Impact of worsening renal function related to medication in heart failure

Hans-Peter Brunner-La Rocca, Christian Knackstedt, Luc Eurlings, Vinzent Rolny, Friedemann Krause, Matthias E Pfisterer, Daniel Tobler, Peter Rickenbacher, Micha T. Maeder & TIME-CHF Investigators

AIMS
Renal failure is a major challenge in treating heart failure (HF) patients. HF medication may deteriorate renal function, but the impact thereof on outcome is unknown. We investigated the effects of HF medication on worsening renal function (WRF) and the relationship to outcome.

METHODS AND RESULTS
This post-hoc analysis of TIME-CHF (NT-proBNP-guided vs. symptom-guided management in chronic HF) included patients with LVEF ≤45% and ≥1 follow-up visit (n = 462). WRF III was defined as a rise in serum creatinine ≥0.5 mg/dL (i.e. 44.2 µmol/L) at any time during the first 6 months. Four classes of medication were considered: loop diuretics, beta-blockers, renin-angiotensin system (RAS)-blockers, and spironolactone. Functional principal component analysis of daily doses was used to comprehend medication over time. All-cause mortality after 18 months was the primary outcome. Interactions between WRF, medication, and outcome were tested. Patients with WRF III received on average higher loop diuretic doses (P = 0.0002) and more spironolactone (P = 0.02), whereas beta-blockers (P = 0.69) did not differ and lower doses of RAS-blockers were given (P = 0.09). There were significant interactions between WRF III, medication and outcome. Thus, WRF III was associated with poor prognosis if high loop diuretic doses were given (P = 0.001), but not with low doses (P = 0.29). The opposite was found for spironolactone (poor prognosis in the case of WRF III with no spironolactone, P <0.0001; but not with spironolactone, P = 0.31). Beta-blockers were protective in all patients (P <0.001), but most in those with WRF III (P <0.05 for interaction). RAS-blockade was associated with improved outcome (P = 0.006), irrespective of WRF III.

CONCLUSION
Based on this analysis, it may be hypothesized that high doses of loop diuretics might have detrimental effects, particularly in combination with significant WRF, whereas spironolactone and beta-blockers might be protective in patients with WRF.