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Optimal cut-off value for LIPS and potential confounders for identifying the risk of developing ARDS

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To the Editor

We reviewed with great interest the comments by Kida et al. (1) regarding our manuscript on the use of the Lung Injury Prediction Score (LIPS) to identify non-emergency department (ED) patients at risk for acute respiratory distress syndrome (ARDS) (2).

First, we would like to address the appropriate cut-off value for the LIPS and the low positive predictive value (PPV) of a LIPS ≥ 4 (17%) to identify patients at risk of ARDS. We evaluated the number of ARDS cases missed at several cut-off points and determined that compared to a threshold LIPS ≥ 5 or ≥ 6 , a LIPS ≥ 4 missed the least number of ARDS cases. With a LIPS ≥ 4 , 17% of patients will develop ARDS and only 10% of them will be missed (sensitivity 90%). Using a LIPS ≥ 5 increased the percentage of patients who develop ARDS by 3% (PPV 20%), but we will miss 21% of them (sensitivity 79%). Lastly, if a LIPS ≥ 6 would be used, the number of ARDS patients identified will increase by another 3% (PPV 23%) but 33% of these patients would be missed (sensitivity 67%). A higher LIPS threshold of 5 or 6 only minimally increased the number of ARDS cases identified with a much higher increase in the number of ARDS patients missed with each increase in LIPS cut-off point.

Furthermore, the low PPV of a LIPS ≥ 4 in this study is similar to the PPV of 18% in the original LIPS study (3). Since the great majority of patients with predisposing conditions do not develop ARDS (4), a LIPS ≥ 4 is clinically useful if the preventive interventions applied to the patients at risk are associated with low costs and risks.

Second, since the aim of the study was to validate the LIPS as a prediction rule to identify non-ED patients at risk of ARDS at the time of clinical deterioration, the data collected included clinical characteristics, laboratory data, and interventions prior to or at the time of critical care contact. We did not include data to determine ARDS severity or evaluate whether the severity of ARDS predicted mortality as these analyses were unrelated to the main scope of this study.

Third, we agree with Kida et al. that some of the patients in this cohort could have developed ARDS if they survived long enough. Out of 200 deaths during the hospitalization, 140 patients died without ARDS, 47 (33%) of these patients died within the first 3 days and 77 (55%) within the first week after critical care contact. Due to the high mortality in this cohort and high number of patients dying within 7 days of clinical deterioration, we additionally performed all analyses including a composite outcome of ARDS or death as well as a competing risk analysis where early mortality was modeled as the competing risk

for ARDS. After accounting for the risk of hospital death, patients with a LIPS 4 had a significant four-fold increased risk of developing ARDS (HR 3.71, 95% CI 2.05–6.72).

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