Abstract

Background

Few sepsis biomarkers accurately predict severity and mortality. Previously, we had reported that first-day histidine-rich glycoprotein (HRG) levels were significantly lower in patients with sepsis and were associated with mortality. Since the time trends of HRG are unknown, this study focused on the time course of HRG in patients with sepsis and evaluated the differences between survivors and non-survivors.

Methods

A multicenter prospective observational study was conducted involving 200 patients with sepsis in 16 Japanese hospitals. Blood samples were collected on days 1, 3, 5, and 7, and 28-day mortality was used for survival analysis. Plasma HRG levels were determined using a modified quantitative sandwich enzyme-linked immunosorbent assay.

Results

First-day HRG levels in non-survivors were significantly lower than those in survivors (mean, 15.7 [95% confidence interval (CI), 13.4–18.1] vs 20.7 [19.5–21.9] μg/mL; $P = 0.006$). Although there was no time × survivors/non-survivors interaction in the time courses of HRG ($P = 0.34$), the main effect of generalized linear mixed models was significant ($P < 0.001$). In

a univariate Cox proportional hazards model with each variable as a time-dependent covariate, higher HRG levels were significantly associated with a lower risk of mortality (hazard ratio, 0.85 [95% CI, 0.78–0.92]; $P < 0.001$). Furthermore, presepsin levels ($P = 0.02$) and Sequential Organ Function Assessment scores ($P < 0.001$) were significantly associated with mortality. Harrell's C-index values for the 28-day mortality effect of HRG, presepsin, procalcitonin, and C-reactive protein were 0.72, 0.70, 0.63, and 0.59, respectively.

Conclusions

HRG levels in non-survivors were consistently lower than those in survivors during the first seven days of sepsis. Repeatedly measured HRG levels were significantly associated with mortality. Furthermore, the predictive power of HRG for mortality may be superior to that of other singular biomarkers, including presepsin, procalcitonin, and C-reactive protein.