Type of the Pape: Supplementary materials

A secondary retrospective analysis of the predictive value of Neutrophil-Reactive Intensity (NEUT-RI) in Septic and Non-septic Patients in Intensive Care

Paolo Formenti1°, Letizia Isidori1, Stefano Pastori2, Vincenzo Roccaforte2, Elena Maria Alessandra Mantovani1 , Massimiliano Iezzi3, Alessandro Menozzi3, Rossella Panella2, Andrea Galimberti1, Giovanni Brenna1, Michele Umbrello4, Angelo Pezzi1, Francesco Vetrone1, Giovanni Sabbatini1, Miriam Gotti1

|  |
| --- |
| **Citation:** To be added by editorial staff during production.  Academic Editor: Firstname Lastname  Received: date  Revised: date  Accepted: date  Published: date    **Copyright:** © 2024 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/). |

1 SC Anestesia, Rianimazione e Terapia Intensiva, ASST Nord Milano, Ospedale Bassini, Cinisello Balsamo, 20097, Italy.

2 S.C. Analisi Chimico Cliniche e Microbiologiche, ASST Nord Milano, Ospedale Bassini; Cinisello Balsamo, 20097, Italy.

3 School of Medicine and Surgery, University of Milano-Bicocca, 20126 Milano, Italy.

4. Department of Intensive Care, New Hospital of Legnano: Ospedale Nuovo di Legnano, 20025, Legnano, Milan, Italy.

° Correspondence: [paolo.formenti@asst-nordmilano.it](mailto:paolo.formenti@asst-nordmilano.it)

**Table S1.** Comparison of inflammatory parameters between patients with "renal failure" and patients with "normal renal function."

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Renal Failure**  (n=70) | **Normal renal function**  (n=130) | P |
| **Age** | 75.50 [67.00 - 80.00] | 71.00 [56.00 - 77.00] | 0.006 |
| **Male%** | 42.9 | 54.6 | 0.150 |
| **Creatinine** | 2.12 [1.59 – 3.73] | 0.89 [0.69 – 1.25] | < 0.001 |
| **CPR** | 21.20 [12.31 - 134.65] | 11.37 [2.25 - 32.53] | < 0.001 |
| **PCT** | 11.91 [1.02 - 63.71] | 0.68 [0.32 - 3.24] | < 0.001 |
| **NEUT-RI** | 52.15 [47.95 - 56.48] | 48.70 [46.60 - 52.58] | 0.002 |

**Table S2**: NEUT-RI, PCT and CPR values for the detection of septic and non-septic patients.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **AUROC  (95% CI)** | **Cut-off** | **Sens  (95% CI)** | **Spec  (95% CI)** | **PPV**  **(95% CI)** | **NPV**  **(95% CI)** |
| **NEUT-RI** | 0.79 [0.73 - 0.86] | 50.75 | 70.9  [60.4 - 79.7] | 80.7  [71.6-88.1] | 75.6  [65.1-84.2] | 77.2  [68.4-84.5] |
| **CPR** | 0.73  [0.66 - 0.80] | 7.38 | 84.6  [75.8-91.2 | 56.2  [45.5-64.0] | 65.8  [56.5-74.3] | 77.8  [65.5-87.3] |
| **PCT** | 0.76  [0.69 - 0.84] | 2.17 | 62.9  [52.8 - 74.2] | 82.9  [76.4-90] | 82.3  [71.2-90] | 63.7  [52.9-73.6] |

There were not statistically significant differences between AUROC of the three parameters (NEUT-RI vs PCT p=0.83, NEUT-RI vs PCR p=0.29, DeLong’s test for two correlated ROC curves). The CPR specificity is statistically different from the NEUT.RI specificity (p=0.01, specificity test for two correlated ROC curves) and from PCT specificity (p=0.007, specificity test for two correlated ROC curves). AUROC= Area Under the ROC curve; Sens = Sensibility; Spec = Specificity; PPV= Positive Predictive Value; NPV= Negative Predictive Value; NEUT-RI= Neutrophil-Reactive Intensity; PCT= procalcitonin; CRP= C-reactive protein

**Table S3.** NEUT-RI and PCT values for discriminating between "survivors" and "deceased" at 28 days.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **AUROC  (95% CI)** | **Cut-off** | **Sens  (95% CI)** | **Spec  (95% CI)** | **PPV**  **(95% CI)** | **NPV**  **(95% CI)** |
| **NEUT-RI** | 0.70[0.56-0.83] | 53.6 | 62.5  [39.5-81.3] | 76.9  [68.7-82.3] | 28.30  [16.8-42.34] | 93.0  [87.17-96.76] |
| **PCT** | 0.76  [0.65-0.88] | 12.18 | 76.2  [54.6-90.5] | 79.9  [71.5-84.6] | 38.09  [23.6-54.3] | 95.10  [88.93-98.39] |

There were not statistically significant differences between AUROC of the two parameters (p=0.57, DeLong’s test for two correlated ROC curves). AUROC= Area Under the ROC curve; Sens = Sensibility; Spec = Specificity; PPV= Positive Predictive Value; NPV= Negative Predictive Value; NEUT-RI= Neutrophil-Reactive Intensity; PCT= procalcitonin

**Table S4.** NEUT-RI and PCT at ICU admission time, after 48 and 96 hours in septic patients.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Admission time** | **48 hours** | **96 hours** | **p-value**  **(ANOVA)** | **P values pairwaise comparisons** | | |
| **0h vs**  **48h** | **0h vs 96h** | **48h vs 96h** |
| **NEUT-RI (FI) (n=59)** | 52.70  [49.65-56.80] | 53  [49.00-57.60] | 50.50  [47.60-52.90] | 0.0002 | 1 | 0.0011 | <0.0001 |
| **PCT (ng/ml) (n=63)** | 6.36  [0.52-36.95] | 5.51  [0.90-34.82] | 1.65  [0.53-5.74] | <0.0001 | 0.01 | <0.0001 | <0.0001 |

**Figure S1.** NEUT-RI and CPR depending on the site of infection in “septic” group.

**A black and white graph

Description automatically generated**

There were no differences in NEUT-RI and CPR depending on the site of infection in “septic” group. There was a statistically significant difference in PCT depending on site of infection (p<0.001, Kruskal-Wallis rank sum test), in particular PCT was higher in patients with kidney or urinary tract infection compared to lung infection (88.50 [24.20-113.00] vs 1.64[0.39-12.54], p<0.001 Pairwise comparisons using Wilcoxon rank sum test with continuity correction.

**Figure S2.** NEUT-RI and PCT stratified for severity classes based on SAPS II.

