STATISTICA, anno LXII, n. 1, 2002

A STATISTICAL COMPARISON OF SIGNAL REPRESENTATIONS AND SPECTRAL ESTIMATORS OF HEART RATE VARIABILITY IN HYPERTENSIVE PATIENTS

M. Congi, G. Calcagnini, S. Lino, S. Damiani, S. Cerutti

1. INTRODUCTION

The investigation of the statistical properties of the heart period spontaneous fluctuation (heart rate variability - IIRV) has obtained increasing attention over the last years. Since the early studies, the definition of a suitable representation for the sequences of time intervals between consecutive beats has challenged the investigators. The uneven nature of this process is evident when the observed value of the heart period is only defined as a beat occurs and it remains undefined until the next beat; this process should thus be modelled as a point event series.

Because of the wide use of spectral estimation in the IIRV data analysis, efforts have been tnade in obtaining a suitable representation for spectral estimation: the most used solutions include 1) the so called Interval Tachogram (IT); 2) the interpolation and uniform resampling of interbeat time intervals (RK intervals) by cubic splines (CSI); 3) the Low Pass Filtering of Event Series (LPFES) (Anonymous, 1996). In IT the absolute occurrence time of each RK interval is not considered and each interval is plotted as a function of the beats' number, thus not considering the original non-uniform sampling of the data. A uniform sampled signal can be obtained interpolating the so-called Discrete Event Series (DES), which is the RR interval plot versus the absolute time. CSI uses a cubic splines interpolation of DES and a uniform resampling. A different approach considers the original occurrence time data as a train of delta functions. Low-pass filtering of this signal provides a regularly sampled series, which is proved to contain the relevant information (LPFES) (Hyndman, 1975; De Boer, 1984).

The HRV data investigation in the frequency domain is aimed to quantify the data power in two specific frequency bands: 1) the High Frequency band (HF, 0.15-0.40 Hz), expression of the parasympathetic control to the heart; 2) the Low Frequency band (LF, 0.04-0.15 Hz), considered expression of both sympathetic and parasympathetic systems, but always increasing during sympathetic activation (Anonymous, 1996).

Two major estimation approaches currently used are: the classical approach uses the Fourier Transform (FT), in which LF and IIF components are calculated integrating the total power (TP) on the 0.04-0.15Hz and 0.15-0.40Hz range, respectively. The autoregressive (AR) approach uses a stochastic modelling of the data and estimates the spectrum from model parameters; LF and HF powers are calculated using the automatic decomposition of spectral peaks. Although these different approaches are considered equivalent (Anonymous, 1996), there are still difficulties comparing quantitatively and interpreting the results of the many published HRV studies, due to the different HRV signals and spectral estimators which were used to obtain the HRV spectra. The use of IT with parametric methods and the regularly sampled interpolation of DES with non-parametric method was suggested in the IIRV guidelines (Anonymous, 1996).

The aim of our study is to analyse quantitatively, from a statistical point of view, the differences obtained using three different HRV signals and two different spectral estimators, in a population of hypertensive patients.

2. METHODS AND MATERIALS

Thirty-two informed, essential hypertensive patients were recruited. None of them received treatment with anti-hypertensive drugs before signal acquisition. ECG, arterial blood pressure and respiration signals have been simultaneously recorded and real-time digitised (sampling frequency 500 Hz, resolution 12 bit) for 15 minutes, at resting condition. Surface ECG (II lead) was obtained through an analog electrocardiograph (Esaote, Italy). Blood pressure was continuously and non-invasively recorded using a photoplethysmographic technique (Finapres, Omheda, USA). We monitored the breathing activity using a thoracic plethysmographic belt. Confidence limits for heart period estimation have been obtained using numerical recognition of R waves, using a derivative-threshold algorithm; we also used a parabolic interpolation of QRS samples to improve the confidence limits recognition (Kitney, 1980).

From R-R intervals we obtained the IT. We then interpolated the DES with cubic splines and resampled (1 Hz) this signal to obtain the CSI. LPFES was obtained using the French-Holden algorithm, which is a computationally efficient way for low-pass filtering (filter cut-off 0.5 Hz) the Event Series (De Boer, 1984).

Spectral estimation was performed over 5 minutes of recordings. AR model identification is obtained using Yule-Walker equations; the model order is the one matching the condition of whitening the model prediction error and minimised an optimality function; the Ljung-Box whiteness test was applied as prediction error whiteness test and the Akaike criterion was used for optimal order.

PSD was calculated using model parameters in the relation:

$$\hat{P}_{AR}(f) = \frac{\sigma^2 \Delta t}{\left| 1 + \sum_{k=1}^{p} \hat{a}_k \exp(-j2\pi f \Delta t k) \right|^2}$$

where $\hat{a}_k$ and σ^2 are the model coefficients and the residual variance, respectively.

Non-parametric spectrum estimation (FT) uses an average periodogram with Hanning windowing. Data were divided in segments of 128 samples, with an overlap of 64.

$$\hat{D}_{FT}(f) = \frac{1}{\Delta t N}\left|\sum_{n=0}^{N-1} x(n)\exp(-j2\Delta tf\ n)\right|^2$$

We compared the different spectra in terms of Total Power (TP), LF and HF normalised powers (LF n.u., HF n.u.), and LF/HF ratio (LF/HF). Normalised LF and HF powers are defined as the relative power of LF and HF in proportion to the total power minus the VLF cotnponents (0 - 0.04 Hz). These spectral parameters are the most relevant from a clinical point of view. For each parameter we thus obtained six estimations. Figure 1 shows an example of AR and FT spectra of IT in one subject.

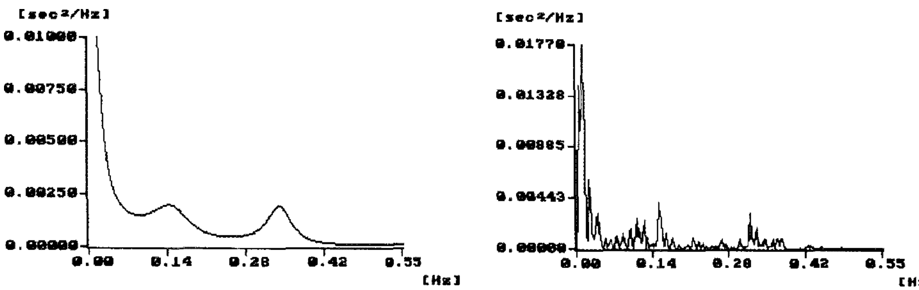

Figure 1 - Example of HRV spectrum of IT by AR modelling (left) and FT (right)

3. STATISTICAL ANALYSIS

All the parameters are tested for departures from normality (Kolmogorov-Smirnov test). Differences are tested using both parametric and non-parametric paired data tests: *t*-Student test is used for those parameters which followed a normal distribution. The non-normal parameters are tested using non-parametric paired data Wilcoxon test; in addition, t-Student test is applied after log transformation. For a given critical level, in fact, the above mentioned test has a higher statistical power.

Correlations among the parameters are also computed.

4. RESULTS

Results are presented as follows: table 1 presents the mean and standard deviation values for the considered parameters; table 2 summarises the results of the normality test.

Tables 3, 4, 5 report the correlation matrixes. Tables 6, 7, 8, 9 report the percentage differences of the mean values over the whole population, for TP, LF n.u., EIF n.u. and LF/HF ratio. Each cell of the table is defined as the percentage difference of the raw parameter versus the column, as illustrated in figure 2. The confidence level p for the difference is reported in the same cell (ns = not significant; *: $0.01 < p$ 50.05; "": $0.001 < p \leq 0.01$; ***: $p < 0.001$).

	yy
xx	$(xx - yy)/xx \cdot 100$

Figure 2 - Construction of the table for the percentage differences

AR and FT spectral estimators does not prove significant differences when compared for the same HRV signals, for all the considered variables. IT vs CSI differ significantly only for IIF n.u., having differently spectral estimator. Significant and relevant differences are found when comparing the LPFES with IT or CSI, with both spectral estimators. Nevertheless all the correlation coefficients (r) are greater than 0.9.

The comparison between IT with parametric methods and between CSI with non parametric methods, which represents the combinations suggested in the HRV Guidelines, shows minimum differences. In addition these differences are statistically significant only for H F n.u.

TABLE 1

Mean ± standard deviation.
Number of observations = 32

	TP (ms^2)	LF n.u.	HF n.u.	LF/HF
IT - AR	2399 ± 4232	57.54 ± 20.05	36.68 ± 17.49	2.30 ± 1.94
IT - FT	2748 ± 4151	58.74 ± 20.57	35.21 ± 17.58	2.59 ± 2.45
LPFES - AR	3126 ± 5614	53.11 ± 20.03	38.77 ± 16.12	1.93 ± 1.65
LPFES - FT	3016 ± 5158	53.77 ± 21.88	40.04 ± 17.08	2.00 ± 1.90
CSI - AR	2421 ± 3690	58.53 ± 19.57	38.14 ± 17.86	2.27 ± 1.98
CSI - FT	2397 ± 3664	57.50 ± 21.11	39.18 ± 18.99	2.32 ± 2.22

TABLE 2

Normality test (Kolmogorov-Smirnov)

	TP	LE' nu	IIF nu	LF/HF
IT - AR	$p < .01$*	$p > .20$	$p > .20$	$p > .20$
IT - FT	$p < .01$*	$p > .20$	$p > .20$	$p < .20$
LPFES - AR	$p < .01$*	$p > .20$	$p > .20$	$p > .20$
LPFES - FT	$p < .01$*	$p > .20$	$p > .20$	$p < .15$
CSI - AR	$p < .01$*	$p > .20$	$p > .20$	$p > .20$
CSI - FT	$p < .01$*	$p > .20$	$p > .20$	$p < .10$

TABLE 3

Low frequency correlation matrix (LF n.u.)

LF n.u.	IT - AR	IT - FT	LPFES - AR	LPFES - FT	CSI - AR	CSI - FT
IT - AR	1.0000	0.9471 ***	0.9822 ***	0.9724 ***	0.9950 ***	0.9685 ***
IT - FT		1.0000	0.9429 ***	0.9605 ***	0.9424 ***	0.9526 ***
LPFES - AR			1.0000	0.9714 ***	0.9797 ***	0.9488 ***
LPFES - FT				1.0000	0.9759 ***	0.9874 ***
CSI - AR					1.0000	0.9779 ***
CSI - FT						1.0000

***: $p < 0.001$.

TABLE 4

High frequency correlation matrix (HF n.u.)

HF n.u.	IT - AR	IT - FT	LPFES - AR	LPFES - FT	CSI - AR	CSI - FT
IT - AR	1.0000	0.9103 ***	0.9791 ***	0.9630 ***	0.9909 ***	0.9609 ***
IT - FT		1.0000	0.8925 ***	0.8983 ***	0.9253 ***	0.9239 ***
LPFES - AR			1.0000	0.9654 ***	0.9737 ***	0.9333 ***
LPFES - FT				1.0000	0.9639 ***	0.9771 ***
CSI - AR					1.0000	0.9759 ***
CSI - FT						1.0000

***: $p < 0.001$.

TABLE 5

LF/HF ratio correlation matrix

LF/HF	IT - AR	IT - FT	LPFES - AR	LPFES - FT	CSI - AR	CSI - FT
IT - AR	1.0000	0.9415 ***	0.9929 ***	0.9086 ***	0.9943 ***	0.9211 ***
IT - FT		1.0000	0.9573 ***	0.9347 ***	0.9478 ***	0.9342 ***
LPFES - AR			1.0000	0.9162 ***	0.9923 ***	0.9219 ***
LPFES - FT				1.0000	0.9232 ***	0.9920 ***
CSI - AR					1.0000	0.9394 ***
CSI - FT						1.0000

***: $p < 0.001$

TABLE 6

Total Power (TP) percentage differences. Statistical analysis using Wilcoxon test for dependent samples

TP	IT - AR	IT - FT	LPFES - AR	LPFES - FT	CSI - AR	CSI - FT
IT - AR	0	- 14.55 ***	- 30.29 ***	- 25.73 ***	- 0.90 **	0.09 (ns)
IT - FT		0	- 13.74 **	- 9.76 **	11.91 (ns)	12.78 (ns)
LPFES - AR			0	3.50 (ns)	22.56 ***	23.32 ***
LPFES - FT				0	19.75 **	20.53 ***
CSI - AR					0	0.98 (ns)
CSI - FT						0

ns = not significant; *: $0.01 < p \leq 0.05$; **: $0.001 < p \leq 0.01$: ***: $p < 0.001$

TABLE 7

HF n.u. percentage differences. Statistical analysis using Student t test for paired data

HF n.u.	IT - AK	1 ' - FT	LPFES - AR	LPFES - P '	CSI - AR	CSI - FT
IT - AR	0	4.02(ns)	- 5.69 **	9.16 ***	3.97 **	- 6.80 *
IT - FT		0	- 10.12 *	- 13.73 **	- 8.32 (ns)	11.28 (ns)
LPFES - AK			0	3.28 ins)	1.63 (ns)	1.05 (ns)
LPFES - FT				0	4.75 *	2.16 (ns)
CSI - AR					0	- 2.73 (ns)
CSI - *F'S*						0

ns = not significant; *: 0.01 c p ≤ 0.05; **: 0.003 < p ≤ 0.01; ***: p < 0.001

TABLE 8

LF n.u. percentage differences. Statistical analysis using Student t test for paired data

LF n.u.	IT - AR	IT - FT	LPFES - AR	LPFES - FT	CSI - AR	CSI - FT
IT - AR	0	- 2.02 (ns)	7.71***	6.56 ***	- 1.72 *	0.08 (ns)
IT - FT		0	9.54 *	8.41 *	0.29 (ns)	2.06 (ns)
LPFES - AR			0	- 1.25 (ns)	- 10.22 ***	- 8.27 ***
LPFES - FT				0	- 8.86 ***	- 6.93***
CSI - AR					0	1.77(ns)
CSI - FT						0

ns = not significant; *: 0.01 c p ≤ 0.05; **: 0.001 < p ≤ 0.01: ***: p c 0.001

TABLE 9

LF/HF n u percentage differences Statistical analysis using Student t test for paired data

1 F/HF ratio	IT \R	IT FT	LPFES - AR	LPFES - FT	CSI - AR	CSI - FT
TT - AR	0	1 (ns)	16.31""":	13.12 *	1.51 (ns)	- 0.52 (ns)
IT -FT		0	25.70 *	22.87 **	12.57 (ns)	10.77 (ns)
LPFES - AR			0	- 3.80 (ns)	- 17.68 ***	- 20.10 *
LPFES - *FT*				0	13.37 (ns)	15.70 ***
CSI - AR					0	2.06 (ns)
CSI FT						0

ns = not significant; *; 0.01 < p ≤ 0.05: **: 0 001 < p ≤ 0.01; ***: p < 0.001

5. DISCUSSION AND CONCLUSIONS

Correlation analysis confirms the substantial (qualitative) equivalence of considered spectral estimations, even if some quantitative differences should be taken into account when comparing the results obtained with different approaches.

Our results confirm that AR and FT produce, as on average, comparable values: the differences observed are relatively small and never significant. As to HRV signals, IT and CSI give the same results, while significant and relatively large differences are obtained comparing the LPFES to the IT or CSI signals. The use of IT with AR spectral estimation and CSI for non-parametric analysis is suggested in EIRV Guidelines. Our data confirm the equivalence of these two approaches.

LPFES tends to overestimate HF and underestimate LF, thus resulting in a noticeable decrease in the LF/HF ratio. This difference can be theoretically explained with the smoothing kernel used to low-pass filtering the Event Series (De Boer, 1984).

The overall comparison reveals minimum differences when IT is used with the parametric (All) methods and the CSI with non-parametric ones. These two combinations are suggested in the IIRV guidelines indeed.

In conclusion, attention has to be paid when comparing data obtained with LPFES. Although this signal is related to a physiologically plausible model, it produces different estimations from IT and CSI when used for spectral analysis.

6. STUDY LIMITATIONS

IIRV spectrum estimation is often conducted with the arterial blood pressure fluctuations and the respiratory activity simultaneous analysis. The choice of the representation for the HRV series, in this extended setting, should also account for the corresponding representation of blood pressure and respiration signals. The investigation of the representation for these signals and the further constraint to the IIRV signal posed are beyond the aim of this study, and have not been addressed.

Department of Statistics, Probability and Statistics MARCO CONGI
"La Sapienza" University of Rome

Department of Information and System Science GIOVANNI CALCAGNINI
"La Sapienza" University of Rome

Clinical Pathophysiology, "La Sapienza" University of Rome STEFANO LINO

Department of Biomedical Engineering, SILVIO DAMIANI
Polythecnic University of Milan SERGIO CERUTTI

REFERENCES

ANONYMOUS (1996), *Heart Rate Variability, Standard of measurement, physiological interpretation and clinical use*, "Circulation", 93, pp. 1043-1065.

B.M. HYNDMAN, R.K. MOHN (1975), *A model of the cardiac pacemaker and its use in decoding the information content of cardiac intervals*, "Automedica", 1, pp. 239-252.

R.W. DE BOER, J.M. KAREMAKER, J. STRACKEE (19841, *Comparing spectra of a series of point events particularly for heart-rate variability spectra*, "IEEE Transactions on Biomedical Engineering", 31, pp. 384-387.

S.M. KAY, S.L. MARPLE (1981), *Spectrum analysis a modern perspective*, "Proceedings of the IEEE", 69, pp. 1380-1419.

R.I. KITNEY, O. ROMPELMANN (1980), *The study of heart rate variability*, Clerendon Press, Oxford.

RIASSUNTO

Un confronto statistico fra le rappresentazioni temporali e gli stimatori spettrali della variabilità della frequenza cardiaca in pazienti ipertesi

Nell'articolo vengono confrontati diversi metodi per la stima dello spettro di serie storiche della variabilità cardiaca. Attraverso lo studio di 32 pazienti ipertesi è stato mostrato che il metodo *low-parr filtering* sovrastima la componente *high-frequency* rispetto a risultati ottenuti sia dalla tecnica *cubic spline interpolation* sia dal metodo *interval tachogram* non è stata rilevata differenza nella stima dello spettro ottenuta per mezzo di modelli autoregressivi e metodi non parametrici quali le trasformate di Fourier.

SUMMARY

A statistical comparison of signal representations and spectral estimators of heart rate variability in hypertensive patients

The paper compares different methods for the estimation of the spectrum in the heart rate variability time series. Studying 32 hypertensive patients it is shown that the low-pass filtering of event series technique drives to an over estimation of the high frequency component of the heart beat when compared with the results of both cubic spline interpolation and interval tachogram techniques. No differences are founded between the spectrum estimation obtained by autoregressive models and non parametric methods like the Pourier transform.