Heart rate variability and severe intraventricular haemorrhage in preterm infants

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Introduction

- Preterm infants are known to be at risk of intraventricular haemorrhage (IVH) and adverse long term neurodevelopmental outcomes.
- Early detection and intervention are key to minimising long term complications.
- Heart rate variability (HRV) is a measure of how heart rate changes over time which can be obtained non-invasively from a bedside monitor.
- HRV can be defined using a variety of metrics.
- HRV has previously been shown to be predictive of severe IVH (grades III and IV) in preterm infants, but due to heterogeneity of the studies, it is unclear which HRV metrics are most useful[1].

Metric	Domain	Definition
SDRRI	Time	Standard deviation of the R-to-R interval
HF	Frequency	Power of the high frequency band of ECG trace
LF	Frequency	Power of the low frequency band of ECG trace
VLF	Frequency	Power of the very low frequency band of ECG trace
SD1	Non-linear	Poincaré plot standard deviation perpendicular to the line of identity
SD2	Non-linear	Poincaré plot standard deviation parallel to the line of identity
$\alpha 1$	Non-linear	Detrended fluctuation analysis short term exponent
$\alpha 2$	Non-linear	Detrended fluctuation analysis long term exponent

Table 1 – Selected metrics of HRV used in present study[2]

Why use heart rate variability in the prediction of intraventricular haemorrhage?

Intraventricular haemorrhage is thought to be caused by a combination of vascular fragility in the germinal matrix and abnormal cerebral blood flow[3]. Cerebral blood flow is controlled by the autonomic nervous system. Importantly, its parasympathetic branch does not reach functional maturity until the third trimester and may therefore be key in the pathogenesis of IVH. The parasympathetic and sympathetic branches have different effects on HRV and specific metrics of HRV should therefore be able to identify infants with autonomic dysfunction predisposing them to IVH.

Aim

The aim of this study was to identify the HRV metric most predictive of severe IVH in preterm infants.

Findings

- 7 infants developed severe IVH (sIVH, full cohort). 5 of those infants were known to be sIVH-free during the period of EKG recording and only developed sIVH later on (late cohort).
- Full cohort - 4/8 HRV metrics were significantly lower in sIVH, including SDRRI, HF, SD1 and SD2. SD1 achieved the highest AUC at 0.89 and 85.7% sensitivity.
- Late cohort - 7/8 metrics were significantly lower including SDRRI, HF, LF, VLF, SD1, SD2 and alpha1. **A drop in SD1 was able to detect sIVH with a 100% sensitivity and 90.2% specificity.**

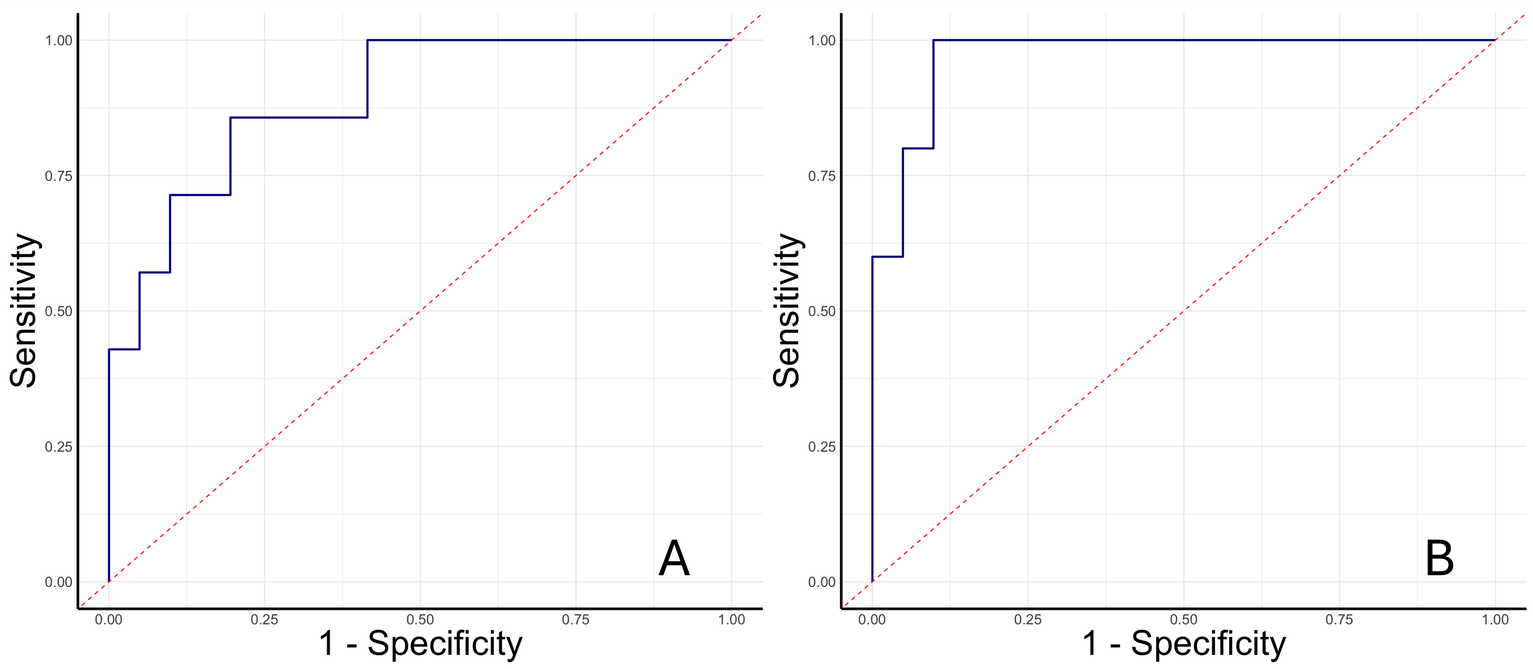


Figure 1 – ROC curves for prediction of sIVH using SD1
A - ROC curve using the full cohort of 48 infants including 7 infants with sIVH,
B - ROC curve using the late sIVH cohort including 5 infants who developed sIVH only after EKG recording.

Methods

- In this prospective cohort study, the EKG traces of 48 preterm infants born at <28 weeks were recorded continuously for 7 days.
- First available 5x2 hour segments free-from movement artefact were used to extract HRV metrics listed in table 1 using MATLAB.
- HRV metrics in infants with severe IVH were compared with infants without severe IVH using Wilcoxon rank sum test.
- Receiver operating characteristic (ROC) curve was used to evaluate each metric as a predictor of severe IVH.
- Differences in baseline characteristics were tested using Wilcoxon rank sum, X^2 or Fisher's exact test and potential confounders evaluated using median regression.

Conclusions

The study has identified SD1 and HF to be the most predictive of severe IVH in preterm infants. Both metrics are thought to be representative of parasympathetic tone.

References

1 – Smolková, M. et al., *Pediatric Research*, 2024
2 – Chiera, M. et al., *Frontiers in Neuroscience,* 2020
3 – Volpe's Neurology of the Newborn (Seventh Edition), 2024

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