The levels of plasma Calprotectin and other biomarkers in early sepsis

Aleksandra Havelka[1,2], Anders Larsson[3], Joachim Johansson[4], Jonas Tydén[4], Miklos Lipcsey[5]

[1] Department of Molecular Medicine and Surgery, Karolinska Institute, Stockholm, Sweden, [2] Gentian Diagnostics AB, Stockholm, Sweden, [3] Department of Medical Sciences, Uppsala University, Uppsala, Sweden, [4] Department of Anaesthesia and Intensive Care Östersund, Umeå University, Umeå, Sweden, [5] Department of Surgical Sciences, Anaesthesiology and Intensive Care, Uppsala University, Uppsala, Sweden

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Introduction

Sepsis is the leading cause of death in ICU with a continuously increasing incidence and a high mortality rate. Early treatment improves outcome suggesting that rapid identification of patients with sepsis is important. Calprotectin is a novel biomarker which is released from neutrophil granulocytes in response to inflammation and/or infection. Rapid turn-around-time for analysis and early release of calprotectin upon inflammation and/or infection suggest that calprotectin can become a useful biomarker with widespread clinical use. We set out to determine the levels of plasma calprotectin in patients with and without sepsis on intensive care (ICU) admission and performance of calprotectin as a marker of mortality day 30 post ICU admission.

Methods

All adult patients with arterial cannula that where primarily admitted to the mixed ICU at Östersund General Hospital between the 1st of February 2012 and 31st of January 2013 were screened for discharge diagnoses. Plasma taken on admission from patients was analysed for Calprotectin, and the more investigated sepsis biomarkers Heparin Binding Protein (HBP) and Procalcitonin. We compared levels of these biomarkers in patients with sepsis (defined according to Sepsis 2) with levels in patients admitted for trauma, i.e. controls with inflammation, patients with other medical conditions (OMC), i.e. medical admissions with no infection, and finally with medical and surgical patients without these pre-specified diagnoses (Miscellaneous conditions). Plasma Calprotectin was analyzed with a particle enhanced turbidimetric immunoassay (PETIA) while HBP and PCT were analyzed by ELISA.

Results

328 patients met the inclusion criteria. 83 patients had sepsis, 33 trauma, 77 OMC as discharge diagnosis and 118 Miscellaneous conditions. Mortality at 30 days was 20% for sepsis patients, 9% for trauma patients, 21% for patients with OMC and 23% for patients with Miscellaneous conditions. The levels of Calprotectin were higher in sepsis vs. trauma patients ($p<0.001$, *** Figure 1a), sepsis vs. OMC ($p<0.01$,**), sepsis vs. Miscellaneous conditions ($p<0.01$,**) and was higher in patients who did not survive to 30 days ($p<0.01$). HPB levels were higher in sepsis vs. trauma patients ($p<0.001$,*** Figure 1b), sepsis vs. OMC ($p<0.001$,***), but were comparable in sepsis vs. Miscellaneous conditions (n.s.). HBP was higher in patients not surviving to 30 days ($p<0.001$). Plasma Procalcitonin did not differ between the groups or for outcome (Figure 1c).

Calprotectin performed best in discrimination between patients with sepsis and trauma patients. ROC curves showed areas under the curve of 0.79 for Calprotectin, 0.72 for HBP and 0.49 for Procalcitonin (Table 1).
Using a cut-off for Calprotectin of 1.27 mg/L rendered a specificity of 70% and a sensitivity of 81%. Using a cutoff for HBP of 26.6 ng/ml rendered a specificity of 52 % and a sensitivity of 86 %. Procalcitonin was not able to distinguish between sepsis and trauma patients.

Figure 1. The levels of Calprotectin, HBP and Procalcitonin in different diagnostic groups

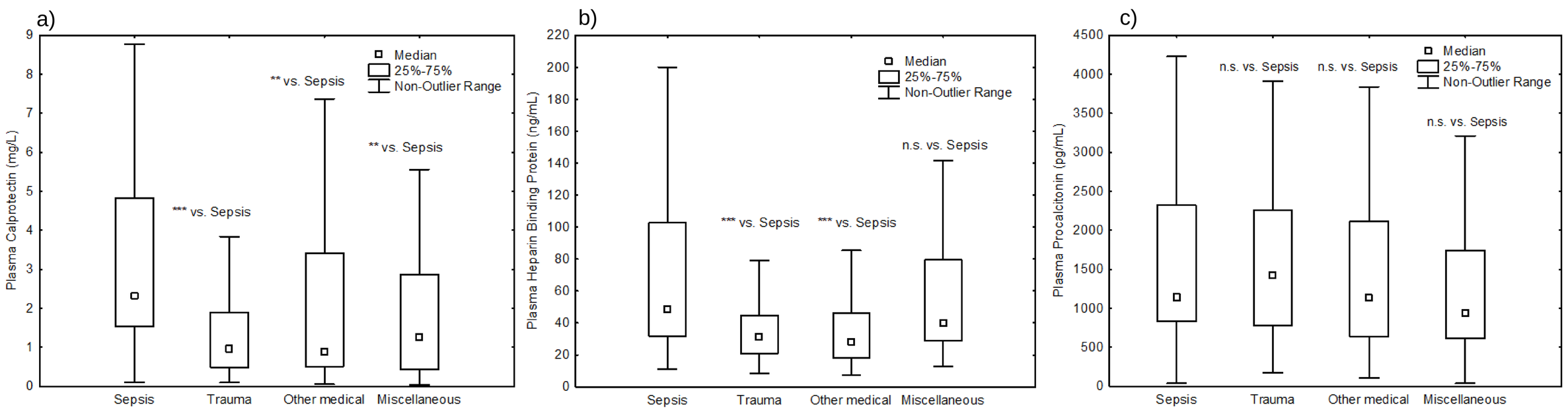

Table 1. Diagnostic and predictive performance of Calprotectin, HBP and Procalcitonin in discrimination between sepsis ans trauma patients

	ROC area (95% CI)	Cut-off	Specificity	Sensitivity	PPV	NPV
Calprotectin	0.79	1.27 mg/L	70%	81%	0.89	0.55
HBP	0.72	26.6 ng/ml	52%	86%	0.82	0.59
PCT	0.49	—	—	—	—	—

Conclusion

Calprotectin may be superior to Procalcitonin and HBP in indicating patients with sepsis as calprotectin, unlike HBP and procalcitonin, was consistently higher in sepsis patients compared to patients with other diagnoses with and without systemic inflammation. Calprotectin performed better then PCT and HBP in diagnosis of sepsis and distinguishing between patients with sepsis and trauma patients. Calprotectin and HBP showed predictive ability regarding 30 days mortality. Procalcitonin did not.

aleksandra.havelka@gentian.no

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