CANCER RATIO-BASED DIAGNOSTIC TOOL IN IDENTIFYING MALIGNANT PLEURAL EFFUSION: SENSITIVITY, SPECIFICITY AND CLINICAL INSIGHTS

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Abstract

Background: Malignant pleural effusion (MPE) is a common cause of exudative lymphocytic pleural effusion. Although pleural fluid evaluation is routinely performed, cytology or histopathology remains the gold standard for MPE diagnosis. The cancer ratio (CR), calculated by comparing serum LDH to pleural fluid ADA levels, has shown promise in diagnosing MPE. However, no studies have investigated its utility in the Thai population, which has a high tuberculosis prevalence.

Objectives: This study aimed to evaluate the diagnostic accuracy of the CR in MPE diagnosis, compare clinical and pleural fluid parameters between MPE and nonMPE cases, determine the appropriate CR cut-off for the Thai population and develop a prediction score for prediagnosing MPE.

Results: Between July 2021 and December 2022, patients presenting exudative lymphocytic pleural effusion were included in the study. Demographics, symptoms, radiographic findings and pleural fluid parameters were collected and cytology/histopathology served as the reference test. CR performance was assessed using receiver operating characteristic curves, and a prediction score was developed using multivariable logistic regression analysis. Among 122 patients, 46.7% received a diagnosis of MPE. The CR exhibited a sensitivity of 87.7% and specificity of 72.3% (AUC 0.83) with a cut-off level >10. Patients with MPE showed longer symptom duration, lower fever and massive pleural effusion, which were more common in MPE than nonMPE cases. A prediction score incorporating symptom duration, fever history, effusion amount and CR demonstrated superior diagnostic performance for MPE (AUC 0.94) compared with the CR alone.

Conclusion: The CR can effectively differentiate MPE from nonMPE among patients with exudative lymphocytic pleural effusion. A cut-off level >10 is recommended for diagnosing MPE in the Thai population. Combining clinical, radiologic and CR data may aid in prediagnosing MPE; however, further research is needed for validation.

Keywords: cancer ratio, malignant pleural effusion, exudative, lymphocytic, pleural effusion

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Introduction

Exudative lymphocytic pleural effusion. is primarily attributed to two leading causes: malignant pleural effusion (MPE) and tuberculous pleural effusion (TPE).[1, 2] These conditions account for 58% of exudative pleural effusion cases in Thailand.[3] Thoracentesis is commonly performed to assess pleural fluid parameters as an initial step in the differential diagnosis of these diseases. A crucial parameter for diagnosing TPE is pleural fluid ADA (pADA), which exhibits a sensitivity of 92% and specificity of 90% when using a cut-off value above 40 IU/L.[4, 5] However, for MPE, the gold standard remains cytology or histopathology with pleural fluid cytology yielding an average diagnostic rate of 60%.[2, 6] Image-guided pleural biopsy increases the diagnostic yield to 87%, while thoracoscopy achieves a rate of 94.8%.[6-8] These latter methods involve more invasive procedures. Related studies have investigated using biochemical markers such as tumor markers (CEA, CA-125, CA 19-9, CA 15-3 and CYFRA 21-1) in pleural fluid. While these markers display a relatively high specificity of approximately 80 to 90%, their sensitivity remains low, ranging from 40 to 60%.[9, 10] Moreover, their routine use in clinical practice remains unfeasible, and additional costs are associated with these tests.

One related study[11] demonstrated the significant predictive value of the cancer ratio (CR) in diagnosing MPE (MPE). The CR is calculated as the serum LDH (sLDH) ratio to pleural fluid ADA (pADA). Using a cut-off value greater than 20, the CR showed a sensitivity of 0.98 (95% CI 0.92-0.99) and a specificity of 0.94 (95% CI 0.83-0.98). Both sLDH and pADA are commonly used to evaluate patients with exudative lymphocytic pleural effusion to distinguish between different diseases.[6, 12] However, noting that the CR has not been investigated in the Thai population is important because it indicates a high prevalence of tuberculosis. As a result, the accuracy of this parameter and the choice of an appropriate cut-off level may be influenced, which forms the basis of the current study. The study aimed to investigate the diagnostic accuracy of the CR for MPE among patients presenting a lymphocytic-predominant profile.

Methods

Participants

From July 2021 to December 2022, a prospective enrollment of patients with recently diagnosed pleural effusion was conducted at Phramongkutklao Hospital. The eligibility criteria encompassed individuals aged ≥20 years, exhibiting an exudative profile ascertained through rigorous adherence to Light's criteria and lymphocytes constituting more than 50% of nucleated cells. Notably, patients receiving a diagnosis of pseudo-exudative pleural effusion, expectant mothers, those who declined to undergo invasive procedures and individuals in an advanced stage of disease or receiving palliative care were excluded from participation. Additionally, conditions that could cause an elevation in serum lactate dehydrogenase (LDH) such as liver disease, severe anemia (hemoglobin <8 g/dL), heart attack within two weeks, bone fractures, muscle trauma, recent organ infections and HIV, were also excluded. This study was approved by the ethics committee of the Royal Thai Army Medical Department (approval No. R003h/65).

Data collection

The demographic data, comorbidities, personal history of cancer, history of tuberculosis exposure, symptoms, initial radiological findings and pleural fluid parameters were collected following patients' diagnosis of exudativelymphocytic pleural effusion. As part of the study protocol, all participants had cytology or histopathology testing, serving as the standard reference test for differentiating between MPE and nonMPE. The pathologists confirmed that the diagnosed MPE revealed the presence of malignant cells in cytology or histopathology.

Outcomes

The primary objective of this study was to determine the diagnostic performance of the CR in diagnosing MPE, explicitly assessing its sensitivity and specificity. The secondary

endpoints included determining the prevalence of MPE, comparing clinical characteristics and pleural fluid parameters between MPE and nonMPE cases and developing a predictive score for diagnosing MPE.

Statistical analysis

Based on the prevalence of MPE reported in a related systematic review on the CR, which was 40.8%[13], the sample size was calculated to be 118 subjects, with a minimum of 48 subjects diagnosed with MPE. Descriptive statistics, such as frequencies, means (SD), or medians (interquartile range [IQR]), were used depending on the distribution of the data. Categorical variables were compared using the chi-square test, while continuous variables were also compared using the Mann-Whitney U test between the MPE and non MPE groups. A two-sided p <0.05 was considered statistically significant. The primary outcome was assessed using the receiver operating characteristic (ROC) curve analysis, and multivariate analyses were conducted using a logistic regression model for the secondary endpoints. The data, including pleural fluid cell analysis, pleural fluid protein, pleural fluid LDH, pleural fluid ADA and serum LDH, underwent categorization into ranges. This categorization was determined by referring to a related study for established reference points.[4, 10, 14, 15] All data were analyzed using statistical software (STATA, Version 14).

Model development

Our model development involved complete-case analysis, meaning we did not perform data imputation. We included all relevant clinical parameters in a multivariable logistic regression model to identify significant predictors of MPE. To decide which predictors to keep, we used backward elimination based on two criteria: statistical significance indicated by the p-value of each predictor and the overall predictive performance of the model measured by the area under the ROC (AuROC) curve. Initially, we eliminated noncontributing factors with large p-values and the lowest effect size (odds ratio closest to 1.00) from the regression model. After removing each predictor, we assessed the model's diagnostic performance using the AuROC. If removing a predictor led to a significant decrease in AuROC, we reintroduced that predictor back into the model. We repeated these steps consecutively until all remaining predictors in the model had a p-value lower than 0.10, ensuring that the reduced model maintained a satisfactory AuROC. To evaluate the discrimination and calibration of the final reduced model, we used AuROC curves and conducted the Hosmer-Lemeshow goodness-of-fit test.

Score derivation and validation

Scores were assigned to each predictor in the final model based on their logit coefficients. During score transformation, the denominator was set as the lowest coefficient among all predictors, and the other coefficients were used as numerators. After dividing the coefficients, the products were rounded to whole numbers. Subsequently, scores were calculated for each patient in the development cohort. We conducted discrimination and calibration measures in the logistic regression model based on the scores. The scores were further divided into three risk groups: low, moderate and high probability of having MPE, using an appropriate cut-off point.

Results

A total of 302 patients were diagnosed with pleural effusion, and after applying the predefined inclusion criteria, 154 patients were considered eligible for the study. Subsequently, 12 cases of undiagnosed pleural effusions, 15 cases with incomplete data, one patient with both TPE and MPE and four patients with palliative or end-stage diseases were excluded. As a result, a final dataset of 122 patients was available for analysis, as depicted in **Figure 1.** Among these patients, 57 individuals (46.7%) received a diagnosis of MPE, while the origins of the MPEs and the etiologies of nonMPE cases are presented in **Table 2.**

Table 1 shows the baseline clinical-radiologic and analytic characteristics of the patients. Most participants were male, comprising

approximately 54% of the total sample. The mean age of the participants was 61 years with the MPE group being significantly older (p=0.01). No significant differences were observed between the two groups regarding smoking history and history of tuberculosis exposure. However, patients with MPE exhibited a higher prevalence of personal cancer history, accounting for 41.8% of cases, significantly greater than that observed in the nonMPE group.

Patients with MPE displayed notable clinical symptoms persisting for more than 30 days (p = 0.01) and a lower incidence of fever than patients with nonMPE. However, the two groups showed no significant difference regarding other symptoms such as dyspnea, chest pain, cough or weight loss. Additionally, a higher proportion of patients with MPE exhibited massive pleural effusion, characterized by the involvement of over two thirds of the hemithorax during the initial evaluation, in contrast to patients with nonMPE (33.3% vs. 10.8%, p=0.002). Furthermore, patients with MPE demonstrated a significantly higher median CR than non-patients with nonMPE (20.7 vs. 5.1, $p < 0.001$).

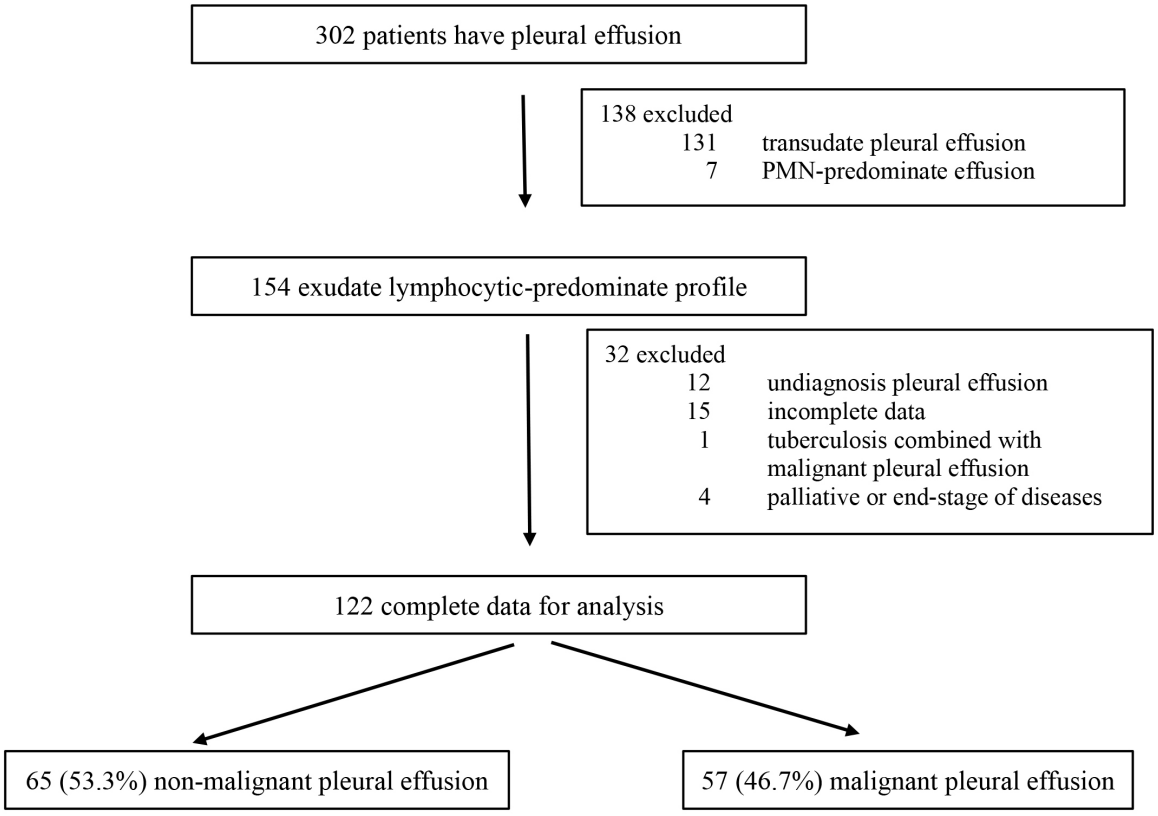

Figure 1. Study flow of patient enrollment

Table 1. Baseline demographic data, presenting symptoms, radiographic data and initial laboratory investigation of derivation cohort, comparison of MPE and nonMPE

Characteristics	non-MPE (N=65)	MPE (N=57)	*p*-value
Age (year), mean ± SD	57.2±18.4	66.2±13.6	0.01*
Male, N (%)	37 (56.9)	29 (50.9)	0.50
Current or ex-smoker, N (%)	20 (35.1)	12 (24.5)	0.24
Contact TB, N (%)	8 (13.8)	4 (7.7)	0.31
Underlying cancer, N (%)	12 (18.8)	23 (41.8)	0.01*
- Lung cancer	1 (1.5)	7 (12.3)	
- Breast cancer	2 (3.1)	7 (12.3%)	
- Hematologic malignancy	3 (4.6)	2 (3.5)	
- Other cancer type	6 (9.2)	7 (12.3)	
CKD over stage 3, N (%)	14 (21.5)	4 (7.4)	0.03*
Duration of symptom (day), median (IQR)	30 (10-60)	30 (30-90)	0.01*
Symptoms, N (%)			
Dyspnea	48 (76.2)	51 (89.5)	0.06
Chest pain	19 (30.6)	17 (31.5)	0.92
Fever	39 (62.9)	2 (3.8)	< 0.001*
Cough	37 (59.7)	33 (62.3)	0.78
- Anorexia	17 (29.3)	15 (31.3)	0.83
- Weight loss	32 (55.2)	25 (52.1)	0.75
Pleural fluid appearance, N (%)			0.14
- Serous	49 (75.4)	34 (61.8)	
- Serosanguinous	15 (23.1)	21 (38.2)	
- Purulent	1 (1.5)	0	
Pleural fluid location, N (%)			0.16
- Right	39 (60)	25 (43.9)	
- Left	19 (29.2)	26 (45.6)	
- Bilateral	7 (10.8)	19 (33.3)	
Massive PF, N (%)	7 (10.8)	19 (33.3)	0.002*
PF WBC, median (IQR)	1443 (555-2560)	1512 (677-2213)	0.05
PF Lymphocytes (%), mean±SD	87.2±11.6	82.9±13.4	0.37

Table 1. Baseline demographic data, presenting symptoms, radiographic data and initial laboratory investigation of derivation cohort, comparison of MPE and nonMPE (Cont.)

Characteristics	non-MPE (N=65)	MPE (N=57)	*p*-value
PF protein (g/dL), mean±SD	5.0±1.1	4.8±1.1	0.08
PF LDH (U/L), median (IQR)	275 (179-514)	364 (232-633)	0.40
PF ADA (U/L), median (IQR)	45 (24.7-58.9)	13.6 (10.3-18.5)	< 0.001*
Serum LDH (U/L), median (IQR)	228 (190-270)	279 (221-352)	0.001*
Cancer ratio, median (IQR)	5.1 (3.6-11.5)	20.7 (16-30)	< 0.001*

* *p*-value < 0.05

MPE malignant pleural effusion, *TB* Tuberculosis, *CKD* chronic kidney disease, *PF* pleural fluid, *LDH* lactate dehydrogenase, *ADA* adenosine deaminase

Table 2. Origin of MPE and etiologies of nonMPE

Origin (n=57)		Etiology (n=65)	
Lung	27 (47.4%)	Tuberculous pleural effusion	49 (75%)
Breast	8 (14.0%)	Others	16 (25%)
Hematologic	3 (5.3%)	- Meigs syndrome or Pseudo-meigs syndrome	
Mesothelioma	1 (1.8%)	- Radiation pleuritis	
Poorly differentiated carcinoma unclassified	7 (12.3%)	- Uremic pleuritis	
Others	11 (19.3%)	- Pulmonary embolism	
		- Post-CABG	
		- Pleural cysticercosis	

CABG coronary artery bypass grafting

As depicted in **Figure 2** and **Table 3**, the primary outcome demonstrates that the CR is highly accurate in predicting MPE when a cut-off level >10 is used with a sensitivity of 87.7% and specificity of 72.3% (AUC 0.83). Regarding the secondary endpoint, no statistically significant differences between the MPE and nonMPE groups were found regarding pleural fluid appearance and location. Similarly, no significant variations were observed in total white blood cell (WBC) count, lymphocyte count (%), protein level and LDH level in the pleural fluid profile between the two groups. However, the pleural fluid adenosine deaminase (pADA) level was significantly lower in the MPE group (median 13.6 vs. 45.0, p <0.001). **Table 4** shows multivariate analysis revealed that only a CR value higher than 10 remained significantly elevated in the MPE group with an adjusted odds ratio of 15.26 (p=0.01). Conversely, a pADA value less than 40 IU/L and sLDH higher than the upper normal limit did not show significant differences.

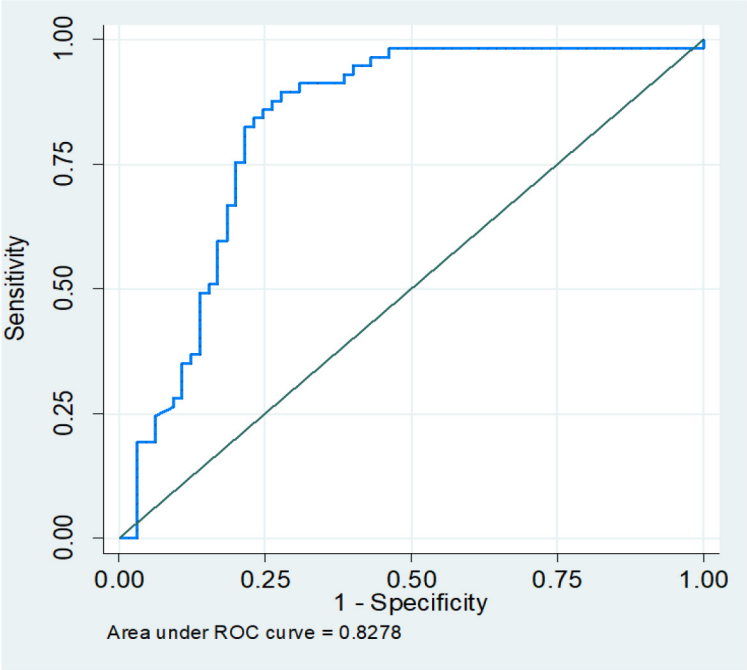

Figure 2. ROC curve of cancer ratio for diagnosis of malignant pleural effusion

Table 3. Cancer ratio sensitivity and specificity at different cut-off levels

Cut-off	Sensitivity (95% CI)	Specificity (95% CI)	ROC area	LR (+) (95% CI)	LR (-) (95% CI)	PPV (95% CI)	NPV (95% CI)
>10	87.7 (76.3-94.9)	72.3 (59.8-82.7)	0.80 (0.73-0.87)	3.17 (2.11-4.75)	0.17 (0.08-0.35)	73.5 (61.4-83.5)	87 (75.1-94.6)
>20	56.1 (42.4-69.3)	83.1 (71.7-91.2)	0.70 (0.62-0.78)	3.32 (1.85-5.96)	0.53 (0.39-0.72)	74.4 (58.8-86.5)	68.4 (56.9-78.4)
>30	24.6 (14.1-37.8)	93.8 (85-98.3)	0.59 (0.53-0.66)	3.99 (1.39-11.44)	0.8 (0.68-0.94)	77.8 (52.4-93.6)	58.7 (48.6-68.2)
>40	10.5 (4-21.5)	96.9 (89.3-99.6)	0.54 (0.49-0.58)	3.42 (0.72-16.28)	0.92 (0.84-1.02)	75 (34.9-96.8)	55.3 (45.7-64.6)
>50	7 (1.9-17)	96.9 (89.3-99.6)	0.52 (0.48-0.56)	2.28 (0.43-11.99)	0.96 (0.88-1.04)	66.7 (22.3-95.7)	54.3 (44.8-63.6)
>60	3.5 (0.4-12.1)	96.9 (89.3-99.6)	0.5 (0.47-0.53)	1.14 (0.17-7.84)	1 (0.93-1.06)	50 (6.8-93.2)	53.4 (44-62.6)

PPV positive predictive value, *NPV* negative predictive value, *PLR* positive likelihood ratio, *NLR* negative likelihood ratio, *CI* confidence interval

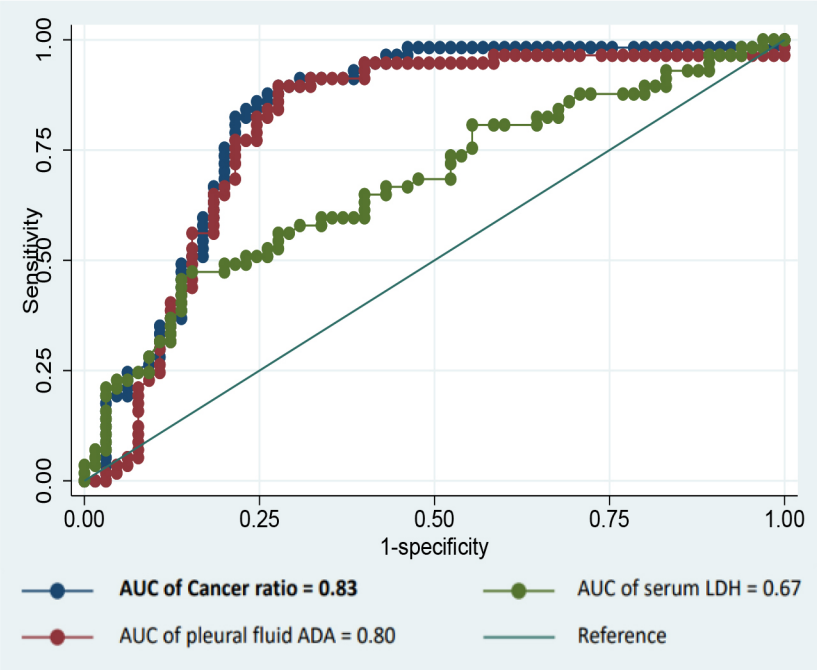

Table 4. Univariable and multivariable analysis of PF profiles with malignant pleural effusion as the outcome variable

Variables	Crude OR (95% CI)	*p*-value	mOR* (95% CI)	*p*-value
PF WBC > 2,000/mm3	1.01 (0.48 – 2.14)	0.97	3.41 (0.41 – 28.57)	0.26
PF %lymphocyte > 80%	0.44 (0.19 – 1.02)	0.06	0.19 (0.02 – 1.80)	0.15
PF protein < 4.0 g/dL	1.32 (0.51 – 3.39)	0.56	4.63 (0.44 – 49.04)	0.20
PF LDH > 1,790 U/L	1.15 (0.07 – 18.75)	0.92	7.17 (0.03 – 2028.93)	0.49
PF ADA < 40 IU/L	25.33 (7.16 – 89.57)	<0.001	18.51 (0.67 – 513.37)	0.09
Serum LDH > 225 U/L	2.34 (1.10 – 4.97)	0.03	2.28 (0.35 – 14.99)	0.39
Cancer ratio > 10	18.65 (7.14 – 48.69)	< 0.001	15.26 (1.88 – 124.10)	0.01

*Logistic regression model adjusted with age > 60 years, gender, comorbidities, duration of symptom > 60 days, symptoms, and radiography.

PF pleural effusion, *WBC* white blood cell, *LDH* lactate dehydrogenase, *ADA* adenosine deaminase

When analyzing patients based on their pADA levels, all three patients with pADA levels of 40 U/L or higher (typically diagnosed as TPE had MPE. The etiology of MPE in these cases was hematologic malignancy, and one of the three patients had a CR greater than 10. Among patients with pADA levels less than 40 U/L, 52 out of 80 cases were diagnosed as MPE. Utilizing a CR > 10 resulted in a high sensitivity of 90.7% in diagnosing MPE. Evaluating the predictability of MPE was performed using the CR, serum LDH (sLDH) and pADA; the CR exhibited the highest area under the receiver operating characteristic (ROC) curve for predicting MPE (**Figure 3**). However, the ROC curve of CR was still comparable with pADA (p=0.22).

Developing a predictive score using the multivariable reduced logistic model for the derivation of the scoring system incorporating clinical factors such as the duration of symptoms and history of fever, radiologic factors such as the amount of pleural effusion and the CR with weighted scores (using a cut-off level >10), we obtained a total score of 17.5 (**Table 5**). Our findings indicated that using this predictive score significantly enhanced the accuracy of diagnosing MPE, as demonstrated by an area under the curve (AUC) of 0.94 (**Figure 4).** The p-value via the Hosmer-Lemeshow goodness-of-fit test was 0.78. The calibration plot of the final model is shown in **Figure 5.** After comparing the predictive score with the clinical score and clinical score plus pleural fluid ADA, the CR demonstrated improved diagnostic performance when added to clinical criteria alone (AUC 0.87, p=0.01) but was comparable with clinical criteria plus ADA (AUC 0.93, p=0.69) **(Figure 6).**

Each potential predictor in the multivariable model was assigned a specific score based on its logistic regression coefficient. The scoring scheme resulted in a total score ranging from 0 to 17.5. They were further divided in three risk subcategories to make the scores more clinically applicable. This categorization was determined by examining the calibration plot, showing the relationship between the probability of having MPE and the distribution of scores. The low risk group had scores ranging from 0 to 5, the moderate risk group had scores ranging from 6 to 14.5 and the high risk group had scores ranging from 14.5 to 17.5. For each risk group, the positive predictive values were calculated. The low risk group had a positive predictive value of 0, the moderate risk group had a positive predictive value of 48.21 (95%CI 35-62), and the high risk group had a positive predictive value of 96.15 (95%CI 80-99) **(Table 6)**.

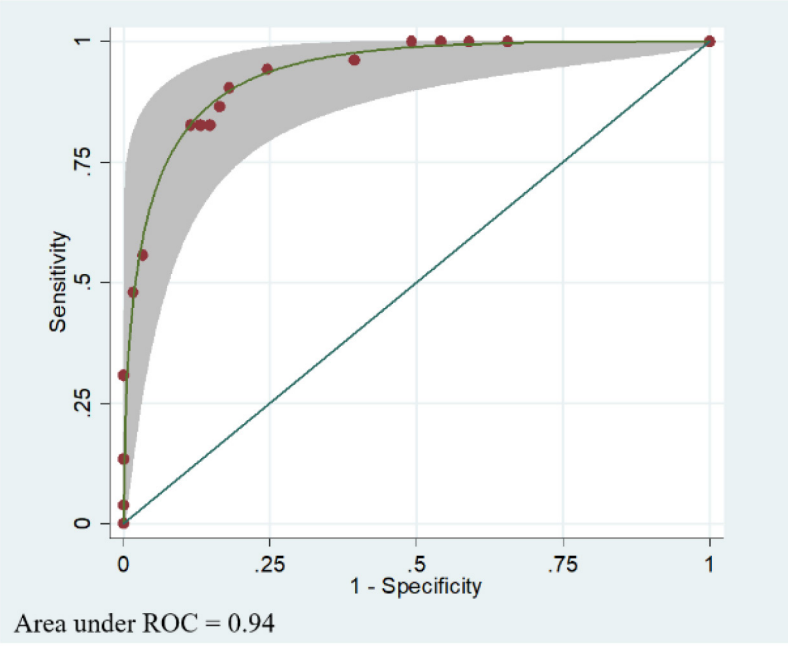

Figure 4. ROC of predicted score to diagnose malignant pleural effusion

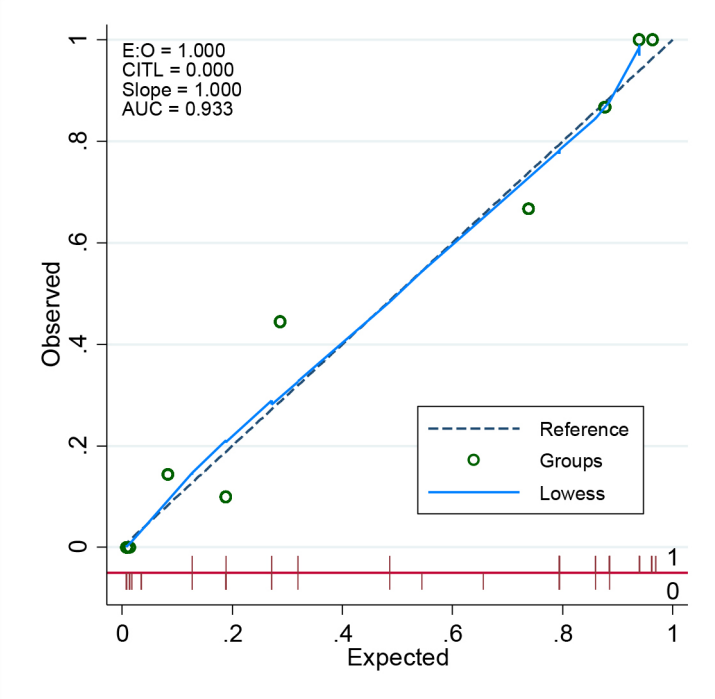

Figure 5. Calibration plot of prediction model performance

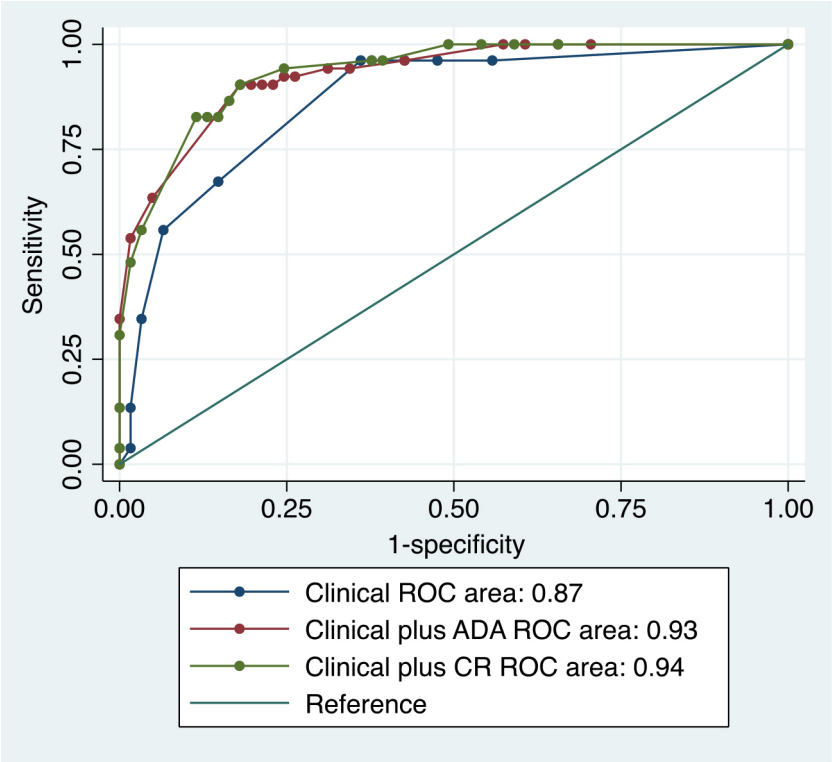

Figure 6. ROC curve compares clinical, clinical with pleural fluid ADA <40 U/L, and predicted model for diagnosis of malignant pleural effusion

Table 5. Risk score deviation using multivariable logistic regression coefficients

Potential predictors	Odds ratio	95% confidence interval	*p*-value	Coefficients	Score
Duration of symptom (days)					
0 – 29 days	1	Reference	-	-	0
30 – 60 days	1.58	0.33 – 7.49	0.56	0.46	1
> 60 days	2.00	0.44 – 8.96	0.37	0.69	1.5
Fever					
Yes	1	Reference	-	-	0
No	29.00	5.31 – 158.57	< 0.001	3.37	7
Chest radiography					
Non-massive PF	1	Reference	-	-	0
Massive PF	4.11	0.89 – 19.02	0.07	1.41	3
Cancer ratio > 10	15.5	4.57 – 52.53	< 0.001	2.74	6
Total score					17.5

Table 6. Distribution of nonMPE vs. MPE across different levels of risk categories (low, moderate, and high risk)

Risk categories	Score	Non-MPE	MPE	PPV	95% confidence interval	*p*-value
Low	0 - 5	31 (100%)	0	0	0 – 11	< 0.001
Moderate	6 – 14.5	29 (51.8%)	27 (48.2%)	48.21	35 – 62	< 0.001
High	> 14.5	1 (3.9%)	25 (96.1%)	96.15	80 – 99	< 0.001

MPE malignant pleural effusion, *PPV* positive predictive value

Discussion

This study constitutes the first to investigate the CR diagnostic accuracy in predicting MPE among Thai patients. The findings demonstrated that the CR displayed good accuracy, as indicated by an AUC value of 0.83, consistent with one related study.[11] Importantly, a CR >10 was identified as the optimal threshold, resulting in a sensitivity of 87.7% and specificity of 72.3%. These results closely resembled those of related studies.[3, 9, 16, 17] The cut-off value for CR was also similar to that in one study conducted in China.[17] However, our values were lower when comparing the sensitivity and specificity of our study to those reported in a related meta-analysis.[13, 18] This difference may be attributed to the specific focus of our study on patients with an exudative lymphocytic profile, while related studies encompassed patients with an exudative profile in general.

In this study, the most common causes of exudative lymphocytic pleural effusion were MPE and TPE, accounting for most cases in the nonMPE group. The prevalence rates for MPE and TPE were 46.7 and 40.2%, respectively. Within the MPE group, a longer duration

of symptoms, a personal history of cancer and an absence of fever were more frequently observed. Furthermore, massive pleural effusion on radiographic findings significantly favored the diagnosis of MPE. These findings are consistent with a related study[3] comparing TPE and MPE. Regarding plNo, a significant difference was observed between MPE and non MPE groups regarding pleural fluid appearance, with a trend toward a higher proportion of serosanguinous fluid in the MPE group (38.2% vs. 23.1%).

This significantly higher CR in the MPE group may be partially attributed to the significantly lower levels of pADA than in the non-MPE group. However, we cannot conclude that a pADA level < 40 indicates the presence of MPE is essential, as currently, a lack of clear studies establishing the accuracy and optimal cut-off level of pADA in MPE diagnosis. Furthermore, the cut-off level of pADA used for diagnosing TPE in the Thai population may be lower than the current standard of 40.[3, 16] The advantage of the CR is that it may assist in diagnosing MPE, especially when pADA levels are low. In routine clinical practice, patients presenting lymphocyte-predominated exudative pleural effusion and diminished pADA levels are frequently excluded from diagnosing TPE. However, those individuals exhibiting elevated CR levels may carry a heightened likelihood of experiencing MPE, warranting a prompt and thorough investigation to establish a definitive diagnosis. Based on ROC curve analysis, the CR still exhibited better diagnostic accuracy for MPE than pADA. However, addressing these questions would require a large scale study with an adequate sample size and additional subgroup analysis. Finally, the predictive score developed in this study, incorporating clinical, radiologic and CR parameters, could enhance the accuracy of MPE diagnosis (AUC = 0.94), aligning with findings from related studies.[19, 20]

This study's strength was its prospective data collection, helping to mitigate the occurrence of missing data. Moreover, the study focused on patients with an exudative lymphocytic profile in their pleural fluid. It reflected a practical approach in real-life clinical settings before considering pADA, cytology or histopathology tests to distinguish among MPE, TPE or other nonMPE conditions. Additionally, all patients in this study underwent cytology or histopathology tests, serving as standard reference tests for discriminating between MPE and nonMPE cases. However, acknowledging certain limitations is essentially required. These included the relatively small sample size and the study's confinement to a single center, restricting the generalizability of the findings on the utility of CR in diagnosing MPE among Thai patients nationwide. Furthermore, external validation of the identified cut-off value of CR >10 was not performed in this study. Consequently, further investigations are warranted to validate the obtained results.

Conclusion

The CR, a predictive tool for diagnosing MPE, has shown good accuracy among Thai patients. The CR, calculated by dividing sLDH by pADA, is already included in the diagnostic evaluation for differential diagnosis and is easily accessible in all healthcare settings, allowing for early detection of the disease during the initial workup. Furthermore, integrating the Clinical-Radiological-CR model can potentially improve the accuracy of MPE diagnosis. However, external validation studies are still needed to confirm these parameters' reliability. Ultimately, the definitive diagnosis of MPE relies on cytology and/or histopathology examinations to determine the specific cancer subtype, which then informs subsequent treatment planning.

Conflicts of interest

We declare we have no conflicts of interest related to the research study. None of the authors had personal or professional relationships that could have influenced the study's outcome or introduced bias in interpreting the results.

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