than procalcitonin and had a better specificity than procalcitonin in differentiating "CAP" from "no-CAP." However, the threshold value of procalcitonin (0.159 ng/ml) used by the authors in their study is different and lower than the previously reported values (2), which would increase the false-positive rates and hence reduce the specificity of a test (3). Further, in routine clinical practice, a clinician's dilemma for correctly diagnosing CAP arises only in the presence of an abnormal chest radiograph, along with incongruous clinical features of CAP; a normal chest radiograph makes the diagnosis of CAP unlikely (4, 5). Also, in severe CAP requiring admission to the intensive care unit, the likelihood of a normal chest radiograph is even bleaker. Thus, we believe that the true predictive power of this novel genomic marker to correctly identify severe CAP would have been more apt if the no-CAP group had included patients with abnormal chest radiograph resulting from other conditions such as pulmonary edema, atelectasis, lung contusions, diffuse alveolar hemorrhage, and others. Despite performing better than protein biomarkers, the negative and positive predictive values of the *FAIM3*:*PLAC8* ratio were 80 and 77.2%, respectively, making it neither a good rule-in nor rule-out test in the diagnosis of severe CAP in the intensive care unit. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Reply

From the Authors:

We are grateful to Dr. Narasimhan and colleagues for their interest in our study on the derivation and validation of the *FAIM3*:*PLAC8* gene expression candidate biomarker for the rapid diagnosis of community-acquired pneumonia (CAP) (1). However, Dr. Narasimhan and colleagues clearly overlooked our stated premise for defining thresholds that favored high sensitivities at the expense of specificity, which reads as follows, "By favoring a high sensitivity we sought to address the potentially serious consequences of false negative predictions (CAP patient classified as no-CAP)." (1). The same rationale was adopted for the evaluation of plasma IL-8, IL-6, and procalcitonin measurements. Thus, the procalcitonin threshold of 0.159 ng/ml reflected our high-sensitivity criterion. We acknowledge that the procalcitonin threshold resides on the lower end of the ranges previously reported by others (2–4), which, together with Dr. Narasimhan and colleagues' comments, motivated us to evaluate the performance of procalcitonin across different thresholds (Table 1). Considering the 0.159-, 0.25-, 0.5-, 1-, and 2-ng/ml thresholds, the performance of plasma procalcitonin measurements in discriminating CAP and no-CAP patients remained poor (Table 1).

With respect to the characteristics of patients in the no-CAP group, we deliberately chose to only include patients who were suspected of having CAP at admission; that is, patients for whom the diagnostic test would be considered. Some of these patients with suspected CAP turned out to have other (noninfectious) reasons for their abnormal chest radiograph in our retrospective analysis, including the reasons mentioned by Dr. Narasimhan and colleagues. Those patients were therefore included in the no-CAP group. In fact, had we included patients with, for example, lung contusions without any clinical suspicion of CAP, our results would have been biased.

Last, we agree with Dr. Narasimhan and colleagues that the *FAIM3*:*PLAC8* gene expression candidate biomarker is not adequate for sole use in diagnosing CAP, as clearly stated in our article. However, we are optimistic that in combination with other biomarkers and/or clinical scores, the *FAIM3*:*PLAC8* expression ratio can be of important clinical utility. ■

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Table 1. Plasma Procalcitonin Performance

Threshold (*ng/ml*)	Sensitivity	Specificity	LR+	LR−	Post p+	Post p−
0.159	0.98	0.1	1.09	0.2	77%	38%
0.25	0.93	0.21	1.17	0.33	78%	50%
0.5	0.78	0.45	1.42	0.48	81%	59%
1	0.67	0.52	1.39	0.72	81%	66%
2	0.55	0.62	1.44	0.7	81%	69%

Definition of abbreviations: LR+ = positive likelihood ratio [sensitivity/(1 − specificity)]; LR− = negative likelihood ratio [(1 − sensitivity)/specificity]; Post p+ = posttest probability of being community-acquired pneumonia positive; Post p− = posttest probability of being community-acquired pneumonia negative.

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