

Novel concept to guide systolic heart failure medication by repeated biomarker testing-results from TIME-CHF in context of predictive, preventive, and personalized medicine

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Background

It is uncertain whether repeated measurements of a multi-target biomarker panel may help to personalize medical heart failure (HF) therapy to improve outcome in chronic HF.

Methods

This analysis included 499 patients from the Trial of Intensified versus standard Medical therapy in Elderly patients with Congestive Heart Failure (TIME-CHF), aged ≥ 60 years, LVEF $\leq 45\%$, and NYHA \geq II, who had repeated clinical visits within 19 months follow-up. The interaction between repeated measurements of biomarkers and treatment effects of loop diuretics, spironolactone, β -blockers, and renin-angiotensin system (RAS) inhibitors on risk of HF hospitalization or death was investigated in a hypothesis-generating analysis. Generalized estimating equation (GEE) models were used to account for the correlation between recurrences of events in a patient.

Results

One hundred patients (20%) had just one event (HF hospitalization or death) and 87 (17.4%) had at least two events. Loop diuretic up-titration had a beneficial effect for patients with high interleukin-6 (IL6) or high high-sensitivity C-reactive protein (hsCRP) (interaction, $p = 0.013$ and $p = 0.001$), whereas the opposite was the case with low hsCRP (interaction, $p = 0.013$). Higher dosage of loop diuretics was associated with poor outcome in patients with high blood urea nitrogen (BUN) or prealbumin (interaction, $p = 0.006$ and $p = 0.001$), but not in those with low levels of these biomarkers. Spironolactone up-titration was associated with lower risk of HF hospitalization or death in patients with high cystatin C (CysC) (interaction, $p = 0.021$). β -Blockers up-titration might have a beneficial effect in patients with low soluble fms-like tyrosine kinase-1 (sFlt) (interaction, $p = 0.021$). No treatment biomarker interactions were found for RAS inhibition.

Conclusion

The data of this post hoc analysis suggest that decision-making using repeated biomarker measurements may be very promising in bringing treatment of heart failure to a new level in the context of predictive, preventive, and personalized medicine. Clearly, prospective testing is needed before this novel concept can be adopted.

Clinical trial registration

isrctn.org, identifier: ISRCTN43596477.

type	journal paper/review (English)
date of publishing	13-05-2018
journal title	EPMA J (9/2)
ISSN print	1878-5077
pages	161-173