Original Article

Predicting Survival in Patients with Malignant Pleural Effusion and Validating LENT Prognostic Score

Petborom P, MD[1], Vassara M, MD[1], Muangnoi P, MD[1]

[1] Department of Medicine, HRH Princess Maha Chakri Sirindhorn Medical Center, Faculty of Medicine, Srinakharinwirot University, Nakhon Nayok, Thailand

Objective: The aim of the present study is to obtain data of patients surviving with malignant pleural effusion, to clarify the prognostic indicators, and to validate LENT prognostic scoring systems.

Materials and Methods: The present study is a retrospective descriptive design. All medical records of patients diagnosed with malignant pleural effusion at HRH Princess Maha Chakri Sirindhorn Medical Center between May 1, 2011, and August 31, 2015 were reviewed. The study included patients with age of 18 years old and above. Their follow-up durations were at least six months, and the complete records of prognostic indicators were available.

Results: Thirty-five patient records were selected. All subjects were stratified into low-risk (score 0 to 1), moderate-risk (score 2 to 4), and high-risk (score 5 to 7) group according to LENT score. Only 30% of patients with high-risk LENT score survived for 1 month from the diagnosis. Nobody survived for 6 months. The analysis of the area under the ROC curve revealed that LENT prognostic scoring system was more reliable than ECOG performance score (PS) in the survival prediction (0.837 vs. 0.827). The sensitivity and specificity of LENT score were 100% and 6%, whereas the values of ECOG PS were 63% and 100% respectively.

Conclusion: LENT prognostic score is a useful prognostic scoring system in malignant pleural effusion for the survival prediction.

Keywords: ECOG PS, LENT prognostic score, Malignant pleural effusion, Prognostic indicators, Survival prediction

J Med Assoc Thai 2019;102(Suppl.6): 91-5
Website: http://www.jmatonline.com

Malignant pleural effusion (MPE) is a common problem in cancer patients and becomes a major problem due to the high mortality rate[1,2]. It usually occurs in patients with advanced neoplastic disease and is associated with a limited life expectancy (3 to 12 months)[3]. Bronchogenic carcinomas and breast cancers are the most common metastatic tumors to the pleura (40% and 25% respectively)[4]. Patients with MPE are considered to have a poor prognosis, and the quality of life is affected by symptoms related to recurrent pleural effusion, such as dyspnea, cough, and pain[5]. The primary goal in the management of MPE should be palliative treatment[4]. Simple therapeutic thoracentesis might be the option, while interventional procedures such as thoracoscopy with talc poudrage or chest tube insertion for pleurodesis are considered only in patients with prolonged life expectancy[5]. The survival prediction in patients with malignant pleural effusion is necessary for the treatment selection and proper management of individuals. Several predictors of survival have been currently used in clinical practice such as tumor characteristics, comorbidities, extent of disease, and the composition of the effusion[6-8]. Recently the LENT scoring system, calculated by using pleural fluid Lactate dehydrogenase (LDH), Eastern Cooperative Oncology Group Performance Score (ECOG PS), serum neutrophil-to-lymphocyte (NTL) Ratio, and malignant cell type in MPE, is the first validated prognostic score which can predict survival with significantly better accuracy than ECOG PS alone and may aid clinical decision making in this diverse patient population[9]. The primary objective is to compare 6-month survival in each group of patients with MPE classified by LENT prognostic scoring system. The second objective is to identify prognostic factors for survival and to compare LENT prognostic score to ECOGS PS in accuracy for survival prediction.

Correspondence to:

Petborom P.

Department of Medicine, HRH Princess Maha Chakri Sirindhorn Medical Center, Faculty of Medicine, Srinakharinwirot University, 62 Moo 7, Rangsit-Nakhon Nayok Road, Ongkharak, Nakhon Nayok 26120, Thailand.

Phone: +66-37-395085 ext. 11001

E-mail: pichaya@g.swu.ac.th

Materials and Methods

This is a retrospective, descriptive study. All medical records of patients diagnosed with malignant pleural effusion at HRH Princess Maha Chakri Sirindhorn Medical Center between May 1, 2011, and August 31, 2015 were reviewed. The study included patients with age of 18 years old and above. Their follow-up durations were at least six months or until death, and the complete records of prognostic indicators were available. Eligible patients were identified by using the International Classification of Diseases, 10th revision

How to cite this article: Petborom P, Vassara M, Muangnoi P. Predicting Survival in Patients with Malignant Pleural Effusion and Validating LENT Prognostic Score. J Med Assoc Thai 2019;102(Suppl.6): 91-5.

(ICD-10) codes associated with malignant neoplasm of the pleura (C38.4) and secondary malignant neoplasm of the pleura (C78.2). The malignant pleural effusion was defined as any one of the followings; a detection of malignant cells from pleural cytology, surgical biopsy, or having pleural lesion without definite cause in a proven cancer of other organs, or with improvement after chemotherapy. Chart reviews were conducted and the data were recorded on the standard case record form. Baseline characteristic of patients included age, sex, site of pleural effusion, method of diagnosis, primary site of malignancy/tumor type, ECOG PS, history of chemotherapy, and history of pleurodesis. Laboratory data consisting of serum neutrophil-to-lymphocyte ratio, pleural fluid differential cell count, and pleural fluid biochemistry (LDH, protein, glucose, and pH) were recorded. Date of diagnosis and date of last visit or death were recorded. LENT score were calculated to divide patients into 3 groups. Table 1 describes the LENT scoring system, which results in a score ranging from 0 to 7. The study was approved by the ethical committee of the faculty of medicine, Srinakharinwirot University, Thailand (SWUEC/E-153/2558).

Statistical analysis

Central limit theorem was used to approximate the sample size for more than 30. Descriptive analysis and Kolmogorov-smirnov test were used for statistical analysis. Overall survival according to the LENT score at 1, 3 and 6 months were assessed using a Cox regression model. Median survival time in each patients group, according to level of LENT score, was analyzed by using Survival analysis and Kaplan-Meier survival curve. Data were analyzed with IBM SPSS statistics for windows, version 22.0 (Armonk, NY: IBM Crop.), and the significance level was set at $p<0.05$.

Table 1. The LENT score calculation

	Variable	Score
L	LDH level in pleural fluid (IU/L)	
	<1,500	0
	>1,500	1
E	ECOG PS	
	0	0
	1	1
	2	2
	3 to 4	3
N	Neutrophil-to-Lymphocyte ratio	
	<9	0
	>9	1
T	Tumor type	
	Lowest risk tumor types	0
	Mesothelioma	
	Hematological malignancy	
	Moderate risk tumor types	1
	Breast cancer	
	Gynecological cancer	
	Renal cell carcinoma	
	Highest risk tumor types	2
	Lung cancer	
	Other tumor types	
Risk categories	Total score	
Low risk	0 to 1	
Moderate risk	2 to 4	
High risk	5 to 7	

ECOG PS = Eastern Cooperative Oncology Group performance score; LDH = lactate dehydrogenase

Results

Thirty-five patients in HRH Princess Maha Chakri Sirindhorn Medical Center, Srinakharinwirot University, Thailand were included. The mean age was 61 years, 57.1% were women and 45.7% of effusions were right sided. The most common tumor type was lung cancer (60%) (Table 2).

LENT score was calculated at the time of presentation. According to the present study 2.8%, 68.6%, and 28.6 % of patients were low-risk, moderate-risk and high risk, respectively. The Kaplan-Meier survival curves of each group were shown in Figure 1. Patients with MPE had lower

Table 2. Baseline characteristics

Variable, total patients	n (%)
Age (years)	61 (25 to 88)*
Female	20 (57.1%)
Side	
Right side	16 (45.7%)
Left side	15 (42.7%)
Both sides	4 (11.4%)
Mode of diagnosis	
Pleural fluid cytology	15 (42.9%)
Pleural biopsy pathology	16 (45.7%)
Pathology from other sites	4 (11.4%)
Primary site/tumor type	
Lung	21 (60.0%)
Gynecologic	5 (14.3%)
Breast	4 (11.4%)
Hematologic	3 (8.5%)
Gastrointestinal	1 (2.9%)
Mesothelioma	1 (2.9%)
ECOG-PS	
0	10 (28.6%)
1	7 (20.0%)
2	6 (17.1%)
3	4 (11.4%)
4	8 (22.9%)
Chemotherapy	25 (71.4%)
Pleurodesis	12 (34.3%)
LENT score	
Low risk	1 (2.8%)
Moderate risk	24 (68.6%)
High risk	10 (28.6%)
Pleural fluid biochemistry	
LDH (U/L)	886 (105 to 6,460)*
Protein (g/dL)	3.9 (1.5 to 7.7)*
Glucose (mg/dL)	96.7 (5 to 203)*

* Mean (range)

survival rate if they had higher LENT score. Patients with low-risk LENT score had 100% survival 6 months from diagnosis. Those with a moderate-risk LENT score, 87.5%, 83.3%, and 62.5% survived at 1 month, 3 months, and 6 months respectively, comparing with those with a high-risk LENT score who had chances of surviving at 1, 3, and 6 months of 30%, 10%, and 0% (none) respectively (Figure 2).

Statistical analysis using Cox regression analysis found that patients with high- risk LENT scores had Hazard ratio (95% CI) for mortality at 6 months of 6.12 (2.25 to 16.79, $p<0.001$), comparing with moderate-risk LENT score. The analysis of other variables for the effect on survival using Cox Regression revealed that only ECOG PS showed a statistically significant effect on survival ($p = 0.020$, 95% CI 1.129 to 4.133) (Table 3).

The receiver operating characteristics (ROC) analysis for mortality using the LENT score showed non-significant higher area under the curve (AUC) value than ECOG performance status alone. The AUC was 0.837 (95% CI 0.71 to 0.97) for LENT compared with 0.827 (0.69 to 0.96) for ECOG PS ($p = 0.050$) (Figure 3). The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of LENT score for predicting survival were 100%, 6%, 55%, and 100% respectively, whereas the values of ECOG PS were 63%, 100%, 100%, and 70% respectively.

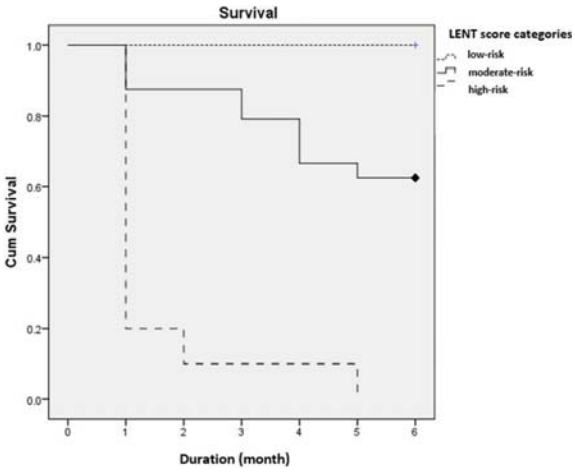

Figure 1. Kaplan-Meier survival curves according to the LENT score.

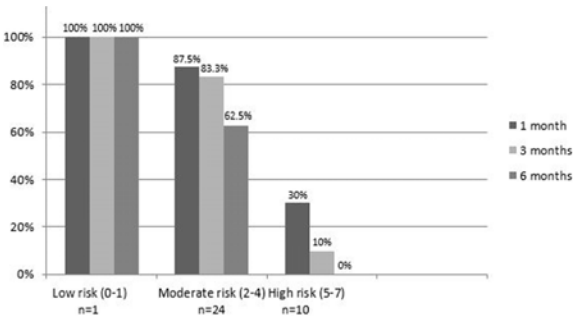

Figure 2. Proportion of patients surviving at 1, 3, and 6 months according to low-risk, moderate-risk, and high-risk LENT scores.

Discussion

Previous study has reported that the LENT score, which is the first validated risk stratification system in MPE, provided valuable additional prognostic information and performed significantly better than ECOG PS in predicting survival[9]. In that study, they collected databases from the UK, Australia and the Netherlands where the incidence of mesothelioma are higher than in Asia[9]. The aim of our retrospective study is to obtain data of patients surviving with malignant pleural effusion, to clarify the prognostic indicators and to validate LENT prognostic scoring systems in Thai populations. In this study lung cancer was the most common tumor type (about 60% of the patients) and only 1 patient (3%) had mesothelioma which was different from previous study in UK[9]. A previous study in Thailand revealed that lung cancer is the most common tumor type in MPE (50.7%) which was similar to the present study[10].

In the present study, patients with low-risk LENT score had 100% survival at 6 months from diagnosis. Those with a moderate-risk LENT score 87.5%, 83.3%, and 62.5% survived at 1 month, 3 months, and 6 months respectively. This compares with those with a high-risk LENT score who had their chances of surviving at 1, 3, and 6 months were 30%, 10%, and 0% respectively. According to this study, LENT prognostic score is associated with the median survival time of patients with malignant pleural effusion. The authors found similar results as the previous study that the death rate at six months among the high-risk group was six times higher than those in the moderate-risk group. The analysis of the AUC of ROC curve revealed that LENT prognostic scoring system was slightly superior (nonsignificant) at predicting survival compared with ECOS PS (0.837 vs. 0.827). This result was different from previous study that showed the LENT score to be significantly superior to ECOG PS at predicting survival at 1 month, 3 months and 6 months[9].

In Asia there was a study about prognostic utility of the LENT score in predicting survival among patients with MPE and showed that high LENT score has lower survival rates[11]. The present study is the first study in Thailand that aim to validate LENT prognostic scoring systems. Seemingly LENT score, together with the use of clinical performance status, could be an interesting scoring system in predicting survival for those patients with malignant pleural effusion. Furthermore the LENT score is easy to calculate, using basic laboratory variables that are available in general hospital, clinically relevant prognostic outcome. ROC curve analysis showed that LENT score was slightly better (nonsignificant) than ECOG PS in predicting survival. Additionally, LENT score was more sensitive than ECOG PS for predicting survival, although the result of the

Table 3. COX Regression on other variables

Variables	Hazard ratio	95%CI	*p*-value
ECOG PS	2.160	1.129 to 4.133	0.02
History of chemotherapy	0.531	0.15 to 1.884	0.327
Pleurodesis	2.635	0.684 to 10.156	0.159
Pleural fluid LDH	1.0	1.0 to 1.0	0.753
NTL ratio	1.015	0.942 to 1.092	0.699

ECOG PS = Eastern Cooperative Oncology Group performance score; LDH = lactate dehydrogenase; NTL = serum neutrophil-to-lymphocyte; CI = confidence interval

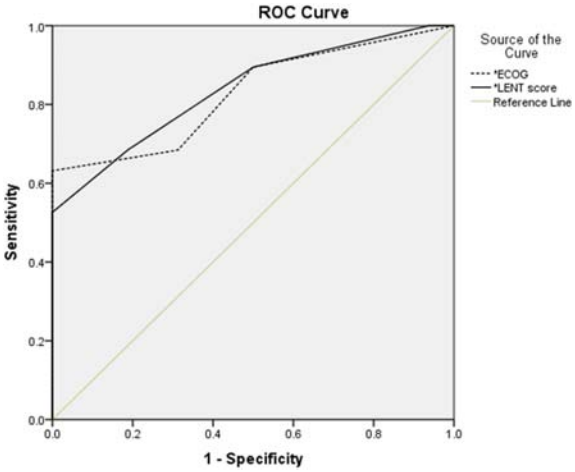

Figure 3. ROC curve analysis for LENT score and ECOG PS for outcome of mortality.

sensitivity and specificity analysis of LENT prognostic score was different from the previous study on LENT score.

There are some limitations of this study. Our study is retrospective descriptive study, has small sample size especially in the low-risk group (n = 1), and data collection in one center. Moreover, as there are the diverse staging systems for the different tumor types and no universal biomarker, the extent of disease were not included as a variable in our analysis. Nevertheless, the present study is the first study that validate LENT prognostic scoring system in the Thai population. Further prospective multicenter studies in Thailand should be useful.

Conclusion

The LENT prognostic score is a useful prognostic scoring system for the survival prediction in malignant pleural effusion.

What is already known on this topic?

The LENT score is the first validated risk stratification system in malignant pleural effusion, providing valuable additional prognostic information and performing significantly better than ECOG PS in predicting survival.

What this study adds?

The present study is the first study in Thailand and confirms the value of this scoring system as additional prognostic information with better than ECOG PS for predicting survival in malignant pleural effusion in the Thai population.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Froudarakis ME. Diagnostic work-up of pleural effusions. Respiration 2008;75:4-13.
2. Froudarakis ME. Pleural diseases in the molecular era - time for more answers: introduction. Respiration 2012;83:2-4.
3. Ozyurtkan MO, Balci AE, Cakmak M. Predictors of mortality within three months in the patients with malignant pleural effusion. Eur J Intern Med 2010;21:30-4.
4. Zarogoulidis K, Zarogoulidis P, Darwiche K, Tsakiridis K, Machairiotis N, Kougioumtzi I, et al. Malignant pleural effusion and algorithm management. J Thorac Dis 2013;5 Suppl 4:S413-9.
5. Anevlavis S, Kouliatsis G, Sotiriou I, Koukourakis MI, Archontogeorgis K, Karpathiou G, et al. Prognostic factors in patients presenting with pleural effusion revealing malignancy. Respiration 2014;87:311-6.
6. Pilling JE, Dusmet ME, Ladas G, Goldstraw P. Prognostic factors for survival after surgical palliation of malignant pleural effusion. J Thorac Oncol 2010;5:1544-50.
7. Bielsa S, Salud A, Martinez M, Esquerda A, Martin A, Rodriguez-Panadero F, et al. Prognostic significance of pleural fluid data in patients with malignant effusion. Eur J Intern Med 2008;19:334-9.
8. Burrows CM, Mathews WC, Colt HG. Predicting survival in patients with recurrent symptomatic malignant pleural effusions: an assessment of the prognostic values of physiologic, morphologic, and quality of life measures of extent of disease. Chest 2000;117:73-8.
9. Clive AO, Kahan BC, Hooper CE, Bhatnagar R, Morley AJ, Zahan-Evans N, et al. Predicting survival in

malignant pleural effusion: development and validation of the LENT prognostic score. Thorax 2014;69:1098-104.
10. Saiphoklang N, Kanitsap A, Nambunchu A. Differences in clinical manifestations and pleural fluid charateristics between tuberculous and malignant pleural effusions. Southeast Asian J Trop Med Public Health 2015;46:496-503.
11. Chan JN, Villalon J. Prognostic utility of the L.E.N.T. score in predicting survival among patients with malignant pleural effusion admitted at the Chinese General Hospital and Medical Center [abstract AP259]. Respirology 2017;22 Suppl 3:191-2.