Systemic Immune-Inflammation Index as a Potential Biomarker for Predicting Acute Pulmonary Embolism: A Systematic Review

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Running head: Systemic Immune-Inflammation Index in Acute Pulmonary Embolism
Abstract

**Background:** Acute pulmonary embolism (APE) is a life-threatening condition with a high mortality rate. The pathophysiology involves various complex processes. The systemic immune-inflammatory index (SII) is a well-known biomarker that reflects the intricate balance between pro-inflammatory and anti-inflammatory immune components. In this systematic review, we aim to determine the significance of SII as a potential biomarker for APE.

**Method:** We utilized PubMed, ProQuest, EBSCOHost, and Google Scholar to search for articles. We assessed bias risk using the Newcastle Ottawa Scale (NOS). The outcomes we examined included in-hospital and long-term mortality, the severity of APE, and the sensitivity and specificity of the SII in predicting APE.

**Results:** Four studies, involving 2,038 patients, were included for analysis. These studies discuss the use of SII in predicting APE severity, APE mortality, high-risk APE, and the occurrence of APE. SII demonstrates significant results in predicting each of these variables. Furthermore, each study establishes different SII cut-off values. Specifically, a cut-off of 1161 predicts massive APE events with a sensitivity of 91% and a specificity of 90%. A cut-off of >1235.35 differentiates high-risk APE with a sensitivity of 87.32% and a specificity of 68.85%. A cut-off of >1111x10⁹ predicts overall mortality with a sensitivity of 72% and a specificity of 51%. Finally, a cut-off at 1839.91 predicts APE events with a sensitivity of 75.8% and a specificity of 61.9%.

**Conclusion:** The SII can be employed as a potential new biomarker to predict outcomes in APE patients, particularly the occurrence, severity, and mortality of APE.

**Keywords:** Immune Marker, Inflammation, Prognosis, Pulmonary Embolism, Vascular Diseases

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**What is new? What is important?**

- First systematic review that examines the usefulness of SII as a potential biomarker in APE.
- SII is effective as a diagnostic and prognostic biomarker in conjunction with existing gold standards.

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**INTRODUCTION**
Acute pulmonary embolism (APE) is a life-threatening condition characterized by the obstruction of pulmonary arteries by blood clots, leading to compromised blood flow to the lungs. Pulmonary embolism (PE) is a manifestation of venous thromboembolism (VTE) with the most severe clinical presentation, capable of causing sudden cardiac death, and is often a result of complications from deep vein thrombosis [1]. PE ranks as the third most common cardiovascular disease after coronary artery disease and stroke. Currently, it is estimated that PE occurs in approximately 60 to 70 cases per 100000 people, with a diagnostic rate of only 30-45% of patients before death [2].

Most PEs result from emboli originating in the lower extremities, which occlude the pulmonary vessels and cause hemodynamic disturbances. The pathophysiology of PE involves various complex processes, including thrombogenesis, inflammation, and hemodynamic disturbances [3,4]. Systemic inflammation and immune dysregulation play vital roles in the pathophysiology of acute PE, contributing to endothelial dysfunction, platelet activation, and the inflammatory cascade. Existing research suggests that inflammation and thrombogenesis can mutually activate each other. Consequently, there is a growing interest in identifying biomarkers that can capture the underlying inflammatory and immune processes to aid in prognostication [5].

The systemic immune-inflammation index (SII) has garnered attention due to its ability to integrate routine peripheral blood counts, such as neutrophils, lymphocytes, and platelets, thereby offering a comprehensive assessment of the systemic inflammatory status. SII has been utilized to determine disease activity in various conditions, including rheumatoid arthritis, cancer, and cardiac arrest. The results of this study indicate that SII exhibits greater potential for evaluating and predicting prognosis and survivability compared to several other markers [6-8].

Several studies have been conducted to determine the potential of SII in predicting VTE events [9,10]. In 2020, SII was used specifically to predict PE for the first time [11]. The prognostic value of SII can be attributed to its ability to reflect the intricate balance between pro-inflammatory and anti-inflammatory components of the immune system. Elevated SII levels indicate a state of increased inflammation and immune activation, which can contribute to vascular damage, thrombus burden, and impaired physiological responses [12].

Based on our knowledge, no systematic review have been found to date that examine the usefulness of SII in APE. The utilization of SII is expected to be a novel breakthrough, particularly in healthcare facilities with limited diagnostic capabilities. Hence, this study aims to determine the significance of SII as a potential biomarker for APE.
MATERIALS AND METHODS

This study adheres to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) as a writing guide and has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the following registration number: CRD42023459350 [13,14]. In this systematic review study, researchers utilized four search engines, namely PubMed, ProQuest, EBSCOHost, and Google Scholar, to identify research articles for inclusion. The selected research articles encompassed publications from July 1st, 2008, to July 1st, 2023. The article retrieval process was concluded in August 2023.

Search strategy

The keywords used in the article search were "Systemic immune inflammation index" OR "SII" AND "biologic marker" OR "biomarker" AND "acute pulmonary embolism" OR "acute PE." The keywords were adapted based on the specific search engine utilized.

Eligibility criteria

This study utilized the PICOS formula for the inclusion criteria as follows: 1) P-Population: Patients diagnosed with acute pulmonary embolism; 2) I-Intervention: Patients who underwent a complete blood count to obtain SII results and confirmed the diagnosis of pulmonary embolism through CT scan; 3) C-Comparison: Severity of APE or patient mortality; 4) O-Primary outcomes: The mortality and severity of APE, sensitivity and specificity of the SII; 5) S-Study: Randomized or non-randomized controlled trials, cohort, case control, case series, and cross sectional.

The exclusion criteria encompassed: 1) Studies not published in English; 2) Literature reviews, systematic reviews, meta-analyses, editorials, letters to the editor, and conference abstracts; 3) Unpublished studies; 4) Studies without full-text or incomplete data.

Selection process

The first step involves independently searching for articles from various search engines by AS and KT. In case of differences in opinion, discussions and consultations will be conducted with the third researcher (SL).

Data collection process
After the initial article selection process, AS and KT independently screened and obtained full-text papers. Subsequently, data collection for each article was conducted independently by AS and KT. The collected data was then merged and validated by AS. In the event of any disagreements, discussions and consultations will take place with the third researcher (SL).

Data items

The outcomes were in-hospital and long-term mortality, as well as the severity of APE (as defined by each study). Other outcomes included the sensitivity and specificity of the SII in predicting APE outcomes, including the occurrence, mortality, and severity of APE (each with an SII cut-off).

Study risk of bias assessment

In this study, we utilized the Newcastle-Ottawa Scale (NOS) to evaluate each observational study conducted. The NOS assesses three criteria for each study: selection, comparability, and outcome [15]. In this study, we used the NOS for the cohort study and adapted NOS for the cross-sectional study [16,17]. The interpretation of the values used is as follows: scores of 7-9 indicate a low risk of bias, scores of 4-6 indicate a high risk of bias, and scores of 0-3 indicate a very high risk of bias. AS and KT performed the assessment, and in the event of any discrepancies, discussion and consultation were conducted with the third researcher (SL).

RESULTS

Study selection

We have conducted a search for articles in the available databases and found a total of 933 articles. After the initial screening based on titles, duplicate articles, and abstracts, we have identified 705 articles that will undergo full-text examination. Ultimately, a total of 35 studies were assessed for eligibility, with four studies included in qualitative synthesis. The conclusion from the PRISMA flowchart for this study can be seen in Figure 1.

Study characteristics

The final four studies were included in the qualitative synthesis. The study designs used retrospective cohort study and cross-sectional study. They were published between 2020 and
2022, with a total of 2038 patients as subjects. The demographic data and characteristics of the studies used are described in Tables 1 and 2.
Risk of bias in studies

The results of the NOS examination (Table 3 and 4) indicate that all the studies used were good quality.

**Figure 1.** PRISMA flow diagram of the studies selection for inclusion in the systematic review.
### Table 1. Basic demographics data of the included studies.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Group</th>
<th>Sample size</th>
<th>Age (years)*</th>
<th>Male (%)</th>
<th>Female (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gok M et al. [11], 2020</td>
<td>Nonmassive APE</td>
<td>117</td>
<td>58 ± 18</td>
<td>47 (40.2)</td>
<td>70 (59.8)</td>
</tr>
<tr>
<td></td>
<td>Submassive APE</td>
<td>211</td>
<td>66 ± 16</td>
<td>101 (47.9)</td>
<td>110 (52.1)</td>
</tr>
<tr>
<td></td>
<td>Massive APE</td>
<td>114</td>
<td>67 ± 15</td>
<td>54 (47.4)</td>
<td>60 (52.6)</td>
</tr>
<tr>
<td>Ösken A et al. [18], 2021</td>
<td>APE survivor</td>
<td>434</td>
<td>59.7 ± 15.8</td>
<td>198 (54.1)</td>
<td>236 (45.9)</td>
</tr>
<tr>
<td></td>
<td>APE non-survivor</td>
<td>80</td>
<td>71.2 ± 14.1</td>
<td>34 (42.5)</td>
<td>46 (57.5)</td>
</tr>
<tr>
<td>Duyan M et al. [19], 2022</td>
<td>Non-high risk APE</td>
<td>122</td>
<td>59.6 ± 16.5</td>
<td>67 (54.9)</td>
<td>55 (45.1)</td>
</tr>
<tr>
<td></td>
<td>High risk APE</td>
<td>71</td>
<td>69.1 ± 15.5</td>
<td>54 (76.1)</td>
<td>17 (23.9)</td>
</tr>
<tr>
<td>Mureșan AV et al. [20], 2022</td>
<td>COVID-19 survivor</td>
<td>746</td>
<td>70.17 ± 12.70</td>
<td>397 (53.22)</td>
<td>349 (46.78)</td>
</tr>
<tr>
<td></td>
<td>COVID-19 non-survivor</td>
<td>143</td>
<td>72.18 ± 13.80</td>
<td>77 (53.85)</td>
<td>66 (46.15)</td>
</tr>
</tbody>
</table>

*Mean ± Standard Deviation
APE: Acute Pulmonary Embolism

### Table 2. Summary of the included studies.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Design</th>
<th>Subjects</th>
<th>Methods</th>
<th>Results</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gok M et al. [11], 2020</td>
<td>Cross-sectional study</td>
<td>442 patients with APE admitted between</td>
<td>The study group was divided based on APE severity (massive, submassive, and massive APE, respectively)</td>
<td>SII levels were higher in patient with higher SII between massive APE, and submassive and massive APE</td>
<td>Significant association between SII levels and APE severity</td>
</tr>
</tbody>
</table>
2015 and 2019. nonmassive) according to European Society of Cardiology Guidelines. APE was diagnosed with symptoms presented no longer than 14 days before diagnosis. APE was confirmed with CTPA. Venous peripheral blood samples was taken for SII measurement. The optimal cut-off value of SII to predict massive APE is 1161, with a sensitivity of 91% and specificity of 90%.

Ösken A et al. [18], 2021 Cross-sectional study 504 consecutive patients followed up with APE between January 2013 to December 2020. The study group was divided into APE survivors and non-survivors. CTPA was carried out to establish the diagnosis of APE. In cases where CTPA was not feasible, confirmation was achieved through ventilation/perfusion lung scanning. A total of 5.4% of patients died within 30 days. During the clinical follow-up period of 29 months, 10.1% of patients died. The SII was a strong predictor of overall mortality in patients with APE. The SII, age, right ventricle end-diastolic basal, and left

massive APE.
multiplying the total peripheral platelet counts by the neutrophil-to-lymphocyte ratio.

Ventricular ejection fraction emerged as an independent predictor of overall mortality within the study population. Results indicate that the SII with a cut-off $>1111 \times 10^9$ can predict mortality with a sensitivity of 72% and specificity of 51%.

There are a total of 71 patients with high-risk APE. The study group was divided based on the PESI values. Patients were diagnosed with APE who presented using multidetector CTPA scanning. The collection of venous peripheral blood was carried out when patients presented to the emergency department of a tertiary hospital. The research results indicate that SII has excellent diagnostic power, while NLR, PLR, SII can be a valuable and potentially useful biomarker for identifying high-risk patients with APE.
between April 2020 and April 2022. Patients arrived at the emergency department to determine the SII value.

and MLR have acceptable diagnostic power. The RLR results show fair diagnostic power. SII can also be used to differentiate high-risk APE from non-high-risk APE with a cutoff of >1235.35, achieving a sensitivity of 87.32% and a specificity of 68.85%.

Mureșa Retrospective cohort study of 899 patients over the age of 18 who had a COVID-19 infection and was confirmed using RT-PCR. Blood examination data used to calculate the SII was collected from the first admission in this study, A higher SII at admission can predict the risk of hospitalization, 16.08% of patients who died during hospitalization, 6.97% of patients with APE, and 4.27% of patients with both APE and DVT.
Modular Intensive Care unit of UMFST “George Emil Palade” of Targu Mures, Romania between January 2020 and March 2021.

Patients suspected of having APE underwent evaluation with computed tomography angiography. Patients with symptoms of DVT undergo evaluation with Doppler ultrasound.

Multivariate analysis indicated that the investigated inflammatory markers were independent predictors of adverse outcomes for all enrolled patients. In this study, the SII cut-off was set at 1839.91, yielding a sensitivity of 75.8% and specificity of 61.9%.

Moreover, higher SII values were associated with a greater risk of APE occurrence and higher mortality.

APE: Acute pulmonary embolism; CTPA: Computed tomography pulmonary angiogram; DVT: Deep vein thrombosis; MLR: Monocyte to lymphocyte ratio; NLR: Neutrophil to lymphocyte ratio; PESI: Pulmonary embolism severity index; PLR: Platelet to lymphocyte ratio
ratio; RLR: Red cell distribution width to lymphocyte ratio; RT-PCR: Real-time-polymerase chain reaction; SII: Systemic immune-inflammation.

### Table 3. Newcastle-Ottawa Scale quality assessment for cross-sectional studies.

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Study design</th>
<th>Selection</th>
<th>Comparability</th>
<th>Outcome</th>
<th>Total score</th>
<th>Result of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gok M al. [11], 2020</td>
<td>Cross-sectional study</td>
<td>****</td>
<td>*</td>
<td>***</td>
<td>8</td>
<td>Low risk</td>
</tr>
<tr>
<td>Ösken A et al. [18], 2021</td>
<td>Cross-sectional study</td>
<td>***</td>
<td>*</td>
<td>***</td>
<td>7</td>
<td>Low risk</td>
</tr>
<tr>
<td>Duyan M et al. [19], 2022</td>
<td>Cross-sectional study</td>
<td>***</td>
<td>*</td>
<td>***</td>
<td>7</td>
<td>Low risk</td>
</tr>
</tbody>
</table>

*aSelection: 1) The degree to which the sample represents the target population; 2) The adequacy of the sample size; 3) The handling of non-respondents; 4) Accuracy in ascertaining the exposure (risk factor). (maximum five stars)*

*Comparability: 1) Ensuring comparability of subjects in different outcome groups through study design or analysis.*

*Outcome: 1) Thoroughness in assessing outcomes; 2) Appropriate use of statistical tests. (maximum three stars)*

### Table 4. Newcastle-Ottawa Scale quality assessment for cohort studies.

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Study design</th>
<th>Selection</th>
<th>Comparability</th>
<th>Outcome</th>
<th>Total score</th>
<th>Result of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mureșan AV et al. [20], 2022</td>
<td>Retrospective cohort study</td>
<td>****</td>
<td>**</td>
<td>**</td>
<td>8</td>
<td>Low risk</td>
</tr>
</tbody>
</table>
Selection: 1) Appropriateness of the exposed cohort's representativeness; 2) Suitability of the non-exposed cohort selection; 3) Accuracy of exposure ascertainment; 4) Verification that the outcome of interest was absent at the study's outset.

Comparability: 1) Comparability of cohorts based on either the study's design or analysis. (maximum two stars)

Outcome: 1) Thoroughness in assessing outcomes; 2) Sufficient duration of follow-up to allow for the occurrence of outcomes; 3) Adequacy of cohort follow-up.

**SII as potential biomarker in APE patients**

The study conducted by Gok et al. in 2020 aimed to determine the relationship between the SII and APE severity and predict mortality in APE patients. This study was the first to analyze the utility of the SII in APE patients. The research results indicated a significant relationship between the SII and APE severity, with a gradual increase in SII values from nonmassive to massive APE (p < 0.001). The SII was found to be an independent predictor of massive APE occurrence \([p < 0.001, \text{ odds ratio (OR) 1.005}]\) and was associated with mortality during hospitalization \([p < 0.001]\) [11].

The use of the SII was further investigated by Duyan et al., who compared two groups of patients: those with high risk APE and those with non-high risk APE. This study involved comparing biomarkers to predict the risk of APE. Several biomarkers were used, including the SII, neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), monocyte to lymphocyte ratio (MLR), and red cell distribution width to lymphocyte ratio (RLR). The area under the receiver operating characteristic curve (AUC) analysis was performed for calculation. The analysis results demonstrated that the SII had excellent diagnostic power with the highest AUC value compared to other biomarkers (AUC: 0.84). Other biomarkers like NLR, PLR, and MLR showed acceptable diagnostic power (AUC: 0.76-0.78), while RLR exhibited fair diagnostic power (AUC: 0.68) [19].

Another study conducted by Mureșan et al. examined the influence of various biomarkers on the occurrence of APE and DVT in patients with COVID-19, where one of the biomarkers investigated was the SII. This study divided the research group into COVID-19 survivors and non-survivors. The results of this study indicated that out of the total patient population, there were 6.97% of patients with APE and 4.27% of patients with both APE and DVT. This study demonstrated a correlation between elevated SII and the occurrence of APE \((p < 0.001)\). Other biomarkers such as MLR, NLR, PLR, systemic inflammation response index (SIRI), aggregate index of systemic inflammation (AISI), prognostic nutritional index (PNI),
and controlling nutritional status (CONUT) score showed associations with the occurrence of APE. [20].

The research on the utility of the SII in predicting mortality in APE patients was further investigated by Ösken et al. in 2021. This study aimed to determine the usefulness of the SII in predicting long-term mortality in APE patients. The study groups in this research were divided based on survivors and non-survivors of APE. Regression analysis results demonstrated several independent predictor factors for mortality in the study population, including age, right ventricle end-diastolic diameter basal, left ventricular ejection fraction, and SII. AUC analysis revealed that the area under the curve value for the SII in predicting overall mortality was 0.703. A high SII could increase the risk of mortality up to 2.129 times [18].

The predictive power of SII in APE patients

Several studies have calculated the sensitivity, specificity, and cut-off value of the SII used to predict APE. The study by Gok et al. obtain a cut-off SII of 1161 to be able to predict massive APE events with a sensitivity of 91% and a specificity of 90% [11]. Duyan et al.’s study also demonstrated the use of SII to differentiate high-risk APE from non-high-risk APE with a cutoff of >1235.35, achieving a sensitivity of 87.32% and a specificity of 68.85% [19]. Apart from this, the study by Ösken et al. shows the SII with a cut-off >1111x10^9 can predict overall mortality with a sensitivity of 72% and a specificity of 51% [18]. Another study by Mureșan et al. shows that the SII with a cut-off at 1839.91 can predict APE events with a sensitivity of 75.8% and a specificity of 61.9% [20]. Calculations performed in these three studies were carried out by AUC analysis.

Quality assessment of observational studies

The Newcastle-Ottawa Scale (NOS) serves as a comprehensive tool for evaluating the quality and potential bias of cross-sectional and cohort studies. In the context of cross-sectional studies, namely those by Gok M et al. (2020), Ösken A et al. (2021), and Duyan M et al. (2022), each study's quality is assessed across three main domains [11,18,19]. The cumulative star ratings across these domains for each cross-sectional study resulted in total scores of eight stars. Notably, all three studies were appraised to exhibit a low risk of bias based on the NOS assessment, thus enhancing their credibility and reliability. Turning to cohort studies, the assessment of the retrospective cohort study conducted by Mureșan AV et al. (2022) adhered to similar criteria [20]. The outcome of this assessment for the retrospective cohort study yielded a total score of eight stars, signifying a low risk of bias according to the NOS.
DISCUSSION

Based on the included studies, there are four studies that have been conducted to understand the utility of SII in APE patients [11,18-20]. Based on these study, SII is one of various mediators that can be used to predict APE events such as predicting APE severity, APE mortality, high-risk APE, and the occurrence of APE. These results suggested that SII could serve as a valuable prognostic marker in APE, aiding in the identification of patients at heightened risk of poor outcomes. Apart from it, SII is also used in various other diseases such as rheumatoid arthritis, cancer, and other VTE diseases such as DVT [6,7,20].

In the presence of APE, the levels of pro-coagulatory and pro-inflammatory microparticles generated by platelets, white blood cells, and endothelial cells in the bloodstream increase. This initial inflammatory reaction has been associated with a grim prognosis and a higher likelihood of short-term mortality in patients with PE, as well as an escalation in subsequent activation of platelets and recruitment of neutrophils [21]. In a study conducted by Araz et al. investigating the predictive accuracy of high-sensitivity-CRP levels in serum for APE outcomes, they discovered a significant connection between elevated levels of high-sensitivity-CRP in the blood and mortality. CRP has previously been recognized as a useful biomarker for assessing the risk of APE due to its association with right ventricular dysfunction, which is a predictive factor for APE outcomes [22].

According to the researchers, this association is probably a stand-in for a more inflammatory condition in large APE compared to non-massive APE [23]. In another recent study by Phan et al., they investigated the potential of NLR and PLR in predicting all-cause mortality among patients with APE. Their findings revealed that higher NLR and PLR were associated with all-cause mortality in APE. It's worth noting that these inflammatory biomarkers involve only two types of inflammatory cells [24].

A distinct marker for predicting the health outcomes of cancer patients is the SII, a precise systemic thrombo-inflammatory index derived from platelet, neutrophil, and lymphocyte counts. Given the independent correlation between SII and major APE, it can serve as a valuable prognostic indicator. While elevated SII levels are strongly associated with the severity of APE, this connection may not always imply a cause-and-effect relationship [25]. It seems more likely that an underlying causal pathway, which also leads to a hypercoagulant state and eventually results in APE, is responsible for the inflammatory condition observed in VTE [26].
Though initial research provided theoretical support for the connection between the inflammatory response and thrombosis, several clinical studies have demonstrated that SII indeed serves as a reliable predictor of VTE [27]. Patients with lung cancer exhibited modified systemic inflammatory responses and active coagulation systems, both directly linked to the initiation and progression of VTE. Various inflammatory mediators, such as interleukin (IL)-1 and IL-6, are released by circulating neutrophils, lymphocytes, and platelets, collectively referred to as the systemic inflammatory immune cells within the human body. These cells also contribute to the activation of nod-like receptor protein three inflammatory vesicles (NLRP3) to stimulate thrombus formation [28].

Until now, pulmonary angiography has been the current gold standard for diagnosing PE. However, the use of pulmonary angiography is invasive, expensive, and not available in all hospital facilities [29]. Based on conducted studies, SII can serve as a diagnostic and prognostic tool for predicting APE events. Gok et al. established an SII cut-off of 1161 to predict massive APE events with a sensitivity of 91% and a specificity of 90% [11]. Duyan et al. demonstrated the use of SII to differentiate high-risk APE from non-high-risk APE, using a cut-off of >1235.35, achieving a sensitivity of 87.32% and a specificity of 68.85% [19]. Ösken et al.’s study indicates that an SII cut-off >1111x10^9 can predict overall mortality with a sensitivity of 72% and a specificity of 51% [18]. Another study by Mureşan et al. suggests that an SII cut-off at 1839.91 can predict APE events with a sensitivity of 75.8% and a specificity of 61.9% [20]. Despite different cut-off values, each study reported results with p <0.05 and AUC >0.7, indicating that SII is effective as a diagnostic and prognostic biomarker in conjunction with existing gold standards.

A recent study by Uslu et al. in 2024 demonstrated a comparison of using SII, D-dimer, and other markers to diagnose PE. This study conducted ROC analysis to evaluate the predictive efficacy of SII, SIRI, NLR, D-dimer, and the Wells score in distinguishing patients with PE from the control group. D-dimer is one of the biomarkers commonly used in determining the diagnosis of PE. The results of the study showed that SII (cut-off >705.6) had a sensitivity of 75.31% and specificity of 71.26%, while D-dimer (cut-off >2.35) had a sensitivity of 75.31% and specificity of 77.01%. The results indicate that the Wells score, D-dimer level, and SII independently influenced the diagnosis of PE. Based on these findings, SII can be used to assist in diagnosing PE [30].

There are several limitations to this study, primarily that all included studies were either case-control or cohort studies, which have a lower level of evidence compared to randomized controlled trials. Utilizing a randomized controlled trial study design would significantly
enhance the quality of research pertaining to the use of SII for predicting APE outcomes. Furthermore, conducting research with larger sample sizes could yield more accurate SII cutoff values, sensitivity, and specificity for various APE outcomes. Large-scale prospective studies could also evaluate SII performance in comparison with other established biomarkers. Additionally, further investigation is warranted to assess the utility of SII as a biomarker in other cardiovascular diseases.

CONCLUSION

In this systematic review, it is demonstrated that the SII can be used as a potential new biomarker to predict the occurrence, severity, and mortality of APE patients. Future studies can be conducted to provide further analysis of the utility of the SII in predicting outcomes in APE patients, especially using randomized controlled trial study designs.

Context: Embolia pulmonară acută (APE) este o afecțiune care pune viața în pericol, cu o rată ridicată a mortalității. Fiziopatologia implică diverse procese complexe. Indicele imuno-inflamator sistemice (SII) este un biomarker binecunoscut care reflectă echilibrul complicat dintre componentele imune proinflamatorii și antiinflamatorii. În această sinteză sistematică, ne propunem să determinăm semnificația SII ca potențiul biomarker pentru APE.

Metodă: Am folosit PubMed, ProQuest, EBSCOHost și Google Scholar pentru a căuta articole relevante. Am evaluat riscul de eroare sistematică utilizând Scala Newcastle Ottawa (NOS). Rezultatele pe care le-am examinat au inclus mortalitatea în spital și pe termen lung, severitatea APE și sensibilitatea și specificitatea SII în prezicerea APE.

Rezultate: Patru studii, care au implicat 2038 de pacienți, au fost incluse pentru analiză. Aceste studii discută utilizarea SII în prezicerea severității APE, a mortalității APE, a APE cu risc ridicat și a aparținut APE. SII demonstrează rezultate semnificative în prezicerea fiecărei dintre aceste variabile. În plus, fiecare studiu stabilește diferite valori prag a SII. Mai exact, o vârf prag de 1161 prezice evenimente APE masive cu o sensibilitate de 91% și o specificitate de 90%. Un prag de >1235,35 diferențiază APE cu risc ridicat cu o sensibilitate de 87,32% și o specificitate de 68,85%. Un prag de >11111x10⁸ prezice mortalitatea globală cu o sensibilitate de 72% și o specificitate de 51%. În cele din urmă, un cut-off la 1839,91 prezice evenimente APE cu o sensibilitate de 75,8% și o specificitate de 61,9%. Concluzie: SII poate fi folosit ca un potențial biomarker nou pentru a prezice rezultatele la pacienții cu APE, în special apariția, severitatea și mortalitatea APE.

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