kidney failure, are exclusion criteria in this study. This study was approved by the medical and health research ethics committee of the Faculty of Medicine, Universitas Andalas, Padang, Indonesia.

Observations on sociodemographic and clinical data were carried out in this study. The LENT score is the total sum of the pleural fluid LDH scores, ECOG, serum NLR, and tumor type. Univariate analysis, namely the analysis used to describe each research variable so that it is obtained in the form of tables and graphs of the frequency distribution of f (%) and the percentage of each variable. Bivariate analysis is to find out the relationship between LENT scores and overall survival and LENT score with progression-free survival patients with malignant pleural effusion in West Sumatera. Hypothesis testing was carried out by survival analysis test using the Kaplan-Meier curve. The Kaplan Meier curve was used to measure OS and PFS, and the endpoint was based on the LENT score of patients with malignant pleural effusion in this study. A test with a log-rank less than 0.05 is considered significant.

3. Results

The characteristics of the study subjects can be seen in Table 1. Out of 198 research subjects, patients were aged ≥60 years (51%) and males (52.5%). The prevalence of smoking patients (38.9%) and former smokers (26.8%). The highest pleural fluid LDH level was in the group <1500 (50.5). Most patients with ECOG 1 (44.9%). The highest serum NLR level was in the group <9 (59.1%). Tumor types were dominated by high-risk tumors (59.1%), with the highest proportion being lung tumors (48.5%)

Table 1. Characteristics of research subjects.

Characteristics	Frequency; (%) (n = 198)
Age	
< 60 years	97 (49)
≥60 years	101 (51)
Gender	
Male	104 (52,5)
Female	94 (47,5)
Smoking status	
Not a smoker	68 (34,3)
Smoker	77 (38,9)
Former smoker	53 (26,8)
LDH	
<1500	100 (50,5)
≥1500	98 (49,5)
ECOG	
0	59 (29,8)
1	89 (44,9)
2	47 (23,7)
3-4	3 (1,5)
NLR	
<9	117 (59,1)
≥9	81 (40,9)
Tumor type	
Low risk	3 (1,5)
Mesothelioma	1 (0,5)
Hematology	2 (1,0)
Moderate risk	78 (39,4)
Breast	23 (11,6)
Gynecology	54 (27,3)
Kidney	1 (0,5)
High risk	117 (59,1)
Lungs	96 (48,5)
Other	21 (10,6)

Kaplan Meier's survival analysis found a median OS (overall survival) of 804 days (95% CI 737 - 871) for MPE patients with a low-risk LENT score, 275 days (95% CI 223 - 327) for MPE patients with a moderate risk LENT score, and 161 days (95% CI 134 - 188) for MPE patients with a high-risk LENT score. There is a difference in survival which is significant between risk groups with the results of the log-rank test, p = 0.000 between low and medium risk, and p = 0.000 between medium and high risk. This means that the median OS of MPE patients with low-risk LENT scores is significantly longer than the moderate-risk group, as well as between medium and high risk.

Table 2 shows the first-year OS probabilities in the low, medium, and high-risk groups are 78%, 36%, and 4%, respectively. The second-year OS probabilities in the low, medium, and high-risk groups were 63%, 0%, and 0%, respectively. Only the low-risk group survived until the third year, namely 18%.

Kaplan Meier analysis found a median PFS (progression-free survival) of 715 days (95% CI 684 – 745 days) for low-risk malignant pleural effusion patients, 202 days (95% CI 168 – 236 days) for moderate-risk patients, and 106 days (95% CI 87 – 125 days) for high-risk patients. There is a difference in survival statistically significant between risk groups using the results of the log-rank test, p=0.000 between low and medium risk, and p=0.000 between medium and high risk. This means that the median PFS in the low-risk group is significantly longer than the medium-risk group and also significantly different between medium and high-risk.

Table 2. Life-table MPE patients based on LENT score.

		Year to-	Total	Death rate	Survival proportions	Cumulative survival probability	Log-rank test
Overall survival	Low risk	1 2 3	63 49 40	14 9 26	78% 82% 28%	78% 63% 18%	0,000
	Moderate risk	1 2	66 24	42 24	36% 0%	36% 0%	0,000
	High risk	1 2	69 3	66 3	4% 0%	4% 0%	0,000

Table 3. Life-table patients with malignant pleural effusion based on LENT score.

		Year to-	Total	Death rate	Survival proportions	Cumulative survival probability	Log-rank test
Progression free survival	Low risk	1 2 3	63 53 23	10 30 18	84% 43% 22%	84% 37% 8%	0,000
	Moderate risk	1 2	66 17	49 17	74% 0%	26% 0%	0,000
	High risk	1 2	69 2	67 2	3% 0%	3% 0%	0,000

Table 3 shows the first-year PFS probabilities in the low, medium, and high-risk groups are 84%, 26%, and 3%, respectively. The second-year PFS probabilities in the low, medium, and high-risk groups were 37%, 0%, and 0%, respectively. Only the low-risk group survived until the third year, namely 8%.

4. Discussion

According to Clive et al.'s study, the median OS in MPE patients based on LENT scores was 319 days, moderate risk 130 days, and high risk 44 days. This research can be a complement as well as a comparison of Clive et al.'s data by providing an overview of the Indonesian population. The population in the study of Clive et al. is a Western country that is classified as a developed country (high-income countries/HIC), which, when compared to Indonesia as a developing country (low-middle income countries/LMIC), has several differences in health systems and services, including the ease and affordability of access to health services to the quality of health services. Differences in the quality and access to health services can affect the quality of health services received by MPE patients so that they can affect the outcome. Clive's research population is dominated by the Caucasian race when viewed from where the data was taken, while this research was conducted on the Indonesian population, especially West Sumatera, which is generally dominated by the Malay race, which can influence the difference, although there is no more direct explanation regarding racial differences in the MPE.[16]

Clive et al.'s study, which is the cornerstone of LENT scoring, found different median OS. The median OS of this study is different from that of Clive et al., but both have the same pattern, namely, the higher the risk based on the LENT score, the lower the OS of the MPE patients. Clive et al.'s study, which is the basis for the LENT score, involved three international cohort studies with a follow-up minimum of 12 months in the UK, Australian, and Dutch populations, with a total of 789 patients enrolled. The three populations in the study showed different cumulative OS, where the United Kingdom population showed an OS of 168 days (95% CI 106 – 228 days); Australia 205 days (95% CI

167 – 238 days); and the Netherlands 84 days (95% CI 72 – 115 days).[16]

Research by Clive et al. illustrates that the differences between the three populations, including the OS observed in this study in the West Sumatera population, can be influenced by various things. Clive et al.'s study, used the Cox regression method to find OS, while this study used the Kaplan-Meier method. The difference between the two lies in the Kaplan-Meier, which is a non-parametric method, while the Cox regression is a parametric method. Kaplan Meier cannot use multiple predictors, while the Cox regression method can use multiple predictors. Another difference could be due to the study design, Clive et al. used a prospective cohort design with follow-up directly for at least 12 months, while this study used a cross-sectional approach. The characteristics of each population can also influence the findings in this study which indicate OS in MPE patients from Indonesia, especially West Sumatra.[16]

Research Taniguchi et al. in Japan, one of the LENT score indicators, namely LDH, was significantly related to PFS, especially in patients with LDH > 240 IU/L with poor PFS ($p<0.05$). Tang et al. in China, obtaining NLR is one of the indicators of LENT scores related to PFS. The results of this study showed a significant relationship between NLR and PFS ($p<0.001$). Patients with NLR ≥5.0 had an average PFS of 6.17±1.23 months, and patients with NLR <5.0 had an average PFS of 13.27±2.11 months. Another research that has been done is PFS analysis, and LENT scores are performed less frequently, so this study can provide a new study on the performance of the LENT score for predicting progression in MPE patients. This study found the median cumulative PFS in patients with MPE to be 202 days (95% CI 160 – 244 days). Follow-up analysis using the Kaplan Meier method found a median PFS of 715 days (95% CI 684 – 745 days) for MPE patients with low-risk LENT scores, 202 days (95% CI 168 – 236 days) for patients with medium-risk LENT scores, and 106 days (95% CI 87 – 125 days) for patients with high-risk LENT scores, with significant differences between risk groups. These findings indicate that the higher the LENT score so that the patient belongs to the higher risk group, the lower the PFS, and vice versa. The results obtained in this study are an indication that the LENT score can also be used to estimate the progression of MPE patients, especially in the population of Indonesia and West Sumatera. Further research needs to be conducted on a larger and more representative population scale to assess the prognostic ability of the LENT score in relation to disease progression.[17,18]

5. Conclusion

Based on the LENT score, Overall survival and progression free survival MPE patients at tertiary hospitals in West Sumatera have a better prognosis compared to previous studies.

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