Correlations between frequency-domain HRV indices and lagged Poincaré plot width in healthy and diabetic subjects

Paola Contreras[1], Rafael Canetti Eng[2] and Eduardo R Migliaro[1]

[1] Departamento de Fisiología, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay
[2] Departamento de Control y Electrónica Industrial, Instituto de Ingeniería Eléctrica, Facultad de Ingeniería, Universidad de la República, Montevideo, Uruguay

E-mail: contreras@fmed.edu.uy

Abstract

The conventional Poincaré plot for heart rate variability (HRV) analysis is a scatterplot of successive (lag 1) pairs of RR intervals (intervals between heartbeats), and its width (SD1) is considered a measure of short-term variability. It has been shown that SD1 correlates better with HF than with LF (high- and low-frequency bands of the spectrum respectively). Our aim was to assess how these correlations were affected when SD1 was obtained for longer lags. 10 min ECGs were used to construct Poincaré plots with lags of 1–10 heartbeats in two groups of subjects, one with normal HRV and the other with impaired HRV (control and diabetic groups respectively, $N = 15$ each). SD1 was quantified for these subjects and HRV spectral indices were estimated. The diabetic group had lower LF, HF and SD1 than the control group ($p < 0.05$). In both groups, SD1 tended to increase as the lag increased. In the control group, SD1 for lags 1 and 2 was highly correlated with HF ($r_s > 0.9$), while SD1 for lags $\geqslant 4$ correlated better with LF ($r_s \geqslant 0.9$) than with HF ($0.65 \leqslant r_s \leqslant 0.73$). However, in the diabetic group, the correlation results did not change in that way for different lags (correlation results between HF and SD1: $r_s \geqslant 0.95$ for lags 1–10). In conclusion, the comparative strength of the correlations between lagged Poincaré widths and spectral indices might be useful to distinguish normal from pathological HRV.

Keywords: heart rate variability, Poincaré plot, diabetes, autonomic nervous system

1. Introduction

Heart rate variability (HRV) analysis seeks mainly to assess autonomic function from fluctuations in the intervals between heartbeats (RR intervals). Spectral analysis of RR interval time series allows us to distinguish rapid from slow heart rate oscillations that correspond respectively to the high- (HF, 0.15–0.40 Hz) and low- (LF, 0.04–0.15 Hz) frequency bands of the spectrum (Task Force of the ESC and the NASPE 1996). HF band has its peak coinciding with the respiratory frequency. Traditionally, the parasympathetic nervous system has been thought to mediate heart rate fluctuations at frequencies corresponding to the HF band of the power spectrum (Akselrod *et al* 1981, Tulppo *et al* 1996). Recently, however, Stein *et al* (2005) have speculated that sometimes increased normalized HF power can also represent non-respiratory sinus arrhythmia and increased beat-to-beat randomness under certain conditions, for example, in post-miocardial infarction patients. LF is associated with vasomotor oscillations, and it has been suggested that it reflects both parasympathetic and sympathetic modulations of heart rate (Akselrod *et al* 1981).

Since the dynamics of the cardiac system are nonlinear, nonlinear methods have been applied to the analysis of HRV (Goldstein and Buchman 1998). One of these techniques is the Poincaré or Lorenz plot (Denton *et al* 1990), a scatterplot of each RR interval as a function of the preceding one. This technique was first used as a qualitative tool (Woo *et al* 1992) and later, the quantification of the Poincaré plot geometry was proposed. Specifically, Tulppo *et al* (1996) fit an ellipse to the shape of the Poincaré plot in order to calculate HRV indices, for example, the standard deviation of instantaneous beat-to-beat RR interval variability or SD1.

However, Brennan *et al* (2001) claimed that this kind of Poincaré plot indices are related to standard time-domain HRV measures. They demonstrate that SD1, which measures the width of the Poincaré plot and therefore indicates the level of short-term variability, is a linear scaling of the linear statistical time-domain index SDSD (standard deviation of the successive differences of the RR intervals). Accordingly, these authors feel that while the Poincaré plot is capable of representing time domain summary statistics graphically, its most potent abilities are being ignored (Brennan *et al* 2001).

A number of variations have been proposed, in order to optimize the use of the Poincaré plot as a quantitative tool (Hnatkova *et al* 1995, Moraes *et al* 2000, Sosnowski *et al* 2005). One of these is the lagged Poincaré plot. The conventional plot has two dimensions and a lag of 1 interval, i.e., each point on the plot consists of a pair of successive intervals ($[RR_i, RR_{i+1}]$). However, Lerma *et al* (2003) used longer lags ($[RR_i, RR_{i+t}]$ with $1 \leqslant t \leqslant 8$) to analyze HRV in chronic renal failure patients and more recently, Thakre and Smith (2006) used lags from 1 to 10 for HRV analysis in patients with chronic heart failure.

Using a model, Brennan *et al* (2002) established that the length and width of a Poincaré plot (lag 1) are a weighted combination of LF and HF, thus, providing a theoretical link between frequency domain spectral analysis and time-domain Poincaré plot analysis. These authors showed that the Poincaré plot width correlated better with HF power than with LF power.

The aim of the present study was to assess how the above-mentioned correlations between SD1 and spectral indices are affected when SD1 is calculated with different lags. Specifically, we hypothesized that the high correlation between SD1 and HF power (Brennan *et al* 2002) should decrease as the lag increases. We applied our hypothesis to two groups of subjects with different HRV, a normal HRV group of healthy volunteers and an impaired HRV group consisting of type 1 diabetic patients. To this end we constructed Poincaré plots with ten different lags (1–10), based on 10 min ECGs, and calculated SD1 for each

Table 1. Definition of HRV indices used in this paper.

HRV index	Definition
LF (ms^2)	Low frequency power
	The energy in the heart period power spectrum between 0.04 and 0.15 Hz
HF (ms^2)	High frequency power
	The energy in the heart period power spectrum between 0.15 and 0.4 Hz
SD1 (ms)	Standard deviation 1
	The dispersion of points perpendicular to the line-of-identity of the Poincaré plot (this is a measure of the width of the Poincaré plot)

lag. We also estimated the spectral HRV indices, HF and LF, and correlated these with lagged SD1.

2. Methods

In carrying our research, we used the data set of a previous study (Migliaro *et al* 2003), which involved subjects with normal and impaired HRV. The data set consists of 15 type 1 diabetic patients (with a history of diabetes extending over 20 years) and 15 healthy volunteers within the same age range (diabetic and control groups respectively). Our study conforms to the principles outlined in the Declaration of Helsinki. All subjects gave their consent.

The healthy volunteers were non-smokers, did not suffer from obesity (body mass index ⩽30) and were not taking any medication. Diabetic patients were allowed to take their usual medication. The most common drugs apart from insulin (15/15) were enalapril (6/15) and amiodarone (3/15). Three diabetic patients had only insulin. Medication for each diabetic patient is specified in an extra table available in the electronic version of this paper. All subjects were instructed to avoid caffeine, alcohol and heavy exercise the day before the study. All tests started between 4 and 6 PM, after at least 4 h of fasting. The subjects relaxed during 20 min before a 10 min recording period in supine position.

2.1. Electrocardiogram (ECG) recording and HRV measurement

Details about these ECG recordings have already been published (Migliaro *et al* 2003). To summarize briefly, electrodes were placed on the chest surface to obtain a bipolar lead (Fukuda FJC-7110 electrocardiograph). The ECG signal was fed into a computer by means of an A/D converter. The sampling rate was 500 Hz. We analyzed the whole 10 min recording. The ECG signal was prefiltered through a Butterworth fourth-order band-pass filter with 0.3–25 Hz passband. Automatic detection recognized the occurrence of an R wave, combining filtered ECG level and slope.

The R wave detections were visually inspected together with the ECG to confirm that only sinusal beats had been detected. Detection of noise or extrasystoles was corrected as well as the lack of detection of a sinusal R wave but the number of corrections was <10% of the total number of intervals. Then, RR intervals (in fact, NN intervals, i.e., normal-to-normal intervals) were measured automatically. Acquisition and off-line processing were done using software written in Labview[R] and Matlab[R].

For this work we estimated two indices in the frequency domain, HF and LF, which are defined in table 1 (Migliaro *et al* 2003). For the frequency-domain analysis of the RR time series, the sequences were interpolated with a cubic spline, uniformly resampled (sampling frequency = 4 Hz) and detrended. The power spectral density of this signal was estimated using

Table 2. Comparisons between diabetic and control groups.

	Diabetic group	Control group	P^a
N (male/female)	15 (7/8)	15 (6/9)	Ns
Age (years)	54 (44–66)[b]	55 (42–70)	Ns
Heart rate (bpm)	78 (59–87)	70 (59–81)	Ns
LF (ms)	65.1 (1.2–627.2)	453.9 (83.4–1595.3)	<0.0001
HF (ms)	21.3 (2.0–354.6)	158.0 (14.8–1218.6)	0.0017
SD1 (ms)	6.2 (1.6–36.0)	14.9 (5.9–28.8)	0.0075

[a] Mann–Whitney test except for gender composition (Fisher's exact test).
[b] All values are given as median (range) except for N.

the Welch method, dividing the data into non-overlapping intervals of length 512 samples, windowed with a Hanning window (Migliaro *et al* 2003).

2.1.1. Poincaré plot indices. The most common Poincaré plot for HRV analysis is a scatterplot of each RR interval against the previous RR interval i.e., it has two dimensions and a lag of 1 interval. In addition to this conventional Poincaré plot, our software constructs plots with any chosen lag. We used lags of 1–10 because it has been reported that any given RR interval can influence up to eight subsequent RR intervals, possibly as a consequence of respiratory sinus arrhythmia (Thakre and Smith 2006, Lerma *et al* 2003). Also, our Matlab[R] routine calculates the Poincaré plot indices for each lag. However, for the purpose of this paper only SD1 was used (see table 1 for definition (Brennan *et al* 2001)). SD1 was not measured from the Poincaré plot but calculated according to the formula: SD1 = SDSD/square root 2 (Brennan *et al* 2001). However, instead of using SDSD (standard deviation of successive differences), we used SDLD (standard deviation of lagged differences, Thakre and Smith 2006), so as to obtain SD1 for lags 1–10. When SD1 was obtained for lags different from 1 interval, the corresponding lag appears as a subindex (e.g.: $SD1_{10}$ refers to the SD1 for lag 10). Although the Poincaré plot was not necessary to calculate SD1, it allowed us to perceive this index in a visual manner and also to confirm that the manual inspection of the R wave detections had been correct.

2.2. Statistical analysis

Statistical analysis was performed using Graphpad Instat[R]. A two-tailed P value <0.05 was considered significant in all analysis. Comparisons between the diabetic and control groups were done using the Mann–Whitney test except for comparison by gender composition (Fisher's exact test). Comparisons within each group were done by means of the Friedman test (non-parametric repeated measures ANOVA). Spearman correlation coefficients (r_s) between frequency-domain HRV indices and lagged SD1 were calculated within each group.

3. Results

3.1. Comparisons between the diabetic and control groups

As shown in our previous study, although the diabetic and control groups had similar gender composition, age and heart rate, the diabetic group had reduced HRV compared to the control group (table 2). Frequency domain indices, as well as SD1, obtained from the Poincaré plot were significantly lower in the diabetic group.
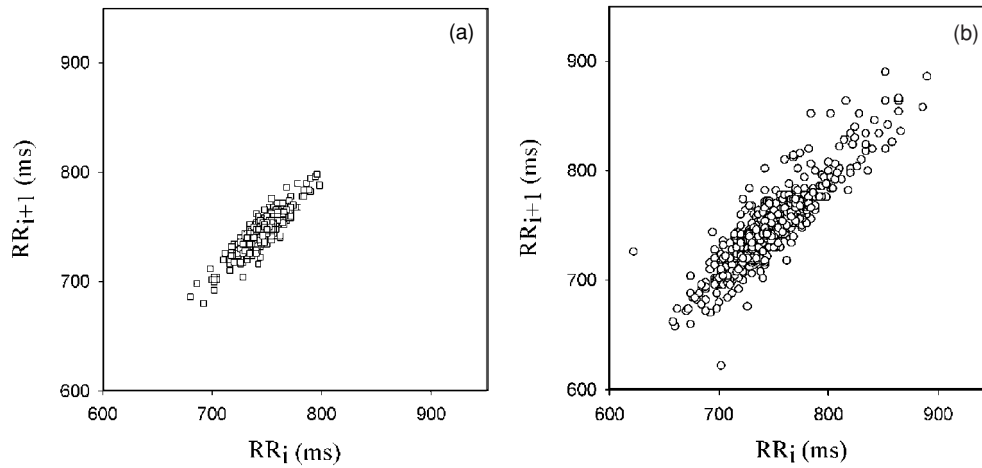
Figure 1. Poincaré plots (lag 1) for a diabetic subject (a) and a control subject (b). SD1 is 4.6 ms for the diabetic subject and 10.5 ms for the control subject. SD1: a measure of the width of the Poincaré plot.
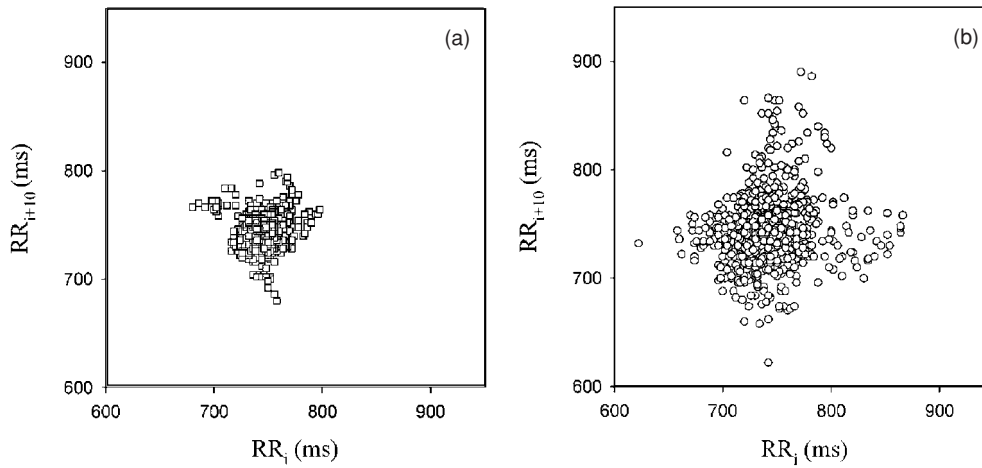

Figure 2. Poincaré plots (lag 10) for the same diabetic subject (a) and the same control subject (b) as in figure 1. $SD1_{10}$ was 11.7 ms for the diabetic subject and 31.9 ms for the control subject. $SD1_{10}$: a measure of the width of the Poincaré plot constructed with a lag of 10 intervals.

Figure 1 shows the Poincaré plots (lag 1) of one female subject from the diabetic group and one male subject from the control group. These examples were chosen by virtue of same heart rate (81 bpm) and similar age (59 and 55 years respectively). Neither represents the extreme values of their corresponding groups.

3.2. Poincaré plots with different lags

For purpose of comparison, figure 2 shows the Poincaré plots with lag 10 for the same diabetic subject and the same control subject as in figure 1. Note that the shape of the plots becomes more circular.
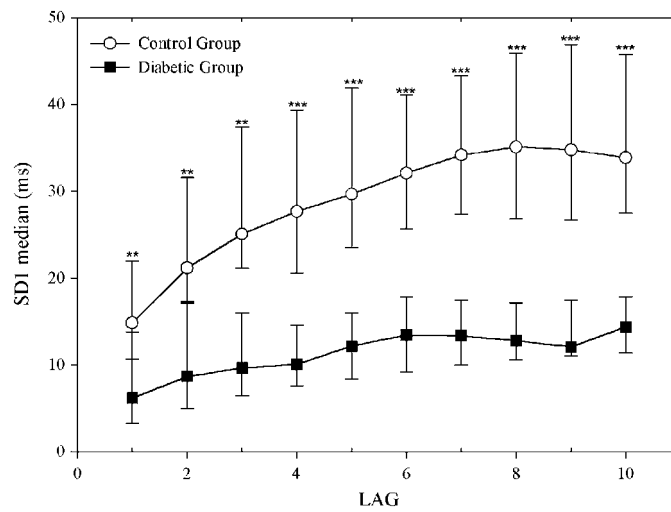
Figure 3. SD1 (median) for different lags in the diabetic group (solid squares) and the control group (hollow circles). The bars represent the 25th and 75th percentiles. Significant differences between both groups (Mann–Whitney test) are indicated by **($P < 0.01$) and ***($P < 0.001$). SD1: a measure of the width of the Poincaré plot.

Table 3. Spearman correlation coefficients (r_s) between frequency domain HRV indices and SD1 (lag 1) within the control and diabetic groups. *P* values appear in parentheses.

	Control group	Diabetic group
SD1 versus LF	0.65 (0.0087)	0.77 (0.0007)
SD1 versus HF	0.95 ($<$0.0001)	0.99 ($<$0.0001)

Figure 3 shows the influence of different lags on SD1 within each group. SD1 increases as the lag increases in both groups ($p < 0.0001$, Friedman test). Figure 3 also shows that SD1 is significantly lower for all lags in the diabetic group than in the control group (Mann–Whitney test). The relative changes of SD1 with increasing lags (taking as the reference SD1 for lag 1) were also significantly lower in the diabetic group than in the control group for lags 2, 3 and 4 (not shown).

3.3. Correlations between frequency domain indices and SD1

Table 3 shows the Spearman correlation coefficients (r_s) between frequency-domain HRV indices and SD1 within each group. As expected, in the control group SD1 correlated highly with HF and to a lesser, yet significant, degree with LF. Comparable results were found in the diabetic group.

Figure 4 shows the Spearman correlation coefficients (r_s) between frequency-domain HRV indices and SD1 calculated from Poincaré plots with lags 1–10 within the control group. Although all the correlations are significant, the high correlation between HF and SD1 diminishes as the lag increases. The opposite is true for the correlation between SD1 and LF, which improves for longer lags. For lags $\geqslant$4, SD1 correlates better with LF than with HF.
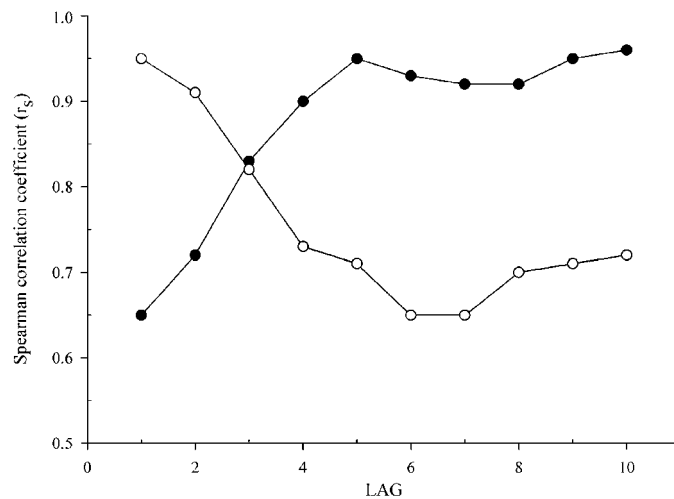
Figure 4. Spearman correlation coefficient (r_s) between spectral indices (HF and LF) and SD1 for different lags in the control group. Hollow circles represent the r_s values between SD1 and HF, and solid circles represent the r_s values between SD1 and LF. P values for each r_s are not given but they were <0.05 in all cases. SD1: a measure of the width of the Poincaré plot, HF: high-frequency power (the energy in the heart period power spectrum between 0.15 and 0.4 Hz), LF: Low frequency power (the energy in the heart period power spectrum between 0.04 and 0.15 Hz).
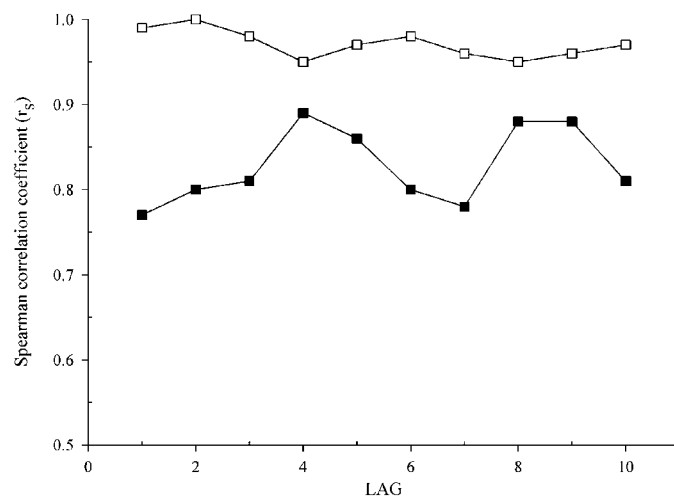
Figure 5. Spearman correlation coefficient (r_s) between spectral indices (HF and LF) and SD1 for different lags in the diabetic group. Hollow squares represent the r_s values between SD1 and HF, and solid squares represent the r_s values between SD1 and LF. P values for each r_s are not given but they were <0.05 in all cases. SD1: a measure of the width of the Poincaré plot, HF: high-frequency power (the energy in the heart period power spectrum between 0.15 and 0.4 Hz), LF: Low frequency power (the energy in the heart period power spectrum between 0.04 and 0.15 Hz).

However, these changes of r_s values as a function of the lag were found only in the control group. As figure 5 shows, in the diabetic group, SD1 has a very good correlation with HF and with LF for all lags from 1 to 10.

In summary, in our control group, correlations between SD1 and HRV spectral indices change depending on the lag. For lags <3, SD1 correlates very well only with HF. At a lag of 3, SD1 correlates very well with LF and HF. For lags >3 (4–10), SD1 correlates very well only with LF (figure 4). However, in the diabetic group, correlations between SD1 and spectral indices do not change as much; and SD1 correlates very well with HF and also with LF for lags 1–10 (figure 5).

4. Discussion

Our finding is that in our healthy group, the Poincaré plot width (SD1) is mainly related to rapid modulations of heart rate only when calculated from Poincaré plots constructed for lag 1 or 2. For lags >3 intervals (4–10), SD1 is mostly related to slow influences on heart rate. However, in our diabetic group, SD1 association with HF and LF does not change as in the control group for all the different lags analyzed (1–10).

Given that both our groups were comparable in age and heart rate (two major determinants of HRV (Tsuji *et al* 1996)), impaired HRV in our diabetic subjects can be ascribed to their illness (Javorka *et al* 2005). After 20 years, they might suffer from diabetic autonomic neuropathy although they did not show clinical symptoms of it at the time of this study (Vinik *et al* 2003).

In both groups SD1 increased as the lag increased (figure 3). Note the different shape of the Poincaré plot for different lags, with cigar-shaped plots for lag 1 (figure 1) and round clouds of points for lag 10 (figure 2). This change was expected, since when intervals are plotted against immediately preceding intervals (lag 1), the correlation between these will be higher than if they were more widely separated. Cigar-shaped plots are typical of high correlation, whereas round clouds of points are typical of lack of correlation (Kaplan and Glass 1995, Otzenberger *et al* 1998). Additionally, for all lags, SD1 was significantly lower in the diabetic group than in the control group (figure 3).

SD1 for lag 1 was very well correlated with HF in both groups (table 3), as expected from the work of Brennan *et al* (2001, 2002) confirming that SD1 is a measure of short-term HRV. Kamen *et al* (1996) suggested that the Poincaré plot width might reflect parasympathetic nervous system activity. One of their results showed that the Poincaré plot width from short-term ECG recordings was reduced during the administration of atropine to healthy volunteers (parasympathetic nervous system activity withdrawal).

The correlations of SD1 in the control group varied markedly depending on the lag. For example, while SD1 correlated very well with HF and only well with LF, $SD1_4$ correlated very well with LF and only well with HF (figure 4).

As stated above, SD1 measures short-term HRV. In fact, on a lag 1 Poincaré plot, SD1 measures the variability from one heartbeat to the next (Brennan *et al* 2001). However, when we consider SD1 from Poincaré plots with longer lags, the term of the variability is extended, from one heartbeat to another separated from it by many beats. The longer the distance between these beats, the higher the mean time interval between the Poincaré plot points which are being summarized by SD1. Therefore, it is expected to find an increasing correlation between SD1 and LF for higher lags as we found in the control group. Indeed, according to Brennan *et al* (2001), the set of lagged Poincaré plots are a complete description of the power spectrum of the RR intervals.

Our results in the control group show that SD1 for lags <3 has better correlations with HF while SD1 for lags >3 (4–10) has better correlations with LF. At a lag of 3, SD1 correlates as well with HF as with LF. Note that a lag of three intervals is the limit only for this specific

group of healthy subjects. A group with a slower mean heart rate, for example, might place the limit in a bigger lag.

The fact that correlations between spectral indices and SD1 for lags 1–10 did not change in the diabetic group (figure 5) might be a consequence of diabetic autonomic neuropathy. In control subjects, the reduction of the correlations between HF and SD1 for lags >3 is probably related to a reduction of the influence of respiration on SD1. On the other hand, in diabetic patients, the low respiratory modulation might explain that the relationship between SD1 and HF remains strong no matter the lag.

This difference between the diabetic and control groups cannot be ascribed to different heart rates, since as earlier stated, both groups are similar in this respect, nor can it be ascribed to medical treatment since most drugs used by our diabetic subjects (enalapril, amiodarone, etc) are reported to increase heart rate variability. However, it is a limitation of our study that medical treatment was not uniform for all the patients in the diabetic group.

In conclusion, the comparative strength of the correlations between lagged Poincaré widths and spectral indices might be useful to distinguish normal from pathological HRV. However, our results need to be validated by a representative number of subjects. Additionally, other studies, including pharmacological and physiological interventions that affect the autonomic nervous system could be used to test hypotheses that may explain our findings.

Acknowledgments

References

Akselrod S, Gordon D, Ubel F A, Shannon D C, Berger A C and Cohen R J 1981 Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control *Science* **213** 220–2

Brennan M, Palaniswami M and Kamen P 2001 Do existing measures of Poincare plot geometry reflect nonlinear features of heart rate variability? *IEEE Trans. Biomed. Eng.* **48** 1342–7

Brennan M, Palaniswami M and Kamen P 2002 Poincare plot interpretation using a physiological model of HRV based on a network of oscillators *Am. J. Physiol. Heart Circ. Physiol.* **283** H1873–86

Denton T A, Diamond G A, Helfant R H, Khan S and Karagueuzian H 1990 Fascinating rhythm: a primer on chaos theory and its application to cardiology *Am. Heart J.* **120** 1419–40

Goldstein B and Buchman T G 1998 Heart rate variability in intensive care *J. Intensive Care Med.* **13** 252–65

Hnatkova K, Copie X, Staunton A and Malik M 1995 Numeric processing of Lorenz plots of R-R intervals from long-term ECGs. Comparison with time-domain measures of heart rate variability for risk stratification after myocardial infarction *J. Electrocardiol.* Suppl **28** 74–80

Javorka M, Javorkova J, Tonhajzerova I, Calkovska A and Javorka K 2005 Heart rate variability in young patients with diabetes mellitus and healthy subjects explored by Poincare and sequence plots *Clin. Physiol. Funct. Imaging* **25** 119–27

Kamen P W, Krum H and Tonkin A M 1996 Poincare plot of heart rate variability allows quantitative display of parasympathetic nervous activity in humans *Clin. Sci. (Lond)* **91** 201–8

Kaplan D and Glass L 1995 Time-series analysis *Understanding Nonlinear Dynamics* ed D Kaplan and L Glass (New York: Springer)

Lerma C, Infante O, Perez-Grovas H and Jose M V 2003 Poincare plot indexes of heart rate variability capture dynamic adaptations after haemodialysis in chronic renal failure patients *Clin. Physiol. Funct. Imaging* **23** 72–80

Migliaro E R, Canetti R, Contreras P and Hakas M 2003 Heart rate variability: short-term studies are as useful as Holter to differentiate diabetic patients from healthy subjects *Ann. Noninvasive Electrocardiol.* **8** 313–20

Moraes R S, Ferlin E L, Polanczyk C A, Rohde L E, Zaslavski L, Gross J L and Ribeiro J P 2000 Three-dimensional return map: a new tool for quantification of heart rate variability *Auton. Neurosci.* **83** 90–9

Otzenberger H, Gronfier C, Simon C, Charloux A, Ehrhart J, Piquard F and Brandenberger G 1998 Dynamic heart rate variability: a tool for exploring sympathovagal balance continuously during sleep in men *Am. J. Physiol.* **275** H946–50

Sosnowski M, Clark E, Latif S, Macfarlane P W and Tendera M 2005 Heart rate variability fraction: a new reportable measure of 24-hour R-R interval variation *Ann. Noninvasive Electrocardiol.* **10** 7–15

Stein P K, Domitrovich P P, Huikuri H V, Kleiger R E and Cast Investigators 2005 Traditional and nonlinear heart rate variability are each independently associated with mortality after myocardial infarction *J. Cardiovasc Electrophysiol.* **16** 13–20

Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996 Heart rate variability: standards of measurement, physiological interpretation and clinical use *Circulation* **93** 1043–65

Thakre T P and Smith M L 2006 Loss of lag-response curvilinearity of indices of heart rate variability in congestive heart failure *BMC Cardiovasc Disorders* **6**   See endnote 1

Tsuji H, Venditti F J Jr, Manders E S, Evans J C, Larson M G, Feldman C L and Levy D 1996 Determinants of heart rate variability *J. Am. Coll. Cardiol.* **28** 1539–46

Tulppo M P, Makikallio T H, Takala T E, Seppanen T and Huikuri H V 1996 Quantitative beat-to-beat analysis of heart rate dynamics during exercise *Am. J. Physiol.* **271** H244–52

Vinik A I, Maser R E, Mitchell B D and Freeman R 2003 Diabetic autonomic neuropathy *Diabetes Care* **26** 1553–79

Woo M A, Stevenson W G, Moser D K, Trelease R B and Harper R M 1992 Patterns of beat-to-beat heart rate variability in advanced heart failure *Am. Heart J.* **123** 704–10

Endnotes

(1) Author: Please provide page number in Thakre and Smith (2006).

Reference linking to the original articles

References with a volume and page number in blue have a clickable link to the original article created from data deposited by its publisher at CrossRef. Any anomalously unlinked references should be checked for accuracy. Pale purple is used for links to e-prints at arXiv.