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Prognostic Indicators in Pleural Effusion: A Retrospective Study

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ABSTRACT

Objective: This study aimed to investigate the association between clinical, biochemical, and hematological indicators and survival outcomes in patients diagnosed with pleural effusion.

Materials and Methods: A retrospective, single-center observational study was conducted, including 365 patients with pleural effusion between January 2020 and December 2024. Clinical data including age, gender, etiology, Eastern Cooperative Oncology Group (ECOG) performance status, Karnofsky score, and laboratory parameters such as albumin, C-reactive protein (CRP), the neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) were extracted from medical records. Survival trends were visualized descriptively using Empirical Cumulative Distribution Function plots.

Results: Among 365 patients, the most frequent etiologies were congestive heart failure and breast cancer. Patients with higher serum albumin (>3.0 g/dL), higher ECOG scores, and lower Karnofsky scores demonstrated shorter survival durations. Elevated CRP, NLR, and PLR levels were also associated with shorter survival. In descriptive analyses, higher NLR and PLR categories were associated with longer survival. No formal time-to-event tests were performed. No formal time-to-event statistical tests were performed.

Conclusion: Several routinely available clinical and laboratory parameters, particularly serum albumin, performance status scores, and inflammatory markers, may be useful for estimating prognosis in pleural effusion. These findings underscore the importance of integrating simple clinical data in the prognostic assessment of patients and warrant further validation in prospective studies using formal survival analysis.

Keywords: Neutrophil–lymphocyte ratio, platelet–lymphocyte ratio, Pleural effusion, Prognosis

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INTRODUCTION

Pleural effusion is a frequently encountered clinical condition with a broad spectrum of underlying causes, including congestive heart failure (CHF), malignancy, infection, pulmonary embolism, systemic inflammatory diseases, and certain drug therapies.[1,2] Among these, malignant and infectious effusions are of particular clinical relevance due to their association with poor prognosis and the frequent requirement for invasive interventions.[1] Malignant pleural effusion (MPE), in particular, is a common complication of advanced-stage cancers such as lung, breast, and mesothelioma and is typically associated with substantial morbidity and limited survival. The pathophysiology of MPE involves either direct tumor infiltration of the pleura or impaired lymphatic drainage, resulting in the accumulation of fluid within the pleural space.[3]

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Recent studies have highlighted the potential prognostic value of various biochemical and inflammatory markers in patients with pleural effusion. Elevated pleural fluid C-reactive protein (CRP) levels have been shown to differentiate parapneumonic effusions from other etiologies with high sensitivity and specificity, supporting its role as a diagnostic and prognostic marker.[4] Similarly, the neutrophil-to-lymphocyte ratio (NLR) in pleural fluid has emerged as a simple yet informative parameter, particularly in distinguishing tuberculosis-related effusions from malignant or parapneumonic causes. Moreover, in pediatric patients with prolonged postoperative pleural effusion, an increased NLR change ratio was found to be significantly associated with poor treatment response and prolonged drainage, indicating its potential utility as a prognostic biomarker for treatment efficacy.[5,6]

This study aims to evaluate the prognostic significance of selected biochemical and hematological parameters – including total protein, hemoglobin, serum albumin, CRP, NLR, and platelet-to-lymphocyte ratio (PLR) – on survival in patients with pleural effusion. In this cohort, inflammatory ratios were analyzed as ordinal categories, and exploratory plots suggested that higher categories of NLR and PLR tended to show longer survival, although these findings require confirmation with formal survival analyses.

MATERIALS AND METHODS

This study was approved by the Local Ethics Committee, December 03, 2024, 4646. Our research was conducted in accordance with the ethical standards of the Declaration of Helsinki. This retrospective, single-center observational study included 365 patients diagnosed with pleural effusion between January 2020 and December 2024. Patients were evaluated and followed at a tertiary care center. Demographic, clinical, and laboratory data were collected from medical records, including age, sex, laterality of effusion, underlying etiology, need for drainage, total protein, hemoglobin, serum albumin, CRP, NLR, PLR, Eastern Cooperative Oncology Group (ECOG) performance status, Karnofsky performance score, treatment modality, and survival outcome.

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics. Survival trends were illustrated using empirical cumulative distribution function (ECDF) plots stratified by clinical and biochemical parameters. These visualizations were descriptive only and not based on Kaplan–Meier estimates or formal statistical tests. No survival comparison tests such as the log-rank test or Cox regression analysis were conducted.

RESULTS

A total of 365 patients diagnosed with pleural effusion were included in the study. The mean age of the patients was 64.9±16.9 years, and the median age was 67 years (range: 13–99). Of the patients, 59.8% were male and 40.2% were female. The most frequently observed etiologies were CHF (n=50, 13.9%) and lung cancer (n=32, 6.4%) (Table 1). Survival was longer in patients with serum albumin levels below 3.0 g/dL compared to those with normal albumin levels (5.0 months vs. 3.0 months). Performance status was also associated with survival. According to ECOG score, the median survival was 5.0 months in patients with ECOG 0–1, whereas it decreased to 1.0 months in those with ECOG 3–4. Similarly, survival decreased as Karnofsky scores declined; while median survival was 5.0 months in patients with a Karnofsky score of 50, it decreased to 1.0–2.0 months in those with scores of 30 or below. Among hematological parameters, patients with higher neutrophil-to-lymphocyte ratio (N/L) had longer survival compared to those with lower N/L (5.0 months vs. 3.0 months). Similarly, survival was also better in patients with higher PLR (5.0 months vs. 4.0 months). Figures 1-7 present ECDF-based survival curves according to various clinical and biochemical indicators.

DISCUSSION

In this retrospective study of 365 patients with pleural effusion, several clinical and biochemical indicators were found to be associated with survival duration. Patients with lower albumin levels (<3.0 g/dL), higher ECOG or lower Karnofsky performance scores, and elevated inflammatory markers such as CRP, NLR, and PLR exhibited differences in survival trends. Although formal survival analysis methods such as Kaplan–Meier or Cox regression were not used, descriptive ECDF plots helped illustrate survival distributions across these subgroups.

According to Light RW's Textbook of Pleural Diseases, serum albumin is frequently considered in the context of pleural fluid evaluation and patient nutritional and inflammatory status.

Table 1. Etiological factors causing pleural effusion

Etiological factor	Number of cases (%)
Congestive heart failure	50 (13.9)
Lung cancer	32 (6.4)
Parapneumonic effusion	28 (7.8)
Breast cancer	26 (7.2)
Traumatic	21 (5.8)
Pleuritis	15 (4.2)
Mesothelioma	8 (2.2)

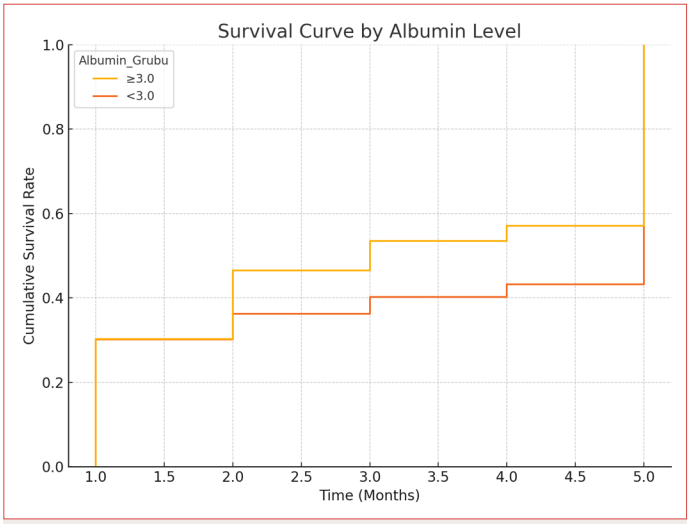

Figure 1. Empirical cumulative distribution function-based survival curve by albumin level (<3.0 vs. ≥3.0 g/dL).

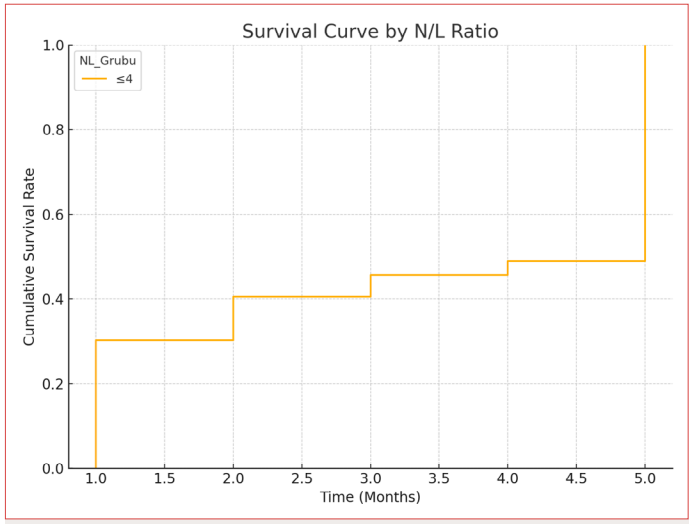

Figure 3. Empirical cumulative distribution function-based survival curve stratified by neutrophil-to-lymphocyte ratio (N/L low vs. high).

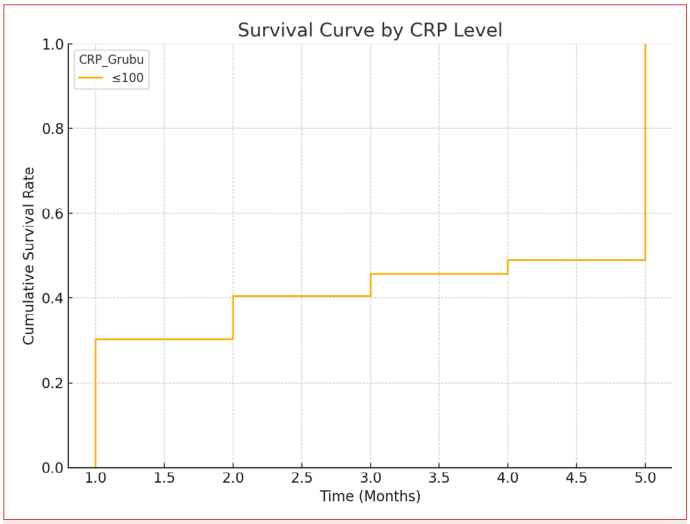

Figure 2. Empirical cumulative distribution function-based survival curve stratified by CRP level (≤100 vs. >100).

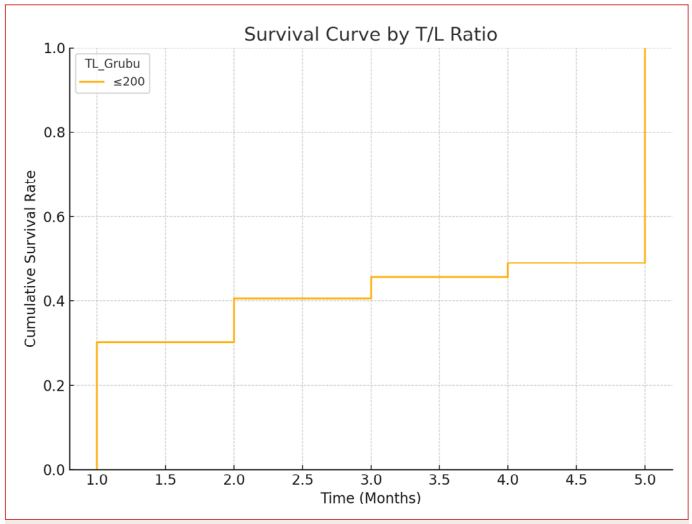

Figure 4. Empirical cumulative distribution function-based survival curve stratified by platelet-to-lymphocyte ratio (T/L low vs. high).

Although not an independent diagnostic marker for pleural effusion etiology, hypoalbuminemia is generally associated with poor functional reserve and increased morbidity, which may influence prognosis indirectly. The textbook also highlights that lower serum protein levels, particularly albumin, may correlate with worse outcomes in chronic or malignant effusions due to underlying systemic illness or cancer cachexia.[7]

The prognostic significance of serum albumin levels has been highlighted in numerous studies across cancer populations. Tang et al.[8] demonstrated, in a large NHANES-based cohort, that lower serum albumin levels were strongly associated with increased cancer-related mortality. Their multivariate Cox regression models revealed that patients with albumin levels ≤4.2 g/dL had significantly worse survival compared to those with higher levels, with hazard ratios exceeding 2.0 in some subgroups. Moreover, their analysis uncovered a consistent non-linear negative relationship between albumin concentration and mortality risk, indicating that even marginal declines in albumin may have prognostic value. These findings are aligned with the current study, where patients with lower albumin levels exhibited divergent survival trends. Although

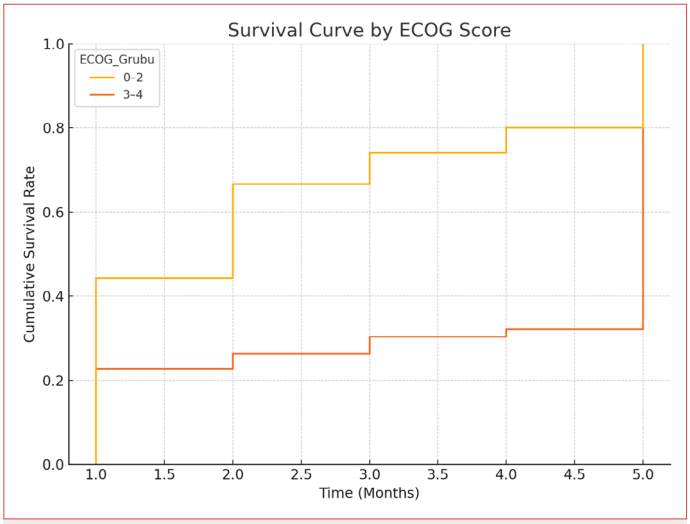

Figure 5. Empirical cumulative distribution function-based survival curve stratified by Eastern Cooperative Oncology Group performance score (0–2 vs. 3–4).

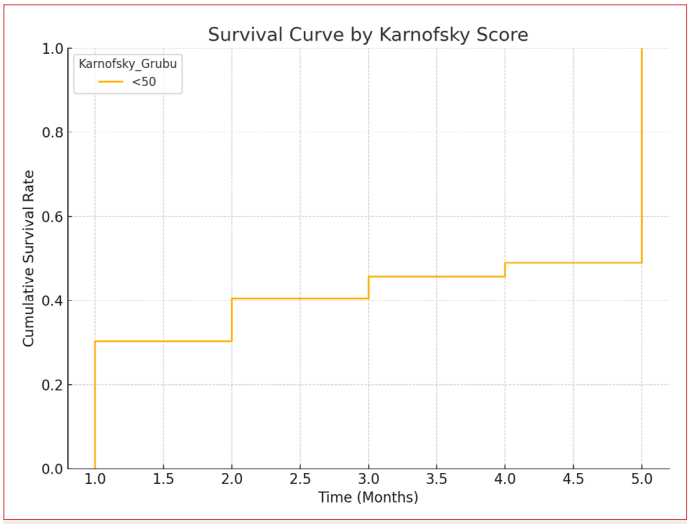

Figure 6. Empirical cumulative distribution function-based survival curve stratified by Karnofsky performance score (≥50 vs. <50).

formal survival modeling was not conducted here, our descriptive ECDF plots reinforce the hypothesis that hypoalbuminemia may be a marker of poorer prognosis in pleural effusion, particularly in malignant or inflammatory conditions.

Performance status has long been recognized as a crucial prognostic indicator in patients with MPE. In a study by Gayaf et al.,[9] ECOG performance status was found to be strongly associated with overall survival. Both ECOG and the LENT prognostic score showed comparable predictive power, with ECOG performing slightly better in long-term survival prediction.

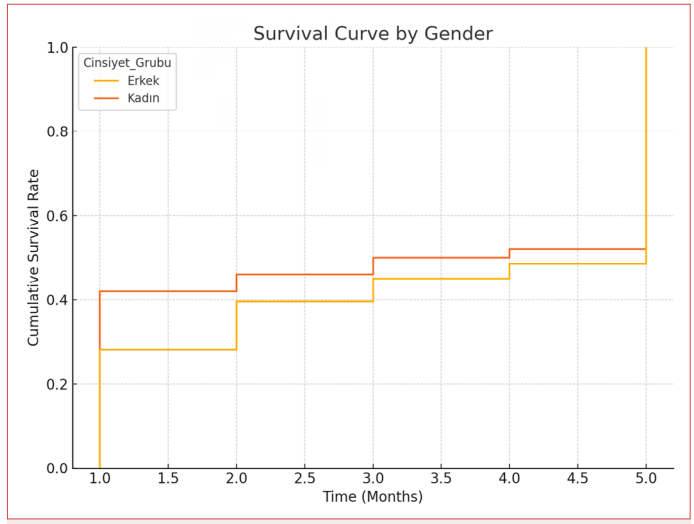

Figure 7. Empirical cumulative distribution function-based survival curve stratified by gender (male vs. female).

These findings align with our observations, where patients with higher ECOG scores had shorter survival. This reinforces the clinical utility of performance-based assessments in guiding prognosis and treatment decisions for MPE patients. In our corrected analysis, poorer performance status (higher ECOG scores) was associated with shorter survival, which is consistent with clinical expectations and prior literature.

Pleural fluid CRP has emerged as a useful biomarker for differentiating parapneumonic effusions from other causes of pleural effusion. In a large retrospective study by Izhakian et al.,[4] pleural CRP levels were significantly higher in parapneumonic effusions (mean 5.38±4.85 mg/dL) compared to effusions related to malignancy, heart failure, or lung transplantation. A CRP cut-off value of 1.38 mg/dL yielded 84.2% sensitivity and 71.5% specificity for identifying infectious etiologies, with a high negative predictive value of 96.7%. Moreover, CRP was selected as the strongest single predictor of parapneumonic effusion in multivariate analysis. These findings support the use of pleural CRP not only as a diagnostic tool but also as a potential marker for prognosis and therapeutic decision-making, especially in cases with suspected infection.

The NLR in pleural fluid has gained attention as an accessible and cost-effective inflammatory marker for differentiating exudative effusion etiologies. In a retrospective study by Akturk et al.,[5] NLR values were significantly lower in tuberculosis-related pleural effusion compared to malignant, para-pneumonic, and para-malignant effusions. While the median NLR was 2.2 in tuberculosis (TB) effusions, it ranged between 3.5 and 4.2 in other etiologies. This suggests that lower NLR values may support a diagnosis of TB pleurisy in the appropriate clinical context, whereas higher NLR values may be more indica-

tive of malignancy or bacterial infection. Although the role of NLR in prognostication remains limited, its diagnostic utility in guiding further investigations should not be underestimated.

Despite the strengths of our study–including a relatively large sample size and a broad spectrum of clinical and biochemical parameters–it has several limitations. First, the retrospective nature of the study limits the ability to control for confounding factors and to establish causal relationships. Second, survival analysis was based solely on descriptive ECDF plots without the use of time-to-event statistical methods such as Kaplan–Meier or Cox regression, which may limit the interpretability of survival differences across groups. Third, the lack of information on treatment specifics, disease stage, and comorbidities may have influenced survival outcomes.

CONCLUSION

Our findings suggest that commonly measured clinical and laboratory parameters – including serum albumin, performance status scores, CRP, NLR, and PLR – may provide prognostic insight in patients with pleural effusion. While these results require validation in prospective cohorts using formal survival analysis, they highlight the potential value of incorporating routine clinical data into early prognostic assessment and management planning in this patient population.

DECLARATIONS

Ethics Committee Approval: The study was approved by Şişli Hamidiye Etfal Education and Research Hospital Ethics Committee (No: 4646, Date: 03/12/2024).

Conflict of Interest: The authors declare that there is no conflict of interest.

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Authorship Contributions: Concept – UT, SK; Design – UT; Supervision – SK; Data collection &/or processing – UT; Analysis and/or interpretation – UT; Literature search – SK; Writing – UT; Critical review – SK.

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