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Title: Copeptin predicts early clinical deterioration and persistent instability in community-acquired pneumonia

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Body: Optimal risk prediction of early clinical deterioration in CAP remains unresolved. We prospectively examined the predictive value of the new biomarkers copeptin and proadrenomedullin (MR-proADM) in comparison to clinical scores and inflammatory markers to predict early high risk prognosis in CAP. Methods: 51 consecutive hospitalised adult patients were enrolled. We measured CRB-65- and PSI-scores, the ATS/IDSA 2007 minor criteria to predict ICU-admission and the biomarkers CRP, procalcitonin, copeptin and MR-proADM on admission. Predefined outcome parameters were combined mortality or ICU-admission after 7 days and clinical instability after 72 hours. Results: Copeptin was the only biomarker significantly elevated in patients with either adverse short term outcome (p=0.003). In ROC-curve analysis copeptin predicted ICU admission or death within 7 days (AUC 0.81, cut-off 35 pmol/l: sensitivity 78%, specificity 79%) and persistent clinical instability after 72 h (AUC 0.74). In Kaplan-Meier-analysis patients with high copeptin showed lower ICU-free survival within 7 days (p=0.001). The diagnostic accuracy of copeptin was superior to the CRB-65 score and comparable to the PSI-score and the ATS/IDSA minor criteria. If copeptin was included as additional minor criterion for combined 7-day mortality / ICU-admission, the diagnostic accuracy of the criteria was significantly improved (AUC 0.85, p=0.045). Conclusion: Copeptin predicts early deterioration and persistent clinical instability in hospitalised CAP and improves the predictive properties of existing clinical scores. It should be evaluated within a biomarker guided strategy for early identification of high risk CAP patients.