Category :**Sepsis: biomarkers**

A271 - ***Extracellular plasma dna levels limit the predictive value of genetic tlr9 variant rs352162 in multimorbidity sepsis patients***

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Introduction:

Extracellular DNA (exDNA) fragments in plasma mediate intercellular signaling in critical illness contributing to systemic inflammation reactions. Most studied mechanism includes binding of exDNA to its receptor TLR9 to induce NFkB gene expression. Carriers of genetic variant CC of TLR9 rs352162 are predisposed to multiple organ failure and/or lethal outcome in post-trauma[1], post-stroke [2]and sepsis[3]. In a novel study, we assess whether the concentration of exDNA in plasma may limit or reveal the predictive value of rs352162 TLR9 CC genotype in multimorbidity sepsis patients.

Methods:

The cohort included 110 post-surgery and diabetes patients with sepsis and multimorbidities (70% with cardiovascular diseases, hypertension, coronary artery diseases), Charlson index value, 7 (4-9), CIRS scale value, 23 (17-27). Circulating exDNA was isolated from plasma and quantified by CYBR Green dye. Genotyping of allelic variants CC, CT and TT of the TLR9 rs352162 polymorphism was performed using a PCR and allele-specific tetra primer set followed by electrophoretic separation of the PCR products. Statistical analysis was performed using SigmaPlot 12.5 software. The Shapiro-Wilk test was used to assess the normality of variable distribution in the groups. Significance between groups was evaluated by Chi-square withYates correction, Fisher's test, Mann-Whitney test and One-was ANOVA

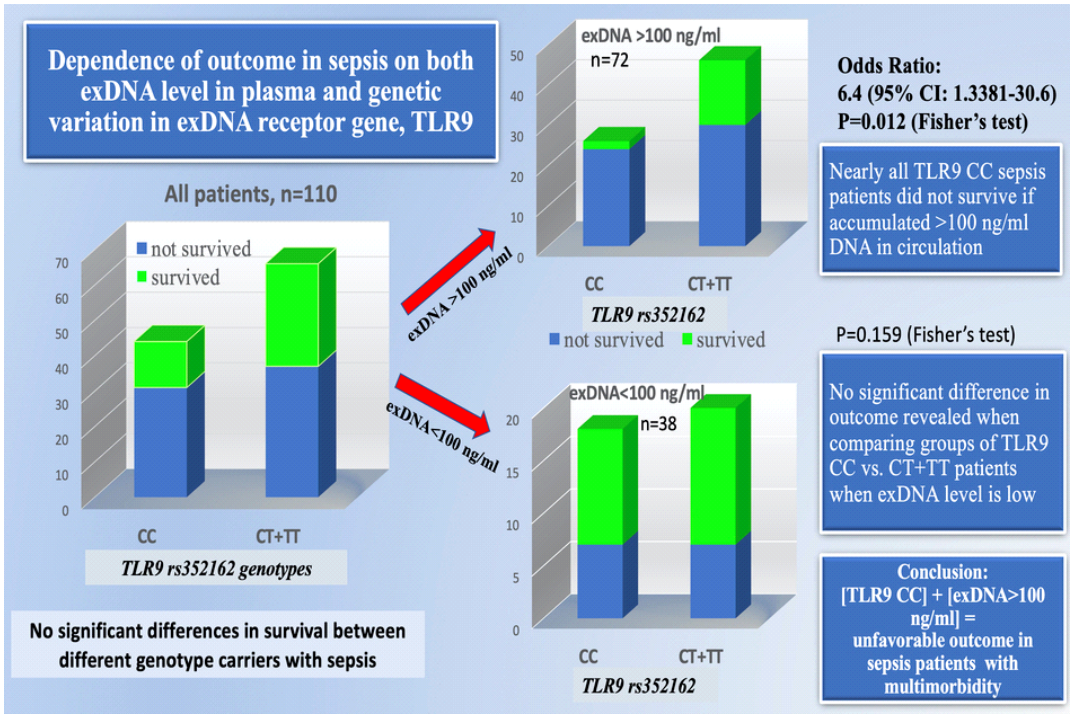
Results:

Carriers of TLR9 CC rs352162 genotype exhibit significantly increased CIRS index for lower GI and hepatic/pancreatic comorbidities. Only subcohort of patients with exDNA >100 ng/ml, however, exhibit significant association of TLR9 CC rs352162 genotype and increased risk for unfavorable outcome (odds ratio 6.4, 95%CI: 1.338-30.6), whereas no linking of TLR9 genotype and outcome are revealed in patients with <100 ng/ml exDNA in plasma.

Conclusion:

Determining the polymorphism of TLR gene and exDNA concentration in plasma might aid in stratification of multimorbid sepsis patients in ICU for early personalized intensive care.

Image :



Increased concentrations of plasma exDNA is required to reveal linking TLR9 genetic polymorphism and outcome in sepsis