

Gender differences in circadian and extra-circadian aspects of heart rate variability (HRV).

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Abstract

Aim. Any gender differences in the broad time structure of HRV were assessed with focus on circadian and infradian (involving frequencies lower than one cycle per day) aspects.

Background. The incidence of cardiovascular diseases such as myocardial infarction tends to occur later in life in women as compared to men (1, 2). Gender differences have also been reported for the circadian pattern of sudden cardiac death in the Absheron Peninsula, Azerbaijan, where the circannual variation was found to be more prominent in men than in women (3). Understanding sex-specific differences in cardiovascular aging is important for public health and biomedical research, given increasingly larger older populations and the need to prevent and treat cardiovascular disease (4). By relying on serial 24-hour ECG records repeated yearly from the same subjects over an about 15-year span, the present investigation lends itself to the scrutiny of infradian changes in HRV by pooling results from all participants.

Subjects and methods. Mostly clinically healthy subjects of both genders (19 males and 22 females, 9 to 66 years of age) contributed 441 24-hour ECG records over an about 15-year span. Several HRV endpoints determined over consecutive 5-min intervals were analyzed by single cosinor to derive estimates of the MESOR (Midline Estimating Statistic Of Rhythm, M; a rhythm-adjusted mean) and the 24-hour amplitude (A; 2A is a measure of the extent of predictable variation within a day). These two parameters and the 24-hour standard deviation (SD) from each HRV endpoint and each record were assigned to the day of monitoring. In view of gender-specific age trends discussed elsewhere, each endpoint was linearly regressed with age, separately for males and females. Residuals (around respective mean values) were pooled across all gender-specific records and used as longitudinal time series. Least squares spectra of these longitudinal series were computed in the frequency ranges of 1 cycle in 15 years to 5 cycles per year, using a 0.2 harmonic increment and of 1 cycle in 52 weeks to 1 cycle in about 80 hours, using integer harmonics. Spectral peaks with an amplitude above the noise level by more than 3SD were identified as putative signals and their periods estimated by nonlinear least squares, using Marquardt's algorithm (5).

Results. On a population basis, a circadian rhythm is detected for all HRV endpoints ($P < 0.001$). Only small gender differences in phase are found for VLF (spectral power around one cycle in 46.5 sec), $\ln(\text{VLF})$, and TP/HF (total spectral power over 5 min/spectral power around one cycle in 3.6 sec), females tending to peak later than men. Small differences in the relative circadian amplitude (expressed as a percentage of the MESOR) are also found for VLF, LF (spectral power around one cycle in 10.5 sec), $\ln(\text{LF})$, and $\ln(\text{HF})$, females tending to have a smaller relative amplitude of VLF but a larger one of LF, $\ln(\text{LF})$, and $\ln(\text{HF})$ than men. Whereas signal detection did not specifically target anticipated components, cycles with an amplitude exceeding the detection threshold were checked against a set of non-photic frequencies characterizing helio-and/or geomagnetic phenomena expected to be reflected in the ECG data.

Apart from a circannual component detected in about 20% of the longitudinal time series, particularly prominent for males, interesting gender differences were found in relation to the cis-half-year (with a period of about 0.4 year) and to an about 2-week cycle. Whereas the cis-half-year reportedly characterizing solar flares (6) as well as sudden cardiac death (3, 7), heart rate of a clinically healthy man monitored over four decades (8), and circulating melatonin (9), was detected only for some HRV endpoints of males (notably related to VLF, inter-beat intervals, IBI, and SDNN, a measure of variability in IBI), the 2-weekly cycle was detected for several HRV endpoints of females but not males. A 2-week cycle was also found to characterize the incidence of sudden cardiac death (7).

Discussion and Conclusion. In view of the non-equidistant sampling of the composite longitudinal population-based series from pooling data across participants, inter-individual variability is unassessed. Some non-photic components detected may be spurious. The simulation of noise series assigned to the same dates and analyzed in the same way suggests that the above results are not an artifact from unequally spaced sampling. The presence of weak signatures of the cosmos on HRV endpoints is in agreement with earlier work, notably that showing cis-half-years in heart rate and sudden cardiac death incidence (3, 7, 8).

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