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Coagulation Profile Variations in Septic Patients with Leukocytosis: A Cross-Sectional Study

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ABSTRACT

Sepsis is a life-threatening dysregulated host response to infection and is frequently associated with hematological and coagulation abnormalities. Leukocytosis reflects the inflammatory burden in sepsis, while alterations in coagulation parameters may indicate evolving sepsis-associated coagulopathy. The present cross-sectional observational study, conducted in the Department of Pathology of a tertiary care teaching hospital in southern India, aimed to evaluate coagulation profile variations in relation to leukocytosis among 40 patients with sepsis and a total leukocyte count >12,000 cells/mm³. Complete blood counts were performed on an automated five-part hematology analyzer, while prothrombin time (PT), international normalized ratio (INR) and activated partial thromboplastin time (APTT) were measured on an automated coagulation analyzer. The majority of patients were 41–60 years old (45.0%), with male predominance (62.5%); respiratory tract infections were the commonest source of sepsis (35.0%) and 57.5% required intensive care unit (ICU) admission. Mild, moderate and severe leukocytosis were observed in 30.0%, 45.0% and 25.0% of patients, respectively. Mean PT, APTT and INR increased progressively across mild, moderate and severe leukocytosis (PT 16.2/18.8/21.1 seconds; APTT 35.4/39.6/44.2 seconds; INR 1.32/1.48/1.65). The frequency of prolonged PT, prolonged APTT and elevated INR rose with increasing leukocyte counts and showed statistically significant associations ($p = 0.01$, 0.04 and 0.003, respectively). ICU patients had significantly greater derangement of PT, APTT and INR than non-ICU patients (all $p \leq 0.002$). Routine coagulation parameters, interpreted alongside leukocyte counts, may provide useful adjunctive information for assessing severity in septic patients in resource-limited settings.

Keywords: *Sepsis; Leukocytosis; Coagulation profile; Prothrombin time; Activated partial thromboplastin time.*

INTRODUCTION

Sepsis represents a dysregulated host response to infection resulting in life-threatening organ dysfunction and continues to pose a major global health challenge. According to the Global Burden of Disease Study, an estimated 49 million cases of sepsis and 11 million sepsis-related deaths occur worldwide each year, accounting for nearly one-fifth of all global deaths[1]. Despite advances in antimicrobial therapy, critical care support and early recognition strategies, sepsis remains associated with high morbidity and mortality, particularly in low- and middle-income countries, where delays in diagnosis and limited resources further exacerbate outcomes[2].

In the Indian context, the burden of sepsis is substantial and often underestimated. Hospital-based studies from India report sepsis-related mortality ranging from 30% to 60%, especially among patients admitted to intensive care units[3,4]. The epidemiology of sepsis in India differs from that in high-income countries, with a higher prevalence of tropical

infections, late presentation and a greater incidence of multi-organ dysfunction at the time of diagnosis[5]. These factors underscore the need for readily available, cost-effective laboratory markers that can assist clinicians in early risk stratification and disease assessment in routine clinical settings.

Hematological abnormalities are among the earliest and most consistently observed laboratory changes in sepsis. Leukocytosis, reflecting activation of the innate immune response, is a common finding and forms part of standard sepsis screening and severity assessment[6]. Elevated leukocyte counts have been associated with increased inflammatory burden, cytokine release and endothelial activation, all of which contribute to the complex pathophysiology of sepsis[7]. However, leukocytosis is not merely an inflammatory marker; emerging evidence suggests that it may be closely linked to downstream disturbances in coagulation pathways.

Sepsis-associated coagulopathy is a well-recognized but incompletely understood phenomenon, ranging from subclinical laboratory abnormalities to overt disseminated intravascular coagulation (DIC). The interaction between inflammation and coagulation in sepsis is bidirectional, with inflammatory mediators activating coagulation cascades, and coagulation abnormalities in turn further amplifying inflammatory responses[8]. Prolongation of prothrombin time (PT), activated partial thromboplastin time (APTT) and elevation of the international normalized ratio (INR) are frequently observed and have been associated with increased disease severity, organ dysfunction and mortality[9,10]. Importantly, these coagulation parameters are routinely available in most tertiary care centres, making them potentially valuable tools for early clinical assessment.

Despite extensive research on sepsis-associated coagulopathy, the existing literature predominantly focuses on severe sepsis, septic shock or patients with overt DIC. Many studies emphasize advanced biomarkers such as D-dimer, fibrin degradation products, protein C levels or thromboelastography, which may not be universally accessible in resource-limited settings[11,12]. Moreover, the relationship between the degree of leukocytosis and routine coagulation profile abnormalities has not been adequately explored, particularly in cross-sectional clinical settings. Whether increasing leukocyte counts parallel the extent of coagulation derangement in septic patients remains an area with limited and inconsistent evidence.

In Indian clinical practice, complete blood counts and basic coagulation profiles are among the most frequently ordered investigations in patients with suspected sepsis. However, these parameters are often interpreted in isolation rather than in relation to each other. Understanding the association between leukocytosis and alterations in PT, APTT and INR may provide clinicians with a simple, integrated approach to identifying patients at higher risk of coagulation dysfunction, especially where advanced diagnostic modalities are unavailable. Addressing this gap is particularly relevant in high-volume government hospitals and peripheral healthcare settings.

Given the substantial burden of sepsis in India, the frequent occurrence of leukocytosis in septic patients and the clinical implications of coagulation abnormalities, there is a clear need to systematically evaluate the relationship between these routinely available laboratory parameters. Therefore, the present study was undertaken to evaluate the coagulation profile—specifically PT, APTT and INR—in relation to the degree of leukocytosis among patients with sepsis in a tertiary care setting.

MATERIALS AND METHODS

Study design and setting

This was a cross-sectional, hospital-based observational study conducted in the Department of Pathology, Clinical Pathology Central Laboratory, Sri Venkateswara Ramnarayan Ruia Government General Hospital, Tirupati, Andhra Pradesh, over a period of nine months. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the Institutional Scientific and Ethics Committee of Sri Venkateswara Medical College (Letter No.: 46/2025). Written informed consent was obtained from all participants or, where applicable, from their legally authorized representatives prior to enrolment.

Study population

Patients diagnosed with sepsis who demonstrated leukocytosis on routine hematological investigations were recruited consecutively from inpatient wards and intensive care units (ICUs) of the hospital during the study period. A total of 40 patients meeting the eligibility criteria were enrolled.

Inclusion and exclusion criteria

Patients of either sex and all age groups diagnosed with sepsis and with a total leukocyte count >12,000 cells/mm³ were included. Patients with known chronic liver disease, those receiving anticoagulant or antiplatelet therapy prior to admission, patients with known inherited coagulation disorders or hematological malignancies, those with bone marrow disorders, and pregnant women were excluded to minimize confounding factors influencing coagulation parameters.

Sample collection
Venous blood samples were collected aseptically under standard precautions. Blood was drawn into two vacutainers: one containing ethylenediaminetetraacetic acid (EDTA) for hematological analysis and another containing 3.2% sodium citrate for coagulation studies. Samples were transported promptly to the central laboratory and processed according to standard operating procedures.

Hematological analysis
Complete blood counts were performed using an automated five-part hematology analyzer (ERBA ELITE 580). Parameters recorded included hemoglobin concentration, total leukocyte count, differential leukocyte count and platelet count. Leukocytosis was categorized on the basis of total leukocyte count into mild (12,000–20,000 cells/mm³), moderate (20,000–30,000 cells/mm³) and severe (>30,000 cells/mm³). Peripheral blood smears were prepared from EDTA samples, stained with Leishman stain and examined by a qualified pathologist for leukocyte morphology, toxic granulation, left shift and platelet adequacy.

Coagulation profile analysis
PT, INR and APTT were measured using an automated coagulation analyzer after centrifugation of citrated blood samples. Prolongation of PT, APTT and elevation of INR were interpreted on the basis of standard laboratory reference ranges. Internal quality control procedures were performed daily to ensure analytical accuracy.

Clinical and severity assessment
Clinical details, including the source of infection, the need for ICU admission and the presence of organ dysfunction, were recorded from patient case records. ICU admission was used as a surrogate marker of disease severity. Laboratory findings were correlated with clinical status to assess the extent of coagulation derangement in relation to leukocyte count and disease severity.

Statistical analysis
All data were entered into Microsoft Excel and analyzed using JASP version 0.18.3.0. Continuous variables were expressed as mean ± standard deviation and categorical variables as frequencies and percentages. Associations between leukocyte count categories and coagulation abnormalities were assessed using the chi-square test. Comparison of coagulation parameters between ICU and non-ICU patients was performed using the independent-samples t-test. A p-value <0.05 was considered statistically significant.

RESULTS
A total of 40 patients with sepsis and leukocytosis were included in the study.

Baseline demographic and clinical characteristics
The baseline demographic and clinical profile of the study population is summarized in Table 1. The majority of patients (45.0%) were 41–60 years of age, with a male predominance (62.5%). Respiratory tract infections (35.0%) were the most common source of sepsis, followed by urinary (25.0%) and abdominal (22.5%) sources. ICU admission was required in 57.5% of patients.

Table 1. Baseline demographic and clinical characteristics of the study population (n = 40).

Variable	Category	Frequency (%)
Age (years)	≤40	11 (27.5)
	41–60	18 (45.0)
	>60	11 (27.5)
Sex	Male	25 (62.5)
	Female	15 (37.5)
Source of sepsis	Respiratory	14 (35.0)
	Urinary	10 (25.0)
	Abdominal	9 (22.5)
	Others	7 (17.5)
ICU admission	Yes	23 (57.5)
	No	17 (42.5)

Distribution of leukocytosis grades
On the basis of total leukocyte count, 30.0% of patients had mild leukocytosis, 45.0% moderate leukocytosis and 25.0% severe leukocytosis (Table 2; Figure 1).

Table 2. Distribution of grades of leukocytosis among septic patients (n = 40).

Total leukocyte count (cells/mm³)	Grade	Number of patients (n)	Percentage (%)
12,000–20,000	Mild	12	30.0
20,000–30,000	Moderate	18	45.0
>30,000	Severe	10	25.0
Total		**40**	**100.0**

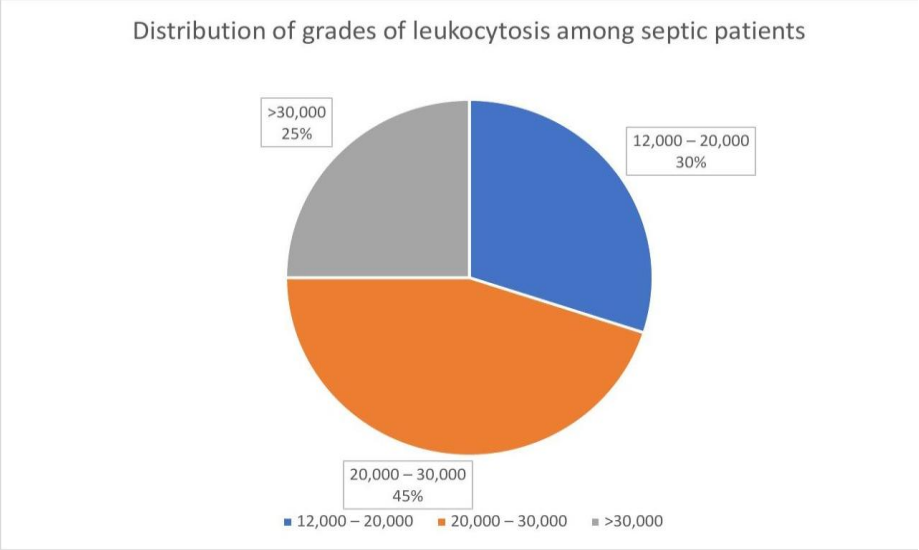

Figure 1. Distribution of grades of leukocytosis among septic patients (n = 40).

Coagulation parameters according to severity of leukocytosis

A progressive increase in mean PT, APTT and INR was observed with increasing severity of leukocytosis (Table 3). Mean PT, APTT and INR were 16.2 seconds, 35.4 seconds and 1.32 in patients with mild leukocytosis; 18.8 seconds, 39.6 seconds and 1.48 in those with moderate leukocytosis; and 21.1 seconds, 44.2 seconds and 1.65 in patients with severe leukocytosis.

Table 3. Correlation between grades of leukocytosis and mean coagulation profile parameters among septic patients (n = 40).

Grade of leukocytosis	Number of patients n (%)	Prothrombin time (seconds), Mean	Activated partial thromboplastin time (seconds), Mean	International normalized ratio, Mean
Mild (12,000–20,000 cells/mm³)	12 (30.0)	16.2	35.4	1.32
Moderate (20,000–30,000 cells/mm³)	18 (45.0)	18.8	39.6	1.48
Severe (>30,000 cells/mm³)	10 (25.0)	21.1	44.2	1.65

Association between leukocytosis severity and coagulation abnormalities

The frequency of abnormal PT, abnormal APTT and elevated INR increased with rising leukocyte counts (Table 4; Figure 2). Among patients with severe leukocytosis, 80.0% had abnormal PT, 60.0% had abnormal APTT and 80.0% had elevated INR, compared with 50.0%, 41.7% and 41.7%, respectively, in patients with mild leukocytosis. These associations were statistically significant for PT (p = 0.01), APTT (p = 0.04) and INR (p = 0.003).

Table 4. Association between severity of leukocytosis and coagulation abnormalities.

Leukocyte count category	Abnormal PT n (%)	Abnormal APTT n (%)	Elevated INR n (%)
12,000–20,000 (n=12)	6 (50.0)	5 (41.7)	5 (41.7)
20,000–30,000 (n=18)	12 (66.7)	10 (55.6)	11 (61.1)
>30,000 (n=10)	8 (80.0)	6 (60.0)	8 (80.0)
p-value	**0.01**	**0.04**	**0.003**

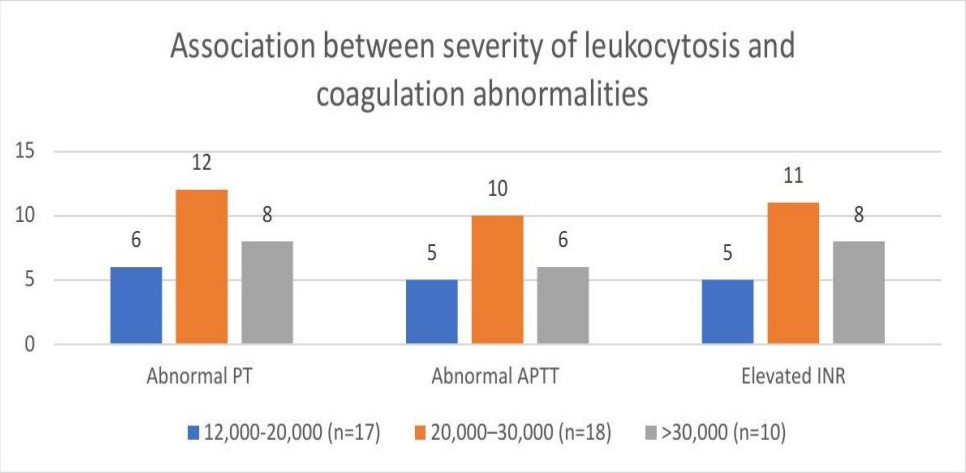

Figure 2. Association between severity of leukocytosis and coagulation abnormalities (n = 40).

Coagulation parameters in ICU versus non-ICU patients

Patients admitted to the ICU demonstrated significantly greater derangement of coagulation parameters compared with non-ICU patients (Table 5; Figure 3). Mean PT (18.2 ± 4.1 vs 14.9 ± 3.2 seconds, $p < 0.001$), INR (1.56 ± 0.38 vs 1.24 ± 0.29, $p = 0.002$) and APTT (45.3 ± 9.1 vs 36.4 ± 6.8 seconds, $p < 0.001$) were all significantly higher in ICU patients than in non-ICU patients.

Table 5. Comparison of coagulation parameters between ICU and non-ICU patients.

Parameter	ICU (n = 23)	Non-ICU (n = 17)	p-value
PT (seconds)	18.2 ± 4.1	14.9 ± 3.2	**<0.001**
INR	1.56 ± 0.38	1.24 ± 0.29	**0.002**
APTT (seconds)	45.3 ± 9.1	36.4 ± 6.8	**<0.001**

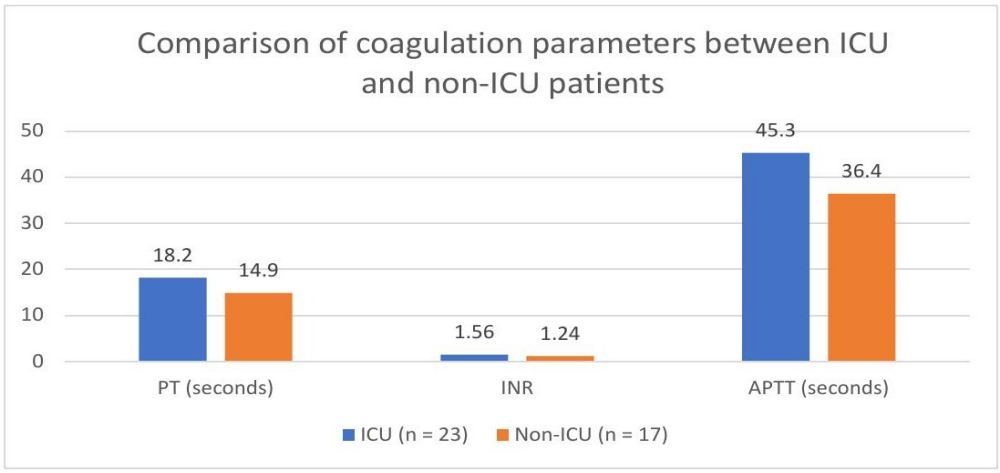

Figure 3. Comparison of coagulation parameters between ICU and non-ICU patients.

DISCUSSION

The present cross-sectional study evaluated coagulation profile variations in septic patients with leukocytosis and demonstrated several clinically relevant findings. The study population predominantly comprised middle-aged and elderly individuals, with a male predominance and respiratory tract infections as the leading source of sepsis. This demographic and clinical profile is consistent with previous Indian and Asian studies, including the MOSAICS study, which reported respiratory infections as a leading cause of sepsis and a higher proportion of male patients requiring intensive care[4]. The high proportion of ICU admissions (57.5%) in the present study reflects the severity of illness in the study population and aligns with observations that sepsis in tertiary care hospitals in India often presents late with significant organ involvement[3,5].

Leukocytosis is a well-recognized manifestation of the systemic inflammatory response in sepsis and reflects activation of innate immune pathways[6,7]. In the present study, moderate to severe leukocytosis constituted 70% of cases (Table 2), highlighting a substantial inflammatory burden in the study population. Importantly, increasing grades of leukocytosis were associated with progressive prolongation of PT and APTT, as well as elevation of INR (Table 3). This graded relationship supports the concept that an escalating inflammatory response in sepsis is closely linked to worsening coagulation abnormalities.

The interplay between inflammation and coagulation in sepsis has been extensively described, with inflammatory mediators triggering activation of the coagulation cascade while simultaneously impairing anticoagulant and fibrinolytic pathways[8,9]. Levi and van der Poll emphasized that coagulation abnormalities in sepsis exist on a continuum, ranging from mild laboratory derangements to overt DIC[8]. The present study reinforces this continuum by demonstrating increasing coagulation derangement with rising leukocyte counts, even in the absence of overt clinical bleeding or formal DIC scoring.

An important finding of the present study is the increasing frequency of coagulation abnormalities with higher leukocytosis severity (Table 4). Patients with severe leukocytosis showed the highest proportion of prolonged PT, prolonged APTT and elevated INR. Although this study did not assess advanced coagulation markers or DIC scores, the observed pattern is consistent with prior literature indicating that worsening inflammatory burden correlates with greater coagulation pathway disruption[9-11]. Gando et al. have highlighted that routine coagulation tests often become abnormal early in sepsis and may precede overt clinical manifestations of coagulopathy[10].

The comparison between ICU and non-ICU patients further strengthens the association between disease severity and coagulation abnormalities (Table 5). ICU-admitted patients demonstrated significantly higher mean PT, APTT and INR compared with non-ICU patients. These findings are concordant with earlier studies reporting more pronounced coagulation derangement among critically ill septic patients requiring intensive care support[4,9]. This observation underscores the relevance of routine coagulation testing in monitoring disease severity rather than as a tool solely for bleeding risk assessment.

From a clinical perspective, the findings of the present study have practical implications. In many Indian healthcare settings, advanced biomarkers of sepsis-associated coagulopathy—such as D-dimer, thrombin–antithrombin complexes or thromboelastography—are not routinely available. However, complete blood counts and basic coagulation profiles are widely accessible. Demonstrating a clear association between leukocytosis severity and routine coagulation abnormalities suggests that these commonly available parameters can be interpreted together to provide a more integrated assessment of disease severity in septic patients[5,8].

Limitations

The present study has certain limitations that merit consideration. The cross-sectional design precludes assessment of temporal changes in coagulation parameters or their prognostic significance. The sample size was modest, and advanced coagulation markers or formal DIC scoring systems were not evaluated. Additionally, leukocytosis was used as a surrogate marker of inflammatory burden without correlation with cytokine levels or with severity scores such as the Sequential Organ Failure Assessment (SOFA). Despite these limitations, the study provides valuable insight into routine laboratory patterns in septic patients and reflects real-world clinical practice in a tertiary care setting.

CONCLUSIONS

The present study demonstrates that coagulation abnormalities are common among septic patients with leukocytosis and tend to worsen with increasing leukocyte counts and clinical severity. Prolongation of prothrombin time, elevation of international normalized ratio and prolongation of activated partial thromboplastin time were frequently observed, particularly in patients requiring intensive care. These findings highlight the close association between inflammatory burden and coagulation derangement in sepsis. Routine hematological and coagulation parameters, when interpreted together, may provide useful adjunctive information for clinical assessment in resource-limited settings. Further prospective studies are warranted to evaluate their prognostic significance and impact on clinical outcomes.

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Conflict of Interest

The authors declare that they have no conflict of interest.

Ethical Approval: Obtained from the Institutional Ethics Committee, Sri Venkateswara Medical College (Letter No.: 46/2025).

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Authors' Contributions
ML Bharathi: concept and design of the study, acquisition of data, statistical analysis, drafting of the manuscript. S Rajasekhar Reddy: concept and design, interpretation of data, critical revision of the manuscript.
U Parameshwari Babu & Govindu Madhavi: laboratory supervision, interpretation of data, critical revision of the manuscript.
K Thulasiram: clinical supervision, interpretation of data, critical revision of the manuscript.
All authors read and approved the final version of the manuscript to be published.

REFERENCES

1. Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395(10219):200–11.
2. Fleischmann C, Scherag A, Adhikari NKJ, et al. Assessment of global incidence and mortality of hospital-treated sepsis: current estimates and limitations. Am J Respir Crit Care Med. 2016;193(3):259–72.
3. Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. Crit Care Med. 2013;41(2):580–637.
4. Phua J, Ngerng WJ, See KC, et al. Characteristics and outcomes of severe sepsis in Asian intensive care units: the MOSAICS study. Intensive Care Med. 2011;37(8):1348–55.
5. Indian Council of Medical Research. Guidelines for the management of sepsis in India. New Delhi: Indian Council of Medical Research; 2017.
6. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801–10.
7. Hotchkiss RS, Moldawer LL, Opal SM, et al. Sepsis and septic shock. Nat Rev Dis Primers. 2016;2:16045.
8. Levi M, van der Poll T. Coagulation and sepsis. Thromb Res. 2017;149:38–44.
9. Iba T, Levy JH, Raj A, Warkentin TE. Advance in the management of sepsis-associated coagulopathy and disseminated intravascular coagulation. J Intensive Care. 2019;7:1.
10. Gando S, Levi M, Toh CH. Disseminated intravascular coagulation. Nat Rev Dis Primers. 2016;2:16037.
11. Bakhtiari K, Meijers JC, de Jonge E, Levi M. Prospective validation of the International Society on Thrombosis and Haemostasis scoring system for disseminated intravascular coagulation. J Thromb Haemost. 2004;2(6):1054–60.
12. Semeraro N, Ammollo CT, Semeraro F, Colucci M. Sepsis-associated disseminated intravascular coagulation and thromboembolic disease. Semin Thromb Hemost. 2015;41(6):650–8.