**Reference Values of Heart Rate Variability**

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We read the contribution by Sammito and Böckelmann [1] with dismay. The article not only describes a problematic study but also reports inconsistent numerical values.

The authors analyzed 24-hour ECG Holter recordings of 695 apparently healthy subjects and report normative heart rate variability (HRV) values summarized by age and sex.

The major problem to note is the substantial difference between the small SDNN and much larger SDANN values. This contradicts previous publications [2-5] and, as we understand, resulted from a methodological error. The authors admittedly removed the heart rate trend over the 24 hours (by “smoothness priors” detrending). This has erroneously reduced reported SDNN values which only reflect short-term variability with ranges consistent with those typically obtained by averaging 5-minute values [6-7]. Also, trend removal completely suppressed and ignored day-night variability, although the day-night differences are a major, if not the major, contributor to 24-hour SDNN. On the contrary, the reported SDANN values include complete 24-hour variability.

Since SDNN reflects the total 24-hour NN interval variance while SDANN relates to the variance below the 0.0033 Hz spectral frequency, i.e. the ultra low (ULF) spectral components [6], it is mathematically impossible to have SDNN values this smaller than SDANN values. SDANN might be as large as SDNN but cannot be larger. Unfortunately, neither the authors nor the Journal reviewers noticed this numerical impossibility.

We also note the heterogeneity of the investigated population. HRV, as well known, quantifies the cardiac period responses to autonomic changes [6]. In healthy subjects, these mainly reflect environment challenges and sleep. Hence, healthy 24-hour HRV significantly depends on activity. Mixing HRV data of subjects with obviously different daily activities is inappropriate and leads to values that are of little use as age and sex-based norms. The authors clearly have a valuable data source in their Holter recordings, but the 24-hour HRV values need to be considered in terms not only of age and sex but also in terms of the level of daily physical and mental activity.

Sammito and Böckelmann also report spectral HRV analyses inconsistent with their stated aims. Indeed, while stating that they “identified reference values for commonly used HRV measures for 24-hour ECG measurements,” they employed a non-parametric Welch spectral analysis with a FFT width of 256 seconds. The reported values thus relate to averages over little less than 5 minutes and do not reflect 24-hour spectral analysis. As reported in the Task Force standards [6] and as more recently discussed in more detail [10], other parameters have been suggested for 24-hour spectral indices, e.g. the α coefficient.

Generally, however, even in stable data analyses [11], the proportion of low (LF) and high (HF) frequency HRV components depends substantially on circumstances. HF power decreases with position changes from supine or sitting/standing. Without controlling the environment, there is little value in reporting 24-hour averages of LF and HF power proportions. In uncontrolled long-term situations, the LF/HF averaged values, even when accurately calculated, have no physiologic or clinical meaning. It might be argued that if similarly diverse population were re-sampled with recordings obtained under similarly variable conditions and if the same short-term HRV techniques were used, the reported LF/HF results would be more or less reproduced. However, that does not make them useful for any physiologic, epidemiological, or clinical purposes.

We are aware of clinically relevant applications of FFT analyses of 24-hour Holter data [2,6,12]. These were primarily based on very low (VLF) and ULF components which are mainly, although not exclusively, influenced by the day-night heart rate differences. The VLF and ULF components can only be derived when the FFT is applied to the entire 24-hour data in one block. They cannot be estimated in very short segments of 256 seconds with subsequent averages. It could be acceptable to report some spectral data in normalized units, even if a non-parametric method is employed, provided that they are properly computed. However, much more importantly, reporting these values without the absolute values of LF and HF power is a methodological mistake.

To return to the SDNN and SDANN values, repeated reports by different groups showed that cardiac patients are at substantially increased risk if their SDNN is below 50-70 ms [6,11-15]. Regrettably, it did not appear strange to Sammito and Böckelmann that the vast majority of their *normal* subjects were apparently in the very high risk category because of the SDNN values.

Although ICD guidelines rely on left ventricular ejection fraction, it is not uncommon for additional factors to be used in borderline situations or when resources are limited. Autonomic indices belong to the most powerful of such factors. Of these, SDNN is the most frequently used 24-hour HRV index. Patients with 24-hour SDNN values around 30-50 ms are at high risk of fatal complications. It is thus most unfortunate that Heart Rhythm accepted a publication that may endanger patients’ lives. Regretfully, we are therefore of the unanimous opinion that the article by Sammito and Böckelmann needs to be revoked and withdrawn.

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