

# Utilizing the lymphocyte-monocyte ratio in predicting the recurrence of spontaneous pneumothorax

## Utilización de la proporción linfocitos-monocitos para predecir la recurrencia del neumotórax espontáneo

Murat Saricam<sup>1</sup>, Oya Guven<sup>2\*</sup>, and Berker Ozkan<sup>3</sup>

<sup>1</sup>Department of Thoracic Surgery, Faculty of Medicine, Kırklareli University, Kırklareli; <sup>2</sup>Department of Emergency Medicine, Faculty of Medicine, Kırklareli University, Kırklareli; <sup>3</sup>Department of Thoracic Surgery, Faculty of Medicine, Istanbul University, Istanbul. Turkey

### Abstract

**Objective:** Lymphocyte-to-monocyte ratio (LMR) has been introduced as a predictor and a prognostic factor for multiple diseases. This study aimed to determine the efficiency of LMR in predicting the recurrence of spontaneous pneumothorax. **Materials and methods:** A total of 374 patients who had received chest tubes at the first episode of primary spontaneous pneumothorax were examined in terms of age, gender, side of the pneumothorax, status of recurrence, LMRs at the time of admittance and recurrence, and the interval until the recurrence. **Results:** Recurrence was diagnosed in 106 (28.3%) patients, whereas the mean time until the recurrence was  $15.32 \pm 5.57$  months. Significantly, the recurrence rate was higher, while the time until the relapse was shorter for patients with elevated levels of LMR. Moreover, LMR counting over 1.25 demonstrated a 70.8% sensitivity and a 94.4% specificity in predicting a potential recurrence. **Conclusions:** Calculation of LMR at the first episode of spontaneous pneumothorax contributes to predict a potential recurrence when combined with traditional risk factors.

**Keywords:** Spontaneous pneumothorax. Recurrence. Lymphocyte-to-monocyte ratio. Prediction. Surgery.

### Resumen

**Objetivos:** La proporción de linfocitos a monocitos (PLM) se ha introducido como un predictor y un factor pronóstico para múltiples enfermedades. Este estudio tuvo como objetivo determinar la eficiencia de LMR en la predicción de la recurrencia del neumotórax espontáneo. **Materiales y métodos:** Un total de 374 pacientes que habían recibido tubos de tórax en el primer episodio de neumotórax espontáneo primario fueron examinados en términos de edad, género, lado del neumotórax, estado de recurrencia, PLM al momento del ingreso y recurrencia, y el intervalo hasta la recurrencia. **Resultados:** Se diagnosticó recidiva en 106 (28.3%) pacientes, siendo el tiempo medio hasta la recidiva de  $15.32 \pm 5.57$  meses. Significativamente, la tasa de recurrencia fue mayor, mientras que el tiempo hasta la recaída fue más corto para los pacientes con niveles elevados de PLM. Además, el recuento de PLM superior a 1.25 demostró una sensibilidad del 70.8 % y una especificidad del 94.4 % para predecir una posible recurrencia. **Conclusión:** Calcular la PLM en el primer episodio de neumotórax espontáneo predice una posible recurrencia cuando se combina con los factores de riesgo tradicionales.

**Palabras clave:** Neumotórax espontáneo. Reaparición. Proporción de linfocitos a monocitos. Predicción. Cirugía.

### \*Correspondence:

Oya Guven

E-mail: ersinoya@yahoo.com

Date of reception: 22-10-2022

Date of acceptance: 20-02-2023

DOI: 10.24875/CIRU.22000523

Cir Cir. 2023;91(6):725-729

Contents available at PubMed

www.cirugiaycirujanos.com

0009-7411/© 2023 Academia Mexicana de Cirugía. Published by Permanyer. This is an open access article under the terms of the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

Primary spontaneous pneumothorax (PSP) is the accumulation of air in the pleural space without any underlying traumatic and iatrogenic etiology or an evident pulmonary disease. Tall and thin body habitus, male gender, smoking, and being aged between 19 and 25 years are frequently encountered clinical features whereas subpleural blebs and bullae appear to play a significant role in the pathogenesis of PSP at a rate as high as 80%<sup>1,2</sup>.

The recurrence rate of PSP has been reported to be ranging over 30% after the first episode<sup>3</sup>. Although there have been conclusive studies that indicate the risks of recurrence, debates mostly consist of similar variables and surgical outcomes while the deficiency of presenting novel predictive factors still exists<sup>1-4</sup>.

The lymphocyte-to-monocyte ratio (LMR) actually compels attention as a diagnostic tool for inflammatory events and a predictor of prognosis in malignancies for the concomitant advantages of easy accessibility and economical benefits.

Regarding that the pathological manifestations of PSP mostly develop in response to the inflammatory reactions produced by the parenchymal injury, this study aimed to investigate the efficacy of LMR in predicting the recurrence of PSP for the first time in the literature.

## Material and methods

This study was approved by the Kırklareli Medical School Scientific Research Ethic Committee (P202200019-01/8.8.22). A retrospective study was conducted to include a total of 374 patients among 442 cases who had been diagnosed with PSP at the University Hospital between 2000 and 2021. Treatment with tube thoracostomy at the first episode and recurrent pneumothorax on the same side of the initial event were the principal inclusion criteria. Patients who had presented a secondary spontaneous pneumothorax, a history of chest surgery and any clinical or radiological suspicion of a local or a systemic infection, were excluded from the study. Regarding the well-accepted impact of smoking on the occurrence and also recurrence of PSP, the current and past history of smoking were accepted as exclusion criteria to provide a valid analysis of LMR as a potential risk factor. Follow-up period for the whole group of patients was 5 years.

In the first episode, all patients received 20 or 24 French chest tubes under local anesthesia. LMRs were calculated through whole blood counts that were obtained before interventions. The patients were invited to follow-up examinations during the 1<sup>st</sup> and 3<sup>rd</sup> weeks after being discharged or any time when they developed complaints similar to the initial admittance. The presence of recurrent pneumothorax was confirmed by chest X-ray or computed tomography. The patients with recurrence received chest tubes or underwent thoracotomy or thoracoscopy where partial parietal pleurectomy in addition to bullectomy or wedge resection was applied.

Whole group of patients was examined in terms of age, gender, side of the pneumothorax, LMR, status of recurrence, and the time until the recurrence. LMR was noted as a numerical value while the time of recurrence was stated as months.

The Statistical Package for the Social Sciences (SPSS) (IBM SPSS for Windows, Ver.24) statistical package program was used for calculations. The descriptive statistics were stated as mean, standard deviation, minimum, and maximum for continuous variables and as number and percentage for categorical variables. The calculations were checked for normal distribution by Kolmogorov–Smirnov ( $n > 50$ ) test and parametric tests were applied. One-way analysis of variance (ANOVA) was performed to compare the mean values of the patient groups. Pearson correlation coefficients were used to reveal the relations between measurements. Sensitivity, specificity, and cut-off values of LMR were assessed by ROC analysis. Chi-square test was used to identify the relation between categorical variables.  $p < 0.05$  were considered as statistically significant.

## Results

The mean age of the patients including 296 (79.1%) males and 78 (20.9%) females was  $22.45 \pm 2.5$  years. Pneumothorax was right sided in 177 (47.3%) and 197 (52.7%) cases. Mean LMR was calculated as  $1.21 \pm 0.31$  at the first episode and  $1.43 \pm 0.58$  at the time of relapse. Recurrent pneumothorax was diagnosed in 106 (28.3%) patients whereas the mean time between the first episode and the recurrence was  $15.32 \pm 5.57$  months. Related data were summarized in table 1.

Statistical studies were unable to determine a significant difference in terms of gender and side of pneumothorax regarding the status of recurrence

**Table 1. Demographic and clinical features of the patients**

Parameters	Values
Age, mean $\pm$ SD (min-max), years	22.45 $\pm$ 2.51 (17-36)
LMR at first episode, mean $\pm$ SD (min-max)	1.21 $\pm$ 0.31 (0.7-2.5)
LMR at recurrence, mean $\pm$ SD (min-max)	1.43 $\pm$ 0.58 (0.9-2.7)
Time until recurrence, mean $\pm$ SD (min-max), months	15.32 $\pm$ 5.57 (6-28)
Gender, n (%)	
Male	296 (79.1)
Female	78 (20.9)
Side of pneumothorax, n (%)	
Right	177 (47.3)
Left	197 (52.7)
Recurrence, n (%)	
Present	106 (28.3)
Absent	268 (71.7)

SD: standard deviation; Min: minimum; Max: maximum; LMR: lymphocyte-to-monocyte ratio.

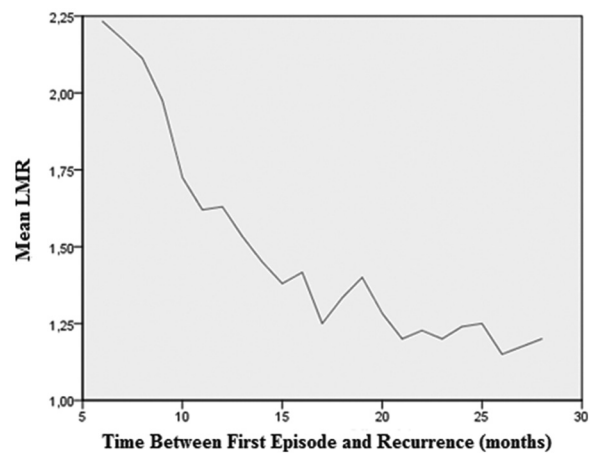
( $p > 0.05$ ). Furthermore, gender or side of the pneumothorax did not constitute a difference in the LMR counts ( $p = 0.075$  and  $0.727$ , respectively). However, mean LMR was  $1.53 \pm 0.35$  for the patients who had developed recurrence and  $1.08 \pm 0.15$  for the rest of the cases, showing that mean LMR was significantly elevated in the patients who would encounter a relapse ( $p < 0.05$ ) (Table 2). With regard to the recurrence-developing group of patients, mean time that had passed until the recurrence was shorter for the cases who had higher counts of LMR considering that statistical analysis indicated a negative if correlation coefficient between these two variables ( $p = 0$ ,  $r = -0.81$ ) (Fig. 1).

LMR demonstrated a 70.8% sensitivity and a 94.4% specificity in predicting a potential recurrence for a cut-off value of 1.25 (area under the curve: 0.931,  $p = 0.001$ ) (Fig. 2).

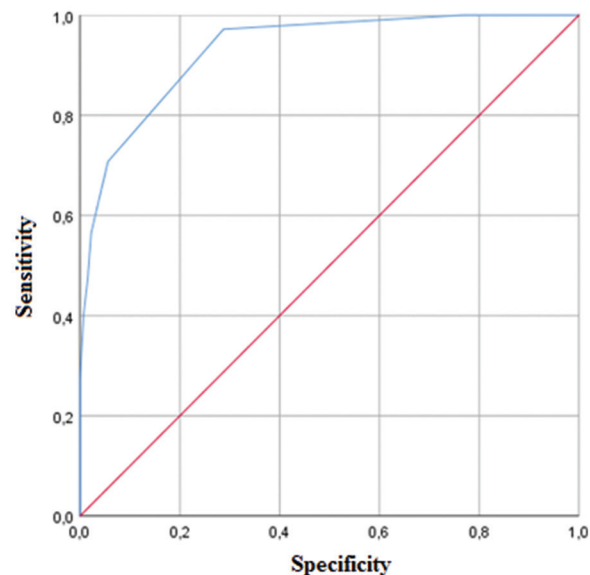
Among a total of 442 cases with the first episode PSP, 68 patients were only observed clinically and radiologically and discharged without any additional treatment or intervention. Thoracoscopy was performed for 78 (73.6%) and thoracotomy for 26 (24.5%) cases who had developed recurrence whereas 2 (1.9%) patients who had disapproved surgery were treated with tube thoracostomy.

## Discussion

The findings of this study show that LMR exceeding the threshold value of 1.25 at the first episode of pneumothorax may contribute to predict a potential recurrence.



**Figure 1.** Relation of lymphocyte-to-monocyte ratio and the time between first episode and recurrence of pneumothorax.



**Figure 2.** Receiver operating characteristic analysis of lymphocyte-to-monocyte ratio as the predictor of recurrent pneumothorax.

PSP more frequently occurs in young males with tall and thin habitus whereas bullous parenchymal lesions and smoking are considered as definite risk factors<sup>2,4-8</sup>. Although the optimal management strategy of first-episode PSP is still controversial, techniques of observing small PSPs without intervention and placing small-bore chest tubes for larger PSPs only if the attempts to success by simple aspiration fail have been approved<sup>9</sup>. A recent study by Brown et al. reported that conservative management of moderate-to-large PSPs provided resolution of pneumothorax within 8 weeks and resulted in lower rates of

**Table 2. Factors associated with the recurrence**

Parameters	Recurrence (n = 106)	Non-recurrence (n = 268)	p-value
Age, mean $\pm$ SD	21.3 $\pm$ 2.42	22.09 $\pm$ 2.26	0.263*
Gender, n (%)			0.081†
Male	83 (28)	213 (72)	
Female	23 (29.5)	55 (70.5)	
LMR at first episode, mean $\pm$ SD	1.53 $\pm$ 0.35	1.08 $\pm$ 0.15	< 0.001*
Side of pneumothorax, n (%)			0.848†
Right	51 (28.8)	126 (71.2)	
Left	55 (27.9)	142 (72.1)	

\*ANOVA: analysis of variance.

†Chi-square.

SD: standard deviation.

recurrence when compared to interventional treatment<sup>10</sup>. Recurrence of PSP ranging from 16% to 52% and progressively increasing incidence of subsequent recurrences constitutes a significant challenge for both patients and physicians<sup>2,5</sup>.

Histopathologic findings in the surgical specimens from the patients with pneumothorax mostly conform with chronic inflammation that demonstrates eosinophilic pneumonia-like changes, pleuritis, and hemosiderin deposition in both pleura and lungs<sup>11</sup>. This evidence has arisen the efforts to consider the inflammatory events associated with pneumothorax to predict a potential relapse. De Smedt et al. reported that peripheral blood analysis in patients with first-episode pneumothorax indicated an increase in white blood cell, neutrophil, monocyte, and eosinophil counts and also a non-significant decrease in lymphocyte counts when compared to the control group of healthy individuals<sup>12</sup>. A study by Selvi et al. also announced that elevated neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios were associated with recurrence in the patients with PSP<sup>13</sup>.

Utilization of LMR was announced to be efficient in the diagnosis and the determination of prognosis in both inflammatory diseases and malignancies. LMR was reported as an independent prognostic factor in the patients following antituberculous treatment and also a valuable independent indicator to identify the extent of involvement for active ulcerative colitis<sup>14-16</sup>. Moreover, recent studies reported that LMR was instructive in obtaining additional prognostic information in malignancies including colon cancer, hepatocellular carcinoma, and follicular lymphoma<sup>17-19</sup>. The current literature does not include any studies that address LMR as a risk or a predictive factor for the recurrence of pneumothorax. In this series, the presence of elevated LMR noticed at the first episode was

related with a relapse. Moreover, the time interval until the recurrence demonstrated a significant negative correlation with higher counts of LMR. All these findings imply that LMR that elevates in relation to the severity of inflammatory processes lends assistance to predict the recurrence of pneumothorax as well as the prognosis of several malignancies. However, multicentered prospective studies with larger study populations and multivariate analysis are needed.

The principal limitations were the retrospective design over a long period of time during which the management for PSP has evolved and the strict norms for the exclusion of cases with secondary spontaneous pneumothorax, smoking, and a past history of chest surgery.

## Conclusion

The value of LMR above the threshold value of 1.25 that is measured at the first episode of PSP may provide supporting evidence to predict a potential recurrence when combined with the traditional risk factors.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Conflicts of interest

The authors have no conflicts of interest to declare.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

## References

1. Tulay CM, Ozsoy IE. Spontaneous pneumothorax recurrence and surgery. *Indian J Surg.* 2015;77:463-65.
2. Noh D, Lee S, Haam SJ, Paik HC, Lee DY. Recurrence of primary spontaneous pneumothorax in young adults and children. *Interact CardioVasc Thorac Surg.* 2015;21:195-9.
3. Primavesi F, Jaeger T, Meissnitzer T, Buchner S, Reich-Weinberger S, Oefner D, et al. First episode of spontaneous pneumothorax: CT-based scoring to select patients for early surgery. *World J Surg.* 2016;40:1112-20.
4. Kepka S, Dalphin JC, Parmentier AL, Pretalli JB, Gantelet M, Bernard N, et al. Primary spontaneous pneumothorax admitted in emergency unit: does first episode differ from recurrence? A cross-sectional study. *Can Resp J.* 2017;2017:2729548.
5. Guo Y, Xie C, Rodriguez RM, Light RW. Factors related to recurrence of spontaneous pneumothorax. *Respirology.* 2005;10:378-84.
6. Olesen WH, Lindahl-Jacobsen R, Katballe N, Sindby JE, Titlestad IL, Andersen PE, et al. Recurrent primary spontaneous pneumothorax is common following chest tube and conservative treatment. *World J Surg.* 2016;40:2163-70.
7. Bobbio A, Dechartres A, Bouam S, Damotte D, Rabbat A, Regnard JF, et al. Epidemiology of spontaneous pneumothorax: gender-related differences. *Thorax.* 2015;70:653-8.
8. Sousa C, Neves J, Sa N, Goncalves F, Oliveira J, Reis E. Spontaneous pneumothorax: a 5-year experience. *J Clin Med Res.* 2011;3:111-7.
9. Grundy S, Bentley A, Tschopp J. Primary spontaneous pneumothorax: a diffuse disease of the pleura. *Respiration.* 2012;83:185-9.
10. Brown SG, Ball EL, Perrin K, Asha SE, Braithwaite I, Egerton-Warburton D, et al. Conservative versus interventional treatment for spontaneous pneumothorax. *N Engl J Med.* 2020;382:405-15.
11. Schneider F, Murali R, Veraldi KL, Tazelaar HD, Leslie KO. Approach to lung biopsies from patients with pneumothorax. *Arch Pathol Lab Med.* 2014;138:257-65.
12. De Smedt A, Vanderlinden E, Demanet C, De Waele M, Goossens A, Noppen M. Characterisation of pleural inflammation occurring after primary spontaneous pneumothorax. *Eur Respir J.* 2004;23:896-900.
13. Selvi F, Bedel C, Ozkaya M. Can we estimate the recurrence of primary spontaneous pneumothorax with simple blood tests? *East J Med.* 2020;25:84-8.
14. Iqbal S, Ahmed U, Zaidi SB. Monocyte lymphocyte ratio as a possible prognostic marker in antituberculous therapy. *J Rawalpindi Med Coll.* 2014;18:178-81.
15. Sibley L, Gooch K, Wareham A, Gray S, Chancellor A, Dowall S, et al. Differences in monocyte: lymphocyte ratio and tuberculosis disease progression in genetically distinct populations of macaques. *Sci Rep.* 2019;9:3340.
16. Okba AM, Amin MM, Abdelmoaty AS, Ebada HE, Kamel AH, Allam AS, et al. Neutrophil/lymphocyte ratio and lymphocyte/monocyte ratio in ulcerative colitis as non-invasive biomarkers of disease activity and severity. *Auto Immun Highlights.* 2019;10:4.
17. Stotz M, Pichler M, Absenger G, Szkandera J, Arminger F, Schabert-Moser R, et al. The preoperative lymphocyte to monocyte ratio predicts clinical outcome in patients with stage III colon cancer. *Br J Cancer.* 2014;110:435-40.
18. Yang YT, Jiang JH, Yang HJ, Wu ZJ, Xiao ZM, Xiang BD. The lymphocyte-to-monocyte ratio is a superior predictor of overall survival compared to established biomarkers in HCC patients undergoing liver resection. *Sci Rep.* 2018;8:2535.
19. Lee SF, Luque-Fernandez MA. Prognostic value of lymphocyte-to-monocyte ratio and neutrophil-to-lymphocyte ratio in follicular lymphoma: a retrospective cohort study. *BMJ Open.* 2017;7:e017904.