

### Abstract

**Background:** N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a useful biomarker for monitoring the status of heart failure. However, the optimal monitoring interval is unknown. This study aimed to investigate its minimal informative monitoring interval in stable heart failure patients, with different risk profiles.

**Methods:** This was a retrospective open cohort study. Consecutive adult patients admitted for acute heart failure at a tertiary hospital during January 2003 to December 2017 with available NT-proBNP measurements were included. NT-proBNP measurements between six months after discharge and the time point where a heart failure medication regimen changed or readmission was identified were subjected to analysis. We fit a random-effects model for progression, biological variability and measurement error of NT-proBNP and adapted a signal-to-noise ratio method to distinguish actual progression of disease from biological variability and measurement error. We conducted the same analysis in subgroups stratified by different underlying risks.

**Results:** We included 368 patients (median age 75.5 years [interquartile range 63.0 – 83.0], 57% male) in our analysis. Patients had six NT-proBNP measurements in median (interquartile range 4 – 10) during the follow-up duration (median 12 months [interquartile range 6.0 – 27.0]). From the estimates of the random-effects model, signal (i.e. actual progression of disease) exceeded noise (i.e. biological variability and measurement error) after 8.1 months (95% confidence interval [CI]: [5.7 – 10.1]). Patients aged 80 years or more had a shorter informative interval compared to patients less than 80 years (< 67 year-old, 16.9 months (95%CI: [7.5 – 21.6]); ≥ 67 and < 80 year-old, 10.0 months, 95%CI: [8.5 – 11.4]; ≥ 80 year-old, 5.7 months, 95%CI: [4.9 – 6.8]). As risk predicted by AHEAD score increases, monitoring intervals consistently shortened, from 12.3 (95%CI: [10.3 – 14.4], AHEAD score 0 or 1) to 3.3 months (95%CI: [.0 – 3.8], AHEAD score 4 or 5).

**Conclusion:** In patients with stable heart failure, the overall informative interval of NT-proBNP measurement is 8.1 months, which varies by the underlying risk. The optimal monitoring interval could be lengthened especially for patients at lower risk.