Decreased levels of plasmacytoid dendritic cells predict survival in critically ill patients

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Background: Critically ill patients admitted to intensive care units (ICUs) exhibit high mortality rates and suffer from a broad variety of life-threatening conditions. Irrespective of the initial cause of hospitalization, many of them experience systemic immune dysregulation accompanied by strong inflammatory activation and subsequent anti-inflammatory response resulting in immune paralysis. Dendritic cells (DCs) are the most potent antigen-presenting cells and play a pivotal role in regulating the immune response by linking the innate to the adaptive immune system. Previous studies already highlighted their prognostic value in sepsis and infectious diseases.

Purpose: DCs may be useful as a biomarker in intensive care medicine. Thus, the aim of this study was to analyse whether DCs or their respective subsets are associated with 30-day mortality in a cohort of unselected patients admitted to a medical ICU with cardiovascular focus.

Methods: 231 patients admitted to a tertiary care medical ICU were consecutively included in this single-centre prospective observational study. Patient characteristics and vital parameters were assessed within 24 hours following ICU admission and 72 hours thereafter. Additionally, blood was drawn at both time points. Subsequently, flow cytometry was utilized for the analysis of DCs and their respective subsets. Patients were prospectively followed up for 30 days or until the primary study endpoint, defined as mortality, was reached.

Results: In the study cohort, low percentages of total DCs were significantly associated with sepsis, respiratory failure, and the presence of shock. Percentages of plasmacytoid dendritic cells (pDCs) were inversely correlated with routinely assessed markers of inflammation, organ dysfunction and hemodynamic derangement. In particular, pDCs at admission showed the most robust association with survival in univariate analysis with a hazard ratio (HR) of 6.5 (95% confidence interval [CI]: 2.5 – 17.2, p < 0.001) comparing the first to the third tertile. In multivariate analysis, pDCs remained a strong and independent predictor of 30-day mortality after adjustment for demographic and clinical variables with an adjusted HR of 4.20 (1.3 - 13.3, p = 0.015). Corresponding Kaplan-Meier curves showing survival according to tertiles of pDCs at day 0 are displayed in figure 2 (log-rank test: p < 0.001).

Conclusion: We observed low percentages of DCs in patients admitted to an ICU suffering from sepsis, respiratory failure, and cardiogenic shock, which potentially contributes to the excessive immune response in critically ill patients. In our cohort, pDCs were identified as the most robust subset to predict 30-day mortality.

Figure 1. Plasma levels of dendritic cells at ICU admission (A) and after 72 hours (B) in 30-day survivors and non-survivors. DCs = dendritic cells, mDCs = myeloid dendritic cells, pDCs = plasmacytoid dendritic cells.
Figure 2. Kaplan-Meier curves illustrating the cumulative survival of patients according to tertiles of total DCs (A, D), plasmacytoid DCs (B, E) and myeloid DCs (C, F) at admission (A-C) and on day 3 (D-F). DCs = dendritic cells.