Stability over time of short-term heart rate variability

Tuula H. Tarkiainen
Kirsi L. Timonen
Pekka Tiittanen
Juha E. K. Hartikainen
Juha Pekkanen
Gerard Hoek
Angela Ibald-Mulli
Esko J. Vanninen

Introduction

Heart rate variability (HRV) has become a valuable non-invasive method to assess cardiovascular autonomic regulation. In 1987, Kleiger et al. reported that reduced HRV was related to increased mortality after myocardial infarction (MI) [11]. In more recent studies, reduced HRV has been related especially to sudden arrhythmic death, but also to other cardiac events, such as death caused by heart failure [6, 13, 15]. HRV as a risk marker for cardiac mortality has been used to study the preven-
tive role of implantable defibrillators in patients early after myocardial infarction (DINAMIT study) [5].

Most studies have used 24-hour ambulatory ECG recordings for the HRV assessments in relation to risk stratification. It is known, however, that also the short-term HRV has prognostic information [1, 2]. In addition, short-term recordings are more feasible to perform than long-term recordings and what is most important, they can be performed under standardized conditions, which should reduce the physiological variation of the HRV measures. The reproducibility of long-term HRV has been shown to be either satisfactory or high both in healthy subjects and patients with stable coronary artery disease (CAD) [8–10, 16]. However, the reproducibility and stability of short-term HRV measurements have not been properly evaluated; this should be done before these measurements are used more widely.

Our study was conducted in the framework with European ULTRA study (Exposure and risk assessment for fine and ultrafine particles in ambient air) [17]. The purpose of the present study was to evaluate the stability of short-term HRV over a three to four month period in patients with CAD.

Methods

■ Study population

The ULTRA study investigated 131 subjects with stable CAD. The main inclusion criteria were a self-report on a physician-diagnosed CAD, being a non-smoker, and age > 50 years. Six subjects were excluded from the HRV analysis because of atrial fibrillation, two subjects because of very frequent supraventricular ectopic beats and one subject because of a second degree atrioventricular block. Finally, 122 subjects were included for the assessment of short-term HRV.

For the reproducibility analyses, we selected the subjects who had at least seven HRV measurements during the first nine consecutive visits. Thus, the investigated time period was between three to four months. Among these 89 subjects, there were 21 female and 68 male subjects; the mean age was 67.3 (SD 8.4, range 40–83 years). Fifty-eight subjects reported a previous myocardial infarction and 57 subjects because of very frequent supraventricular ectopic beats and one subject because of a second degree atrioventricular block. Finally, 122 subjects were included for the assessment of short-term HRV.

■ Study protocol

The subjects made a clinical visit every two weeks, whenever possible on the same week day and at the same time of the day during the winter of 1998–1999. Their medication was not changed for the visits. During the visits the subjects were subjected to a standardized 40-minute protocol which included 5-minute periods of rest, paced breathing and standing, a 6-minute submaximal exercise test and a 10-minute period of recovery. During the paced breathing period the subjects were in the supine position and were asked to breathe with 0.2 Hz frequency (5 s breathing cycles). The exercise test was performed with a bicycle ergometer and the heart rate was aimed to be 90–100 bpm for five minutes. The methods used in the ULTRA study have been published in the Standard Operating Procedures (SOP) developed for the ULTRA study [17]. The subjects gave written informed consent before participating in the study and the study protocol was approved by the local ethics committee. The investigation conforms with the principles outlined in the Declaration of Helsinki.

■ Ambulatory ECG recordings

Two-channel ambulatory ECG recordings were performed with the analogous Medilog MR63 recorders (Oxford Instruments, Abington, U. K.) with standard electrode positions for lead V5 and V1. The ECG recordings were interactively edited and the HRV analyses performed with the commercial Exel Medilog II V7.5 system (Oxford Instruments, Abington, UK) in one core laboratory (Kuopio University Hospital) by experienced nurses.

The recordings were digitized with a sampling rate of 128 Hz. Because of the low sampling rate, the software used an algorithm of interpolation to refine the R wave fiducial point and to improve the time resolution in R-peak detection. The computer classifications (normal, supraventricular, ventricular, unclassified or artifact) were manually reviewed and, if necessary, edited. A premature beat was defined to differ more than 20% from preceding ones. The recordings in which the number of ectopic beats exceeded 10% were excluded from the HRV analyses. A triple-beat filter was used before HRV analyses and only normal-to-normal beat (NN) intervals between 300 and 2000 ms were included. An interpolated tachogram was used for the HRV analysis. Linear detrending and a Hanning window function were applied before performing spectral analysis based on fast Fourier transformation.

Time domain measurements calculated from the whole 40-minute recording and 5-minute periods of rest and paced breathing were the mean normal-to-normal interval, mean NN (ms), standard deviation of all NN intervals, SDNN (ms), and the square root of the mean of the sum of the squares of differences between adjacent NN intervals, r-MSSD (ms). The total power (TP) in the frequency range from 0 to 0.40 Hz was divided into very low frequency (VLF; 0.003–0.04 Hz), low frequency (LF; 0.04–0.15 Hz), and high frequency (HF; 0.15–0.40 Hz) bands. The 5-min period was considered too short for VLF power calculation [17]. The integrals under respective power spectral density functions were calculated and expressed in absolute units (ms²). Moreover, the ratio between LF and HF power (LF/HF ratio) was calculated.

■ Statistical methods

The statistical analyses were performed using the SPSS 10.0 software package for Microsoft Windows (SPSS Inc., Chicogo IL, USA). The coefficient of variation (CV) (%) was used to assess the stability of the HRV measurements over time. The coefficient of variation as well as the confidence intervals for the coefficient of variation were calculated using the formulas for the definition of short-term precision presented by Šišler et al. [4]. Šišler et al. have investigated the assessments of precision errors with a technique demanding very high reproducibility, i.e., bone densitometry techniques. They emphasize especially that the short-term precision errors (expressed as CVs) should be calculated as root-mean-square averages of standard deviations of repeated measurements and is not given by the arithmetic mean of individual subjects’ precision errors, because this leads to underestimation of the true imprecision.

The frequency domain heart rate variability as well as r-MSSD showed a skewed distribution and, thus, the logarithmic values were used in the analyses. The LF/HF ratio was used as percentage to enable the logarithmic transformation.

Heart rate is known to be a determinant of SDNN. Therefore, we assessed the possible effect of HR increase during the submaximal exercise, i.e., change in mean NN between rest and exercise, on SDNN by Spearman correlation coefficient. Because there were many consecutive HRV measures from each subject, the differences between each