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Dear Colleagues,

I am delighted to present you with the first issue of our journal in 2026. Our most important goal is to offer new information to the academic world and medical literature, to share new analyses, and to disseminate the most consistent studies together. This issue is now ready for publication with three original articles, a letter to the editor, and a case presentation of significant importance from an emergency medicine perspective. Our original articles address important topics and make valuable contributions to the literature.

Our first article highlights the importance of lactate biomarkers in determining the prognosis of infectious disease patients requiring intensive care, for emergency medicine specialists. Another article contains findings that could serve as important warnings for future generations regarding the COVID-19 pandemic, which has profoundly affected the entire world. Our final original article is a bibliometric analysis of prostate cancer, highlighting the latest trends in the literature on this subject. This issue also features a letter to the editor regarding the relationship between essential amino acids and suicidal attempts, a common occurrence in emergency medicine practice. Ultrasonography is now frequently used for diagnostic purposes in emergency departments. The case presentation we published in this issue is a trap case that can be seen on lung ultrasonography. The articles we present to you in this issue are addressed to all physicians.

First and foremost, the efforts of the researchers and authors in the creation of this work are immense. And I would also like to thank the reviewers who dedicated their valuable time to ensuring the quality of the articles. I would also like to thank the editorial board and the publishing team who were behind this entire work. In our next steps, we will work even harder for Emergency Medicine and continue to bring you the latest current topics.

Sincerely,

Assoc. Prof. Ahmet Burak ERDEM, MD
Editor in Chief

Volume: 4 Issue: 1 Year: 2026

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Trends and patterns in prostate cancer screening in primary care (2016-2025): a bibliometric study

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ABSTRACT

Aims: The aim of this study is to examine the scientific output, impact, and collaboration patterns of the literature on prostate cancer screening in primary care over the past decade using bibliometric methods.

Methods: The study was conducted on original English research articles published between 2016 and 2025 in journals indexed in the Science Citation Index Expanded within the Web of Science Core Collection database. Bibliometric analyses were carried out using Biblioshiny, the web-based interface of the Bibliometrix package running in the RStudio environment, and the VOSviewer software. Scientific output, citation performance, and keyword patterns were examined using Biblioshiny, while the network structures of co-authorship and co-citation relationships were visualized and evaluated with VOSviewer.

Results: A total of 266 original research articles were analyzed. These publications appeared in 139 journals and were produced by 2008 authors, with a mean of 8,87 authors per article and an international collaboration rate of 21,8%. Annual publication output showed a fluctuating pattern, reaching its peak in 2021. The average number of citations per article was 35,44. In the keyword analysis, “prostate cancer,” “prostate-specific antigen,” “primary care,” and “screening” were the most frequently used terms. Co-authorship analysis revealed clear clustering among authors, with the presence of core research groups. In the country-level co-authorship network, the United States of America emerged as the most dominant hub, followed by England and Australia as other major contributors. Co-citation analysis indicated that the literature is mainly structured around large-scale screening trials and clinical guidelines.

Conclusion: This bibliometric analysis highlights the production, impact, and collaboration dynamics of the literature on prostate cancer screening in primary care, making the intellectual structure of the field visible and offering a guiding framework for future research.

Keywords: Prostatic neoplasms, early detection of cancer, mass screening, primary health care, bibliometrics

INTRODUCTION

Prostate cancer is a common disease among men, and survival improves markedly with early detection. The most widely used method for early detection is the prostate-specific antigen (PSA) test. However, the balance between the benefits of PSA-based screening and the risks of overdiagnosis and overtreatment remains controversial.¹ Screening decisions are most commonly made in primary care, as asymptomatic men usually first enter the health system through family physicians. However, some patients may initially present to emergency departments with suspicion of prostate cancer, which makes coordinated functioning between different levels of care essential for timely diagnosis and referral.

The use of PSA in primary care is known to vary between countries and according to different guidelines. In many settings, screening is performed opportunistically rather than through organized programs, which may negatively affect rates of early-stage diagnosis.¹ In addition, deficiencies in

primary care physicians' knowledge and practices regarding prostate cancer screening have been reported.² Moreover, although risk-based and individualized approaches to screening are increasingly being recommended, the extent to which these models are reflected in primary care practice remains unclear. While some studies emphasize the benefits of screening, others highlight potential drawbacks such as overdiagnosis, patient anxiety, and increased burden on the healthcare system.³⁻⁵ This situation makes it difficult to draw a comprehensive picture of how prostate cancer screening is positioned in primary care. Therefore, there is a need for a bibliometric evaluation that can identify general trends, areas of concentration, and gaps in the scientific output on prostate cancer screening in primary care.

The aim of this study is to examine the literature on prostate cancer screening in primary care using bibliometric methods and to provide a more systematic framework.

Based on original research published over the last ten years, publication volume, citation impact, leading authors and countries, collaboration patterns, and main research themes were analyzed, thereby presenting an up-to-date overview of scientific output in the field of prostate cancer screening in primary care.

METHODS

Ethics

As this study is a bibliometric analysis based on data extracted from the Web of Science Core Collection, it did not involve human participants, patient data, or animal experiments; therefore, ethics committee approval was not required.

Literature Search and Data Retrieval

This bibliometric study was conducted using the Web of Science (WoS) platform, which includes publications from many disciplines and provides detailed citation data. The WoS Core Collection database was selected as the data source, and the analysis was limited to publications between 2016 and 2025. Data were obtained through comprehensive searches performed in the WoS system using the "topic" (TS) field. The search strategy was constructed as follows: TS= (("prostate cancer" OR "prostatic cancer" OR "prostate carcinoma") AND ("screening" OR "early detection" OR "PSA" OR "prostate-specific antigen") AND ("primary care" OR "family medicine" OR "general practice" OR "family physician*" OR "general practitioner*")). Data download was carried out on January 15, 2026.

The inclusion criteria were defined as publication in journals indexed by WoS and covered by the Science Citation Index Expanded (SCIE), being written in English, having the characteristics of an original research article, and being retrieved using the defined search strategy. Articles directly related to the topic were manually selected. Publication types other than original research, such as case reports, case series, reviews, systematic reviews, and meta-analyses, were excluded from the study.

Data Analysis Tools

Microsoft Excel 2016 was used for organizing the obtained data and for the preliminary preparation stages.⁶ For bibliometric analyses, Biblioshiny (version 4.1.3), the web-based interface of the Bibliometrix R package, was used; network and visual analyses were performed with the VOSviewer software (version 1.6.20).⁷⁻⁹

Data downloaded from WoS were transferred to the Biblioshiny environment, and before analysis, duplicate records and missing information were checked and necessary corrections were made. Using the Main Information module, basic bibliometric variables such as number of publications, number of journals, number of authors, collaboration structure, references, and citation indicators were planned to be calculated.

To examine publication output by year, the annual scientific production function in Biblioshiny was used. With this analysis, the number of studies published each year was determined and changes in publication volume over time were presented graphically.

The average article citation per year tool was used to evaluate the annual citation performance of the articles. At this stage,

the mean number of citations per article for each publication year was calculated, and changes in citation trends over time were examined comparatively.

To identify the prominent concepts in the literature, a word cloud analysis was performed using Biblioshiny. In this analysis, author keywords were taken as the basis, and terms above a certain frequency threshold were selected and visualized according to their frequency of use. In this way, it was aimed to present a general outline of the conceptual structure of the research field.

Network and relationship analyses were carried out using the VOSviewer program. In the study, co-authorship and co-citation analyses were performed. In all analyses, the full counting approach was adopted as the counting method, and the association strength method was used to balance the strength of the links. In the layout algorithm, the random start value was set to 1000 and the maximum number of iterations was set to 1000. These settings were chosen to ensure that the most appropriate layout could be found by starting from different initial positions. In network structures, the units were defined as nodes, and the relationships between units were defined as links. To indicate the overall density of connections in the network, the Total Link Strength (TLS) value was used.

In the co-authorship analysis, two separate networks were created for authors and countries. In the author network, each node represented an author, and the node size indicated the author's weight within the network. Nodes were shown in different colors according to their clusters, and only the names of prominent authors were labeled. The lines between nodes represented collaborations between authors, and shorter and thicker lines were arranged to indicate stronger collaborations. In this analysis, the minimum number of documents for authors was set to 3, and the minimum number of citations was set to 0. Weighting was based on TLS.

In the country-based co-authorship analysis, each node represented a country, and the node size reflected the country's relative weight within the network. Countries were colored according to their clusters, and only the names of prominent countries were displayed. The lines between countries indicated collaboration, and line length was arranged to be inversely proportional to the strength of the relationship. For countries, the minimum number of documents was set to 1 and the minimum number of citations was set to 0, and total link strength was used for weighting. Weighting was based on TLS.

To examine the intellectual structure of the field, a co-citation analysis was performed. In this analysis, cited sources were taken as the unit of analysis, and sources that had received at least five citations were included. The analysis was carried out using VOSviewer, and the strength of the relationships between co-cited sources was weighted according to their citation counts.

RESULTS

Using the defined search strategy, a total of 918 publications focusing on prostate cancer screening in primary care were identified in the Web of Science database. After applying

the predefined inclusion and exclusion criteria, 266 original research articles suitable for bibliometric analysis were included in the study (Figure 1).

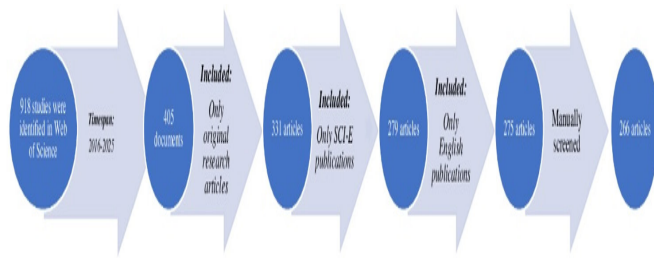


Figure 1. Flow diagram of the selection process

Figure 2 presents the main information data summarizing the basic bibliometric indicators of the publications included in the study. In the analysis covering the years 2016-2025, a total of 266 documents were obtained from 139 different sources. A total of 2008 authors contributed to these studies, and 5 of them produced single-authored publications. The international co-authorship rate was calculated as 21.8%, and the average number of authors per article was found to be 8.87. The annual growth rate of publications was 0.86%. The total number of references used in the analysis was 8226, and the average age of the documents was determined as 5.61 years. The average number of citations per article was 35.44. In addition, author keywords consisted of a total of 590 different terms.



Figure 2. Main information

Annual publication output by year is presented in Table 1. Overall, publication numbers showed a fluctuating pattern across the years, with a marked increase in 2021 and a gradual recovery trend in the following years (Figure 3).

Citation performance by publication year is summarized in Table 1 and illustrated in Figure 4.

When the annual average number of citations per article was examined by year, the highest value was observed in 2016, and studies published in that year received an average of 16.60 citations per article per year. This was followed by 2019, in which the annual average citation rate was 14.08. In 2017 and 2018, annual citation averages were notably low, calculated as 1.34 and 2.30, respectively. In 2020 and 2021, annual average citation numbers were at similar levels (2.74 and 2.54, respectively), while in 2022 this value decreased to

Table 1. Citation performance of articles by year, showing mean total citations per article (MeanTCperArt), number of articles (n) and mean total citations per year (MeanTCperYear)

Year	MeanTCperArt	n	MeanTCperYear
2016	182.56	25	16.6
2017	13.41	29	1.34
2018	20.71	35	2.3
2019	112.63	19	14.08
2020	19.15	20	2.74
2021	15.23	43	2.54
2022	8.33	24	1.67
2023	7.24	21	1.81
2024	7.52	23	2.51
2025	1.7	27	0.85

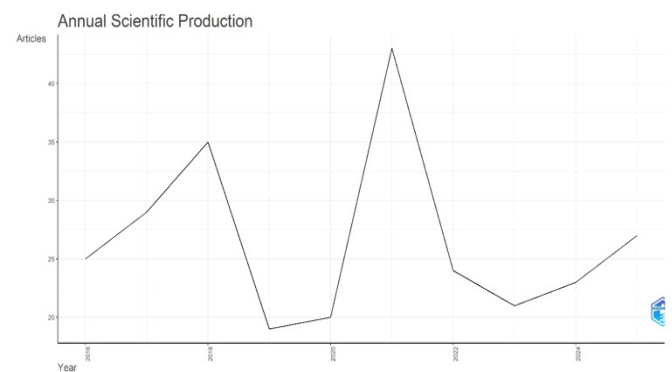


Figure 3. Annual scientific production showing the number of articles published each year between 2016 and 2025

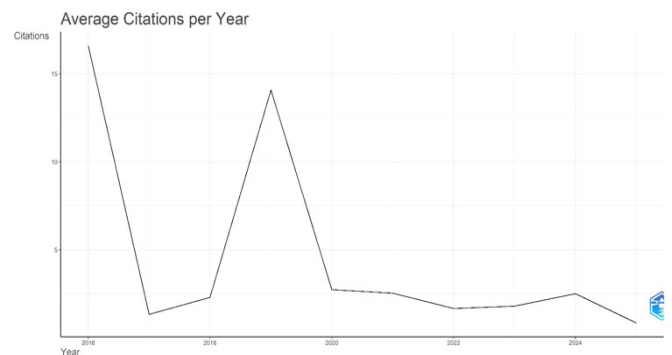


Figure 4. Distribution of average citations per year by publication year

a lower level of 1.67. A slight increase was observed in 2023 and 2024, with annual average citation values of 1.81 and 2.51, respectively. The lowest annual average citation value was identified in 2025, when articles published in that year received an average of 0.85 citations per article per year.

The average total number of citations per article also varied by year. The highest value was observed in 2016, followed by 2019. In the subsequent years, the average total citations per article were markedly lower. Overall, studies published in the earlier years were found to have higher values in terms of both annual and total citations.

In the word cloud and frequency table, the most frequently used term was "prostate cancer," appearing 93 times (Table 2, Figure 5). This was followed by "prostate-specific antigen" (37 occurrences), "primary care" (34 occurrences), and "screening"

(33 occurrences). In the visualization, the term “prostate cancer” is clearly displayed in a larger size compared with the other words.

Table 2. Most frequently used keywords and their number of occurrences

Terms	Frequency
Prostate cancer	93
Prostate-specific antigen	37
Primary care	34
Screening	33
Cancer screening	29
Cancer	19
Prostatic neoplasms	15
Early detection of cancer	14
PSA	13
Oncology	10
Primary health care	10

PSA: Prostate-specific antigen



Figure 5. Word cloud showing the most frequently used keywords in studies on prostate cancer screening in primary care, with word size reflecting the number of occurrences

The network map created to demonstrate scientific collaboration among authors is presented in **Figure 6**. Within the scope of the analysis, a total of 76 authors with a minimum of 3 publications and a minimum citation threshold of 0 were identified. Co-authorship analysis was conducted based on these 76 authors. In weighting institutional relationships, the TLS metric was used. The total number of clusters was 16, with 197 links and a TLS of 548. In this analysis, the authors with the highest TLS and citations were Ahmet Hashim U, Burak Paula, Day Emily, Fiorentino Francesca, Gammon Martin, Klimowska Nassar Natalia, Padhani Anwar R, Price Derek, Sokhi Heminder, Tam Henry, and Winkler Mathias, and all of these authors had 3 articles, 129 citations, and 30 TLS. The authors with the highest number of publications were Pollack Craig E (6 articles, 108 citations (cit), 16 TLS) and Roobol Monique J (6 articles, 26 cit, 4 TLS).

The network map created to demonstrate scientific collaboration among countries is presented in **Figure 7**. Within the scope of the analysis, a total of 44 countries with at least 1 publication and a minimum citation threshold of 0 were evaluated. The analysis was conducted on 37 countries that were interconnected among these 44 countries. The TLS metric was used to weight the relationships between countries. In the generated network structure, the total

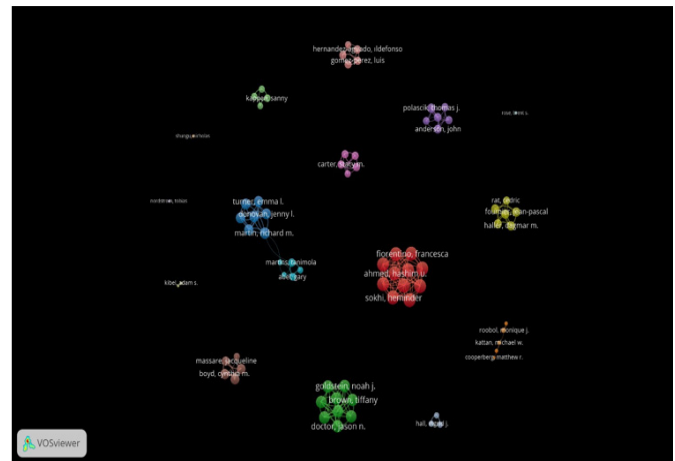


Figure 6. Network visualization of author co-authorship in prostate cancer screening research in primary care

number of clusters was 9, the number of links was 93, and TLS was 137. The countries with the highest number of publications and the highest citation counts were United States of America (124 articles, 5550 cit, 37 TLS), England (50 articles, 1248 cit, 34 TLS), and Australia (22 articles, 350 cit, 14 TLS), respectively. The countries with the highest TLS values were United States of America, England, Spain (12 articles, 178 cit, 17 TLS), and the Netherlands (13 articles, 86 cit, 17 TLS), respectively.

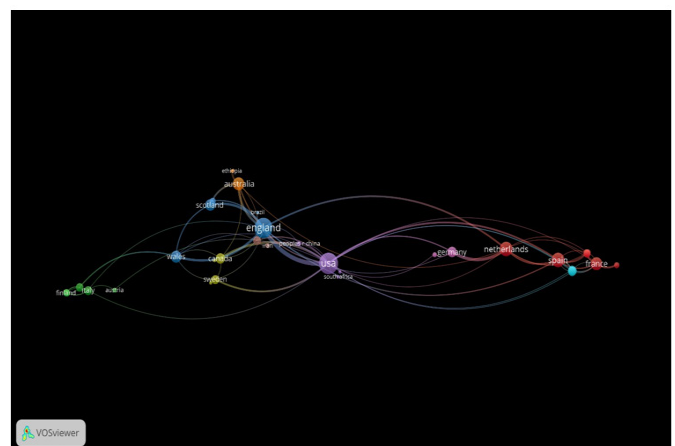


Figure 7. Network visualization of country co-authorship in prostate cancer screening research in primary care

To examine the intellectual structure of studies on prostate cancer screening in primary care and the network of relationships among co-cited publications, a co-citation analysis was performed (**Figure 8**). A minimum threshold of 3 citations was applied for cited sources. According to this criterion, 147 of the total 8213 references were included in the analysis. All of these 147 references were found to be interconnected, and the analysis was conducted based on this group. The weighting of links was based on the number of citations received by the references. As a result of the analysis, 6 clusters were formed, with a total of 3234 links and 5851 TLS calculated. The five documents with the highest citations and also the highest TLS, ranked according to citation counts, were as follows: Moyer VA, 2012, Ann Intern Med, v157, p120, doi:10.7326/0003-4819-157-2-201207170-00459 (53 cit, 439 TLS); Schröder FH, 2014, Lancet, v384, p2027, doi:10.1016/S0140-6736(14)60525-0 (43 cit, 386 TLS); Carter HB, 2013,

Informed Consent

This bibliometric study used only publicly available data and did not involve human subjects or personal information; therefore, informed consent was not required.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

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Author Contributions

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Retrospective evaluation of the inflammatory response in patients diagnosed with COVID-19 based on hematological and biochemical parameters

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ABSTRACT

Aims: This study aimed to compare the demographic characteristics, clinical symptoms, comorbidities, and hematological, biochemical, and inflammatory parameters of individuals with COVID-19 positivity with those of a healthy control group. Additionally, the relationship between the Systemic Inflammatory Index (SII) and the disease, the interaction between symptom presence and hematological variables, the association of thoracic computed tomography (CT) findings with clinical and laboratory parameters, and the effect of applied treatment protocols on length of hospital stay were evaluated.

Methods: This retrospective, observational study included a total of 286 individuals aged 18–80 years who presented to Yozgat City Hospital between January 1, 2020, and January 1, 2021. The study group consisted of 143 patients diagnosed with COVID-19 based on RT-PCR positivity, while the control group included 143 individuals had COVID-19-like symptoms with negative RT-PCR results and no known comorbid diseases. Demographic data and hematological, biochemical, and inflammatory parameters were recorded retrospectively, and SII values were calculated. Statistical analyses were performed using SPSS version 20.0. Appropriate parametric and non-parametric tests were applied, and a p-value <0.05 was considered statistically significant.

Results: In the COVID-19 group, the female/male ratio was 31.5%/68.5%, and the mean age was similar to that of the control group. The most common comorbidities were hypertension, diabetes mellitus, and chronic kidney disease. The most frequently reported symptoms were myalgia, cough, and fever. Thoracic CT findings compatible with COVID-19 were observed in 37.8% of the cases, and these patients had a longer duration of hospital stay. Compared with the control group, the COVID-19 group showed increased leukocyte and neutrophil counts as well as elevated C-reactive protein (CRP), erythrocyte sedimentation rate, and D-dimer levels, while lymphocyte counts were decreased. The SII value was significantly higher in the COVID-19 group than in the control group (p<0.001). Patients with longer hospital stays were more likely to have received combination therapy.

Conclusion: COVID-19 is characterized by marked hematological and inflammatory alterations. In particular, elevated SII and lymphopenia are important indicators reflecting disease severity. Monitoring these parameters may provide valuable guidance in the clinical management of COVID-19.

Keywords: COVID-19, Systemic Inflammatory Index, length of hospital stay

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in late 2019 and rapidly evolved into a global public health emergency. The clinical presentation of COVID-19 is highly heterogeneous, ranging from asymptomatic infection to severe respiratory failure, multiorgan dysfunction, and death. This variability has underscored the need for reliable, easily accessible biomarkers to support early risk stratification and clinical decision-making.¹⁻³

A dysregulated systemic inflammatory response plays a central role in the pathophysiology of COVID-19. Previous studies have consistently demonstrated that hematological and biochemical abnormalities -including neutrophilia, lymphopenia, and elevated levels of C-reactive protein (CRP), ferritin, and D-dimer- are closely associated with disease severity and adverse outcomes.^{1,2,4-6} Lamichhane et al.¹ and Bairwa et al.² reported marked deterioration in these parameters among severe and fatal cases, highlighting their prognostic relevance. Similarly, comprehensive reviews have

emphasized the clinical utility of inflammatory biomarkers in predicting disease progression.³

Despite their clinical value, individual biomarkers may be insufficient to fully reflect the complex and multidimensional inflammatory processes involved in COVID-19. This limitation has led to growing interest in composite inflammatory indices that integrate multiple immune components. The Systemic Inflammatory Index (SII), calculated using neutrophil, lymphocyte, and platelet counts, has emerged as a practical marker that reflects both immune activation and overall inflammatory burden. Prior studies have suggested that SII may serve as a prognostic indicator in various infectious and inflammatory conditions.^{1,3,4}

In severe COVID-19, excessive immune activation and cytokine-mediated inflammation may result in endothelial injury, coagulopathy, and multiorgan involvement.^{4,5} Elevated inflammatory markers during this process have been associated with poor clinical outcomes across different populations.⁶⁻⁸ Moreover, longitudinal analyses have shown that temporal changes in laboratory parameters parallel disease progression, while persistent inflammatory activity may have implications beyond the acute phase of infection.^{9,10}

In this context, the present study aimed to evaluate the relationship between the SII and clinical, laboratory, and radiological findings in patients hospitalized with COVID-19. In addition, the potential prognostic value of SII in relation to disease severity and length of hospital stay was investigated. By focusing on a readily available composite inflammatory marker, this study seeks to contribute to practical risk assessment strategies and support the integration of SII into routine clinical evaluation of COVID-19 patients.

METHODS

The study was approved by the Non-interventional Clinical Researches Ethics Committee of Yozgat Bozok University (Date: 05.11.2025, Decision No: 2025-GOKAEK-2519_2025.11.05_653). Due to the retrospective nature of the study, written informed consent was not obtained from participants. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. All data were anonymized prior to analysis and protected in accordance with the Personal Data Protection Law. No additional diagnostic tests or interventions were performed as part of the study.

This study was designed as a retrospective and observational investigation. Individuals aged 18–80 years who presented to Yozgat City Hospital between January 1, 2020, and January 1, 2021, were included. The study group consisted of patients who tested positive for reverse transcription–polymerase chain reaction (RT-PCR) at presentation, were diagnosed with COVID-19, and were admitted to the inpatient ward. Diagnostic criteria were applied uniformly to all cases, based on the same laboratory infrastructure and national diagnostic algorithms.

The control group consisted of individuals who presented to the same emergency department during the same time period with COVID-19–like symptoms, underwent similar laboratory evaluations, had confirmed negative RT-PCR

test results, showed no evidence of acute pathology, and had no known chronic diseases. To minimize selection bias, particular attention was paid to ensuring that the control group was comparable to the study group in terms of age and sex distribution. The control group was selected such that the numbers of female and male participants were equal between the compared groups, with the difference in mean age by sex being less than 5 years and the difference in age distribution ranges not exceeding ± 5 years. Patients with missing hematological or biochemical data at the time of diagnosis, those admitted to the intensive care unit, and those managed on an outpatient basis were excluded from the study.

All data were obtained retrospectively from the hospital's electronic medical record system. Demographic characteristics, including age, sex, and medical history, were recorded. Laboratory parameters were evaluated using samples obtained at the time of presentation or within the first 24 hours of hospitalization, in order to reduce variability related to sampling time.

Hematological analyses included routine parameters such as erythrocyte count, hemoglobin, and haematocrit. In addition, white blood cell subtypes (neutrophils, lymphocytes, monocytes, eosinophils, and basophils) and platelet counts were recorded. Biochemical assessments focused on parameters reflecting inflammatory response and organ function. These included inflammatory markers such as CRP, ferritin, and procalcitonin; liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], bilirubin); renal function indicators (urea, creatinine); and coagulation parameters (D-dimer). All laboratory measurements were performed in the hospital's accredited laboratory using standard analytical methods.

The SII was calculated for each individual using neutrophil, lymphocyte, and platelet counts obtained within the same time frame ($SII = \text{neutrophil} \times \text{platelet} / \text{lymphocyte}$). Calculations were performed on a standardized dataset to minimize potential bias arising from differences in measurement timing or methodology.

Statistical Analysis

The data analyses were conducted using SPSS version 20.0 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. For normally distributed data, comparisons between two groups were performed using the independent samples t-test, and comparisons among more than two groups were conducted using one-way analysis of variance (ANOVA). For data that did not follow a normal distribution, the Mann–Whitney U test was used for two-group comparisons, and the Kruskal–Wallis test was applied for comparisons involving three or more groups.

Relationships between variables were evaluated using Pearson correlation analysis when parametric assumptions were met, and Spearman correlation analysis when they were not. To reduce the risk of type I error in multiple comparisons, results were interpreted within the framework of clinical relevance. In all analyses, p-values < 0.05 and < 0.01 were considered statistically significant.

RESULTS

During the study period, a total of 816 patients who presented to Yozgat City Hospital with suspected COVID-19 were assessed for eligibility. Of these, 96 patients who required intensive care unit admission at initial presentation and 21 patients who were referred to another medical center were excluded. Among the 149 hospitalized patients with RT-PCR-confirmed COVID-19, 6 patients were excluded due to missing hematological or biochemical laboratory data at admission. Consequently, 143 COVID-19-positive patients were included in the final analysis. The control group consisted of 143 RT-PCR-negative individuals without known comorbid diseases. There were no statistically significant differences between the COVID-19 and control groups with respect to age ($p=0.703$) or sex distribution ($p=1.000$), baseline demographic features are summarized in **Table 1**.

Characteristic	COVID-19 patients (n=143)	Control group (n=143)	p value
Age, years (mean±SD)	42.1±19.8	41.5±17.4	0.703
Sex, n (%)			1.000
Female	45 (31.5)	45 (31.5)	
Male	98 (68.5)	98 (68.5)	

SD: Standard deviation

Briefly, hypertension, diabetes mellitus, and chronic kidney disease were the most frequently observed comorbidities among COVID-19-positive patients, while no comorbid conditions were present in the control group. The distribution of comorbid diseases is presented in **Figure 1**.

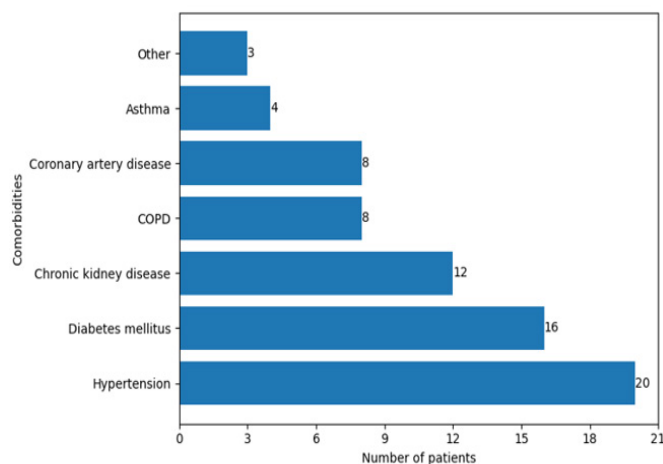


Figure 1. Distribution of comorbidities in COVID-19 positive patients

The most common presenting symptoms were myalgia, cough, and fever, and typical COVID-19-compatible findings on thoracic CT were observed in approximately one-third of patients (**Figure 2, 3**).

Hydroxychloroquine-based treatment regimens were the most frequently administered therapies (**Table 2**).

Comparison of hematological parameters between COVID-19 patients and controls demonstrated that platelet counts were significantly lower in the COVID-19 group ($p=0.008$),

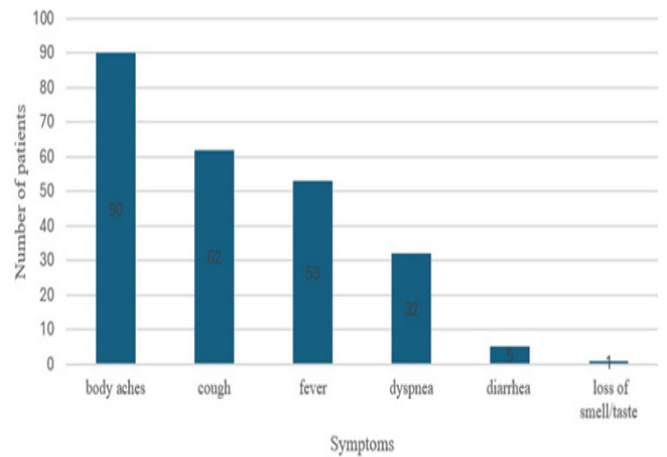


Figure 2. Distribution of symptoms in the COVID-19 positive patient group

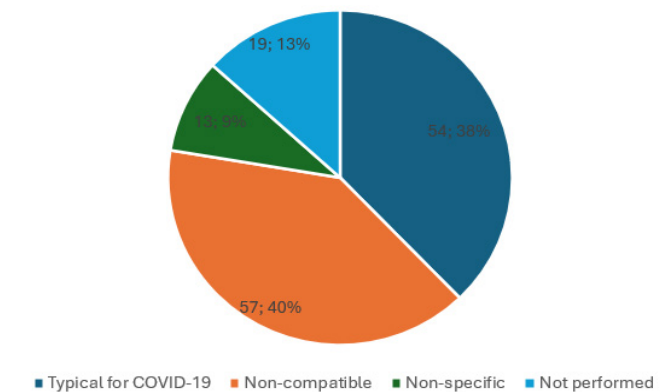


Figure 3. Distribution of thoracic CT findings by number and percentage of patients
CT: Computed tomography

Table 2. Treatment regimens and the number of COVID-19 positive patients received each therapy

Treatment protocols	Number of patients	% patients
Only HCQ	30	20.98
Only azithromycin	10	6.99
HCQ+azithromycin	48	33.57
HCQ+oseltamivir	14	9.79
HCQ+oseltamivir+azithromycin	28	19.58
HCQ+favipiravir+azithromycin	8	5.59
No treatment	5	3.50

HCQ: Hydroxychloroquine

while lymphocyte counts were markedly reduced ($p<0.001$) and neutrophil counts were significantly higher ($p=0.032$). Leukocyte and hemoglobin levels did not differ significantly between groups (**Table 3**). Symptom-based analyses showed that patients presenting with fever had significantly lower hemoglobin and lymphocyte levels (both $p<0.001$), whereas patients reporting myalgia exhibited higher leukocyte ($p=0.027$) and neutrophil counts ($p=0.030$).

Inflammatory marker analysis revealed that mean CRP and erythrocyte sedimentation rate (ESR) values were significantly higher in COVID-19 patients compared with controls (both $p<0.001$). Although CRP and ESR levels did not differ according to symptom presence, both markers demonstrated significant negative correlations with

Table 3. Hematological parameters in COVID-19 positive and control groups

Parameter	COVID-19 positive (mean±SD)	Control group (mean±SD)	p value
Leukocyte (10 ³ /μL)	7.21±3.95	6.49±1.76	p>0.05
Hemoglobin (g/dl)	13.6±2.81	13.84±2.6	p>0.05
Platelet (10 ³ /μL)	229.55±100.29	239.69±47.96	p=0.008
Lymphocyte (10 ³ /μL)	1.71±1.25	2.04±0.62	p<0.001
Neutrophil (10 ³ /μL)	4.78±3.37	3.91±1.59	p=0.032

SD: Standard deviation

lymphocyte count (CRP: ρ=-0.17, p=0.039; ESR: ρ=-0.20, p=0.017).

Evaluation of cardiac and coagulation biomarkers showed wide variability in troponin, pro-BNP, and D-dimer levels, indicating marked elevations in a subset of patients. D-dimer levels correlated positively with CRP (p<0.001) and neutrophil count (p=0.019), and inversely with hemoglobin (p<0.001) and lymphocyte count (p=0.042). Troponin levels were positively associated with CRP, neutrophil, and leukocyte counts and negatively correlated with hemoglobin. Pro-BNP levels increased in parallel with CRP (p=0.003) and ESR (p<0.001). Clinically, patients presenting with fever had significantly higher D-dimer levels (p<0.001), while those presenting with dyspnea had markedly elevated troponin (p=0.004) and pro-BNP (p<0.001) levels (Table 4).

Table 4. Marker relationships according to symptoms

Symptom	Marker	Result	p-value
Fever	D-dimer	Higher in patients with fever	<0.001
Dyspnea	Troponin	Higher in patients with dyspnea	0.004
Dyspnea	pro-BNP	Significantly higher in patients with dyspnea	<0.001
Body aches	pro-BNP	Difference observed, due to a few patients with high values	0.012

BNP: B-type natriuretic peptide

Mean SII values were significantly higher in COVID-19 patients (910.3±1146.1) compared with controls (599.7±670.9; p<0.001) (Figure 4). SII showed strong positive correlations with neutrophil (ρ=0.73) and platelet counts (ρ=0.35), and a negative correlation with lymphocyte count (ρ=-0.37). In addition, SII demonstrated weak but significant positive correlations with D-dimer (ρ=0.20; p=0.021), troponin (ρ=0.18; p=0.029), and CRP (ρ=0.22; p=0.016).

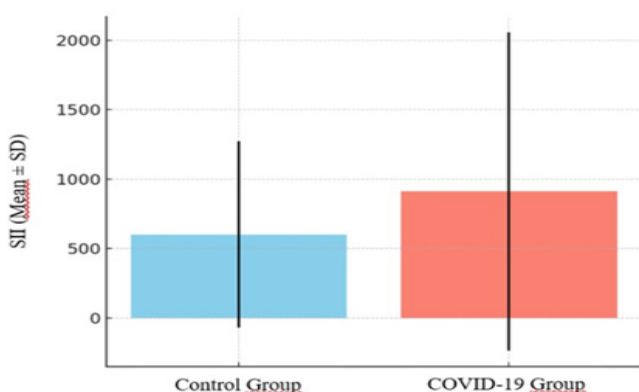


Figure 4. Comparison of the mean Systemic Inflammatory Index (SII) between COVID-19 and control groups

ROC curve analysis evaluating the discriminative performance of SII for COVID-19 positivity yielded an area under the curve of 0.623. The optimal SII cut-off value determined by the Youden index was 711.56, corresponding to a sensitivity of 41.4% and a specificity of 91.6%. In univariable logistic regression analysis, higher SII values were associated with increased odds of COVID-19 positivity (OR 1.73; 95% CI 1.22–2.47; p=0.002 per log-transformed SII). However, multivariable logistic regression analyses performed within the COVID-19 cohort and adjusted for age, sex, and major comorbidities demonstrated that SII was not an independent predictor of CT compatibility or prolonged hospitalization (p>0.05 for both outcomes).

Patients presenting with fever had significantly higher SII values than those without fever (median 871.6 vs. 526.3; p=0.010). No statistically significant correlation was observed between SII and length of hospital stay (r=-0.155; p=0.067). The mean length of hospital stay among COVID-19 patients was 12.8±4.8 days. Hospitalization duration was significantly prolonged in patients with hypertension, diabetes mellitus, and chronic kidney disease (all p<0.05).

DISCUSSION

In this study, hospitalized patients with COVID-19 demonstrated distinct hematological and inflammatory alterations compared with the control group, supporting the central role of systemic inflammation in disease pathophysiology. The similarity in age and sex distribution between the patient and control groups represents an important methodological strength, allowing interpretation of laboratory findings with minimal demographic confounding. Although advanced age and male sex have been widely reported as risk factors for severe disease and mortality,¹⁻³ the balanced design of the present study enabled a clearer evaluation of biomarker-associated differences.

Hypertension, diabetes mellitus, and chronic kidney disease were the most prevalent comorbidities among COVID-19-positive patients and were associated with significantly prolonged hospital stay. These findings are consistent with previous reports indicating that chronic comorbid conditions adversely affect clinical course and recovery in COVID-19.^{14,20,22} Renal dysfunction and metabolic disorders have been shown to amplify inflammatory responses and reduce physiological reserve, thereby contributing to delayed clinical improvement and extended hospitalization.^{5,13,23}

The clinical presentation observed in this cohort reflects the heterogeneous nature of COVID-19. Myalgia, cough, and fever were the most frequently reported symptoms, consistent with earlier studies.³ Fever was associated with lymphopenia, while myalgia correlated with leukocytosis and neutrophilia, highlighting the close interaction between clinical manifestations and underlying inflammatory responses. Similar symptom-associated hematological patterns have been reported previously and are considered indicative of disease severity.^{4-6,8}

Thoracic computed tomography (CT) findings were heterogeneous, with typical COVID-19-compatible patterns identified in only a subset of patients. Patients with typical CT findings experienced longer hospital stays and received more intensive treatment regimens, suggesting a higher

inflammatory burden. Previous studies have reported discordance between RT-PCR results and CT findings, particularly in early disease stages, while also emphasizing the association between typical radiological patterns and adverse clinical outcomes.^{9,26} These observations support the role of thoracic CT not only in diagnosis but also in assessing disease severity and guiding clinical management.⁵

Hematological analysis revealed characteristic features of COVID-19, including lymphopenia and neutrophilia, which have consistently been associated with poor prognosis.⁶⁻⁸ Elevated CRP and ESR further confirmed the presence of a pronounced systemic inflammatory response. The observed negative correlations between inflammatory markers and lymphocyte counts suggest immune dysregulation proportional to inflammatory intensity, in line with previous studies identifying CRP and ESR as reliable indicators of disease severity and outcome.^{14,21,22}

Alterations in coagulation and cardiac biomarkers further underscore the multisystem involvement of COVID-19. Elevated D-dimer, troponin, and pro-BNP levels in a subset of patients indicate hypercoagulability and myocardial stress, both of which have been associated with unfavorable outcomes.^{9,16,19,21} The positive correlations between these biomarkers and inflammatory parameters support the concept that cardiovascular involvement in COVID-19 is largely mediated by systemic inflammation.

A key finding of the present study is the significantly elevated SII observed in COVID-19 patients compared with controls. As a composite marker integrating neutrophil, lymphocyte, and platelet counts, SII provides a comprehensive reflection of immune activation and inflammatory burden. The associations observed between SII and hematological as well as biochemical parameters -including D-dimer and cardiac biomarkers- suggest that SII captures both inflammatory and prothrombotic processes. Consistent with these findings, previous studies have highlighted the prognostic value of SII in COVID-19, particularly when interpreted alongside conventional inflammatory markers.²⁸⁻³²

Although no strong correlation was identified between SII and length of hospital stay, higher SII values in febrile patients suggest a relationship with clinical severity. The lack of association with hospitalization duration may reflect the influence of additional factors such as treatment strategies, comorbidities, and institutional discharge practices. Overall, our findings are also consistent with previous reports evaluating hematological, biochemical, and inflammatory biomarkers in COVID-19 across different populations.^{17-19,23-25,27,30,34-38}

Limitations

This study has several limitations. Its retrospective and single-center design limits generalizability, and laboratory parameters were assessed primarily at admission, precluding evaluation of dynamic changes over time. In addition, length of hospital stay is influenced by multiple clinical and organizational factors beyond inflammatory burden. Finally, given that SII is mathematically derived from hematological parameters, its correlations with these components should be interpreted cautiously. Despite these limitations, the study provides real-world evidence supporting the role of SII as a practical inflammatory marker in COVID-19.

CONCLUSION

COVID-19 infection is associated with significant alterations in hematological and inflammatory parameters, including lymphopenia, neutrophilia, and elevated inflammatory markers. In this study, SII values were significantly higher in COVID-19-positive patients compared with healthy controls, suggesting that SII may reflect the overall inflammatory burden of the disease. Given that SII can be easily derived from routine complete blood count parameters, it may serve as a practical adjunct marker in clinical assessment. In addition, the presence of comorbid conditions such as hypertension, diabetes mellitus, and chronic kidney disease was associated with prolonged hospital stay, indicating a more severe clinical course. Further prospective studies are warranted to clarify the prognostic value of SII and its role in clinical decision-making.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was approved by the Non-interventional Clinical Researches Ethics Committee of Yozgat Bozok University (Date: 05.11.2025, Decision No: 2025-GOKAEK-2519_2025.11.05_653).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

Author Contributions

Concept: İA; Design: İA, İG; Supervision: İA, İG; Resources: İA; Materials: İA; Data Collection and/or Processing: İA; Analysis and/or Interpretation: İG; Literature Review: İG; Writing-Original Draft: İA, İG; Writing-Review & Editing: İA, İG.

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Prognostic significance of early lactate clearance in patients with suspected infection admitted to the intensive care unit from the emergency department

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ABSTRACT

Aims: To evaluate the association between early lactate clearance and short-term outcomes in patients admitted to the intensive care unit (ICU) from the emergency department with suspected infection.

Methods: This single-center, retrospective observational study included adult patients admitted to the internal medicine ICU between January 1, 2023 and June 30, 2025. Serum lactate levels measured at admission and approximately 6 hours later were used to calculate lactate clearance. Patients were stratified into two groups based on lactate clearance: inadequate (<20%) and adequate (≥20%). The primary outcome was 28-day all-cause mortality.

Results: Among the 117 patients analyzed, those with inadequate lactate clearance had significantly higher 28-day mortality than those with adequate clearance (p=0.025). Inadequate lactate clearance was also associated with older age, whereas APACHE II scores, routine biochemical parameters and arterial blood gas values did not differ significantly between groups.

Conclusion: Early lactate clearance was associated with short-term mortality in critically ill patients admitted from the emergency department with suspected infection. Serial lactate assessment may provide complementary prognostic information beyond baseline severity scores and routine laboratory findings.

Keywords: Lactate clearance, intensive care unit, suspected infection, mortality, emergency department

INTRODUCTION

Patients admitted to the intensive care unit (ICU) from the emergency department with suspected infection represent a clinically heterogeneous population characterized by variable disease severity and a substantial risk of adverse outcomes. Early identification of individuals at increased risk is a key challenge in critical care, especially during the initial phase of ICU admission when resuscitation and management strategies are being implemented.¹

Serum lactate serves as a marker of tissue hypoperfusion and metabolic stress in critically ill patients. Elevated lactate concentrations are associated with increased mortality; however, a single measurement offers limited insight into the dynamic response to initial treatment.²

Changes in lactate levels, known as lactate kinetics or clearance, reflect the physiologic response to illness. Evidence suggests that lactate clearance during the initial hours of illness has greater prognostic value than baseline lactate measurements, supporting its use in early risk assessment.³

Most research on lactate kinetics has focused on patients with sepsis or septic shock. In contrast, limited data exist on the prognostic significance of lactate clearance in ICU patients with suspected infection, particularly in clinical practice.⁴

This study considers the relationship between lactate clearance within the first 6 hours and clinical outcomes in ICU patients admitted from the emergency department with suspected infection.

METHODS

This study was conducted with the approval of the Ethics Committee of the Health Sciences Researches Center at Sivas Cumhuriyet University (Date: 08.01.2026, 2026-01/57). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study was designed as a single-center, retrospective, observational cohort study. Data were obtained from the electronic medical records of patients admitted to the

Emergency Department of Sivas Cumhuriyet University Faculty of Medicine Hospital and subsequently transferred to the Internal Medicine ICU.

The study population included adults admitted between January 1, 2023 and June 30, 2025, with suspected infection. Suspected infection was defined as a clinical presentation, such as respiratory symptoms with imaging infiltrates or urinary symptoms with pyuria, that prompted the attending emergency physician to initiate empirical antibiotic therapy. To ensure a standardized and objective triage process, the final decision on ICU admission was made by the investigating Internal Medicine specialist in accordance with established institutional protocols. These protocols prioritize patients presenting with acute organ dysfunction or those requiring advanced monitoring and life-sustaining interventions, such as vasopressor support or mechanical ventilation, regardless of the specific pathogen. This recruitment strategy intentionally prioritized a pragmatic, real-world triage model over formal sepsis-3 criteria, recognizing that intensive care management often commences before definitive microbiological confirmation is available.

To be included, patients had to meet all of the following criteria: I) Admission to the internal medicine ICU from the emergency department with suspected infection or sepsis. II) An initial serum lactate measured before or immediately after ICU admission. III) At least one more measurement, about 6 hours (± 2 hours) after the first. Patients were excluded if: I) their ICU stay was less than 6 hours. II) Serial lactate measurements were missing. III) Baseline clinical or laboratory data were incomplete. Additionally, to ensure that lactate kinetics primarily reflected the response to infection rather than alternative pathologies, patients with non-infectious conditions known to cause significant hyperlactatemia, such as major trauma, acute mesenteric ischemia or primary metabolic disorders, were excluded during the initial specialist-led triage. This rigorous selection process was maintained to minimize diagnostic uncertainty regarding the etiology of elevated lactate levels at presentation. The detailed process of patient screening, including specific reasons for exclusion and the subsequent stratification into study groups, is illustrated in the patient flow chart (Figure).

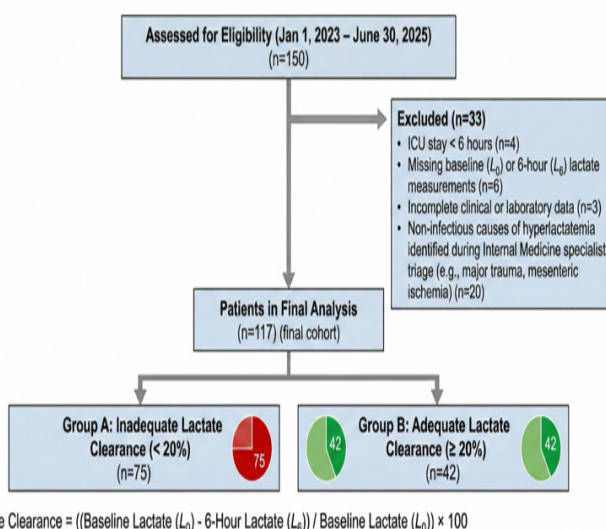


Figure. Patient enrollment and study flow chart. The diagram illustrates the standardized triage and selection process for patients admitted with suspected infection, including the systematic exclusion of non-infectious causes of hyperlactatemia

Serum lactate was first measured at emergency department presentation or ICU admission. A repeat measurement was taken about 6 hours later, allowing a ± 2 -hour tolerance window. If multiple lactate values were within the time window, the value closest to the target time was used in the analysis.

Lactate clearance (%) was calculated according to the formula previously described in the literature:

$$\text{"Lactate clearance"} = (L_0 - L_6) / L_0 \times 100$$

where L_0 represents the baseline serum lactate level and L_6 represents the serum lactate level measured approximately 6 hours later.⁵

Patients were grouped by lactate clearance, using cutoffs from previous studies on critically ill patients. Lactate clearance of less than 20% was considered inadequate. Clearance of 20% or higher was considered adequate.^{5,6}

Patients in whom the 6-hour lactate level exceeded the baseline value ($L_6 > L_0$) were considered to have negative lactate clearance and were included in the inadequate lactate clearance group, consistent with prior methodological strategies.⁷

Demographic data (age, gender), clinical characteristics and ICU treatment variables were pulled from medical records. Indicators of disease severity included the need for vasopressors within the first 6 hours (yes/no) and the APACHE II score. Source of infection, comorbidities and 28-day mortality were also recorded.

Baseline laboratory parameters were defined as the first available tests collected within 24 hours after ICU admission. These included: serum albumin, electrolytes (sodium, potassium, chloride, magnesium, calcium), blood urea nitrogen, creatinine, hemoglobin, white cell and platelet counts, CRP and arterial blood gas values (pH, pCO_2 , bicarbonate, base excess [BE] and lactate).

Comorbidities were classified based on the presence of coronary artery disease, chronic kidney disease, chronic heart failure, active malignancy or liver cirrhosis and were summarized as major comorbidity (yes/no).

The primary outcome was 28-day all-cause mortality, defined as death occurring within 28 days following ICU admission.

Statistical Analysis

The data analyses were performed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality and are presented as mean \pm standard deviation or median (interquartile range), as appropriate. Categorical variables are expressed as counts and percentages. Between-group comparisons were conducted using the independent sample t-test or Mann-Whitney U test for continuous variables and the Chi-square test for categorical variables. Associations with secondary outcomes were analyzed using appropriate parametric or non-parametric methods. A two-sided p-value < 0.05 was considered statistically significant.

RESULTS

A total of 117 patients admitted to the ICU from the emergency department with suspected infection were

included in the final analysis. The study cohort was evaluated for lactate clearance status and categorized into inadequate (<20%) and adequate (\geq 20%) groups. Demographic characteristics, laboratory parameters and clinical outcomes were compared between these groups.

The most common suspected source of infection was the respiratory tract (88,9%). Procedure-related (4.3%), urinary tract (3.4%), bloodstream (1.7%) and unknown origin infections (1.7%) were less frequent.

Baseline serum lactate levels at admission (lactate₀), serum lactate levels measured at approximately 6 hours (lactate₆) and calculated lactate clearance values for the overall study population are summarized in **Table 1**. Descriptive statistics include measures of central tendency and distribution for each parameter. Baseline lactate levels showed a wide range (0.6–12.9 mmol/L), with a right-skewed distribution. The mean baseline lactate level was 2.63 mmol/L, while the mean 6-hour lactate level was 2.25 mmol/L. Similar distributional characteristics, including right skewness and increased kurtosis, were observed for 6-hour lactate values.

Lactate clearance values showed substantial variability, ranging from –252.00% to 84.85%, with a heterogeneous, negatively skewed distribution. Measures of central tendency and dispersion indicated considerable inter-individual variation in lactate clearance within the study population.

Baseline hematological and biochemical parameters were compared between patients with inadequate and adequate lactate clearance (**Table 2**). Patients with inadequate lactate clearance had a significantly higher median age than those in the adequate clearance group ($p=0.034$). No significant differences were observed between groups in APACHE II score, serum albumin levels, electrolyte parameters or renal function markers ($p>0.05$ for all).

White blood cell counts were significantly lower in the inadequate lactate clearance group ($p=0.018$), whereas CRP levels were significantly higher in the adequate lactate clearance group ($p=0.035$). No statistically significant differences were identified between groups in arterial blood gas parameters, including the pH, bicarbonate, pCO₂ or BE ($p>0.05$ for all).

The association between lactate clearance status and 28-day mortality is presented in **Table 3**. A statistically significant difference in 28-day mortality was observed between patients with inadequate and adequate lactate clearance ($p=0.025$), with a higher proportion of deaths in the inadequate lactate clearance group. No statistically significant differences were observed between groups for gender, comorbidity or vasopressor use within the first 6 hours after ICU admission ($p>0.05$ for all).

Table 2. Baseline characteristics according to lactate clearance status

Variable	Inadequate lactate clearance (n=75)	Adequate lactate clearance (n=42)	p value
Age, years	79 (66-84)	72.50 (52.52-80.25)	.034*
APACHE II score	25.88±8.87	25.62±8.34	.876
Albumin, g/L	23.96±4.68	24.01±4.70	.957
Chloride, mmol/L	104 (100-108)	103 (99.75-108.50)	.733
Sodium, mmol/L	143 (139-147)	141 (138.75-146.50)	.477
Potassium, mmol/L	3.90 (3.43-4.30)	3.88 (3.51-4.35)	.495
Calcium, mg/dl	7.92±0.82	7.99±0.79	.617
Magnesium, mg/dl	1.87 (1.65-2.10)	1.89 (1.6 8-2.07)	.814
BUN, mg/dl	35.90 (23.50-53.30)	33.45 (22.60-55.30)	.765
Creatinine, mg/dl	0.77 (0.52-1.04)	0.36 (0.53-1.77)	.619
WBC, $\times 10^3/\mu\text{L}$	10.28 (7.98-14.49)	13.8 (9.09-18.57)	.018*
Hgb, g/dl	11.83±2.40	11.38±2.70	.347
PLT, $\times 10^3/\mu\text{L}$	254.05±119.14	292.57±118.62	.096
CRP, mg/L	45.5 (15.2-100.3)	81.90 (27.52-199.52)	.035*
pH	7.41 (7.31-7.44)	7.39 (7.32-7.43)	.552
Bicarbonate, mmol/L	24.81±7.18	23.46±4.77	.276
pCO ₂ , mmHg	41.3 (33.2-49.0)	38.25 (34.00-48.32)	.845
BE, mmol/L	-0.50 (-3.8-4.1)	-1.70 (-5.45-2.10)	.085

Data are presented as mean±standard deviation for normally distributed variables and as median (interquartile range) for non-normally distributed variables. Between-group comparisons were performed using the independent-samples t-test or the Mann-Whitney U test for continuous variables and the Chi-square test for categorical variables, as appropriate. p-values <0.05 were considered statistically significant and are indicated with an asterisk. APACHE II indicates Acute Physiology and Chronic Health Evaluation II, BUN: Blood urea nitrogen, WBC: White blood cell count, Hgb: Hemoglobin, PLT: Platelet count, CRP: C-reactive protein, pCO₂: Partial pressure of carbon dioxide

Table 3. Clinical characteristics and 28-day mortality according to lactate clearance status

Variable	Inadequate lactate clearance (n=75)	Adequate lactate clearance (n=42)	p value	
28-day mortality	Yes	66 (68.8%)	30 (31.3%)	.025*
	No	9 (42.9%)	12 (57.1%)	
Gender	Female	36 (64.3%)	20 (35.7%)	.968
	Male	39 (63.9%)	22 (36.1%)	
Comorbidity	Absent	9 (56.3%)	7 (43.8%)	.481
	Present	66 (65.3%)	35 (34.7%)	
Vasopressor use	Yes	51 (63%)	30 (37%)	.700
	No	24 (66.7%)	12 (33.3%)	

Comparisons between groups were performed using the Chi-square test as appropriate. A p-value <0.05 was considered statistically significant and is indicated with an asterisk. Vasopressor use refers to the requirement for vasopressor support within the first 6 hours following ICU admission

DISCUSSION

In this study of patients admitted to the ICU from the emergency department with suspected infection, early lactate clearance within the first 6 hours was associated with short-term mortality. This finding supports the growing body of

Table 1. Descriptive statistics of baseline lactate, 6-hour lactate and lactate clearance values

	Min	Max	\bar{X}	SD	Median	Skewness	Kurtosis
Lactate ₀	0.6	12.9	2.63	2.27	2.00	2.42	6.45
Lactate ₆	0.5	12.7	2.25	1.94	1.70	2.77	9.39
Lactate clearance	-252	84.85	-0.49	52.32	5.26	-1.56	4.88

Min: Minimum, Max: Maximum, SD: Standard deviation

evidence suggesting that dynamic changes in lactate levels provide more clinically meaningful prognostic information than a single static admission measurement. Recent studies have emphasized that early lactate trajectories reflect the balance between ongoing tissue hypoperfusion, metabolic stress and the physiologic response to initial resuscitative interventions, thereby giving insight into early disease evolution in critically ill patients.^{8,9}

Importantly, the association between impaired lactate clearance and mortality observed in the present cohort was identified in a population defined by suspected infection, rather than by strict sepsis or septic shock criteria. This distinction is clinically relevant, as many patients admitted to the ICU from the emergency department fall into this intermediate diagnostic category during the early phase of illness. Emerging literature indicates that lactate kinetics may retain prognostic value across a broad spectrum of critical illness severity, including varied populations encountered in routine clinical practice.¹⁰ In this context, early lactate clearance may serve as a practical adjunct for early risk stratification during the transition from emergency care to intensive care management.

Although patients with inadequate lactate clearance were older, no significant differences were observed between clearance groups in APACHE II scores, serum albumin levels, electrolyte profiles or renal function markers. This result suggests that impaired lactate clearance may not be adequately accounted for by conventional severity scoring systems or static biochemical measurements obtained at admission. Global scores such as APACHE II primarily summarize physiological derangement at a single time point, whereas lactate clearance reflects an evolving process that integrates tissue perfusion, metabolic adaptation and early response to treatment.¹¹

Current international guidelines emphasize that early assessment of patients with suspected infection should incorporate dynamic indicators of tissue perfusion rather than depending solely on static severity scores or single laboratory measurements.¹² In this context, serial lactate measurements are recommended to monitor changes in global perfusion and metabolic stress during early resuscitation. From this perspective, lactate clearance may serve as a complementary indicator of evolving physiologic responses not fully captured by routine laboratory values or composite severity scores.

Previous studies have shown that a substantial proportion of critically ill patients may exhibit impaired lactate clearance despite similar baseline severity scores, indicating that dynamic metabolic markers can provide prognostic information beyond classic static indices.^{13,14} In this context, lactate clearance may capture early physiological trajectories that are not fully reflected by composite severity scores or routine laboratory measurements, supporting its function as a complementary tool in early risk assessment.

In this study, differences in inflammatory markers between lactate clearance groups should be interpreted with caution. Patients with inadequate lactate clearance had lower white blood cell counts, whereas higher C-reactive protein levels were observed in patients with adequate clearance.

This pattern may reflect differences in the timing and heterogeneity of the inflammatory response rather than absolute differences in inflammatory burden. As previously highlighted, traditional inflammatory markers, such as leukocyte count and CRP, may exhibit discordant behavior during early infection and critical illness, depending on the phase and regulation of the host response.¹⁵

Furthermore, growing evidence suggests that lactate is not simply a marker of tissue hypoperfusion but may actively interact with immune cells, influencing cytokine production and immune cell function. Such metabolic-immune interactions may contribute to early biological phenotypes in which inflammatory markers and metabolic recovery do not evolve in parallel.¹⁶ From this perspective, the observed dissociation between WBC, CRP and lactate clearance may indicate heterogeneous immune-metabolic responses during the early course of critical illness.

In addition to inflammatory and immune responses, recent observational studies have shown that integrating lactate dynamics with conventional severity scores improves prognostic value. A large retrospective cohort study demonstrated that the combination of lactate levels, lactate clearance and APACHE II scores predicted short-term outcomes more reliably than any single indicator, suggesting that dynamic metabolic changes capture prognostic information not fully reflected by static assessments.¹⁷

Similarly, a pilot study in patients with cardiogenic shock found that lower lactate clearance was significantly associated with worse outcomes and correlated negatively with both fluid balance and APACHE II scores, supporting the relevance of early lactate kinetics for risk stratification across several critical care settings.¹⁸

Together, these outcomes support the notion that lactate clearance, particularly when considered alongside other clinical indicators, may help identify patients with a distinct metabolic and inflammatory phenotype in the early phases of critical illness. This integrated perspective may guide clinicians toward more customized monitoring and clinical strategies to modify both perfusion and immune-metabolic responses.

Clinically, these data indicate that early lactate clearance may enhance risk stratification for patients admitted to the ICU from the emergency department with suspected infection. Given that serum lactate is routinely measured and readily available, serial evaluation of lactate dynamics during the initial hours of admission may help clinicians distinguish patients with different physiological trajectories, even when clinical presentations appear similar. Variability in lactate clearance may reveal underlying heterogeneity in metabolic stress and recovery that is not fully reflected in baseline severity scores or single laboratory values. Lactate clearance should be interpreted as a complementary marker, integrated with clinical assessment and additional physiological parameters, rather than as a standalone indicator. This approach is consistent with recent observational studies and current clinical guidelines, which underline the importance of serial lactate monitoring for early risk assessment in patients with suspected infection.^{19,20}

Limitations

There are various limitations on this study. The results may not be generalizable to other ICU settings due to the retrospective, single-center design and small sample size. Although multivariable analyses were performed, residual confounding cannot be excluded, as treatment-related factors such as timing of resuscitation, fluid management and antibiotic strategies were not fully captured. In addition, lactate clearance was categorized using a 20% cutoff, consistent with prior studies; different thresholds or alternative modeling approaches may yield different prognostic performance. Finally, inclusion was based on suspected infection rather than strict sepsis definitions, reflecting real-world ICU admission practices but potentially introducing clinical heterogeneity. Further prospective, multicenter studies are needed to validate these findings.

CONCLUSION

Early lactate clearance was significantly associated with short-term mortality in critically ill patients admitted to the ICU from the emergency department with suspected infection. Serial assessment of lactate dynamics may offer clinically relevant prognostic information beyond baseline severity scores and routine laboratory parameters, supporting early risk stratification during the initial phase of critical illness. Although the results should be interpreted in light of the retrospective design, they suggest a potential role for lactate clearance as a practical adjunct to early intensive care assessment and warrant confirmation in prospective studies.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of the Ethics Committee of the Health Sciences Researches Center at Sivas Cumhuriyet University (Date: 08.01.2026, 2026-01/57).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

Conceptualization: ST; Design: ST; Project Control and Supervision: ST, ED; Resources: ST; Materials: ST; Data Collection and/or Processing: ST, ED; Analysis and/or Interpretation: ED; Literature Review: ST; Writing the Article: ST; Critical Review: ST, ED.

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Pitfalls of lung ultrasound interpretation in malignant pleural mesothelioma: an emergency department case report

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ABSTRACT

Lung ultrasound (LUS) is widely used in emergency departments (ED) for rapid evaluation of acute dyspnea and chest pain, but certain conditions may lead to misinterpretation of sonographic artifacts. We report a 70-year-old woman with malignant pleural mesothelioma (MPM) who presented with chest pain and dyspnea, in whom LUS demonstrated diffuse B-lines and pleural-based anechoic lesions mimicking cardiogenic pulmonary edema. The patient required non-invasive mechanical ventilation and was subsequently diagnosed with non-ST-elevation myocardial infarction. This case emphasizes that B-lines in oncologic patients may reflect pleural or subpleural pathology rather than interstitial edema and should be interpreted in conjunction with clinical and laboratory findings.

Keywords: Lung, ultrasonography, mesothelioma, emergency medicine, pleura

INTRODUCTION

Lung ultrasound (LUS) is increasingly utilized in emergency medicine (EM) as a rapid, bedside, radiation-free imaging tool for the evaluation of acute respiratory failure and chest pain. The fundamental principles and standardized interpretation of LUS artifacts were first systematically described by Lichtenstein,¹ forming the basis of modern LUS practice. The technique relies on the interpretation of pleural motion and ultrasound artifacts generated at the pleural-air interface rather than direct visualization of lung parenchyma.²

Under normal conditions, the presence of lung sliding and horizontal reverberation artifacts, known as A-lines, indicates normal lung aeration. In contrast, vertical hyperechoic artifacts extending from the pleural line to the bottom of the screen, referred to as B-lines, are typically associated with increased lung density and are most interpreted as interstitial syndrome, such as pulmonary edema. However, B-lines are not disease-specific and may also arise from non-cardiogenic causes, including pneumonia, pulmonary fibrosis, acute respiratory distress syndrome, and pleural-based malignancies.^{3,4} Malignant pleural mesothelioma (MPM) is an aggressive neoplasm originating from mesothelial cells and is frequently associated with pleural thickening, nodularity, and effusions, all of which may alter LUS findings.⁵

Although LUS has been described as a useful tool in detecting pleural masses and guiding biopsies in mesothelioma, reports focusing on LUS findings of mesothelioma patients presenting to the emergency department (ED) are scarce. In

this case report, we aim to emphasize the potential pitfalls in interpreting B-lines in patients with MPM from an EM perspective.

CASE

A 70-year-old woman presented to the ED with acute onset chest pain and progressive shortness of breath. Her medical history was significant for MPM, for which she was receiving active chemotherapy.

On arrival, her peripheral oxygen saturation was 88% on room air and increased to 94% with 2 L/min supplemental oxygen via nasal cannula. Vital signs revealed a blood pressure of 122/75 mmHg and sinus rhythm on electrocardiography, without ST-segment elevation. Physical examination demonstrated bilateral basal crackles without wheezing.

Initial laboratory analysis showed a serum creatinine level of 1.07 mg/dl and an elevated C-reactive protein of 84 mg/L. High-sensitivity cardiac troponin levels were elevated and demonstrated a rising trend (40 ng/L initially, followed by 57 ng/L and 85 ng/L on serial measurements).

Chest radiography findings are shown in **Figure 1**. Thoracic computed tomography revealed pleural irregularities and subpleural involvement consistent with known malignancy (**Figure 2**). LUS examination demonstrated multiple B-lines bilaterally. A diagnostic LUS was performed using a handheld ultrasound device (Butterfly iQ+, Butterfly Network Inc., Boston, MA, USA) with the lung preset and a depth set to

13 cm. **Figure 3** demonstrates the right lung, where multiple B-line artifacts attributable to pleural involvement secondary to malignant mesothelioma are observed. In contrast, **Figure 4** shows the left lung, with preserved A-lines interrupted by focal B-line artifacts.

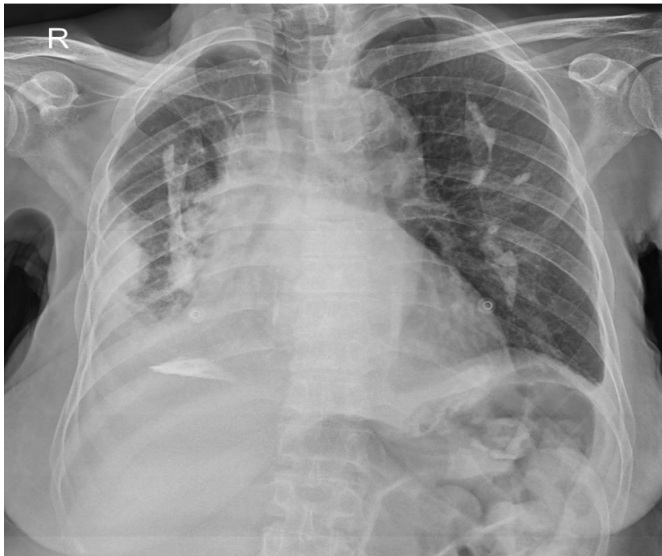


Figure 1. Posteroanterior chest radiograph demonstrating asymmetric right-sided pleural abnormalities with associated volume loss, consistent with known pleural disease

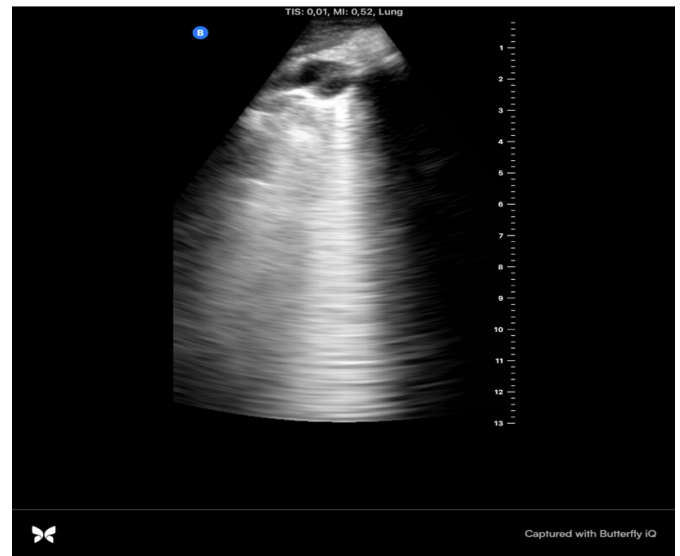


Figure 3. Lung ultrasound image obtained from the right upper lung zone demonstrating multiple vertical hyperechoic artifacts consistent with B-lines, attributed to pleural involvement secondary to malignant pleural mesothelioma

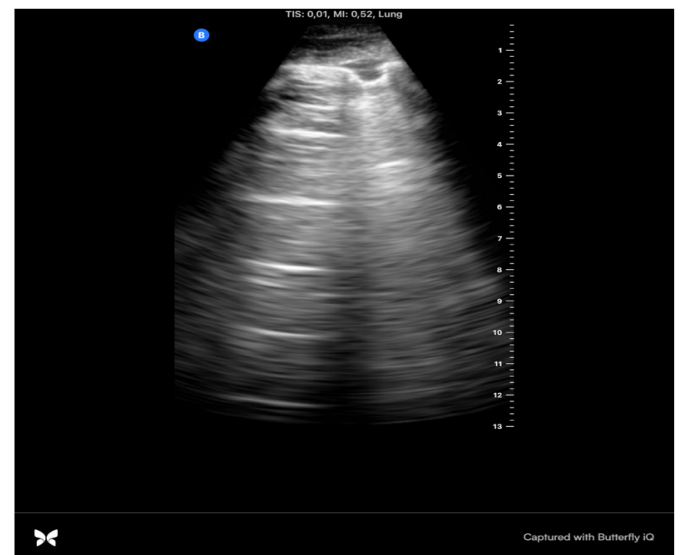


Figure 4. Lung ultrasound image obtained from the left upper lung zone demonstrating preserved A-lines with focal interruption by vertical hyperechoic B-line artifacts

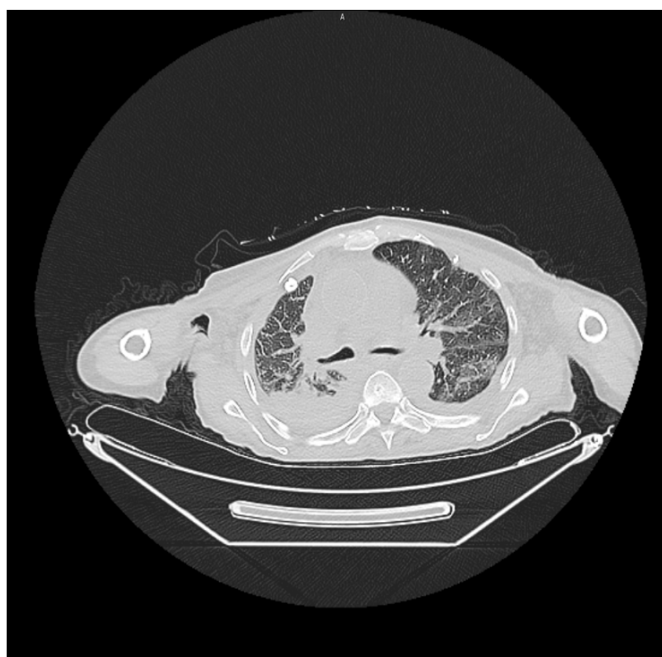


Figure 2. Non-contrast axial chest computed tomography image showing irregular pleural thickening and pleural-based lesions consistent with malignant pleural mesothelioma

On admission, arterial blood gas analysis revealed significant respiratory acidosis with a pH of 7.18 and a PaCO₂ level of 68 mmHg. Following initiation of non-invasive mechanical ventilation, repeat arterial blood gas analysis demonstrated improvement in gas exchange, with the pH increasing to 7.30 and PaCO₂ decreasing to 41 mmHg. Due to the continued rise in cardiac troponin levels, cardiology consultation was obtained. The patient was diagnosed with non-ST-elevation myocardial infarction and transferred to the coronary intensive care unit, where coronary angiography was subsequently performed.

DISCUSSION

This case highlights a key diagnostic challenge in the ED: the interpretation of LUS artifacts in patients with underlying pleural malignancy. Although B-lines are frequently associated with pulmonary edema in acute care settings, they are nonspecific artifacts reflecting increased acoustic interfaces caused by alterations in lung aeration or pleural integrity rather than a single pathological process.

In MPM, pleural thickening, nodularity, subpleural infiltration, and loculated effusions disrupt the normal pleural surface and may generate multiple B-lines that mimic diffuse interstitial syndrome.⁶ Additionally, pleural-based anechoic or hypoechoic lesions, as observed in our patient, are atypical for cardiogenic pulmonary edema and should prompt consideration of alternative diagnoses. These findings underscore the risk of misinterpretation when LUS is used in isolation, particularly in oncologic patients with complex pleuropulmonary pathology.

MPM is an aggressive disease with nonspecific clinical manifestations, often presenting with dyspnea, chest pain, or pleural effusion—symptoms that overlap with more common cardiopulmonary conditions encountered in the ED.⁷ While LUS provides valuable real-time bedside information regarding pleural morphology and subpleural involvement, its findings must be interpreted within the broader clinical context. Previous studies have shown that LUS can reliably detect pleural thickening, nodularity, and pleural-based masses, and in selected settings may even surpass computed tomography in identifying chest wall invasion.⁸ However, the presence of B-lines in malignant pleural disease should not be automatically attributed to pulmonary edema, as these artifacts may instead reflect pleural surface disruption or adjacent compressive atelectasis.

In our patient, although the presence of diffuse B-lines initially suggested an interstitial syndrome such as cardiogenic pulmonary edema, several clinical and sonographic features argued against volume overload as the primary mechanism. The patient did not demonstrate signs of acute fluid overload, such as hypertension, peripheral edema, or rapid radiographic progression compatible with pulmonary congestion. Moreover, LUS revealed that many of the B-lines originated directly from irregular, thickened pleural surfaces and pleural-based anechoic lesions corresponding to known malignant involvement on computed tomography. This spatial relationship between the pleural masses and the vertical artifacts supports the interpretation that the B-lines were generated by pleural and subpleural disruption caused by malignant mesothelioma rather than by diffuse interstitial edema. While concomitant pulmonary edema cannot be completely excluded in the setting of acute coronary syndrome, the overall clinical picture and imaging findings favored malignancy-related ultrasound artifacts as the predominant cause.

From an EM perspective, this case reinforces the importance of integrating LUS findings with clinical history, laboratory data, and complementary imaging modalities. Awareness that B-lines are not pathognomonic for pulmonary edema is essential to avoid diagnostic pitfalls and inappropriate management decisions, particularly in patients with known or suspected pleural malignancy.

CONCLUSION

This case highlights the potential for misleading LUS findings in patients with MPM presenting to the ED. Awareness of pleural-based pathology as a cause of B-lines is essential to avoid diagnostic pitfalls, and LUS findings should always be interpreted in conjunction with clinical context and complementary investigations.

ETHICAL DECLARATIONS

Informed Consent

Written informed consent was obtained from the patient included in this report. Signed consent forms are retained by the authors and are available upon request.

Peer Review Process

This report underwent external peer review.

Conflict of Interest

The author declare no conflicts of interest.

Financial Disclosure

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Author Contributions

The author is solely responsible for the conception, design, data collection, analysis, interpretation, literature review, writing, and critical review of the article.



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Comment “essential amino acids levels in individuals that attempted suicide”

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Keywords: Amino acids, depression, nutrition

Dear Author,

I read and examined your study with pleasure about the essential amino acid levels in suicide cases in the emergency room. In your study, it was found that the amino acids methionine, leucine, isoleucine, valine, lysine, threonine, phenylalanine and tryptophan were lower in the patient group. Essential amino acids are amino acids that are taken from external sources with food. Suicidal people with depression may have low levels of these amino acids since they also have malnutrition.

Depression may also occur indirectly due to methionine and tryptophan deficiency. Intake of adequate amino acids through proper nutrition reduces depression and reduces suicide attempts. This information is promising for the future. We hope you will conduct new studies with more patient groups.

In the study conducted by Rao et al.,¹ protein intake and therefore individual amino acids may affect brain functions and mental health. Most neurotransmitters in the brain are made from amino acids. The neurotransmitter dopamine is made from the amino acid tyrosine and the neurotransmitter serotonin from tryptophan. In case of deficiency of any of these two amino acids, there is not sufficient synthesis of the relevant neurotransmitters and this is associated with low mood and aggression in patients.

In the study conducted by Hees et al.,² essential amino acid levels were found to be low in celiac disease due to the decrease in the intake of plant proteins. In the same study, essential amino acid levels were low in patients with major depression, but no difference was detected between celiac patients and major depression patients. Essential amino acid deficiency due to celiac disease was found to be low. No relationship was found between major depression.

In the study conducted by Koochakpoor et al.,³ a relationship was found between low dietary intake of essential amino acids and depression and anxiety.

In the study conducted by Baranyi et al.,⁴ they found an inverse relationship between low levels of essential amino acids such as valine, leucine and isoleucine, and major depression.

In the light of this information, although your study shows a relationship between major depression and a decrease in essential amino acid intake, the number of patients in your study is small and your study is single. At the same time, there are other factors that cause major depression. In this regard, we recommend that patients be selected by eliminating other factors. There is not enough descriptive information about amino acids in your study. We also recommend that you conduct a study with a higher level of evidence by keeping a larger number of patients.

ETHICAL DECLARATIONS

Peer Review Process

This letter was externally peer-reviewed.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Disclosure

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Author Contributions


Conceptualization: EV, NE; Design: EV, NE; Supervision: EV, NE; Resources: EV, NE; Materials: EV, NE; Data Collection and/or Processing: EV, NE; Analysis and/or Interpretation: EV, NE; Literature Review: EV, NE; Writing–Original Draft: EV, NE; Writing–Review and Editing: EV, NE.

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Author reply “essential amino acids levels in individuals that attempted suicide”

 Tansu Gençer

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Dear Editor,

We would like to thank the author for the interest shown in our study entitled “basic amino acid levels in individuals with suicide attempts” and for the valuable comments provided.

In the letter, it was noted that the sample size of our study was limited and that studies conducted with larger patient groups may provide stronger evidence. In this regard, we would like to state that the sample size of our study was determined based on a statistical power analysis performed before the study was initiated. According to the analysis conducted by a biostatistics specialist, the inclusion of 35 participants in both the patient and control groups was sufficient to detect differences between the groups with respect to the variables evaluated in the study, and the statistical power was calculated as 0.90744. Accordingly, the study groups were established on the basis of this power analysis.

Nevertheless, as also highlighted in the literature, studies with larger sample sizes and multicenter designs would further strengthen the level of evidence on this subject. Therefore, future research involving larger patient populations may provide important contributions to the field.

We would like to thank the author for the constructive comments on our study and acknowledge that these contributions add valuable insight to the scientific discussion on this topic.

Sincerely,