



## NRBC Counts for Risk Assessment in Hospitalized Patients

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The peripheral blood of healthy adults is generally free of nucleated red blood cells (NRBC), but in the blood of patients with a variety of severe diseases, NRBCs are often found. In such patients, the prognosis is relatively poor. Therefore, we evaluated the diagnostic and prognostic significance of this parameter for hospitalized patients without haematological diseases. Using a Sysmex XE-2100, we measured NRBC concentrations in 15,541 blood samples from 4,173 patients of a university over the course of 12 weeks. 7.5% of all patients were NRBC-positive at least once. The incidence of NRBC increased with age. The mortality of NRBC-positive patients (n=313) was 21.1% (n=66); this was significantly higher than the mortality of NRBC-negative patients (1.2%, n=3860). The mortality increased with increasing NRBC concentration. In terms of in-hospital mortality, NRBC in blood showed a sensitivity and specificity of 57.9% and 93.9%, respectively. NRBC were detected for the first time on average 21 days (median, 13 days) before death. Furthermore, in intensive care patients the incidence of NRBC was up to 30%. The mortality of NRBC-positive intensive care patients was >40 %. Mortality in NRBC-negatives was about 5%. Eighty three percent of deceased patients who were treated in a surgical intensive care unit were NRBC-positive at least once. In those patients a NRBC concentration >2000/ $\mu$ l was associated with a mortal outcome.

Whether a malfunction of the bone marrow leads to the detection of NRBC is as unknown as the possible role that cytokines could play in this process.

Therefore, erythropoietin, interleukin-3 (IL-3), interleukin-6 (IL-6), and interleukin-12p70 (IL-12p70) were analysed in the blood of 301 patients with circulating NRBC. 250 NRBC-negative patients served as control.

Multiple logistic regression revealed a significant association between the appearance of NRBC in the blood and erythropoietin, IL-3, IL-6, and age, respectively. Gender and IL-12p70 were not significantly associated with the appearance of NRBC in the blood. To estimate the red blood cell production in the bone marrow the increase in the reticulocyte concentration in blood was measured. The reticulocyte concentration in NRBC-positive patients was  $69 \pm 2$ /nl, being significantly higher than in NRBC-negative patients ( $60 \pm 2$ /nl;  $P < 0.01$ ).

Taken together, the routine analysis of NRBC in blood is of high prognostic power with regard to in-hospital mortality. Therefore, this parameter may serve as an early indicator for patients at increased mortality risk. Furthermore, as indicated by the cytokine profile NRBC could be a marker which sums up hypoxic and inflammatory injuries. Moreover, the increased number of reticulocytes in the blood of NRBC-positive patients may indicate that the appearance of NRBC is not associated with disturbed bone marrow function as far as the erythropoiesis is concerned.