Reliability of ultrashort electrocardiographic indices in hypertension: the quest for a clinically applicable prognostic marker

Keren Politi,[1] Keren Kaminer,[2] Udi Nussinovitch [3]

[1]Neonatal Neurology Clinic, Schnider Children's Medical Center, Alyn Children and Adolescent Rehabilitation Center, Petach Tikva, Israel
[2]Department of Endocrinology, Rabin Medical Center, Petach Tikva, Israel
[3]Department of Cardiology, Meir Medical Center, Kfar Saba, Israel

Correspondence to
Dr Udi Nussinovitch, Department of Cardiology, Meir Medical Center, Kfar Saba 44281, Israel; udi.nussinovitch@gmail.com

Accepted 27 July 2019
Published Online First 16 August 2019

To cite: Politi K, Kaminer K, Nussinovitch U. *J Investig Med* 2020;**68**:364–370.

ABSTRACT

Heart rate variability (HRV) is an accepted clinical tool for evaluating autonomic nervous system function and a marker of adverse cardiac outcome. Although 5 min long HRV recordings are considered methodologically acceptable, it remains impractical in most clinical settings. Also, while some ultrashort HRV (usHRV) parameters were found useful in healthy individuals, their applicability to patients with cardiovascular risk factors is largely unknown. Therefore, our goal was to evaluate the reliability of ultrashort ECG (usECG) indices for HRV among patients with hypertension. One-hundred and two patients with essential hypertension were included. HRV was recorded for 5 min in strictly monitored settings. HRV parameters from randomly chosen 1 min and 10 s series were analyzed. Excellent correlations were found between 1 min SD of RR interval (SDNN) (intraclass correlation coefficient (ICC) 0.973), 10 s SDNN (ICC 0.92) and 5 min SDNN results. An excellent correlation was also found between 1 min root mean square of successive differences in RR intervals (RMSSD) (ICC 0.992), 10 s RMSSD (ICC 0.982) and 5 min RMSSD. Logarithmic transformation of ultrashort 1 min HRV-triangular index using the natural logarithm (Ln) also had excellent correlation with 5 min measurements (ICC 0.9). Also, excellent correlations were found between 10 s and 1 min Ln(RMSSD), 10 s Ln(RMSSD) and 5 min measurements. Other HRV parameters measured from 1 min and 10 s periods showed lower correlations. In conclusion, evaluation of SDNN, RMSSD or Ln(RMSSD) from 10 s ECG recordings can be used to estimate autonomic nervous system function in patients with hypertension. These appealing markers can be readily calculated from any standard ECG tracing. The prognostic significance of ultrashort SDNN and ultrashort RMSSD in patients with cardiovascular risk factors needs to be determined in future prospective cohort studies.

Significance of this study

What is already known about this subject?

- Autonomic nervous system function can be evaluated according to heart rate variability (HRV), yet current measurement techniques for HRV makes it clinically impractical.
- HRV may be used as a marker of adverse cardiac outcomes, especially for patients with cardiovascular diseases or risk factors.
- Some 10 s ultrashort HRV (usHRV) parameters were found to be useful in healthy individuals but their applicability for patients with hypertension is unknown.

What are the new findings?

- Ultrashort SD of RR interval (usSDNN), ultrashort root mean square of successive differences in RR intervals (usRMSSD) and 1 min ultrashort natural logarithm (usLn(HRV-triangular index (TI))) were found to be equivalent to 5 min SDNN, RMSSD and Ln(HRV-TI), respectively, in the study population.
- Evaluation of SDNN and RMSSD and the natural logarithm value of RMSSD from ultrashort 10 s ECG recordings can be used to estimate autonomic nervous system (ANS) function in patients with hypertension.
- Other usHRV variables were found to be unreliable for evaluating ANS in patients with hypertension.

How might these results change the focus of research or clinical practice?

- Study of 10 s usSDNN, usRMSSD, and Ln(RMSSD) can be easily implemented in any emergency department or clinic.
- These ultrashort indices have promising prognostic implications in patients with hypertension, which require further confirmation in future studies.
- Ultrashort Ln(HRV-TI) and Ln(SDNN) may be of clinical value, but the need for 1 min measurements limit its use.

INTRODUCTION

Heart rate variability (HRV) is a clinical tool for measuring cyclic changes in heart rate. HRV is influenced by autonomic nervous system (ANS) function and is commonly used to estimate this.[1 2] Also, HRV has been successfully utilized for cardiac risk stratification in certain patients.[3 4] Five-minute long recordings are considered methodically acceptable for HRV evaluation.[5] In recent years, low-cost commercial devices for evaluating HRV have become increasingly accessible, and even heart rate monitor watches have proven useful for HRV study.[6] The average patient appointment time for most general practitioners and family doctors rarely exceeds 10–15 min.[7–9] Therefore, unlike resting ECG and blood pressure, which take a few seconds to measure, evaluating HRV remains impractical for most practitioners. For this reason, more practical tools for ultrashort (us) evaluation of HRV and ANS function is warranted for inpatient clinical risk stratification. Several studies have shown that specific usHRV parameters are clinically useful. Karp *et al* demonstrated that SD of RR intervals (SDNN) calculated from a 10 s ECG have prognostic implications for patients with a recent myocardial infarction.[10] Our research group reported that some us parameters of HRV are more reliable than others for HRV measurements in healthy individuals (ie, average RR interval and root mean square of successive differences in RR intervals (RMSSD)).[11] Schroeder *et al* also reported high correlation coefficients of mean RR and RMSSD between 10 s and 2 min measurements, and 6 min HRV measurements in healthy controls.[12] Nevertheless, the results of the latter studies differ regarding SDNN reliability; presumably due to factors associated with patient selection.[11 12] Similar results were reported by Munoz *et al*, namely that RMSSD computed from 10 s long measurements is sufficiently reliable.[13] Yet, they did not evaluate ECG-based HRV, but rather studied pulse variability based on non-invasive continuous blood pressure monitoring. Also, Munoz *et al* included individuals followed for deteriorating renal function (Prevention of Renal and Vascular Endstage Disease (PREVEND) study) and did not focus on other specific patient populations.

Some ultrashort frequency domain HRV measures were found to be reliable markers for longer measurements in healthy adults.[11] Yet, it should be emphasized that experience gained from healthy volunteers does not necessarily reflect the expected results in other patient groups, including those with cardiovascular risk factors, such as hypertension.

Hypertension is a common medical condition associated with increased risk for end-organ damage and arrhythmias, and may be associated with abnormal ANS function. Hypertension was also reported to be associated with abnormal HRV parameters measured from 5 min intervals,[14] and from 24 hours measurements.[15] Due to a paucity of knowledge regarding the reliability of ultrashort indices of HRV in patients with hypertension, we sought to study the association between usHRV indices and a standardized HRV test, and estimate which parameters were more reliable for usHRV evaluation. The present study focuses both on time and frequency domains of HRV parameters.

MATERIALS AND METHODS

Study design

A case series study design was used. The participants were included after they provided written informed consent.

Study subjects

One-hundred and two volunteers with hypertension were included in the study. Participants were recruited after a routine health check-up in the outpatient clinic. All participants were interviewed regarding their health history. Their medical records were screened and complete physical examinations were conducted to determine health status. Hypertension was defined as blood pressure threshold of 140/90 mm Hg according to the 2018 European Society of Cardiology/European Society of Hypertension guideline.[13] Patients were diagnosed with essential hypertension following a medical workup and exclusion of secondary causes. They had been under continuous treatment for their hypertension for at least 3 months prior to enrollment. None of the patients had an acute condition known to have an effect on heart rate or other electrocardiographic parameters.

Procedure

For at least 3 hours prior to the test participants were asked not to drink caffeinated beverages, smoke or take other stimulants. The test was conducted during the morning hours in order to avoid circadian influences on ANS function. Studies were carried out in a quiet room where temperature was maintained at approximately 22°C. Participants were asked to remain in a supine position for 10 min prior to commencement of the study. Blood pressure was measured twice and the results were averaged. Measurements were carried out with a digital ECG device with a sampling rate of 2000 Hz (Norav Medical, Yokne'am, Israel). Recordings were made from the limb leads for 5 min. Poor quality recordings were repeated. The data were saved and processed using designated commercial computer software (PC-ECG, HRV V.5.514, Norav Medical).[5]

Time-domain measures were based on the normal-to-normal (NN) intervals. The mean heart rate and the square root of the mean of the squares of the successive differences between adjacent NN intervals (RMSSD) were calculated. Additional time domains were computed by the software, including SDNN (the SD of RR intervals); the absolute NN intervals that were >50 ms from the preceding ones (NN50) and the ratio of NN50 to the total number of RR intervals recorded (pNN50).

Table 1 Baseline characteristics of study subjects

Characteristics	Study sample (n=102)
Male/female	81 (79.4%)/21 (20.6%)
Age, years	59.7±11.1
Height, m	1.72±0.08
Body mass index, kg/m^2	28.5±4.3
Systolic blood pressure, mm Hg	137.9±17.3
Diastolic blood pressure, mm Hg	82.2±10.8
Dyslipidemia, n (%)	70 (68.6)
Diabetes mellitus, n (%)	24 (23.5)
Smoking, n (%)	13 (12.7)
Family history, n (%)	56 (54.9)
ACE inhibitors/ARBs, n (%)	62 (60.8)
Diuretics, n (%)	32 (31.4)
β-Blockers, n (%)	49 (48.0)
Calcium channel blockers, n (%)	38 (37.2)
Antiplatelet drugs, n (%)	52 (51.0)
Anti-arrhythmic drugs (type 1, 3), n (%)	5 (4.9)
Lipid-lowering statin drugs, n (%)	51 (50.0)

ARBs, angiotensin receptor blockers.

Table 2 Correlation of electrocardiographic measurements of HRV from 1 min to 5 min recordings

	1 min		5 min			
	Mean	SD	Mean	SD	ICC	95% CI
Maximal RR (ms)	1050.9	176.55	1095.2	176.55	0.986*	0.979 to 0.990
Minimal RR (ms)	897.9	139.76	838.9	139.76	0.951*	0.928 to 0.967
Average RR (ms)	972.4	154.96	970.2	154.96	0.998*	0.997 to 0.999
Average HR (bpm)	63.1	10.91	63.0	10.91	0.995*	0.993 to 0.997
SDNN (ms)	34.0	24.18	41.1	24.18	0.973*	0.960 to 0.982
RMSSD (ms)	32.5	29.98	34.3	29.98	0.992*	0.988 to 0.995
HRV-TI	7.9	2.53	12.2	2.53	0.786	0.683 to 0.855
NN50	28	4.12	14.9	4.12	0.542	0.323 to 0.691
pNN50	2.0	3.05	5.2	3.05	0.785	0.682 to 0.855
VLF (ms^2)	167.8	109.11	220.2	109.11	0.656	0.490 to 0.767
LF (ms^2)	160.2	89.65	136.7	89.65	0.726	0.594 to 0.815
HF (ms^2)	161.9	92.42	112.7	92.42	0.832	0.751 to 0.886
Total power (ms^2)	495.6	101.01	520.4	101.01	0.863	0.798 to 0.908
LF/HF	1.7	2.07	1.8	2.07	0.85	0.777 to 0.898
Ln(SDNN)	3.351	0.560	3.584	0.489	0.947*	0.922 to 0.964
Ln(RMSSD)	3.230	0.664	3.310	0.614	0.981*	0.972 to 0.987
Ln(HRV-TI)	2.019	0.322	2.421	0.397	0.9*	0.853 to 0.933
Ln(VLF)	4.853	0.836	5.311	0.455	0.634	0.459 to 0.753
Ln(LF)	4.923	0.571	4.820	0.465	0.88	0.823 to 0.919
Ln(HF)	4.883	0.697	4.552	0.617	0.874	0.813 to 0.915
Ln(total power)	6.172	0.316	6.241	0.169	0.648	0.478 to 0.762
Ln(LF/HF)	0.041	0.981	0.268	0.823	0.88	0.823 to 0.919

Correlation of 1 min and 5 min electrocardiographic HRV measurements.
*Excellent correlation.
HF, high frequency components; HRV, heart rate variability; HRV-TI, HRV-triangular index; ICC, intraclass correlation; LF, low frequency components; NN50, number of intervals differing by >50 ms from preceding interval; pNN50, NN50 divided by total number of intervals; RMSSD, root mean square of successive differences in RR intervals; SDNN, SD of RR interval; VLF, very low-frequency components.

HRV-triangular index (HRV-TI) was calculated from an integral of the density distribution (count of all NN QRS intervals) divided by the maximum of the density distribution. Power spectral analysis was further performed using a fast Fourier transform-based non-parametric algorithm. The power spectrum was then converted into frequency-domain indices, which consisted of the low-frequency power (0.04–0.15 Hz), the high-frequency (HF) power (0.15–0.4 Hz) and the total power. The latter was computed as the sum of all spectra (ie, variance of all NN intervals <0.4 Hz). HRV indices were log-transformed using the natural logarithm (Ln).

HRV parameters were reanalyzed from a randomly chosen 1 min long series and another randomly chosen 10 s series. None of the recordings included premature beats.

Statistical analysis

Results were expressed as mean and SD. Intraclass correlation coefficient (ICC) was used in order to quantify the agreement between measurements obtained from the entire 5 min recording with the 1 min and 10 s interval recordings. An ICC significantly ($p<0.05$) above 0.9 was considered to have excellent correlation, and an satisfactory measure of reliability.[16] Analyses were performed using JMP V.7.0 (SAS Institute, Cary, North Carolina, USA) and SPSS V.25 for Windows software (SPSS, Chicago, Illinois, USA).

RESULTS

The demographic and clinical characteristics of the study group are described in table 1. There were 81 men; mean age was 59.7±11.1 years. Some patients had additional cardiovascular risk factors, such as dyslipidemia (68.6%), diabetes mellitus (23.5%), smoking (12.7%) and family history of heart disease (54.9%). Mean systolic blood pressure was 137.9±17.3 mm Hg; mean diastolic blood pressure was 82.2±10.8 mm Hg. All patients were treated with antihypertensive drugs, such as ACE inhibitors or angiotensin receptor blockers (60.8%), diuretics (31.4%), β-blockers (48.0%) or calcium channel blockers (37.2%). Antiplatelet drugs were administrated to 51.0%, and antiarrhythmic drugs (type 1, 3) were used by 4.9%. Half of the patient group used lipid-lowering therapy.

Table 2 and figure 1 include the correlations between 1 min and 5 min HRV parameters. Excellent correlations were found between 1 min and 5 min average RR results (ICC 0.998, 95% CI 0.997 to 0.999). An excellent correlation was also found between 1 min RMSSD and 5 min RMSSD (ICC 0.992, 95% CI 0.988 to 0.995) as well as between 1 min SDNN and 5 min SDNN (ICC 0.973, 95% CI 0.960 to 0.982). Ln of 1 min SDNN and 1 min RMSSD also had excellent agreement with the 5 min measurements (table 2). In addition, 1 min Ln(HRV-TI) had excellent correlation with 5 min Ln(HRV-TI) (ICC 0.9, 95% CI 0.853 to 0.933). The other HRV parameters had lower correlations.

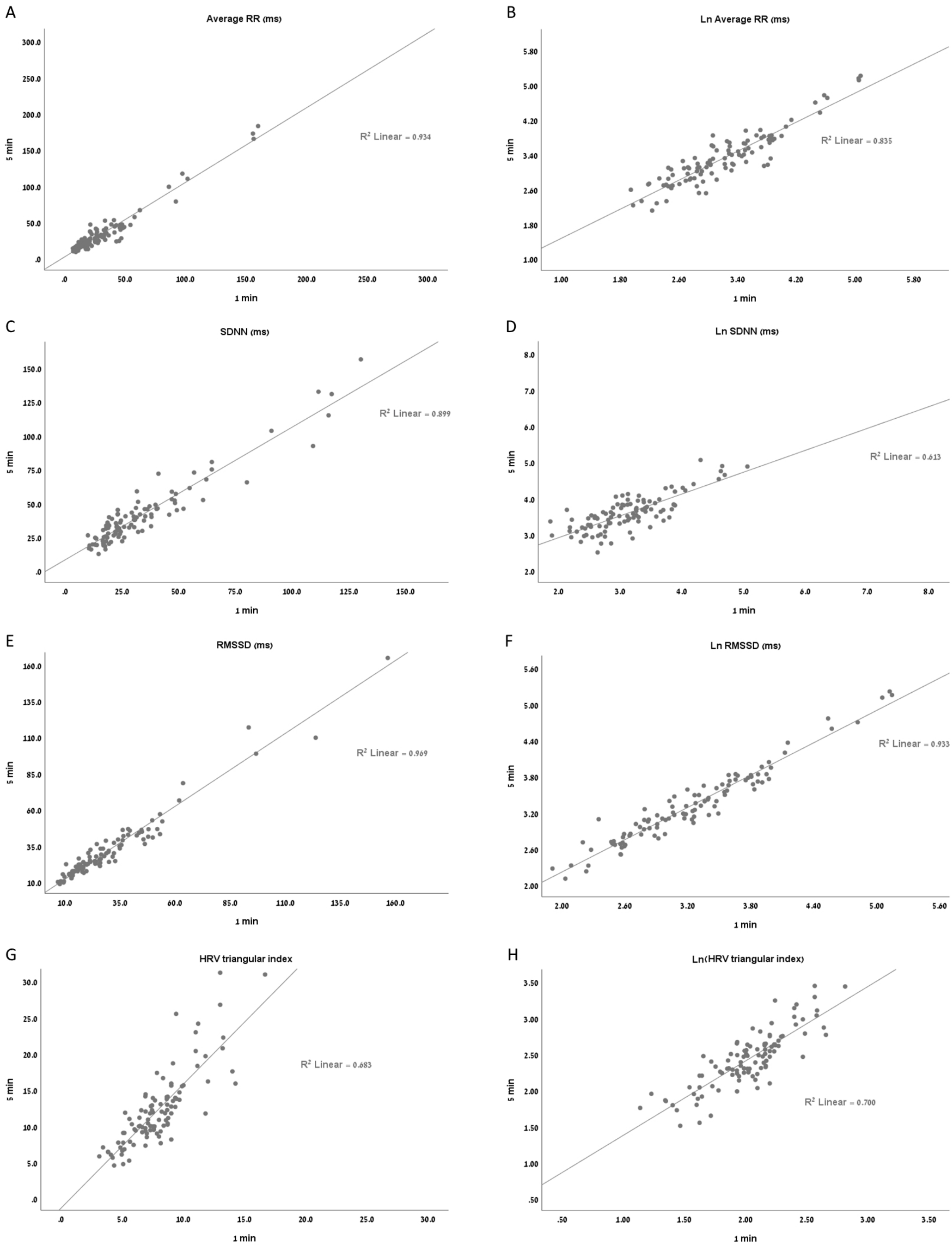

Figure 1 Correlation between 1 min heart rate variability (HRV) parameters and 5 min HRV parameters. (A) Average RR; (B) Ln(average RR); (C) SD of RR interval (SDNN); (D) Ln(SDNN); (E) RMSSD; (F) HRV-triangular index; (G) Ln(HRV-triangular index).

Table 3 and figure 2 include the correlations between 10 s and 5 min HRV parameters. Excellent correlations were found between 10 s and 5 min average RR results (ICC 0.99, 95% CI 0.985 to 0.993). Excellent correlations were also found between 10 s RMSSD and 5 min RMSSD (ICC 0.982, 95% CI 0.973 to 0.988; figure 2), as well as between 10 s and 5 min SDNN (ICC 0.92, 95% CI 0.882 to 0.946). Ln of 1 min RMSSD (but not SDNN or HRV-TI) had excellent

Table 3 Correlation of 10 s and 5 min electrocardiographic HRV measurements

	10 s		5 min			
	Mean	SD	Mean	SD	ICC	95% CI
Maximal RR (ms)	1023.3	169.3	1095.2	180.6	0.975*	0.963 to 0.983
Minimal RR (ms)	936.6	148.0	838.9	128.4	0.931*	0.897 to 0.953
Average RR (ms)	976.8	154.5	970.2	152.1	0.99*	0.985 to 0.993
Average HR (bpm)	62.6	10.9	63.0	10.8	0.993*	0.989 to 0.995
SDNN (ms)	28.6	24.1	41.1	25.0	0.92*	0.882 to 0.946
RMSSD (ms)	31.9	28.7	34.3	30.7	0.982*	0.973 to 0.988
HRV-triangular index	4.8	1.8	12.2	5.2	0.371	0.068 to 0.575
NN50	0.42	0.78	14.9	20.3	0.108	−0.321 to 0.397
pNN50	0.45	0.83	5.2	7.7	0.271	−0.079 to 0.507
LF (ms^2)	168.3	106.1	136.7	58.2	0.564	0.354 to 0.705
HF (ms^2)	239.3	105.5	112.7	63.4	0.463	0.205 to 0.637
Total power (ms^2)	446.9	88.6	520.4	89.0	0.849	0.776 to 0.898
LF/HF	1.33	1.99	1.81	1.70	0.625	0.445 to 0.747
Ln(SDNN)	3.351	0.560	3.584	0.489	0.862	0.796 to 0.907
Ln(RMSSD)	3.230	0.664	3.310	0.614	0.953*	0.931 to 0.968
Ln(HRV-triangular index)	2.019	0.322	2.421	0.397	0.634	0.459 to 0.753
Ln LF (ms^2)	4.923	0.571	4.820	0.465	0.561	0.350 to 0.703
Ln HF (ms^2)	4.883	0.697	4.552	0.617	0.573	0.368 to 0.712
Ln(total power)	6.172	0.316	6.241	0.169	0.727	0.596 to 0.816
Ln(LF/HF)	0.041	0.981	1.820	1.700	0.646	0.477 to 0.761

*Excellent correlation.
HF, high frequency components; HRV, heart rate variability; HRV-TI, HRV-triangular index; ICC, intraclass correlation; LF, low frequency components; NN50, number of intervals differing by >50 ms from preceding interval; pNN50, NN50 divided by total number of intervals; RMSSD, root mean square of successive differences in RR intervals; SDNN, SD of RR interval.

agreement with the 5 min measurements. The other 10 s HRV parameters had lower correlations with 5 min HRV parameters.

DISCUSSION

The scientific community has begun to appreciate usHRV as a useful clinical tool, especially in the context of cardiovascular risk stratification. Nevertheless, its use extends beyond merely evaluating ANS function. For example, Adjei *et al* evaluated 10 s SDNN changes in subclinical electroencephalographic seizure patterns, although the study yielded limited results.[17] Kon *et al* evaluated the coefficient of variation of the RR interval from a 2 min recording and suggested that lower values were associated with higher CRP levels.[18] Bikkina *et al* evaluated HRV (calculated in this particular study by subtracting the minimal from the maximal RR interval, and corrected to a heart rate of 75 bpm) from 10 consecutive RR intervals prior to the electrophysiological study. They reported that inducible VT was associated with lower variability.[19] de Bruyne *et al* reported that 10 s SDNN, when either excessively low or high, reflected increased risk for mortality in the elderly.[20]

The current study is an extension of our previous research in which we found that us measurements of average RR and RMSSD are useful for evaluating 5 min values of these parameters in healthy individuals.[11] Nevertheless, our previous study did not include patients with cardiovascular risk factors such as hypertension, and this population has not been adequately investigated.

The present study included a large cohort of patients with essential hypertension, some of whom had other cardiovascular risk factors. Notably, there is a paucity of knowledge as to the reliability of usECG indices for HRV, and no study has previously included large cohorts of patients with hypertension. We found that average RR, RMSSD, SDNN, Ln(RMSSD), L(SDNN) and Ln(HRV-TI) measured from 1 min recordings have an excellent correlation with 5 min measurements of these variables. Also, average RR, RMSSD, SDNN and Ln(RMSSD) calculated from 10 s long periods also have excellent correlations with 5 min recordings. These results extend our previous findings in healthy individuals,[11] in that more usHRV variables were found to be reliable for patients with hypertension. This difference may stem from the known tendency towards autonomic dysregulation among patients with hypertension.[21] Other variables showed lower correlations, and therefore are less reliable markers for 5 min HRV. These results are important in light of the higher accessibility and practicality of usHRV compared with 5 min measurements. Our results are similar to those of Hamilton *et al* who reported that RMSSD reflected cardiac vagal tone in a heterogeneous group of 50 patients.[22] Our results are also supported by those of McNames and Aboy who found that mean heart rate and RMSSD are less affected by the measured duration (although they also reported high reliability of HF, which was not found in our two studies).[23] Salahuddin *et al* demonstrated that mean RR interval and RMSSD measured from 10 s intervals are comparable to longer measurements.[24]

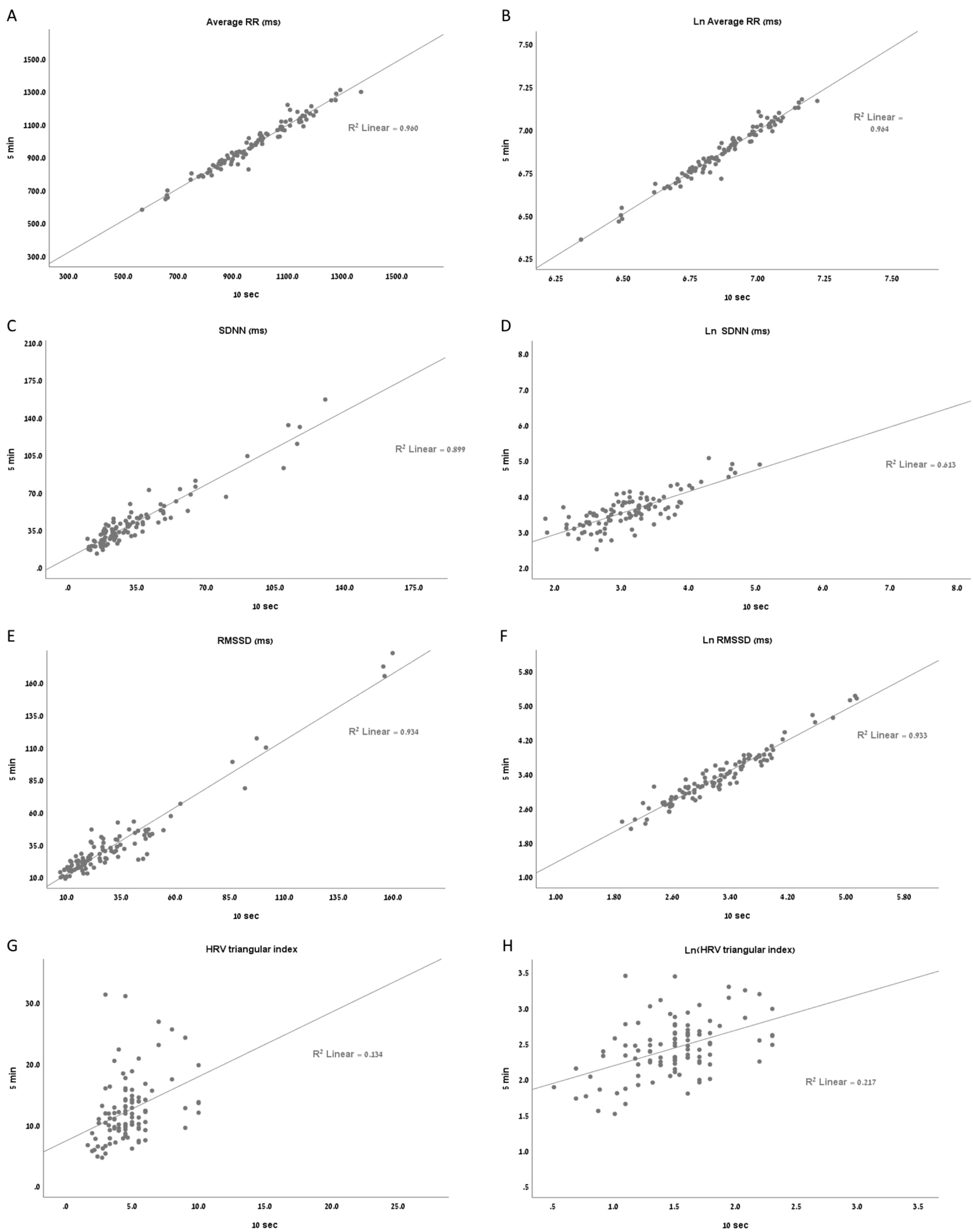

Figure 2 Correlation between 10 s heart rate variability (HRV) parameters and 5 min HRV parameters. (A) Average RR; (B) Ln(average RR); (C) SDNN; (D) Ln(SDNN); (E) root mean square of successive differences in RR interval (RMSSD); (F) HRV-triangular index; (G) Ln(HRV-triangular index).

Thong *et al*, by using ECGs from the Physionet database, reported that 10 s RMSSD, but not SDNN, was a reliable index for 5 min results, and suggested that the reliability of HF merits further research.[25] Munoz *et al* reported that a single 10 s recording yields a valid RMSSD measurement, although they concluded that an average over multiple 10 s ECGs is preferable.[13] Nevertheless, all the above studies included heterogeneous groups of patients, and did not focus on patients with hypertension. Also, the reliability of all parameters was not evaluated in some studies, while others did not use standard ECG-based methods for HRV quantification, which limit comparisons with the current research.

Limitations

HRV measurements were conducted under strict conditions (controlled environment, appropriate preceding rest, etc) that do not necessarily reflect the conditions found in the emergency department or outpatient clinics, where ECG are regularly recorded. Also, HRV measurements were conducted in the present study without paced breathing to simulate a typical ECG recording. This method is also in agreement with the accepted methodological approach towards routine HRV evaluation. We cannot predict whether a study conducted in an uncontrolled environment or using paced breathing would have yielded different results. It also remains to be explored whether specific usHRV parameters can reflect on circadian-associated or long-term ANS alterations, and if the current findings are applicable in persons with undiagnosed hypertension, patients with drug-resistant hypertension and those who are non-compliant with medical therapy.

CONCLUSIONS

Ultrashort 10 s long evaluation of RMSSD, SDNN, and Ln(RMSSD) should be used for evaluating 5 min HRV and therefore, as an estimate of ANS function in patients with hypertension. These parameters represent appealing markers that can be readily calculated in various clinical settings from any ECG tracing.

Acknowledgements The authors would like to thank Phyllis Curchack Kornspan and Faye Schreiber for editorial assistance. The authors would also like to thank Dr Gabriel Chodik from Tel Aviv University and Navah Jelin from Meir Medical Center for help with the statistical analyses.

Contributors KP and KK collected the data. KP and UN planned the study. KK and UN performed the statistical analysis. UN wrote the paper.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The Institutional Review Board approved the research protocol.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Data are available on reasonable request.

ORCID iD

Udi Nussinovitch http://orcid.org/0000-0002-3931-8003

REFERENCES

1 Raffin J, Barthélémy JC, Dupré C, *et al*. Exercise frequency determines heart rate variability gains in older people: a meta-analysis and meta-regression. *Sports Med* 2019;49:719–29.
2 Dalal J, Dasbiswas A, Sathyamurthy I, *et al*. Heart Rate in Hypertension: Review and Expert Opinion. *Int J Hypertens* 2019;2019:1–6.
3 Sajadieh A, Nielsen OW, Rasmussen V, *et al*. C-reactive protein, heart rate variability and prognosis in community subjects with no apparent heart disease. *J Intern Med* 2006;260:377–87.
4 Sandercock GR, Brodie DA. The role of heart rate variability in prognosis for different modes of death in chronic heart failure. *Pacing Clin Electrophysiol* 2006;29:892–904.
5 Anon. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Eur Heart J* 1996;17:354–81.
6 Nunan D, Donovan G, Jakovljevic DG, *et al*. Validity and reliability of short-term heart-rate variability from the Polar S810. *Med Sci Sports Exerc* 2009;41:243–50.
7 Radecki SE, Kane RL, Solomon DH, *et al*. Do physicians spend less time with older patients? *J Am Geriatr Soc* 1988;36:713–8.
8 Sandella JM, Roberts WL, Langenau EE. Relationship between encounter time and candidate performance on COMLEX-USA Level 2-PE. *J Am Osteopath Assoc* 2011;111:38–43.
9 Chambers KA, Boulet JR, Gary NE. The management of patient encounter time in a high-stakes assessment using standardized patients. *Med Educ* 2000;34:813–7.
10 Karp E, Shiyovich A, Zahger D, *et al*. Ultra-short-term heart rate variability for early risk stratification following acute ST-elevation myocardial infarction. *Cardiology* 2009;114:275–83.
11 Nussinovitch U, Elishkevitz KP, Katz K, *et al*. Reliability of Ultra-Short ECG Indices for Heart Rate Variability. *Ann Noninvasive Electrocardiol* 2011;16:117–22.
12 Schroeder EB, Whitsel EA, Evans GW, *et al*. Repeatability of heart rate variability measures. *J Electrocardiol* 2004;37:163–72.
13 Munoz ML, van Roon A, Riese H, *et al*. Validity of (Ultra-)Short Recordings for Heart Rate Variability Measurements. *PLoS One* 2015;10:e0138921.
14 Pavithran P, Mithun R, Jomal M, *et al*. Heart rate variability in middle-aged men with new-onset hypertension. *Ann Noninvasive Electrocardiol* 2008;13:242–8.
15 Havlicekova Z, Tonhajzerova I, Jurko A, *et al*. Cardiac autonomic control in adolescents with primary hypertension. *Eur J Med Res* 2009;14(Suppl 4):101–3.
16 Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *J Chiropr Med* 2016;15:155–63.
17 Adjei P, Surges R, Scott CA, *et al*. Do subclinical electrographic seizure patterns affect heart rate and its variability? *Epilepsy Res* 2009;87:281–5.
18 Kon H, Nagano M, Tanaka F, *et al*. Association of decreased variation of R-R interval and elevated serum C-reactive protein level in a general population in Japan. *Int Heart J* 2006;47:867–76.
19 Bikkina M, Alpert MA, Mukerji R, *et al*. Diminished short-term heart rate variability predicts inducible ventricular tachycardia. *Chest* 1998;113:312–6.
20 de Bruyne MC, Kors JA, Hoes AW, *et al*. Both decreased and increased heart rate variability on the standard 10-second electrocardiogram predict cardiac mortality in the elderly: the Rotterdam Study. *Am J Epidemiol* 1999;150:1282–8.
21 Mancia G, Grassi G. The autonomic nervous system and hypertension. *Circ Res* 2014;114:1804–14.
22 Hamilton RM, McKechnie PS, Macfarlane PW. Can cardiac vagal tone be estimated from the 10-second ECG? *Int J Cardiol* 2004;95:109–15.
23 McNames J, Aboy M. Reliability and accuracy of heart rate variability metrics versus ECG segment duration. *Med Biol Eng Comput* 2006;44:747–56.
24 Salahuddin L, Cho J, Jeong MG, *et al*. Ultra short term analysis of heart rate variability for monitoring mental stress in mobile settings. *Conf Proc IEEE Eng Med Biol Soc* 2007;2007:4656–9.
25 Thong T, Li K, McNames J, *et al*. *Accuracy of ultra-short heart rate variability measures. of the 25th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2003:2424–7.