

Galectin-3 is an independent predictor of survival in systemic sclerosis

Authors:

R. Faludi¹, M. Tokes-Fuzesi², G. Nagy³, L. Czirjak³, A. Komocsi¹, ¹Heart Institute, University of Pecs - Pecs - Hungary, ²University of Pecs, Department of Laboratory Medicine - Pecs - Hungary, ³University of Pecs, Department of Rheumatology and Immunology - Pecs - Hungary,

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Galectin-3 is a beta-galactoside-binding member of the lectin family. In previous studies, it has been shown to be an independent marker for outcome in heart failure and appeared to be particularly useful in heart failure with preserved left ventricular ejection fraction. High serum levels of galectin-3 have been described in a number of other conditions such as COPD, pneumonia, sepsis and kidney disease. In systemic sclerosis (SSc) galectin-3 may be related to organ sclerosis and aberrant activation of angiogenesis. The aim of our study was to determine the associations between galectin-3 levels and patient characteristics, as well as to investigate the long term prognostic value of galectin-3 in a large cohort of SSc patients.

Patients and methods: 152 SSc patients (55±11 years, 138 female) were included in the study. Blood samples and baseline clinical data were collected between 1st January 2005 and 31st December 2008. Primary outcome was all-cause mortality. Cardiovascular mortality was also investigated.

Results: After adjustments for age, gender and BSA, galectin-3 levels showed positive correlation with the grade of left ventricular diastolic function ($r=0.193$; $p=0.026$) and with the laboratory parameters of inflammation such as erythrocyte sedimentation rate ($r=0.172$; $p=0.036$) and CRP ($r=0.200$; $p=0.015$). Negative correlation was found between galectin-3 and diffusing capacity for carbon monoxide ($r=-0.228$; $p=0.006$). During the follow-up time of 7.2 ± 2.3 years, 35 SSc patients (23%) died, 16 of them suffered cardiovascular death. In Cox multivariate regression analysis galectin-3 was independent predictor of the all-cause mortality (HR: 2.780; $p=0.007$) and cardiovascular mortality (HR: 3.346; $p=0.031$) even after the inclusion of age, gender, BSA and NTproBNP levels. Using ROC analysis, galectin-3 >10.25 ng/ml and NT-proBNP >140.1 pg/ml were the best predictors of the all-cause mortality. When evaluated by comparing groups above and below the cut-off value for each biomarker,

NTproBNP and galectin-3 were discordant for 58 subjects (38.2%), divided approximately equally between high galectin-3/low NTproBNP (n=27) and low galectin-3/high NTproBNP (n=31). Compared with the reference group of low galectin-3/low NTproBNP, high galectin-3/low NT-proBNP (HR: 4.884, p=0.024) and low galectin-3/high NT-proBNP (HR: 4.196, p=0.026) groups had similarly higher mortality rate while the highest mortality was observed in the high galectin-3/high NT-proBNP group (HR: 12.180, p<0.0001) (Figure 1).

Conclusion: Our results suggest that galectin-3 is an independent predictor of all-cause and cardiovascular mortality in SSc. Added to NT-proBNP, galectin-3 provided complementary prognostic information, mainly by reflecting mortality risk associated to organ sclerosis and inflammation. Validation studies are required to establish whether galectin-3 may be considered as a useful and simple biomarker for selecting patients with high mortality risk in SSc.

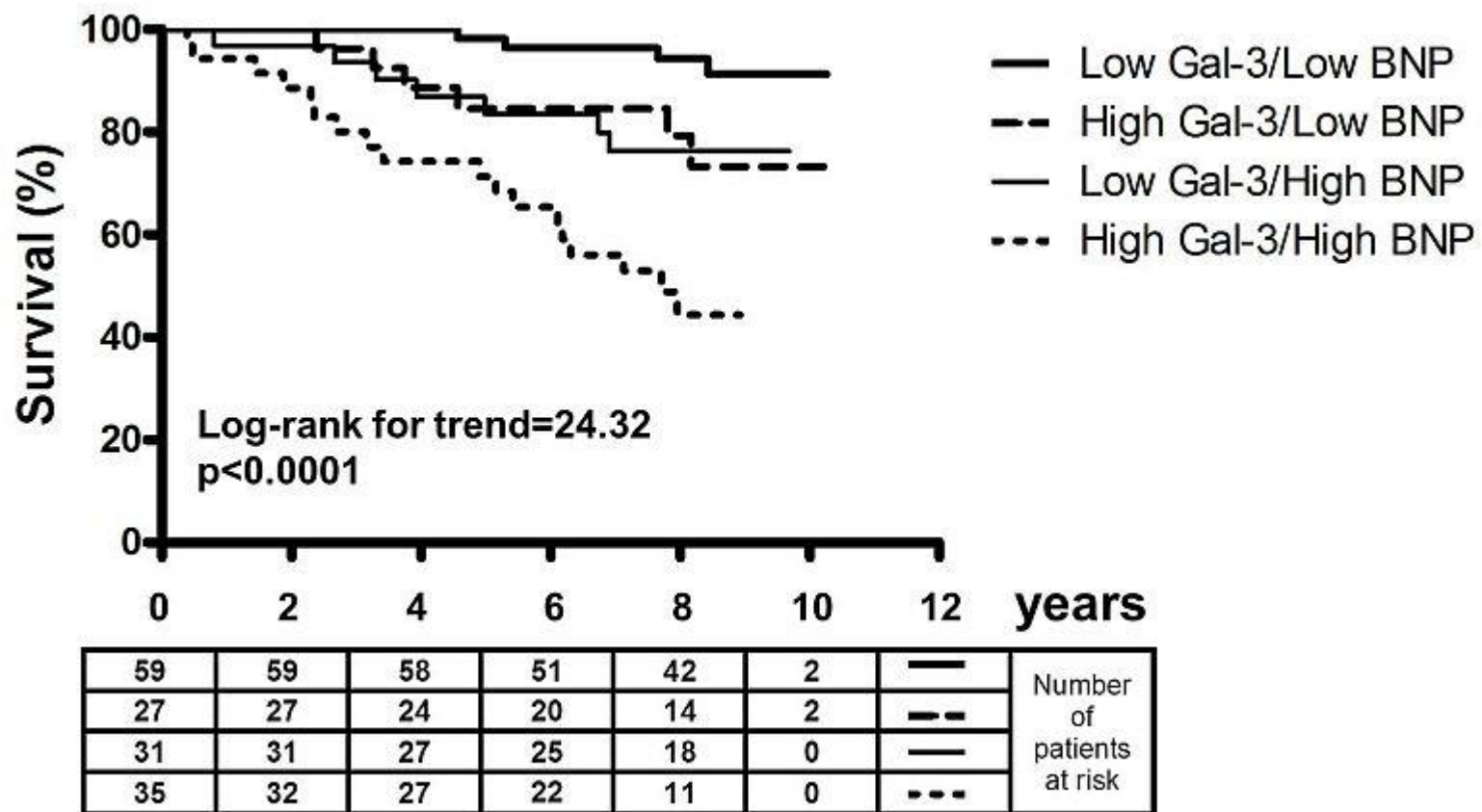


Figure 1