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Oral Contributions
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Background: A novel polygenic response predictor (PRP) for beta blocker (BB) survival benefit in heart failure (HF) was recently described which separated European ancestry BB responders from non-responders using a score derived from 44 genetic loci. We tested whether this would replicate in the United Kingdom Biobank (UKB) dataset.

Methods: UKB data pull identified patients with a HF diagnosis, genetic data and prescription data. Ejection fraction (EF) data was not available. BB exposure was quantified using BB dose and prescription frequency. The PRP was calculated using the genetic loci, weights, and cutoff value from the original description. Cox models were constructed of time to all-cause mortality adjusted for clinical risk (MAGGIC score), BB propensity score, BB exposure and BB exposure*PRP interaction.

Results: Among 7502 HF patients included, 34% were women, 54% had coronary disease, 33% atrial fibrillation, 51% baseline BB usage, and 22% (n=1651) were PRP-predicted responders. Patients in the PRP responder group had strong survival benefit associated with BB exposure (HR=0.55, p=0.016), while PRP non-responders showed little BB effect (HR=0.92, p=0.466) and this difference was significant (p-interaction =0.051). Survival curves by PRP group and dichotomized BB exposure (high vs. low) are shown in the figure.

Conclusion: The polygenic BB response predictor replicated in HF patients from the UKB regardless of EF. This innovative genomic medicine tool requires testing in a clinical trial.