Ultra-short heart rate variability over 15 seconds is associated with increased long-term risk of cardiovascular disease

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Background: Heart rate variability (HRV) is an established cardiac autonomic marker with prognostic value, whose application at scale is limited by the fact it requires relatively long ECG recordings (≥ 5-min). Ultra-short HRV (usHRV) is derived from much shorter recordings and can be measured at scale using standard and wearable ECGs, but its association with cardiovascular events is undetermined.

Purpose: (1) To validate usHRV measured using 15-second ECGs and (2) To investigate association with multiple outcomes in individuals without cardiovascular disease.

Methods: Data from the National Survey for Health and Development (N=1,337) was used to assess the agreement between usHRV and standard HRV (which requires ≥5-minute ECGs). Participants from the first visit of the UK Biobank study (2009-2013), without cardiovascular disease and with an ECG (N=51,628, 64% male, median age 58) were recruited to assess association of usHRV with outcomes. Exposures included usHRV time-domain indices RMSSD and SDSD, which measure fast heart rate variations related to cardiac vagal modulation, and usHRV spectral index PHF, which is related to respiratory sinus arrhythmia. Outcomes included incident atrial fibrillation (AF), major adverse cardiovascular events (MACE), stroke and mortality.

Results: HRV indices RMSSD and SDSD measured in 15-second ECGs showed excellent agreement (median correlation coefficient ≥0.84 and narrow limits of agreement in Bland-Altman analyses, Fig. 1) with indices measured from 6-minute ECGs, while PHF showed good agreement (median correlation coefficient 0.70 and small positive bias). In the UK Biobank, after a median follow-up of 11.5 (11.4-11.7) years, incidence of AF, MACE, stroke, and mortality was 3.8%, 3.9%, 1.7% and 4.3%, respectively. An inverse linear association was found between usHRV and AF and stroke, with hazard ratios between 1.07 and 1.13 for a standard deviation decrease in RMSSD, SDSD and PHF, p<0.05. Non-linear cox regressions (Fig. 2) showed that the association of RMSSD (and SDSD) with MACE and mortality was U-shaped with individuals in the bottom quintiles of usHRV indices showing increased risk with respect to those in the third quintile (hazard ratios between 1.16 and 1.29, p<0.05).

Conclusions: Cardiac autonomic dysfunction measured with usHRV from 15-second ECGs is associated with increased risk of AF, MACE, stroke, and mortality in individuals without cardiovascular disease. usHRV can be measured from both standard clinical ECGs and novel wearable devices and may have a role to monitor autonomic function at scale and improve understanding and prevention of cardiovascular disease.
Fig1: 6-min vs 15-sec HRV
Fig2: usHRV association with outcomes