Evaluation of the Diagnostic Value of Neutrophil-to-lymphocyte Count Ratio (NLR) and Platelet-to-lymphocyte Ratio (PLR) for Identifying Serious Infection (SI) and Serious Bacterial Infection (SBI) in Febrile Young Infants < 90 Days Old

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Abstract

Background:

Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are simple and easy to calculate biomarkers. They have been reported as a predictor of severity and prognosis in adult patients with bacteremia. However, there is a paucity of literature examining the use of NLR and PLR as a diagnostic biomarker in pediatrics. This study aims to evaluate the diagnostic value of the NLR and PLR for identifying serious infections (SI) and serious bacterial infections (SBI) in febrile young infants <90 days old.

Methods:

A retrospective review of neonates and infants who were admitted for evaluation of fever between 1\textsuperscript{st} July 2018 and 31\textsuperscript{st} December 2018 were reviewed retrospectively. Patients aged less than 90 days of life admitted for fever from the emergency department were included. Patient age, gender, comorbidities, body temperature, clinical findings and initial laboratory results including white blood cell (WBC) count, NLR, PLR, serum levels of C-Reactive Protein (CRP) were assessed, and the microbiological investigations and final clinical diagnoses were evaluated.

Results:

There were 561 patients identified for inclusion. SI and SBI were diagnosed in 166 (29.6\%) and 98 (17.5\%) patients. Mean absolute neutrophil count, NLR were significantly higher in the SI group compared to the non-SI group (1.39±1.04 vs 1.09±0.87, p=0.001). The NLR was also significantly different in the SBI compared to the non-SBI group (1.38±0.88 vs 1.13±0.94, p=0.019). PLR did not show statistical significance in differentiating SI or SBI from non-SI or SBI group. For SI and SBI, the area under the Receiver Operating Characteristic (AUROC) curve value of NLR was 0.57 (95 \% CI 0.46-0.69) and 0.61 (95 \% CI 0.48-0.73), respectively. Although we found significantly higher NLR values in infants with SI and SBI, our results indicate that CRP was more accurate at detecting SI and SBI.

Conclusion: Our study provided initial evidence on the use of the NLR in combination with other biomarkers in the diagnosis of serious infection and serious bacterial infection in young infants < 90 days’ of life. Prospective evaluation of this finding is needed to assess further its clinical value in the evaluation of young febrile infants for SI and SBI.

Background

The evaluation of the young febrile infant (from 0 to 90 days’ of life) remains clinically challenging. Multiple prediction rules have been investigated to rule out serious infections (SI) and serious bacterial infections (SBI), especially for those age group 29–60 days of life.[1] Inflammatory biomarkers e.g procalcitonin (PCT) and C-reactive protein (CRP) are commonly used investigations in the evaluation of young febrile infants. However, these acute phase reactants may not be readily available in resource limited clinical care areas or in circumstances for which the turn-over may be longer than required for rapid clinical decision making. [2, 3] This is especially important for emergency physician and intensive care unit physician, who need the test run in real time and make quick decision about patient treatment. In our center, procalcitonin (PCT) is not available in the emergency department (ED) because it is an expensive assay and has slow turn-around-time (2–3 hours).

During acute sepsis and bacteremia, the number of neutrophils increase, while the number of lymphocytes decreases.[4–8] There are also evidence indicates that inflammatory process also results in accelerated megakaryocyte proliferation with associated thrombocytosis and lymphopenia.[9, 10] The mediators of these hematological changes are mainly due to endogenous cortisol and catecholamines release; while cytokines and other hormones are also likely involved.[11, 12]
The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are two new composite inflammatory biomarkers for sepsis. NLR increases rapidly following acute physiologic stress (< 6 hours) unlike other hematological indices (such as white blood cell count) which may be slower to respond.[8, 13] PLR is more stable than a single blood parameter that can vary because of multiple factors such as dehydration and treatment of blood specimens. [10] Studies on NLR and PLR have been extensively published in the adult literature for evaluation and prognostication of systemic bacterial infections, surgical abdomen, major trauma, and oncology patients.[14–16] There have been also recent publications on its use in the neonatal population for its prognosticative value in the evaluation of neonatal sepsis.[17–20] However, studies on its use in the pediatric population in the evaluation of infection severity is very limited.

We aimed to study the utility of NLR distinguishing a serious infection from a more benign cause of fever in infants 0–90 days’ of life. We hypothesize that NLR would provide discriminatory value because of the physiologic response among this group of neonates and young febrile infants when they encounter a SI or SBI.

**Methods**

**Setting**

We performed a single-center retrospective study of infants 0–90 days old presenting with fever without source and who underwent an evaluation for serious infection. Our center is a tertiary pediatric institution that sees about 150,000 children a year, and about 2000 febrile young infants < 90 days old, annually.[21] In our institution, all infants 0–90 days old presenting with fever to the Emergency Department (ED) are admitted and undergo limited or full septic evaluation to identify those at risk of SI, thus forming a natural pool for more detailed study. This includes complete blood count, urinalysis, urine cultures, blood culture, cerebrospinal fluid (CSF) cytology, glucose, protein and CSF culture. Patients are admitted for observation range from 24 to 72 hours.

Institutional ethic board review was obtained with the approval for waiver of informed consent. (2020/2256)

**Patient population**

Using the institutional data repository of electronic medical records, we identified all children less than 90 days of age presenting to the ED with fever without source between July 1, 2018, and December 31, 2018. We screened all children less than 90 days old with an initial triage axillary temperature of > 37.5°C. Temperature is measured at the triage by a nurse using an axillary thermometer. Subsequently if the repeat temperature was less than 38°C (e.g. in cases of overwrapping) and the child remained clinically well with no subsequent investigations performed, this child was excluded from the analysis.

**Exclusion Criteria**

The following are the exclusion criteria: (a) Patient was admitted for other diagnosis or have stayed inpatient ≥ 48 hours; (b) pre-term infants with gestational age < 37 weeks, (c) any pre-treatment of oral or intravenous antibiotics within past 1 week; (d) patients with co-morbid conditions predisposing to severe or recurrent bacterial illness, including genetic, congenital, chromosomal, malignancy, neuromuscular or neurodevelopment abnormalities; (e) patients with central venous catheters or ventriculoperitoneal shunts; (f) patients transferred from another hospital inpatient setting; and (g) patients with any obvious source of infection, e.g. omphalitis, pneumonia, bronchiolitis

**Data collection**
We collected data on patient demographics, vital signs at the triage, and clinical presentation. The initial complete blood count at admission, CRP, microbiological investigations, critical interventions, and their final diagnoses were collected. NLR value were obtained by dividing the neutrophil count by the lymphocyte count. PLR were obtained by dividing the platelets by the lymphocyte count.

**Definition**

SI was defined as sepsis (including bacteremia), meningitis, lobar pneumonia, osteomyelitis, abscess, and urinary tract infection. [22]

SBI was defined as growth of any bacterial pathogen in one or more of the following cultures: CSF, blood, urine, stool, or any other aspirated fluid from a sterile location; and any disease commonly associated with bacterial pathogens, including osteomyelitis, septic arthritis, enterocolitis, and pneumonia. [23]

**Statistical analysis**

All data were entered into Microsoft Excel database. Statistical analysis was performed using IBM SPSS Statistics Version 26.0. Normally distributed data were expressed as mean ± SD, non-normally distributed data as median & interquartile range, and categorical data were reported as percentages. Statistical comparison was performed using Fischer’s exact test if the data were normally distributed, whereas Mann-Whitney U tests were used to compare nonparametric data. A comparison of the diagnostic accuracy of biomarkers was performed using receiver operating characteristics (ROC) curves analysis. Significance was set at p < 0.05.

**Results**

Between 1st July 2018 and 31st December 2018, 561 infants age 0–90 days were admitted from the emergency department for fever with no clear source. The median age of the study population of SI was 32 days old (IQR 15–58) and SBI was 37.5 days old (IQR15-61). There were 345 (61.5%) males. All infants had complete blood count data available.

Of these 561 infants, 166(29.6%) had a diagnosis of SI and 98(17.5%) had a diagnosis of SBI. All SI patients demonstrated significantly higher absolute neutrophil count (ANC) (5.60 ± 3.70 × 10⁹ vs 4.45 ± 2.44 × 10⁹, p < 0.001). When the mean NLR level was compared between two groups it was significantly elevated in the SI group than the non-SI group (1.39 ± 1.04 vs 1.09 ± 0.87, p = 0.001). However, the absolute lymphocyte count (ALC), platelet count, and PLR were not significant between the groups (p = 0.53 for ALC, p = 0.23 for platelet count, p = 0.14 and p = 0.56 for PLR).

SBI infants also demonstrated significantly higher ANC (6.56 ± 4.21 × 10⁹ vs 4.45 ± 2.44 × 10⁹, p < 0.001) and platelet count (428.7 ± 113.7 × 10⁹/L vs 399.4 ± 115.4 × 10⁹/L, p = 0.019) when compared to non SBI group. The mean NLR level was significantly elevated in SBI group than non-SI group (1.38 ± 0.88 vs 1.13 ± 0.94, p = 0.019). ALC and PLR were not significant between the groups (p = 0.22 for ALC, p = 0.96 for PLR).

**Diagnostic performance of the hematological markers**

Figure 1 shows Receiver Operating Characteristic (ROC) curves and Area Under Receiver Operating Characteristic (AUROC) curve of ANC, CRP and NLR for differentiating young infants 0–90 days old with SI from non-SI (Fig. 1a) and SBI from non SBI (Fig. 1b).

The AUROC of NLR to detect SI was 0.57(95% CI 0.51–0.62). We compared four cut-off values found in previous studies, namely 0.97, 1.35, 1.77 and 2.7. (Table 2a & 2b) Using a cut-off value of 0.97, it has the highest sensitivity amongst the
four and its sensitivity and specificity of NLR for predicting SI was 56.6% (95% CI 48.7–64.3) and 57.7% (95% CI 52.7–62.7), respectively. In the SBI group, the AUROC of the NLR to detect SBI was 0.60 (95% CI 0.54–0.66). Similarly using a cut-off value of 0.97, the sensitivity and specificity of the NLR to detect SBI was 62.2% (95% CI 51.9–71.8) and 56.8% (95% CI 52.2–61.4), respectively.

The AUROC to detect SI was highest for CRP level with AUROC of 0.69 (95% CI 0.64–0.74) and ANC level with 0.58 (95% CI 0.52–0.63). In SBI, the AUROC was also highest for CRP, 0.74 (95% CI 0.68–0.81) and ANC, 0.66 (95% CI 0.59–0.72).

Discussion

In this study, we investigated the diagnostic value of NLR and PLR to detect SI and SBI. Although we found significantly higher NLR values in infants with SI and SBI, our results indicate that CRP level show more accuracy to detect SI and SBI. PLR did not show statistical significance in differentiating SI or SBI from non-SI or non-SBI group.

The need to clinically distinguish SI and SBI from more benign causes of fever in young infants remains clinically challenging. Patient outcomes are determined not only by virulence of invading pathogens, but also by host response. Neonates and infants are the most immunocompromised because of their poorly developed innate and adaptive immunity system responses. [24–26] This has resulted them in increased susceptibility to develop severe infections from various pathogens.[27, 28] Therefore, early recognition and detection of sepsis is of high importance in neonates and infants because it improves the outcome of the patients.

Multiple biomarkers have been proposed but improvement is still needed for clinical management. To date, most biomarkers are discussed in terms of sepsis prognosis and duration of antibiotics. [29–31] Early in the course of sepsis, most biomarkers fail to predict ongoing bacterial infection when fever is the only symptom.[32] Some studies advise to use a combination of biomarkers to improve the sensitivity and specificity.[33] However, these employ biomarkers that are costly and require a turnaround time. We need a biological marker that must be easily accessible, cheap, rapid, sensitive, and specific as much as possible. Nevertheless, WBC and CRP remain the most widely used biomarkers for bacterial infection diagnosis.

Many clinical studies suggested NLR in addition to CRP, WBC and neutrophil count as an important marker in early bacteremia diagnosis and evaluation of sepsis outcomes. [34–37] Also NLR was observed in some studies to be more efficient than regular inflammation biomarkers among adults. [34, 38] A study of adults with suspected bacteremia and sepsis, which grouped the patients according to procalcitonin levels, showed procalcitonin and NLR has the highest correlation value. [34] Thus, NLR was shown to be significant in adult population in early sepsis prediction compared to standard diagnostic biomarkers. [34, 36, 38] However, there were very few neonatal or paediatric studies conducted to evaluate the use of NLR for prediction of sepsis and the optimal cut-off values are still under debate. In the study by Alkan et al, NLR values were much higher in septic newborn babies. Using NLR cut-off value at 1.77, the sensitivity and specificity were 78% and 78%, respectively. [17] In our study using similar NLR cut-off point of 1.77, the sensitivity and specificity for SI was 25.3% and 82.8%, respectively, and sensitivity and specificity for SBI, 26.5% and 81.9%, respectively. This lower performance could be due to the different patient spectrum included in the studies, as the two previous studies were performed in NICU in which the prevalence of neonatal sepsis was higher, compared to infants presented to emergency department. This might affect the SI or SBI diagnosis and its prevalence. We found that NLR with cut-off at 0.97 proposed by Sun Y et al. has better sensitivity and specificity especially for SBI, 62.2% and 56.8% respectively. However, this cut-off point was used to predict bronchopulmonary dysplasia in premature babies < 32 weeks with congenital pneumonia and therefore the result is not generalizable. [39]

For our cohort, we found that CRP 20 or more had the highest positive likelihood for both SI and SBI (5.68 and 7.97 respectively) and positive predictive value (73.44% and 65.62% for SI and SBI respectively). (Tables 2a and 2b). ANC
1.5K or less had the highest sensitivity for SI (95.78%, 95% CI 91.5-98.29%) and SBI (96.94%, 95% CI 91.31–99.36%) and negative predictive value for SI 76.67% (95% CI 58.98–88.25%) and SBI (90%, 95% CI 73.58–96.68%). ANC 10K or more has the highest specificity for SI (96.2%, CI 93.81–97.86%) and SBI (96.54%, CI 94.45–98.01%). While we found a correlation between NLR with SI and SBI, as a blood count index, it did not fare better than using specific neutrophil cut-offs. However, NLR is a simple and easy to calculate biomarker using routine laboratory data without additional technique or cost. Our study provided initial evidence for NLR in the evaluation of young febrile infants less than 90 days old. It is unknown, however, if when combined with other biomarkers, there might be of synergistic value when evaluating serious infection and serious bacterial infection in young febrile infants, especially in resource limited settings.

PLR is a blood ratio that is largely used in chronic diseases and malignancies in adults. [40–42] Arcagok et al. evaluated the role of PLT in early onset neonatal sepsis and identified that PLR levels of suspected and definite early onset sepsis were significantly higher than that of control group, with 91.3% sensitivity & 97.6% specificity using a cut off level of 57.7. [43] In contrast to our study, we did not find any significant association between PLR and serious infection or serious bacterial infection.

The present study had several limitations. First, the study was designed as a retrospective study lacking longitudinal observation. Therefore, we could not measure the biomarkers in the following hours or days after sepsis diagnosis. While the baseline NLR is undoubtedly of prognostic value, increase or decrease in the NLR during the course of illness may also be importance. Second, there is lack of consensus regarding the most appropriate cut-off value for NLR. This was variably reported in the literature and for the NLR to be useful as a screening tool for clinicians, there needs to be consensus on the definitions of “high” versus “low” NLR. Third, though all infants have complete blood count performed, CRP were not performed in all presenting infants. Only 89.5% of the infants included in the study had CRP done. This could have led to a certain selection of children.

**Conclusions**

Our study provided initial evidence on the use of the NLR in combination with other biomarkers in the diagnosis of serious infection and serious bacterial infection in young infants. However, these findings still need to be confirmed by future studies with larger numbers of neonates and further evaluation with combination of various biomarkers.

**Abbreviations**

ANC
Absolute neutrophil count
ALC
Absolute lymphocyte count
AUROC
Area under Receiver Operating Characteristic
CRP
C-Reactive Protein
CSF
Cerebro-spinal fluid
ED
Emergency department
FBC
Full blood count
IQR
Declarations

Ethics approval and consent to participate

This study was retrospective and exempted for review by SingHealth Centralised Institutional Review Board (CIRB).

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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This work received no financial support.
Author’s contributions

KZX conceived the study, collected the data, coordination, writing the manuscript

CSL perform statistical analyses and revised manuscript

GO conceived the study, writing the abstract and introduction, revised manuscript

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## Tables

**Table 1: Epidemiology and baseline characteristics**
|                          | Non SI(N=395) | SI(N=166) | p-Value | Non-SBI(N=465) | SBI(N=98) | p-Value |
|--------------------------|---------------|-----------|---------|----------------|-----------|---------|
| Age, median(IQR)         | 16(4-49)      | 32(15-58) | <0.001  | 20(5-49)       | 37.5(15-61)| <0.001  |
| Age, in days of life, n(%)| <0.001        |           |         |                |           | <0.001  |
| 0-28 days                |               |           |         |                |           |         |
| 29-60 days               | 244(61.8)     | 76(45.8)  |         | 281(60.4)      | 39(39.8)  |         |
| 61-90 days               | 76(19.2)      | 51(30.7)  |         | 96(20.6)       | 34(34.7)  |         |
|                          | 75(19.0)      | 38(22.9)  |         | 88(18.9)       | 25(25.5)  |         |
| Gender, n(%)             | <0.001        |           | <0.001  |                |           |         |
| Male                     | 222(56.2)     | 123(74.1) |         | 264(56.8)      | 80(81.6)  |         |
| Female                   | 173(43.8)     | 43(25.9)  |         | 201(43.2)      | 18(18.4)  |         |
| Biomarkers               |               |           |         |                |           |         |
| ANCs, x10^9/L            | 4.45±2.44     | 5.60±3.70 | <0.001  | 4.42±2.40      | 6.56±4.21 | <0.001  |
| ALC, x10^9/L             | 5.08±2.17     | 4.95±2.40 | 0.53    | 4.99±2.23      | 5.29±2.26 | 0.22    |
| Platelet, x10^9/L        | 399.4±115.4   | 412.5±121.7| 0.23  | 397.9±117.5   | 428.7±113.7 | 0.019   |
| NLR, mean (SD)           | 1.09±0.87     | 1.39±1.04 | 0.001   | 1.13±0.94      | 1.38±0.88 | 0.019   |
| PLR, mean (SD)           | 1.33±0.61     | 1.29±0.81 | 0.56    | 1.32±0.67      | 1.32±0.67 | 0.96    |

Legend: SI – Serious infection, SBI – serious bacterial infection, IQR – interquartile range, SD – standard deviation, ANC – absolute neutrophil count, ALC – absolute lymphocyte count, NLR – neutrophil to lymphocyte ratio, PLR – platelet to lymphocyte ratio.

**Table 2:**

(a) Comparison of the hematological parameters of the SI group
| Parameter | SI | Non-SI | p-value | OR (95%CI) | Sen | Spec | NPV | PPV | LR- | LR+ |
|-----------|----|--------|---------|------------|-----|------|-----|-----|-----|------|
| ANC ≤1.5K | 7 | 23 | 0.44 | 1.40 (0.59-3.34) | 95.78 (91.5-98.29) | 5.82 (3.73-8.61) | 76.67 (58.98-88.25) | 29.94 (29.11-30.79) | 0.72 (0.32-1.65) | 1.02 (0.98-1.06) |
| ANC > 1.5K | 159 | 372 |       |          |     |      |     |     |     |      |
|ANC ≤4K | 63 | 198 | 0.008 | 1.64 (1.14-2.38) | 62.05 (54.20-69.46) | 50.13 (45.08-55.17) | 75.86 (71.65-79.63) | 34.33 (30.93-37.90) | 0.76 (0.61-0.94) | 1.24 (1.07-1.45) |
|ANC > 4K | 103 | 197 |        |          |     |      |     |     |     |      |
|ANC <10K | 147 | 380 | 0.001 | 3.27 (1.62-6.62) | 11.45 (7.03-17.30) | 96.20 (93.81-97.86) | 72.11 (70.92-73.26) | 55.88 (39.75-70.86) | 0.92 (0.87-0.98) | 3.01 (1.57-5.79) |
|ANC ≥10K | 19 | 15 |        |          |     |      |     |     |     |      |
|NLR ≤0.97 | 72 | 228 | 0.002 | 1.782 (1.24-2.57) | 56.63 (48.73-64.29) | 57.72 (52.68-62.65) | 76.00 (72.30-79.35) | 36.02 (32.07-40.16) | 0.75 (0.62-0.91) | 1.34 (1.12-1.60) |
|NLR > 0.97 | 94 | 167 |        |          |     |      |     |     |     |      |
|NLR ≤1.35 | 105 | 286 | 0.031 | 1.52 (1.04-2.24) | 36.75 (29.41-44.57) | 72.41 (67.71-76.76) | 73.15 (70.50-75.64) | 35.88 (30.24-41.95) | 0.87 (0.77-1.00) | 1.33 (1.03-1.72) |
|NLR > 1.35 | 61 | 109 |        |          |     |      |     |     |     |      |
|NLR ≤1.77 | 124 | 327 | 0.028 | 1.63 (1.05-2.52) | 25.30 (18.88-32.62) | 82.78 (78.69-86.38) | 72.51 (70.48-74.44) | 38.18 (30.55-46.44) | 0.90 (0.82-1.00) | 1.47 (1.05-2.06) |
|NLR > 1.77 | 42 | 68 |        |          |     |      |     |     |     |      |
|NLR ≤2.79 | 148 | 373 | 0.027 | 2.06 (1.08-3.96) | 10.84 (6.55-16.60) | 94.43 (91.69-96.48) | 71.59 (70.39-72.76) | 45.00 (31.07-59.76) | 0.94 (0.89-1.00) | 1.95 (1.07-3.53) |
|NLR > 2.7 | 18 | 22 |        |          |     |      |     |     |     |      |
|CRP ≤20 | 119 | 324 | <0.001 | 7.53 (4.16-13.62) | 28.31 (21.60-35.82) | 95.01 (92.14-97.07) | 73.14 (71.16-75.03) | 73.44 (62.11-82.34) | 0.75 (0.68-0.83) | 5.68 (3.37-9.58) |
|CRP > 20 | 47 | 17 |        |          |     |      |     |     |     |      |

(b) Comparison of the hematological parameters of the SBI group
| Parameter | SBI  | Non-SBI | p-value | OR (95%CI) | Sen | Spec | NPV | PPV | LR- | LR+ |
|-----------|------|---------|---------|-----------|-----|------|-----|-----|-----|-----|
| ANC ≤ 1.5K<sup>a</sup> | 3    | 27      | 0.27    | 1.96 (0.58-6.60) | 96.94 (91.31-99.36) | 5.83 (3.88-8.37) | 90.00 (73.58-96.68) | 17.89 (17.28-18.51) | 0.52 (0.16-1.7) | 1.03 (0.99-1.07) |
| ANC > 1.5K | 95   | 436     |         |           |     |      |     |     |     |     |
| ANC ≤ 4K<sup>b</sup> | 27   | 234     | <0.001  | 2.69 (1.66-4.34) | 72.45 (62.5-80.99) | 50.54 (45.89-55.19) | 89.66 (86.13-92.36) | 23.67 (21.02-26.54) | 0.55 (0.39-0.76) | 1.46 (1.26-1.71) |
| ANC > 4K  | 71   | 229     |         |           |     |      |     |     |     |     |
| ANC < 10K<sup>c</sup> | 80   | 447     | <0.001  | 6.29 (3.08-12.84) | 18.37 (11.26-27.47) | 96.54 (94.45-98.01) | 84.82 (83.55-86.01) | 52.94 (37.30-68.03) | 0.85 (0.77-0.93) | 5.32 (2.81-10.05) |
| ANC ≥ 10K | 18   | 16      |         |           |     |      |     |     |     |     |
| NLR ≤ 0.97<sup>d</sup> | 37   | 263     | 0.001   | 2.17 (1.39-3.39) | 62.24 (51.88-71.84) | 56.80 (52.15-61.37) | 87.67 (84.49-90.27) | 23.37 (20.20-26.87) | 0.66 (0.51-0.87) | 1.44 (1.20-1.74) |
| NLR > 0.97 | 61   | 200     |         |           |     |      |     |     |     |     |
| NLR ≤ 1.35<sup>e</sup> | 63   | 328     | 0.199   | 1.35 (0.85-2.14) | 35.71 (26.29-46.03) | 70.84 (66.47-74.95) | 83.89 (81.63-85.92) | 20.59 (16.10-25.95) | 0.91 (0.77-1.06) | 1.22 (0.91-1.66) |
| NLR > 1.35 | 35   | 135     |         |           |     |      |     |     |     |     |
| NLR ≤ 1.77<sup>f</sup> | 72   | 379     | 0.06    | 1.63 (0.98-2.71) | 26.53 (18.12-36.41) | 81.86 (78.04-85.26) | 84.04 (82.26-85.66) | 23.64 (17.44-31.20) | 0.90 (0.79-1.02) | 1.46 (1.00-2.14) |
| NLR > 1.77 | 26   | 84      |         |           |     |      |     |     |     |     |
| NLR ≤ 2.7<sup>g</sup> | 90   | 431     | 0.662   | 1.197 (0.53-2.68) | 8.16 (3.59-15.45) | 93.09 (90.38-95.22) | 82.73 (81.79-83.62) | 20.00 (10.62-34.46) | 0.99 (0.93-1.05) | 1.18 (0.56-2.48) |
| NLR > 2.7  | 8    | 32      |         |           |     |      |     |     |     |     |
| CRP ≤ 20<sup>h</sup> | 56   | 387     | <0.001  | 13.19 (7.34-23.73) | 42.86 (32.9-53.25) | 94.62 (91.97-96.60) | 87.36 (85.32-89.15) | 65.62 (54.49-75.27) | 0.60 (0.51-0.72) | 7.97 (5-12.7) |
| CRP > 20  | 42   | 22      |         |           |     |      |     |     |     |     |

<sup>a</sup> Rochester criteria[44]

<sup>b</sup> Kupperman et al[1]

<sup>c</sup> “Step-by-Step”[45]

<sup>d</sup> Sun Y et al.[39]

<sup>e</sup> Tamelytė E et al.[46]

<sup>f</sup> Alkan et al.[17]

<sup>g</sup> Omran et al.[20]
Figures

Figure 1

(a) ROC and AUROC for SI (b) ROC and AUROC for SBI