REPLY TO: NEUTROPHIL TO LYMPHOCYTE RATIO AS A RISK STRATIFICATION TOOL FOR OLDER ADULTS WITH PNEUMONIA

To the Editor: We thank Karakonstantis and colleagues for their letter[1] regarding our recent paper on the role of neutrophil to lymphocyte ratio (NLR) in the prognosis stratification of pneumonia in elderly adults.[2] Their questions will no doubt lead to fruitful exchanges of comments on the meaning of our data. First of all, our study was conducted in 195 individuals consecutively hospitalized for pneumonia according to the following criteria: presence of a new infiltrate on plain chest radiography 103 or chest computed tomography associated with one or more suggestive clinical features such as dyspnea, hypo- or hyperthermia, cough, sputum production, tachypnea (respiratory rate >20 breaths per minute), altered breath sounds upon physical examination, hypoxemia (partial pressure of oxygen <60 mmHg), and leukocytosis (white blood cell count >10,000/μL). Hypoxemia occurred in 69% of the participants. Overall, at this stage, no conclusion from our study can be extrapolated to outpatients with pneumonia. We encouraged early discharge only of individuals with a NLR of less than 11.12, but this does not mean that individuals with these NLR values could be treated as outpatients. Karakonstantis and colleagues[1] in their letter many times referred to the Confusion, Urea, Respiratory rate, Blood pressure, aged ≥65 (CURB-65) score, which a large meta-analysis[3] and our study[2] showed had worse performance in risk stratification of pneumonia than the Pneumonia Severity Index (PSI), although in our study, mortality in individuals with a CURB-65 score of 2 or less was 41%. As Karakonstantis and colleagues[1] requested, characteristics of survivors and nonsurvivors are reported in Table 1. Regarding the possibility of overfitting of our results, our statistical evaluation has been performed using 1,000 randomizations of the original sample with a logistic regression classifier. In each randomization, we assigned half of the cases to a training group and the other half to a testing group. We applied this approach uniformly and in the same way for all of the analyzed variables: NLR, CURB-65, and PSI. Using this strategy, although overfitting cannot be completely excluded, the prediction of prognosis would be robust. The NLR cut-off in our study was similar to that of de Jager and colleagues,[4] which had been obtained in a mixed population, and not in elderly adults, as we in our study. Therefore, our data, coming from a proof-of-concept study, need to be confirmed in larger, multicenter studies focusing on the additional prognostic value of NLR in elderly outpatients with pneumonia. We confirm that individuals undergoing chronic immunosuppressive therapy were excluded from our study. Fifty-eight individuals, as is likely before hospital admission, who were given small doses of corticosteroids for less than 1 week to obtain an antiinflammatory effect were included in our study. Our analysis clearly showed that the administration of corticosteroids did not influence prognosis prediction. Moreover, as Karakonstantis and colleagues suggested,[1] we reran our model after excluding those 58 individuals given corticosteroids; NLR resulted in an area under the receiver operating characteristic curve (AUC) of 0.94, whereas PSI resulted in an AUC of 0.86, and CURB-65 an AUC of 0.58, confirming that NLR performed much better than the PSI and CURB-65. This further analysis clearly shows that, in our study, the confounding effect of corticosteroids, related to their stimulation of leukocytosis,[5] has no effect on the performance of NLR in the risk

Table 1. Characteristics of Survivors and Nonsurvivors

Parameter	Survivors	Nonsurvivors
	Mean ± Standard Deviation	
Age	78.9 ± 7.6	84.5 ± 5.3
Confusion, urea, respiratory rate, blood pressure, aged ≥65 score	2.4 ± 0.8	2.7 ± 0.7
Pneumonia severity index score	114.9 ± 27.3	152.2 ± 22.3
Heart rate, beats per minute	89.5 ± 18.7	90.3 ± 17.4
Systolic blood pressure, mmHg	130.9 ± 24.5	135.6 ± 32.9
Diastolic blood pressure, mmHg	73.9 ± 14.0	74.1 ± 14.4
White blood cell count, cells/μL	12.2 ± 5.5	13.8 ± 6.2
Neutrophil count, cells/μL	9.2 ± 4.4	13.2 ± 5.8
Lymphocyte count, cells/μL	1.3 ± 0.9	0.9 ± 0.8
Neutrophil-to-lymphocyte ratio	8.2 ± 6.0	27.3 ± 16.2
Hemoglobin, g/dL	11.7 ± 2.2	11.0 ± 2.3
Hematocrit, %	37.6 ± 6.6	36.4 ± 7.2
Erythrocyte sedimentation rate, mm/h	38.9 ± 16.2	37.3 ± 14.5
C-reactive protein, mg/dL	13.9 ± 11.0	15.5 ± 12.4
Ferritin, ng/mL	529.5 ± 461.3	407.9 ± 422.3
Serum creatinine mg/dL	1.1 ± 0.5	1.7 ± 0.6
Glomerular filtration rate, mL/min per 1.73 m^2	66.1 ± 24.4	38.2 ± 19.5
Chronic kidney disease, stage	2.3 ± 0.8	3.4 ± 0.8
Blood urea nitrogen, mg/dL	64.1 ± 34.1	100.1 ± 60.0
Glycemia, mg/dL	134.0 ± 63.3	153.0 ± 80.9
Sodium, mmol/L	138.2 ± 5.9	140.1 ± 5.1
Potassium, mmol/L	4.0 ± 0.7	4.0 ± 0.6
Chloride, mmol/L	99.1 ± 7.3	100.7 ± 9.5
D-dimer, ng/mL	682.2 ± 715.5	1,391.8 ± 1,416.9
Brain natriuretic peptide, pg/mL	219.9 ± 235.6	230.5 ± 192.4
pH	7.3 ± 0.3	7.4 ± 0.3
Partial pressure of carbon dioxide, mmHg	48.0 ± 17.1	46.6 ± 13.8
Partial pressure of oxygen, mmHg	54.9 ± 12.3	56.5 ± 13.8
Bicarbonate, mmol/L	29.1 ± 5.7	31.9 ± 9.0
Overall hospital stay, days	14.1 ± 5.1	13.3 ± 4.8

This letter comments on the letter by Karakonstantis et al.

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stratification of pneumonia in elderly adults. In conclusion, given the weak performance of PSI and CURB-65 in risk stratification of individuals with pneumonia, the results of our study would encourage exploration in larger multicenter surveys of whether the addition of NLR can improve the performance of these scores in older adults with pneumonia and whether NLR can be used for this purpose in an outpatient setting.

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