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Cardiovascular disease, risk factors, and heart rate variability in the general population

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Abstract The results of studies into the prognostic value of heart rate variability (HRV) for cardiac and all-cause mortality in the general population are briefly reviewed, and the effect of various recording durations of the electrocardiogram (ECG) on HRV parameters is assessed. Heart rate variability parameters offer prognostic information beyond that of traditional risk factors. In the elderly, increased HRV measured on a 10-second ECG is an even stronger indicator of cardiac death than decreased HRV. Estimated of HRV obtained from 10-second ECGs have moderate to poor correlation with those from 5- or 20-minute ECGs.

Keywords: Heart rate variability; ECG; Population-based studies

Introduction

Abnormal heart rate variability (HRV, a marker of cardiac autonomic control) has been put forward as a harbinger of cardiac and other trouble. Heart rate variability is influenced by various physiologic and pathologic conditions, such as age, fitness level, respiration, diabetic neuropathy, congestive heart failure, and coronary artery disease.[1] There is ample evidence that decreased HRV is associated with adverse prognosis in patients after myocardial infarction.[2] However, relatively few studies investigated the prognostic value of HRV in the general population.

During the past decade, reports have appeared from 4 major studies in this field, 2 from the United States (the Framingham Heart Study[3,4] and the Atherosclerosis Risk in Communities Study[5,6]) and 2 from the Netherlands (the Zutphen Study[7] and the Rotterdam Study[8]). Recently, a fifth study was started in Germany, the CARdiovascular disease, Living and Aging in Halle (CARLA) Study.[9]

In this article, the results of these studies regarding the prognostic value of HRV in the general population are briefly reviewed. Data from the CARLA Study are used to assess the effect of various electrocardiogram (ECG) recording durations on HRV measurement results.

Population-based HRV studies

Study characteristics are given in Table 1. There are large differences between studies in size, composition, follow-up, end points, and duration of the ECG recordings. For the CARLA Study, follow-up is in progress and data on the prognostic value of HRV cannot yet be given.

The first 2 reports on the prognostic value of reduced HRV in the general population came from the Framingham Study.[3,4] Heart rate variability measures were based on 2-hour ambulatory ECGs. The relatively short follow-up time only allowed to look at associations with all-cause mortality and with fatal and nonfatal cardiac events combined. In the first report,[3] all frequency-domain measures except the ratio of low-frequency (LF) to high-frequency (HF) power were significantly associated with all-cause mortality (hazard ratios [HRs] from 1.43 to 1.70), after adjustment for age, sex, and clinical risk factors. The SD of normal RR intervals (SDNN) proved to be the only significant time-domain predictor (HR, 1.38). In the second report,[4] all HRV measures, again except LF/HF ratio, were significantly associated with new cardiac events, with HRs around 1.4.

In the Atherosclerosis Risk in Communities Study, a case-cohort design was followed.[5,6] Two-minute ECG recordings were acquired, after a 20-minute supine rest period. In a first report,[5] a few HRV indices (HF power, LF power, LF/HF ratio, SDNN) were divided into quartiles, and the risks of a cardiac event (fatal and nonfatal) for subjects in the lowest quartile and those in the upper 3 quartiles were compared. High-frequency power was the only variable that

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Table 1
Study characteristics of population-based HRV studies

Study	n	Age (y)	Follow-up (y)	End point	ECG
Framingham	736	72 (63-93)	4	All-cause death	2 h
	2501	53 (±13)	3.5	Cardiac events	2 h
ARIC	2389 (case-cohort)	55 (45-64)	3	Cardiac events	2 min
	1694 (case-cohort)	53 (45-64)	4-6	Cardiac events, cardiac death, noncardiac death, all-cause death	2 min
Zutphen	878 men	40-60	15	(Sudden) cardiac death, noncardiac death, all-cause death	15-30 s
	885 men	65-85	5		15-30 s
Rotterdam	5272	69 (≥55)	3-6	Cardiac death, noncardiac death, all-cause death	10 s
CARLA	1779	45-83	NA	NA	20 min

remained a significant predictor after adjustment for age, sex, and other risk factors. In a second report,[6] only time-domain measures were considered. Indices were divided in tertiles, taking the intermediate group as the reference. Elevated risks were observed for incidence of coronary heart disease (pNN50, percentage of successive normal interval differences of >50 milliseconds) and for cardiac or all-cause death (all indices). Risks remained virtually unchanged when the analyses were restricted to subjects without hypertension, diabetes, cancer, or symptomatic heart disease at baseline.

The Zutphen Study[7] started in 1960 with a sample of middle-aged men in the city of Zutphen, The Netherlands. In 1985, this sample was combined with a new sample of elderly men to create an elderly cohort of sufficient size. Electrocardiographic recordings had a duration of 15 to 30 seconds, and only SDNN was studied. Hazard ratios compared the lowest and highest quartiles with the intermediate 2 quartiles (reference group) and were adjusted for age, body mass index, systolic blood pressure, cholesterol, and smoking. Reduced HRV was significantly associated with increased risks for cardiac death and all-cause mortality. Interestingly, high HRV values were also associated with a higher risk of mortality, though not significantly.

Finally, the Rotterdam Study examined the association between both decreased and increased SDNN on 10-second ECGs and cardiac and all-cause mortality in an elderly population.[8] Subjects with non–sinus rhythm and those with less than 6 normal RR intervals were excluded. The lowest and highest quartiles of SDNN were compared relative to those in the third quartile. Reduced HRV carried an 80% increased risk for cardiac mortality, after adjustment for possible confounders. Like in the Zutphen Study, this risk was even more pronounced for subjects in the highest quartile, that is, with higher than normal HRV (HR, 2.3). A possible explanation may be that increased HRV is due to sinus node dysfunction.

Electrocardiographic recording duration and HRV

The variety of ECG recording durations in these studies raises the question how HRV indices obtained from differing recording durations relate to each other. For an answer we turn to the CARLA Study, in which a 10-second and a 20-minute 12-lead ECG were recorded for each participant.[9] The recordings were controlled for major physiologic mechanisms influencing short-term HRV by prescribing a supine resting period of 20 minutes or more before the recordings were taken, and by requesting metronome-guided respiration at 0.25 Hz (15/min) for the 20-minute ECGs[10]; the 10-second ECGs were recorded under free respiration. Four HRV time-domain parameters were derived for the free-respiration 10-second ECGs, and for the first 10 seconds, 2 minutes, and 5 minutes of the metronome-guided 20-minutes ECGs. The parameters computed for these short-term recordings were compared with those of the 20-minute recordings by means of Spearman correlation (Fig. 1). There is a clear improvement in correlation with increasing recording length, with excellent correlations for the 5-minute recordings. The correlations for 10-second free respiration and 10-second controlled respiration were comparable, and poor to moderate at best.

Conclusions

Multiple studies have shown that low HRV is a predictor of cardiac and all-cause mortality in general populations. Heart rate variability parameters offer prognostic information beyond that of traditional risk factors. In the elderly, increased HRV measured on the standard 10-second ECG

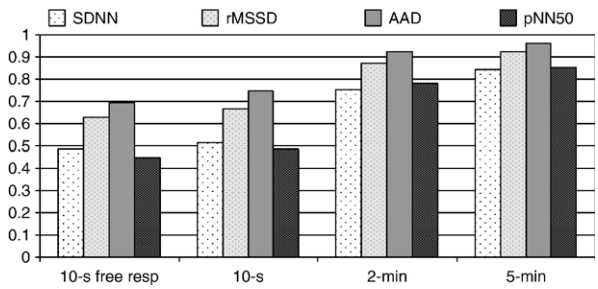

Fig. 1. Correlations between HRV indices from short-term ECGs and 20-minutes ECGs. rMSSD indicates root mean square of successive normal interval differences; AAD, average of absolute successive normal interval differences; pNN50, percentage of successive normal interval differences of more than 50 milliseconds.

is an even stronger indicator of cardiac mortality than decreased HRV. Finally, HRV estimates obtained from 10-second ECGs have moderate to poor correlation with those from 5- or 20-minute ECGs. Further studies are needed to clarify the physiologic meaning of HRV measures based on 10-second ECGs.

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