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Liver-specific microRNA-122 as a prognostic biomarker in patients with chronic heart failure

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Background. Several circulating microRNAs (miRs) have been proposed as potential diagnostic biomarkers in heart failure. However, studies investigating the prognostic value of circulating miRs in patients with chronic heart failure (CHF) are scarce.

Purpose. The aim of this study was to investigate the potential role of circulating miRs as prognostic biomarkers in patients with CHF.

Methods. A pathway-focused microRNA array was performed in pooled plasma samples of 40 patients with CHF who died during the follow-up and 40 age- and sex-matched survivors to screen for potential prognostic miR-candidates. In a second validation step, circulating levels of differentially expressed miRs were assessed using quantitative polymerase chain reaction in 234 patients with CHF admitted to our outpatient department for heart failure. Primary study endpoints were defined as all-cause and cardiovascular mortality.

Results. In the first phase, pathway-focused array analysis revealed differential expression of miR-122, miR-126 and miR-423 between CHF survivors and non-survivors. Circulating levels of these 3 miRs were then assessed in a large validation cohort of 234 patients. During a median follow-up time of 3.2 years, 76 patients (32.5%) died. miR-122 and miR-423 were strong, independent predictors of the primary endpoint even after comprehensive multivariable adjustment for age, sex, LVEF, NYHA class, renal function, CRP and BNP with respective HR per 1-SD of 1.16 (95% CI: 1.05-1.29, p=0.005) and 1.24 (95% CI: 1.09-1.41, p=0.001). In contrast, miR-126 showed no association with primary endpoint in univariate cox regression analysis (HR per 1 increase of standard deviation (1-SD) 1.01, 95% CI: 0.84-1.21, p=0.915). Interestingly, adding miR-122 to multivariable model improved Harrell's C index from 0.78 (95% CI: 0.73-0.83) to 0.81 (95% CI: 0.76-0.86, p=0.030), whereas no improvement was observed after adding miR-423 to the same model (C-index 0.79, 95% CI: 0.76-0.85, p=0.259).

Conclusion. Circulating miR-122 and miR-423 are independent predictors of all-cause and cardiovascular mortality in CHF patients. Furthermore, miR-122 improves risk stratification in this vulnerable group of patients. Thus, miR-122 might be a new, valuable and easily accessible biomarker for enhanced risk assessment in CHF.