Reference values for time- and frequency-domain heart rate variability measures

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BACKGROUND The analysis of heart rate variability (HRV) has become an established procedure in recent decades. Because there are no appropriate reference values available, HRV findings can still only be compared within a group or in individuals in longitudinal studies.

OBJECTIVE The objectives of the present study were to examine a group of healthy subjects of different ages and sexes and to identify reference values for common HRV parameters.

METHODS Long-term 24-hour electrocardiograms of 695 voluntary subjects were recorded by using a 2-channel Holter system over a period of 24 hours during daily activities.

RESULTS Reference values for men and women in 10-year age groups were calculated for standard deviation of NN intervals, root mean square of successive differences of NN intervals, standard deviation of the average of all consecutive 5-minute NN intervals, percentage of consecutive NN intervals that deviate from one another by more than 50 ms, low-frequency power normalized unit, high-frequency power normalized unit, low frequency/high frequency ratio, SD1, and SD2. The 5th and 95th percentiles were given for each sex and for the age groups 20–30, 30–40, 40–50, and 50–60 years. We observed a consistent decrease in HRV measures with increasing age as well as a sex dependency of HRV findings.

CONCLUSION We studied a large group of healthy subjects and identified reference values for commonly used HRV measures for 24-hour ECG measurements. The reference values differed considerably from the values published in 1996 in the Guidelines of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. In the future, steps should be taken to expand the database and define reference values for the age groups under 20 and over 60 years. It would be desirable to obtain reference values for short-term recordings (eg, 5-minute recordings) as well.

KEYWORDS Autonomic nervous system; Heart rate; Analysis; Electrocardiogram; NN intervalsicus

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Introduction

The measurement and analysis of heart rate variability (HRV), which is based on the variation between consecutive NN intervals, has become an established procedure over the past 2 decades[1–4] since the publication of the first guidelines.[5] Not only there have been advances in recording technology (smaller, more mobile, more accurate devices),[6] but NN intervals can now be measured by small chest strap and pulse watch systems.[7,8] Technological developments have decreased the costs of recording and analysis and have facilitated applications in an outpatient setting.

In 1996, Malik et al introduced possible "normal values" in the Guidelines of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology.[5] However, they pointed out that these values had been measured only in a small number of subjects and recommended further studies. In a 2010 review that included 44 previously published studies, Nunan et al[9] reported mean values unrelated to age for the 5-minute short-term recording of commonly used HRV measures. They identified mean values lower than those published in the above-mentioned guidelines of 1996.[5] Because HRV is not only sex-related[10–12] but also age-related,[10,13,14] the values from Nunan et al[9] being not correlated with age are applicable only to a limited extent.

Since there are no appropriate reference values available, HRV findings can only be compared within a group or in individuals in longitudinal studies. The objectives of the present study were to examine a group of healthy subjects of different ages and sexes and to identify reference values for common time- and frequency-domain HRV measures as well as for both Lorenz plot variables.

Methods

Long-term electrocardiograms (ECGs) of voluntary subjects were recorded by using a 2-channel Holter system (Schiller MT-101, Firma Schiller AG, Baar, Switzerland) over a

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period of 24 hours during daily activities, and the intervals between the individual R waves were calculated with a sampling frequency of 1000 Hz. During recording time, subjects were asked to follow their normal daily activities except performing physical exercise or taking a shower/bath. This corresponds to the recommendations in the Guidelines of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology[5] as well as to current recommendations for measuring NN intervals for HRV analysis.[7]

Exclusion criteria were diagnosis of coronary heart disease with or without stent implantation, heart attacks, strokes, night shifts during recording time, diagnosed diabetes mellitus (irrespective of type), use of psychiatric medication, and pregnancy. Subjects younger than 20 years and older than 60 years were also excluded.

All subjects were informed about the study in writing before participation and signed informed consent forms. The study protocol conforms to the ethical guidelines of the Declaration of Helsinki and was presented to and approved by the ethics committee of Otto von Guericke University Magdeburg, Magdeburg, Germany.

A total of 695 subjects were included in the study. Most of the subjects were volunteer participants from the normal population of Magdeburg, Germany (n = 267). The other subjects came from preventive studies in several different workplaces: bank employees (n = 89), military servicemen (n = 57), doctors' assistants (n = 46), students (n = 45), government employees (n = 44), public transportation servicemen (n = 38), employees at the university (n = 38), police servicemen (n = 33), rescue servicemen (n = 30), nurses (n = 5), and doctors (n = 3). On the day of 24-hour ECG measurement, subjects spend the day as normal as usual and did not have night shift.

After the data were recorded, they were analyzed using the Schiller MT-200 Holter ECG program (version 2.54, Firma Schiller AG) on a personal computer. Long-term ECGs were analyzed both by computer and manually by a physician.

After the NN intervals were exported, an HRV analysis was performed with Kubios HRV Version 2.0 (University of Kuopio, Kuopio, Finland)[15] with artifact correction (settings: "custom" and "0.3") and a trend component (method: "smooth priors" and "Lamda = 500").[16] The frequency analysis was conducted using a fast Fourier transformation (window width 256 seconds; overlap ratio 50%). The following frequency bands were used: low frequency (LF) from 0.04 to 0.15 Hz and high frequency (HF) from 0.15 to 0.40 Hz.[5] Recordings with a total length of <22 hours were excluded.

In addition to time-domain measures (standard deviation of NN intervals [SDNN], root mean square of successive differences of NN intervals [RMSSD], standard deviation of the average of all consecutive 5-minute NN intervals [SDANN], and percentage of consecutive NN intervals that deviate from one another by more than 50 ms [pNN50]), low-frequency power normalized unit (LFnu), high-frequency power normalized unit (HFnu), and LF/HF ratio as frequency-domain measures and SD1 and SD2 as HRV parameters of the Poincaré plot were calculated.[7] It must kept in mind that LFnu and HFnu are linearly dependent and that both parameters always add together to 100 (LFnu + HFnu = 100). Also, SD1 and SD2 are related to linear indices and can be transferred to SDNN and RMSSD, respectively.

In order to compute age- and sex-related reference values, the subjects were allocated to the following 10-year age groups according to their sex (male/female):

- age ≥20 and <30 years,
- age ≥30 and <40 years,
- age ≥40 and <50 years, and
- age ≥50 and <60 years.

A total of 695 subjects were included in the study; 319 (45.9%) subjects were men with a mean age of 40.2 ± 10.4 years, a body height of 179.8 ± 7.2 cm, and a body weight of 85.9 ± 13.6 kg (body mass index [BMI] 26.6 ± 3.8 kg/m^2); 376 (54.1%) of the subjects were women with a mean age of 40.4 ± 11.3 years, a body height of 167.3 ± 6.9 cm, and a body weight of 69.0 ± 12.6 kg (BMI 24.7 ± 4.4 kg/m^2). Only body height, body weight, and BMI show significant differences between men and women ($P < .001$). Systolic blood pressure was 132.4 ± 15.3 mmHg and diastolic blood pressure was 83.3 ± 10.4 mmHg for men and 124.5 ± 15.3 mmHg and 81.5 ± 10.6 mmHg, respectively, for women (significant difference between sex: $P < .001$ for systolic blood pressure and $P = .027$ for diastolic blood pressure). More men than women were smoker and ex-smoker (28.8% (n = 92) vs 17.8% (n = 67) and 17.6% (n = 56) vs 13.3%, (n = 50) respectively; $P < .001$). Also, 44.4% (n = 143) of the men and 45.5% (n = 172) of the women underwent athletic training, with an average of 3.0 ± 1.4 times/wk and 2.3 ± 1.3 times/wk, respectively ($P < .001$ for both sexes). The number of subjects in different age groups is listed in Table 1.

The 5th, 25th, 50th, 75th, and 95th percentiles were calculated for all age groups separately for men and women. A regression analysis of each HRV measure was performed for the total group, separately for men and women and additionally for each sex and for each age group, with age as an independent variable to prove the effect of age. The normal distribution was

Table 1 Number of subjects categorized according to their age and sex (N = 695)

Sex	Age group (y)	No. of patients
Male	20–30	71
	30–40	73
	40–50	106
	50–60	69
Female	20–30	97
	30–40	75
	40–50	110
	50–60	94