KIR haplotype A is associated with mortality in sepsis

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OBJECTIVE: Natural killer (NK) cells are regulated by a set of activating and inhibitory cell surface receptors named killer immunoglobulin-like receptors (KIR). KIR haplotypes fall within two broad types: A and B. Haplotype B has been associated with better clinical outcomes in several diseases. Here we report an analysis of KIR gene haplotypes impact on clinical outcomes in critical care patients.

METHODS: DNA was genotyped using the polymerase chain reaction method with sequence-specific oligonucleotide (PCR-SSO kit, One Lambda® Inc, Woodland Hills, USA) for 16 KIR genes. Haplotype A was identified by the presence of a single activating gene, KIR2DS4. The presence of more than one activating gene defined haplotype B. Comparison of the KIR haplotype between groups was done with Pearson chi-square. To evaluate the influence of individual genotypes on outcomes, Cox multivariate logistic regression

analysis was used. Kaplan–Meier survival analysis was performed for survival curves. A $p \leq 0.05$ after correction was considered to indicate a statistically significant difference. The study was approved by the institutional Research Ethics Committee.

RESULTS: Forty-three different KIR gene combinations were found. Haplotype A was identified in 28.41%, and haplotype B in 71.59% samples. Haplotype A was identified in 29.38% septic patients and 8.33% controls, whereas B was identified in 70.62% septic patients and 91.67% controls (non-significant). Haplotype B was significantly associated with increased hospital survival ($p = 0.035$) and was more frequent in ICU survivors compared to non-survivors, although this latter comparison fell just short of significance ($p = 0.055$). Logistic regression adjusted for APACHE II revealed that haplotype A was associated with a hospital mortality risk of about 50% (HR=1.501; IC 95%: 1.036-2.175; $p = 0.032$) for critical care patients, and with a hospital mortality risk of about 56% (HR=1.556; IC 95%: 1.057-2.28; $p = 0.025$) for patients with sepsis.

CONCLUSION: KIR haplotype A may be a marker of higher probability of hospital mortality in septic patients. If confirmed by larger studies, these early findings might have implications on prognosis and therapies based on NK cell function in sepsis.