VALIDATION OF CLINICAL PROMISE SCORE IN PREDICTING 3-MONTH MORTALITY IN MALIGNANT PLEURAL EFFUSION PATIENTS

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ABSTRACT

Background: Pleural effusion is a frequent complication of malignancy. Malignant pleural effusion accounts for 15% to 35% of all pleural effusion cases and the incidence rate reaches 660 people per 1 million population globally. Several prediction models have been evaluated to predict mortality in malignant pleural effusion patients. The PROMISE score is a prediction model for 3-month mortality in patients with malignant pleural effusion.

Methods: A retrospective cohort study was conducted on patients with malignant pleural effusion registered in 2015-2022 at Cipto Mangunkusumo National Central General Hospital. A three-month mortality assessment was carried out. The collected data was analyzed using the Hosmer-Lemeshow goodness-of-fit test to determine the calibration performance and creation of a Receiver Operating Curve (ROC) curve to determine the discrimination performance of the Clinical PROMISE score on three-month mortality outcomes.

Results: A total 120 subject were included in the study. The majority of subjects were women (73.3%), mean age 55 years and other types of cancer (78.3%). The Clinical PROMISE score had good calibration performance (p = 0.230, coefficient of correlation r = 0.945). The discrimination performance of the Clinical PROMISE score was good with an AUC of 0.849 (95% CI 0.776 –0.922).

Conclusion: The calibration and discrimination performance of Clinical PROMISE score to predict 3-month mortality of malignant pleural effusion is good.

Keywords: Malignant pleural effusion, mortality, Clinical PROMISE score

ABSTRAK

Latar Belakang : Efusi pleura merupakan salah satu komplikasi dari kanker atau penyakit keganasan yang sering terjadi. Efusi pleura maligna termasuk dalam 15% sampai dengan 35% dari seluruh kejadian efusi pleura dan angka kejadiannya mencapai 660 orang per 1 juta populasi secara global. Beberapa model prediksi telah dievaluasi untuk memprediksi mortalitas pada pasien efusi pleura maligna. Skor PROMISE merupakan sebuah model prediksi mortalitas 3 bulan pada pasien dengan efusi pleura maligna.

Tujuan : Penelitian ini bertujuan untuk mengevaluasi performa kalibrasi dan diskriminasi skor Clinical PROMISE dalam memprediksi mortalitas tiga bulan pada pasien efusi pleura maligna.

Metode : Penelitian ini menggunakan metode kohort retrospektif yang melibatkan pasien efusi pleura maligna yang teregistrasi tahun 2015-2022 di Rumah Sakit Umum Pusat Nasional Dokter Cipto Mangunkusumo. Dilakukan penilaian mortalitas tiga bulan. Data terkumpul dianalisis dengan uji Hosmer-Lemeshow goodness-of-fit untuk mengetahui performa kalibrasi dan pembuatan kurva Receiver Operating Curve (ROC) untuk mengetahui performa diskriminasi skor Clinical PROMISE terhadap luaran mortalitas tiga bulan.

Hasil : Diperoleh 120 subjek yang disertakan dalam penelitian dengan proporsi mortalitas 60,8%. Mayoritas subjek adalah perempuan (73,3%), rerata usia 55 tahun, kanker tipe lain (78,3%). Skor Clinical PROMISE memiliki performa kalibrasi yang baik (p = 0,230, koefisien korelasi r = 0,945). Performa diskriminasi skor Clinical PROMISE baik dengan AUC 0,849 (IK95% 0,776 –0,922).

Kesimpulan : Performa kalibrasi dan diskriminasi skor Clinical PROMISE dalam memprediksi mortalitas tiga bulan pada pasien efusi pleura maligna adalah baik.

Kata Kunci : Efusi pleura maligna, mortalitas, skor Clinical PROMISE

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INTRODUCTION

Pleural effusion is a frequent complication of malignancy diseases. Malignant pleural effusion accounts for 15% to 35% of all pleural effusion events and the incidence rates reaches 660 people per 1 million population globally.[1-3] The presence of malignant pleural effusion usually represents advanced or metastatic disease, and consequently poor prognosis, from an average of 3 months to 12 months depending on patient factors and underlying cancer.[4] A study conducted by Kuniati R et al. in 2018 shows that 90-day mortality in malignant pleural effusion patients at RSCM was 63.8%.[5]

The PROMISE score is a prediction model for 3-month mortality in patients with malignant pleural effusion. The PROMISE score has good performance in predicting the risk of mortality in patients with malignant pleural effusion (AUC 0.78; 95% CI 0.72 – 0.83). Components that are evaluated in PROMISE score is history of chemotherapy, history of radiotherapy, hemoglobin value, leukocyte value, CRP, ECOG Performance status, and type of cancer.[6] This study aim to evaluate the performance of the PROMISE score in predicting mortality in patients with malignant pleural effusion.

METHODS

Patients, study design, and variables

A retrospective cohort study based on medical health record was conducted on subjects with malignant pleural effusion cases registered from 2015-2022 at Cipto Mangunkusumo National General Hospital. The inclusion criteria for this study were patients over the aged of 18 years who were diagnosed with malignant pleural effusion based on pleural fluid cytology. Patients with incomplete medical record data were excluded.

Independent variables in this study were previous chemotherapy, previous radiotherapy, hemoglobin, serum white blood cell (WBC) count, C-reactive protein (CRP), ECOG performance status, and cancer type. Hemoglobin divided into ≥16, 14 to <16, 12 to <14, 10 to <12, and <10. Serum WBC was classified into <4,000, 4,000 to <6,300, 6,300 to 10,000, 10,000 to <15,800, and ≥15,800. Meanwhile, CRP consist of <3, 3 to <10, 10 to <32, 32 to <100, and ≥100. ECOG performance status was classified into 0-1, and 2-4. Cancer type divided into mesothelioma, all other type of cancer, and lung cancer. The minimum sample size required for this research is 120 samples. Consecutive sampling method was done on all medical record on malignant pleural effusion patients registered at RSUPN-CM from 2015-2022.

Statistical analysis

Data processing was carried out using SPSS version 25. Univariate analysis was carried out to describe the characteristics of the research subjects. The calibration test with Hosmer-Lemeshow were carried out to predict three-month mortality in patients with malignant pleural effusion. The Hosmer-Lemeshow test is a test of the goodness of fit of the logistic regression model. The Hosmer-Lemeshow test is considered to have good calibration performance if the p value is more than 0.05. Meanwhile, discrimination uses the area under receiving operator characteristic (AUROC).

Ethical Issues

This study has permission from the Health Research Ethics Committee, Faculty of Medicine Universitas Indonesia with number KET-460/UN2.F1/ETIK/PPM.00.02/2024 and the study location permit was issued by the Innovation and Intellectual Property Management Installation of the Cipto Mangunkusumo National General Hospital with number YR.02.01/D.IX.2.3/416/2024. All patient data confidentiality is protected in this study.

RESULTS

There were 120 study subjects who met the eligibility criteria for this research. The mean age in this study was 55 years. The majority research subjects were female (73.3%). The most common type of cancer in this study were all other type of cancer (78.3%). In other type of cancer, with the largest proportion was breast cancer (27.5%). Most patients have no history of previous chemotherapy or radiotherapy. The mean Clinical PROMISE score was 25. Demographic data of study subjects is displayed in table 1.

Table 1. Characteristic of Study Subjects

Characteristic	Value (n = 120)
Age,mean (years) ± SD (years)	55,19 ± 11,78
Sex, n (%)	
Male	32 (26,7)
Female	88 (73,3)
Previous chemotherapy, n (%)	
No	81 (67,5)
Yes	39 (32,5)
Previous radiotherapy, n (%)	
No	104 (86,7)
Yes	16 (13,3)
Hemoglobin, n (%)	
≥16	1 (0,8)
14 - <16	11 (9,2)
12- <14	26 (21,7)
10 - <12	51 (42,5)
<10	31 (25,8)
Serum WBC counts, n (%)	
<4.000	0 (0)
4.000 - <6.300	10 (8,4)
6.300 - <10.000	36 (30)
10.000 - <15.800	37 (30,8)
≥15.800	37 (30,8
CRP, n (%)	
<3	7 (5,8)
3 - <10	23 (19,2)
10 - <32	28 (23,3)
32 - <100	37 (30,8)
≥100	25 (20,8)
ECOG PS, n (%)	
0-1	61 (50,8)
2-4	59 (49,2)
Cancer type, n (%)	
Mesothelioma	1 (0,8)
All other type of cancer	94 (78,3)
Lung	25 (20,8)
Clinical PROMISE score	25,16 (6,42)

CRP : C-reactive Protein. ECOG PS : Eastern Cooperative Oncology Group (ECOG) Performance Status. SD : Standard Deviation. WBC : white blood cells.

In this study, the three-month mortality was 60.8%, with the highest mortality rate coming from other type of cancer group (79.5%). The highest proportion of mortality was in ECOG 2-4.

Table 2. Characteristics of subjects based on three-month mortality

Characteristics	Mortality	
	Yes (n=73)	No (n=47)
Sex, n (%)		
Male	19 (26)	13 (27,7)
Female	54 (74)	34 (72,3)
Previous chemotherapy, n (%)		
No	46 (63)	35 (74,5)
Yes	27 (37)	12 (25,5)
Previous radiotherapy, n (%)		
No	64 (87,7)	40 (85,1)
Yes	9 (12,3)	7 (14,9)
Hemoglobin, n (%)		
≥16	0 (0)	1 (2,1)
14 - <16	5 (6,8)	6 (12,8)
12- <14	16 (21,9)	10 (21,3)
10 - <12	31 (42,5)	20 (42,6)
<10	21 (28,8)	10 (21,3)
WBC counts n (%)		
<4.000	0 (0)	0 (0)
4.000 - <6.300	4 (5,5)	6 (12,8)
6.300 - <10.000	17 (23,3)	19 (40,4)
10.000 - <15.800	26 (35,6)	11 (23,4)
≥15.800	26 (35,6)	11 (23,4)
CRP, n (%)		

<3	3 (4,1)	4 (8,5)
3 - <10	8 (11)	15 (31,9)
10 - <32	17 (23,3)	11 (23,4)
32 - <100	27 (37)	10 (21,3)
≥100	18 (24,7)	7 (14,9)
ECOG PS, n (%)		
0-1	22 (30,1)	39 (83)
2-4	51 (69,9)	8 (17)
Cancer type, n (%)		
Mesothelioma	0 (0)	1 (2,1)
All other type of cancer	58 (79,5)	36 (76,6)
Lung	15 (20,5)	10 (21,3)

CRP : C-reactive Protein. ECOG PS : Eastern Cooperative Oncology Group (ECOG) Performance Status. WBC : white blood cells.

Calibration and Discrimination Test

The performance of Clinical PROMISE score calibration in predicting three-month mortality in malignant pleural effusion was well-calibrated (p = 0.230; correlation coefficient r = 0.945). Discrimination performance in this study was classified as good with an AUC of 0.849 (CI 95% 0.776 - 0.922).

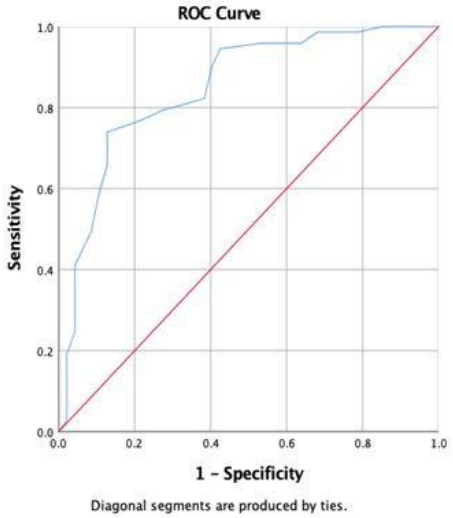

Figure 1. Receiver Operating Characteristic (ROC) Clinical PROMISE score.

DISCUSSION

In this study, it was found that three-month mortality rate in malignant pleural effusion patient 60.8%. The mortality rate obtained was similar compared to previous study done in the same hopsital in 2018 conducted by Kurniati R et al[5] found that the three-month mortality rate was 63.8%. This result is higher compared to other studies done in other countries. One study done in Singapore by Quek et al[7] have three-months mortality rate of 15% while study done in Hong Kong by Wong et al[8] have three-months mortality rate of 39.6%. This study found that the 90-day mortality rate in patients with malignant pleural effusion was 15%. The mortality rate in this study is also much higher compared to the study conducted by Wong et al.[8] The study by Wong et al[8] found that the three-month mortality rate in patients with malignant pleural effusion was 39.6%.

The mean age of the subjects in this study was 55.19+11.78 years, which is almost the same average age with other studies published regarding malignant pleural effusion. Study done by Kurniati et al[5] and Amin et al[9] have mean age of 52 years and 51 years respectively. Other study done by Özyurtkan et al[10] also have similar mean age 59 years. research which found a mean age of 52 years and Amin et al[9] research which found an age of 51 years in patients with malignant pleural effusion. Research conducted by Quek et al[7] found that most of the subjects were aged 56-71 years with a median of 65 years. Research that conducted by Özyurtkan et al[10] also had a higher mean age than this study, namely 59 years. It appears that the average age of the subjects used in this study is not much different from previous studies.

The types of cancer that most commonly cause malignant pleural effusion shows different result comparing data from Cipto Mangunkusumo Hospital with study from other country. In this study, other types of cancer, including breast cancer and gynecological

cancer are the main cause, while Kurniati et al have similar result that is breast and ovarian cancer. This is different from the study conducted by Quek et al[7], where the most common type of primary cancer was lung cancer. The results of this study are different from the literature where lung cancer is still the first cause of death due to cancer.

Based on the results of this study, it appears that the performance of the Clinical PROMISE score calibration in predicting three-month mortality in malignant pleural effusion patients is classified as good using the Hosmer-Lemeshow test and the p value = 0.230. This study also shows that the discrimination performance of the Clinical PROMISE score is relatively good with an AUC of 0.849 (95% CI 0.776 – 0.922). To date, there has been no other research that has validated the Clinical PROMISE score in Indonesia. From the original research developed by Psallidas et al, the Clinical PROMISE score also showed good performance (AUC 0.90; CI95% 0.85 – 0.94). The discrimination ability for the mortality outcome of malignant pleural effusion is relatively good. The original study conducted by Psallidas et al[6] also compared the performance of this score with the LENT score, where it was found that the performance of the LENT score was lower than the Clinical PROMISE score, namely AUC 0.62 (95% CI 0.58 – 0.66). The results of this study compare favorably with the study conducted by Quek et al.[7] In this study, it was found that the Clinical PROMISE score performed quite well with an AUC value of 0.72 (95% CI 0.53 – 0.91). This could be because the age of the subjects in this study was younger compared to the study conducted by Quek et al[7] with the average age of the subjects in this study being 55 years, while the average age of the subjects in Quek et al study was 65 years.[7]

Conclusion

We can conclude that the calibration and discrimination performance of the Clinical PROMISE score is relatively good in predicting three-month mortality in patients with malignant pleural effusion.

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Conflict of Interest

Authors declare no conflicts of interest.

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