CORRESPONDENCE

Philipp Schuetz
Beat Mueller

Biomarker-guided de-escalation of empirical therapy is associated with lower risk for adverse outcomes

Dear Editor,
We would like to congratulate Dr. Garnacho-Montero and colleagues for their prospective study suggesting a mortality benefit for patients in whom antibiotic therapy was de-escalated early [1]. As acknowledged by the authors and due to the observational study design, causal inference remains somewhat unclear. Although the authors used a state-of-the-art statistical approach that includes multivariate regression and propensity score analysis, residual confounding cannot be excluded. Thus, a prospective randomized trial is warranted for ultimate proof.

In line with these authors' study, we have recently analyzed data from similar trials in which patients were treated according to a procalcitonin algorithm for antibiotic de-escalation and control patients were not treated with this approach [2, 3]. We included all published randomized controlled trial data in an individual patient data (IPD) meta-analysis. The main purpose of this analysis was to demonstrate the safety of using procalcitonin protocols. Surprisingly, as demonstrated in Fig. 1, there was a significantly lower risk for treatment failure in patients with community-acquired pneumonia and patients treated in the emergency department when procalcitonin protocols were used for antibiotic stewardship. In terms of the mortality endpoint, there were no significant differences. However, the point estimate of 0.84 for intensive care unit patients with systemic infections treated according to a procalcitonin protocol is reassuring and may prompt future randomized trials to *de-escalate* antibiotic therapy with the aim of reducing mortality and morbidity using a similar biomarker approach.
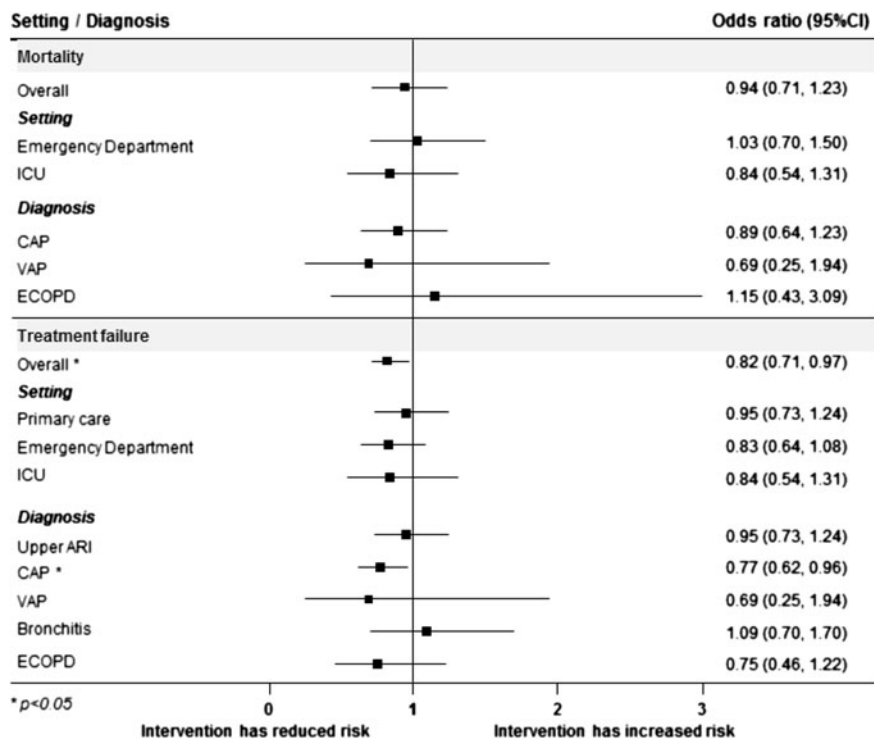
Fig. 1 Mortality and adverse outcomes associated with procalcitonin de-escalation protocols. *ICU* intensive care unit, *CAP* community-acquired pneumonia, *VAP* ventilator-associated pneumonia, *ECOPD* exacerbation of chronic obstructive pulmonary disease, *ARI* acute respiratory infection, *CI* confidence interval

References

1. Garnacho-Montero J, Gutierrez-Pizarraya A, Escoresca-Ortega A, Corcia-Palomo Y, Fernandez-Delgado E, Herrera-Melero I, Ortiz-Leyba C, Marquez-Vacaro JA (2013) De-escalation of empirical therapy is associated with lower mortality in patients with severe sepsis and septic shock. Intensive Care Med. doi: 10.1007/s00134-013-3077-7
2. Schuetz P, Briel M, Mueller B (2013) Clinical outcomes associated with procalcitonin algorithms to guide antibiotic therapy in respiratory tract infections. JAMA 309:717–718
3. Schuetz P, Muller B, Christ-Crain M, Stolz D, Tamm M, Bouadma L, Luyt CE, Wolff M, Chastre J, Tubach F, Kristoffersen KB, Burkhardt O, Welte T, Schroeder S, Nobre V, Wei L, Bhatnagar N, Bucher HC, Briel M (2012) Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections. Cochrane Database Syst Rev 9:CD007498

P. Schuetz (✉) · B. Mueller
Medical University Department, Kantonsspital Aarau, Tellstrasse, 5001 Aarau, Switzerland
e-mail: schuetzph@gmail.com
Tel.: +41-62-8389524; +41-79-3651006