Přehledový článek | Review article

Relationship of Neutrophil-Lymphocyte Ratio (NLR) as Diagnostics and Prognostics Tools of Deep Vein Thrombosis (DVT): Current Status

Zanella Yolanda Lie, Yan Efrata Sembiring

Department of Thoracic, Cardiac and Vascular Surgery, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
Department of Thoracic, Cardiac and Vascular Surgery, Dr Soetomo General Academic Hospital, Surabaya, Indonesia

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SOUHRN

Zdá se, že by poměr neutrofilů a lymfocytů (neutrophil-lymphocyte ratio, NLR) mohl být slibným biomarkerem u trombózy hlubokých žil (deep vein thrombosis, DVT), neboť odráží spletitý vztah mezi zánětem a trombózou. Tento přehledový článek zkoumá dvojí úlohu NLR jako diagnostického i prognostického nástroje při léčbě DVT. Současné důkazy ukazují, že zvýšené hodnoty NLR (> 3,0) těsně korelují s výskytem DVT, její závažností a s rizikem recidivy, zvláště u vysoce rizikových populací, jako jsou pacienti po operaci a pacienti s onkologickým onemocněním. Z hlediska mechanismu NLR zaznamenává protrombotické účinky neutrofilních extracelulárních pastí (neutrophil extracellular trap, NET) a antitrombotickou regulaci lymfocyty, a umožňuje tak bližší poznání patogeneze onemocnění. Pokud se zkombinuje s tradičními nástroji, jako jsou Wellsova kritéria, zvyšuje NLR z klinického hlediska diagnostickou přesnost, a ve specificitě při DVT asociované s onkologickým onemocněním je spolehlivější než D-dimer. Z hlediska prognózy predikují hodnoty NLR > 4,0 nepříznivější výsledný stav včetně post-trombotického syndromu a kratšího přežití pacientů s malignitami. Přes existující limitace v oblasti standardizace a specificity činí nákladová účinnost a běžná dostupnost z NLR cenný přídatný parametr při léčbě DVT. V budoucnu se výzkum musí zaměřit na stanovení standardizovaných mezních hodnot a posouzení významu monitorování NLR při použití antikoagulace.

Keywords:
Deep vein thrombosis
Diagnostic marker
Neutrophil-lymphocyte ratio

ABSTRACT

The neutrophil-lymphocyte ratio (NLR) has emerged as a promising biomarker in deep vein thrombosis (DVT), reflecting the intricate relationship between inflammation and thrombosis. This literature review examines NLR's dual role as both a diagnostic and prognostic tool in DVT management. Current evidence demonstrates that elevated NLR (>3.0) correlates strongly with DVT occurrence, severity, and recurrence risk, particularly in high-risk populations such as postoperative and cancer patients. Mechanistically, NLR captures the pro-thrombotic effects of neutrophil extracellular traps (NETs) and the anti-thrombotic regulation by lymphocytes, offering insights into disease pathogenesis. Clinically, NLR enhances diagnostic accuracy when combined with traditional tools like Wells' criteria and outperforms D-dimer in specificity for cancer-associated DVT. Prognostically, NLR >4.0 predicts poorer outcomes including post-thrombotic syndrome and reduced survival in malignancy. While limitations exist regarding standardization and specificity, NLR's cost-effectiveness and routine availability position it as a valuable adjunct in DVT management. Future research should focus on establishing standardized cut-offs and exploring therapeutic implications of NLR monitoring during anticoagulation.

Address: Yan Efrata Sembiring, Jl. Mayjen Prof. Dr. Moestopo 6-8 Surabaya 60286, Indonesia, e-mail: yan-e-s@fk.unair.ac.id
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Introduction

Deep vein thrombosis (DVT) is a serious medical condition characterized by the formation of blood clots within the deep veins, most commonly in the lower extremities. As a major component of venous thromboembolism (VTE), DVT not only increases the risk of morbidity but also mortality, particularly when progressing to pulmonary embolism (PE).[1,2] The incidence of DVT is reported to range from 50 to 100 cases per 100,000 people annually, with recurrence rates reaching 10% in the first year and 30% within 5–8 years after initial diagnosis.[3,4] Current diagnosis of DVT relies on clinical assessment, imaging, and biomarkers such as D-dimer, which, although sensitive, has limitations in specificity.[5]

Recent studies have highlighted the potential of the neutrophil-lymphocyte ratio (NLR) as a novel biomarker for DVT. NLR, derived from routine complete blood counts (CBC), reflects the balance between pro-inflammatory neutrophils and anti-inflammatory lymphocytes, offering insights into the inflammatory state associated with thrombosis.[6] This literature review explores the role of NLR as both a diagnostic and prognostic tool in DVT, examining its pathophysiological basis, clinical correlations, and prognostic value.

Inflammation in DVT pathogenesis

Inflammation plays a pivotal role in the pathogenesis of DVT, as described by Virchow's triad, which emphasizes endothelial injury, stasis, and hypercoagulability as key contributors.[7] Neutrophils, the primary mediators of innate immunity, contribute to thrombus formation through the release of neutrophil extracellular traps (NETs). These structures promote coagulation by activating platelets and providing a scaffold for fibrin deposition.[8] Concurrently, inflammatory cytokines such as IL-6 and TNF-α enhance endothelial activation and tissue factor expression, further driving the hypercoagulable state.[9] The neutrophil-lymphocyte ratio captures this inflammatory imbalance, with elevated levels (>3.0) strongly correlating with DVT severity and recurrence risk.[10]

Neutrophil-lymphocyte ratio

The Neutrophil-lymphocyte ratio is a simple, cost-effective biomarker derived from routine CBC, reflecting systemic inflammation and immune response dynamics.[11] NLR has gained attention as a diagnostic and prognostic marker in various conditions, including cardiovascular diseases and cancer, due to its ability to indicate the balance between pro-inflammatory and anti-inflammatory pathways.[12] In the context of DVT, elevated NLR values signify increased neutrophil activity and reduced lymphocyte-mediated immune regulation, both of which contribute to thrombogenesis.[13] Studies have demonstrated that NLR is an independent predictor of DVT, particularly in high-risk populations such as postoperative and cancer patients.[14]

Neutrophils in DVT pathophysiology

Neutrophils play a central role in DVT development through mechanisms involving NETosis and cytokine release. NETs, composed of DNA, histones, and proteases, not only trap pathogens but also promote thrombosis by activating coagulation factors such as factor XII and inhibiting fibrinolysis.[15] Pro-inflammatory cytokines like IL-6 further amplify neutrophil recruitment and NET formation, creating a vicious cycle of inflammation and coagulation.[16] Elevated neutrophil counts and persistent NETosis are associated with larger thrombi and delayed resolution, as observed in patients with high NLR (>4.0).[17] These findings underscore neutrophils as key players in bridging inflammation and thrombosis in DVT.

Role of lymphocytes in DVT pathophysiology

Lymphocytes, particularly regulatory T cells (Tregs), modulate the immune response and play a protective role against excessive thrombosis. Tregs suppress endothelial activation and tissue factor expression, thereby reducing thrombin generation and fibrin deposition.[18] Lymphopenia, or reduced lymphocyte counts, disrupts this balance, leading to unopposed inflammation and hypercoagulability.[19] In DVT patients, low lymphocyte counts are associated with higher recurrence rates and poorer outcomes, highlighting the importance of lymphocyte-mediated immune regulation in thrombus resolution.[20]

Hypercoagulability and NLR

The neutrophil-lymphocyte ratio serves as a biomarker of hypercoagulability, integrating both cellular and mo-

Table 1 – Pathophysiological mechanisms linking neutrophils, lymphocytes, and IL-6 to NLR elevation in DVT

Factors	Pathophysiology	Impacts on NLR
↑ **Neutrophile**	- Activation of factor XII & platelets via NETs - Increased TF	↑ NLR
↓ **Lymphocyte**	- Decreased IL-10 production (anti-inflammatory) - Failure to inhibit thrombosis	↑ NLR
↑ **IL-6**	- Stimulation of fibrinogen production - Inhibition of fibrinolysis	↑ NLR

lecular mechanisms of thrombosis. Elevated NLR reflects increased neutrophil activity (e.g., NET release) and diminished lymphocyte function (e.g., reduced Treg activity), both of which contribute to a pro-thrombotic state.[21] Clinically, high NLR values correlate with DVT severity, recurrence, and complications such as post-thrombotic syndrome (PTS) (**Table 1**).[22] This ratio provides a practical tool for risk stratification, particularly in cancer patients, where NLR ≥3.5 is associated with higher VTE rates and reduced survival.[23]

Clinical correlation in diagnostics

NLR has emerged as a valuable adjunct in DVT diagnosis, particularly in settings where imaging is not immediately available. Studies have shown that NLR >3.5–4.0 independently predicts DVT occurrence, with sensitivity and specificity comparable to traditional biomarkers like D-dimer.[24] For example, in emergency departments, NLR integration with clinical scoring systems (e.g., Wells' criteria) improves diagnostic accuracy.[25] Additionally, NLR's cost-effectiveness and routine availability make it an attractive tool for early DVT detection, especially in resource-limited settings.[26]

Prognostic value

Beyond diagnosis, NLR serves as a robust prognostic marker in DVT. Elevated NLR (>4.0) is associated with larger thrombus burden, higher recurrence rates, and increased risk of PTS.[27] In cancer-associated DVT, NLR ≥3.5 predicts poorer survival outcomes, with pancreatic cancer patients exhibiting median survival of 6 months compared to 12 months in those with low NLR.[28] Furthermore, NLR dynamics during anticoagulation therapy may reflect treatment efficacy, with persistently high levels indicating resistance or occult malignancy.[29] These prognostic insights highlight NLR's potential in guiding personalized management strategies for DVT patients.

Conclusions

The Neutrophil-Lymphocyte Ratio represents a promising biomarker for DVT, bridging inflammation and thrombosis in both diagnostic and prognostic contexts. While NLR alone cannot replace imaging, its integration into clinical workflows enhances risk stratification and personalized care, particularly for high-risk populations. Future research should focus on standardizing NLR cut-offs and exploring its therapeutic implications, such as targeting NETosis or modulating lymphocyte function. With ongoing advancements, NLR may become an indispensable tool in the comprehensive management of DVT.

Conflict of interest
None.

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Ethical statement
This article was written in line with the principles of the Declaration of Helsinki.

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