

Time domain and non-linear heart rate variability (HRV) parameters

The time domain indices of HRV were calculated from 5-minute-long segments of the electrocardiogram (ECG) waveform, which were used to obtain the frequency domain indices (low frequency [LF], high frequency [HF], LF/HF, and total power). The parasympathetic nervous activity, which is mediated by a respiratory sinus arrhythmia, contributes to 1) the standard deviation of the RR intervals of normal sinus beats originating from the sinoatrial node of the right atrium (SDNN); 2) the percentage of adjacent normal-to-normal sinus beat RR intervals that have a more than 50 milliseconds difference between them (pNN50); 3) the standard deviation of the successive differences in the RR interval (SDSD); 4) the root mean square of the successive differences in the RR interval (rMSSD); 5) the interquartile range of the successive differences in the RR interval (IRRR); and 6) the median of the absolute values of the successive differences in the RR interval (MADRR).

The baseline width of the triangular interpolation of the normal-to-normal RR intervals histogram (TINN) was calculated as

$$TINN = \frac{\text{total number of RR intervals} \times 7.8125 \text{ milliseconds} \times 2}{\max(\text{number of RR intervals in each bin})}$$

where 7.8125 milliseconds is the size of a bin. The HRV index was calculated as

$$HRV \text{ index} = \frac{\text{total number of RR intervals}}{\max(\text{number of RR intervals in each bin})}$$

TINN and HRV index represent the overall activity of HRV but are more affected by LF than by HF [1].

A Poincaré plot is a scatter plot where each pair of preceding and succeeding RR intervals is plotted on the abscissa and ordinate, respectively. After fitting the ellipse around the plot, SD1 and SD2 were calculated as the standard deviation of the distance of each point from the line of

identity ($y = x$) and from the line passing through the centroid, which vertically intersects the line of identity, respectively. SD1 and SD2 reflect the short-term and long-term HRV as the lengths of the transverse and long axes of the ellipse, respectively. SD1, SD2, and SD1/SD2 correlate with the baroreflex sensitivity and HF, with the baroreflex sensitivity and LF, and with the LF/HF, respectively [1].

Sample and approximate entropy

Using the RR interval data obtained from a 5-minute-long segment of an ECG waveform, sample entropy and approximate entropy were calculated by setting $m = 2$ and $r = 0.2 \times$ *standard deviation of the data*, where m is the length of sequences to be compared and r is the tolerance value below which a match is deemed to be achieved [2]. The length of the data, n , was the number of RR intervals. Sample entropy decreases the bias caused by the self-comparison of vectors, which occurs when approximate entropy is calculated. Sample and approximate entropy measure the regularity and complexity of the data, with high values indicating the low predictability of the changes in the successive RR intervals.

R packages for time domain and non-linear HRV parameters and sample and approximate entropy

All the time domain and nonlinear HRV parameters were calculated using the RHRV package (version 4.2.5, <https://CRAN.R-project.org/package=RHRV>). Sample and approximate entropies were calculated using the TSEntropies package (version 0.9, <https://CRAN.R-project.org/package=TSEntropies>). The two packages were installed in the R program (version 4.0.1, R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>).

Generation of spectrogram

To show the longitudinal changes in the HRV parameters of one patient who developed a hypotensive bradycardic event (HBE), a spectrogram was generated using the whole ECG waveform between the beginning of the study and the end of the surgery. The whole waveform was divided into 100-second-long segments that overlapped adjacent segments by 90% (90 seconds). Each segment sequentially underwent detrending, Hamming windowing, and fast Fourier transform. The calculated spectral power was natural-log-transformed, and its values, which ranged from 0 to 10 [$\ln(\text{ms}^2/\text{Hz})$], are displayed with rainbow color shading in a density plot, where the x, y, and z axes represent time in seconds, frequency in Hz, and spectral power in log scale, respectively. The spectrogram was drawn with DADiSP software.

References

1. Shaffer F, Ginsberg JP. An overview of heart rate variability metrics and norms. *Front Public Health* 2017; 5: 258.
2. Byun S, Kim AY, Jang EH, Kim S, Choi KW, Yu HY, et al. Entropy analysis of heart rate variability and its application to recognize major depressive disorder: A pilot study. *Technol Health Care* 2019; 27: 407-24.