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Heart rate – A complex prognostic marker in acute heart failure

We read with interest the article by Agra Bermejo et al. [1] on the results of resting heart rate (HR) as a predictor of hospital readmission and mortality in acute heart failure (HF). A plethora of studies have investigated the predictive value of resting HR in acute and chronic HF [2]. HR predicts the outcome in chronic HF with a steep rise in cardiovascular mortality at an HR $\geq$ 80 b.p.m. in patients with sinus rhythm [3], whereas an elevated resting HR in atrial fibrillation (AF) patients may not be associated with cardiovascular mortality [4,5].

The authors have reported a study population of 1398 consecutive patients admitted for acute HF and investigated the predictive values of discharge HR and the change in HR between admission and discharge on one-year probability of readmission and mortality.

Importantly, the authors have analyzed patients in sinus rhythm and in AF separately and include both HF with reduced and preserved ejection fraction in their analysis. In all these groups, HR at discharge predicted one-year mortality, with higher HR portending a higher mortality risk. In contrast, the change of HR between admission and discharge wasńt a predictor of mortality in sinus rhythm nor in patients with AF. Of note, after correction for other predictors, readmission for HF was not significantly associated with those two HR-based parameters in this study population.

These results are in contrast to findings of Takahama et al. [6], who reported that the difference in HR, but not the discharge HR, was predictive of a composite end point of readmission and all-cause death in a registry of 421 Japanese patients hospitalized for acute HF. On the other hand, the current study results are supported by a large American registry by Laskey et al. [7]. The authors analyzed 46,217 acutely decompensated HF Medicare patients >65 years and found a significant and linear positive correlation with one-year mortality. Notable differences between the latter two studies are the ethnic origin of the study participants, the definition of heart failure event and study design.

Despite all these differences, there are also commonalities. First, crude mortality rates are still sobering. The raw one-year mortality in the study by Agra Bermejo et al. was around 20%. The fact that HR appears to be a better predictor of 30-day mortality than of mortality from day 31 through day 365 is a finding which has also been corroborated by Laskey et al. [7]. Also, HR at discharge appears to be not very predictive of readmission for HF as opposed to mortality. This suggests that the readmission and mortality potentially underly different pathophysiological mechanisms. Additionally, this may also indicate, that the probability of readmission seems to be more difficult to predict, even with multivariate models [8]. Importantly, HR itself is a complex variable which is influenced by multiple factors: e.g. physiological variables like age or the tone of the autonomous nervous system [9]; the circadian rhythm; environmental factors like medication, but also neuropsychological factors like mood, stress or a depressive mental state. All these factors may impact the prognostic value of HR in HF patients.

While the authors shed an important light on this complex relation between HR and mortality, we would caution to jump from this correlation between HR at discharge and mortality to a conclusion of causality all too quickly. Of note, the current guidelines for acute and chronic HF recommend that in general, beta-blocker therapy should be initiated cautiously due to the potential of bradycardia and aggravating HF symptoms [10]. In this line, tolerability of initiation and up-titration of HF medication during the hospital stay may well influence the individual patients acute state of convalescence and thereby HR at discharge, apart from the discharge dose of negatively dromotropic medications like beta-blockers and ivabradine. Furthermore, ambulatory up-titration of HF medication is not only depending on the recommendations at discharge, but also on the continued dose adjustments made by office-based cardiologists and General Practitioners [11]. As the predictiveness of HR at discharge for mortality seems to be highest early after discharge from the hospital (within 30 days), it would also be interesting to see HR explored as a time-varying covariate in future studies (e.g. through continuous analysis of HR in implanted ICD). Besides, unknown confounding factors of the studied population that may have significantly contributed to the reported observations cannot be excluded. Thus, the study remains interesting and hypothesis generating but needs to be varified in a randomized trial.

In summary, while we have gained valuable insights into the complex phenomenon of HF, many questions remain open. The study shows, that discharge HR may predict one-year mortality, with higher HR portending a higher mortality risk in HF patients. However long-term outcomes were not reported. Future randomized studies are warranted to assess the (true) prognostic significance of discharge HR and to determine, whether discharge HR may be used for risk stratification and to initiate a more personalized and intense follow-up or rehabilitation program. We thank the authors for their important contribution and are looking forward to the adjustments in clinical pathways that this study may open.

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