COMPARISON OF LINEAR AND NON-LINEAR ANALYSIS OF HEART RATE VARIABILITY IN SEDATED CARDIAC SURGERY PATIENTS

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***Abstract*— Heart rate variability (HRV) provides a non-invasive method to monitor functioning of the autonomous nervous system. HRV has been proposed as a potential tool for objective assessment of the level of sedation in critical care. In this paper we studied whether different linear and non-linear analysis methods may discriminate different levels of sedation in cardiac surgery patients. In addition we studied the interrelationships between the different parameters. The results show that HRV is modified by changes in the level of sedation, and that it is not completely recovered by the next day after the cardiac surgery. Both linear time and frequency domain parameters, and non-linear parameters discriminate the different levels, but especially the method based on Poincare plot analysis seems promising. As different parameters are closely correlated, a sub-set of parameters may be sufficient in the quantification of HRV in sedation.**

Keywords: Heart rate variability, level of sedation, intensive care, Poincare plot, entropy.

I. INTRODUCTION

Heart rate variability (HRV) provides a non-invasive marker of the functioning of the autonomous nervous system (ANS). It is well known that the status of the ANS is modified by anaesthetic or sedative drugs, and that noxious stimulus causes sympathetic activation. Hence, HRV has been proposed as a possible measure of anaesthetic depth [1,2] or level of sedation [3,4].

Traditionally, HRV has been quantified by linear time-domain measures such as standard deviation (SD) and root mean square of the successive R-R-intervals (RMSSD), or by spectral analysis of the HRV power in low frequency (LF, around 0.04-0.15Hz) and high frequency (HF, around 0.15.0.4Hz) bands [5]. However, ANS is not a linear system and it has been argued that non-linear analysis would be more optimal for HRV. Furthermore, there is no agreement, which parameters would be the most optimal for the analysis of HRV during anaesthesia or sedation.

The objectives of this study were to: 1) study whether different linear and non-linear HRV measures may discriminate different levels of sedation in cardiac surgery patients; and 2) compare different linear and non-linear HRV measures in their performance and interrelationships with the sama data.

II. METHODS

A. *Patients and protocol*

The study was approved by the local Ethics committee of Kuopio University Hospital. All patients gave written informed consent. 26 patients scheduled for elective coronary artery bypass grafting surgery were included in the study. Anaesthesia regime (propofol-alfentanil) and postoperative sedation (propofol) were standardised.

Data were recorded from patients in five different situations: 1) baseline; 2) pre-medication; 3) after cardiac surgery at intensive care unit at deep sedation (Ramsay score 6 [6]); 4) in intensive care in moderate sedation (Ramsay score 4); 5) post-operatively (the next day).

B. *Data acquisition and signal processing*

Standard patient monitor (CS/3 monitor, Datex-Ohmeda, Instrumentarium Corporation, Helsinki, Finland)) was used to record the vital signals. Electrocardiograph (ECG) was recorded at 300Hz sampling rate, and the R-waves were automatically detected from the ECG off-line. The R-wave detection was manually verified and corrected when necessary. Beat-to-beat RRI (R-to-R-interval) signal was constructed as a series of time difference between the successive heart beats. For spectral analysis purposes, the beat-to-beat data were linearly interpolated and re-sampled at 2 Hz prior to spectral estimation.

C. *Heart rate variability analysis*

5-min stationary periods of RRI were selected in each measurement situation for further analysis. From the origina 26 patients, 4 patients were excluded from the study at this phase due to a pacemaker or severe arrhythmia. If no stationary RRI could be identified from a certain period, the

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period was excluded from the further analysis.

Linear parameters: Linear parameters were computed both in time and frequency domain. Time domain parameters were the standard deviation (SD) of the beat-to-beat RRI signal, which describes the overall HRV, and RMSSD, which is mostly related to the respiratory sinus arrhythmia (RSA). Frequency domain analysis was based on power spectral estimation, which was carried out by Welch method with FFT length of 512 points. Linear frequency domain analysis included quantification of the spectral power in the LF and HF bands, and their ratio, LF/HF ratio. The HF power relates mainly to the parasympathetic activity and respiratory modulation of HRV, while the LF power is affected both by the sympathetic and parasympathetic activities and includes so-called 10-second rhythm [5]. The LF/HF ratio has been associated with the so-called sympathovagal balance [7], but the physiological basis for the use of this parameter has also been criticised [8]. In any case, this ratio is largely used in HRV analysis and is hence included here, too.

Non-linear parameters: Non-linear analysis was carried out by two different approaches. The first one was the calculation of the spectral entropy H, which is defined as [9]

$$H = \sum_f p_f \log(1/p_f) \tag{1}$$

where p_f is the spectral power of the RRI signal on frequency f, and the summation goes over whole spectrum. The spectral entropy H ($0 \le H \le 1$) describes the complexity of the RRI signal: the higher the entropy, the more complex the signal, or the more processes are involved in the generation of the signal [9].

Another non-linear approach was based on the analysis of the return maps (Poincare plots) of the RRI signal. The Poincare plot is a diagram where each RRI(i) is plotted as a function of RRI(i-τ), where τ is a predefined delay (Fig. 1). Typically, τ=1 has been used for the RRI signal. Visual inspection of the Poincare plot has been largely used in the analysis of HRV. The Poincare plot may be analysed quantitatively by calculating the standard deviations of the distances of the RRI(i) to the lines $y = x$ and $y = -x + 2$*RRI$_m$, where RRI$_m$ is the mean of all RRI(i) (Fig. 1) [10]. These standard deviations are referred to as SD1 and SD2, respectively. SD1 is related to the fast beat-to-beat variability in the data, while SD2 describes the longer-term variability of RRI [10]. The ratio SD1/SD2 may also be computed to describe the relationship between these components. This analysis does not require any pre-processing or stationarity of the data [10], and is hence especially attractive.

Statistical analysis: The data were statistically analysed by plotting the mean and standard error of mean (SEM) for each parameter in each situation for all patients. In addition, Pearson's correlation coefficient R was computed between different parameters to study their interrelationships.

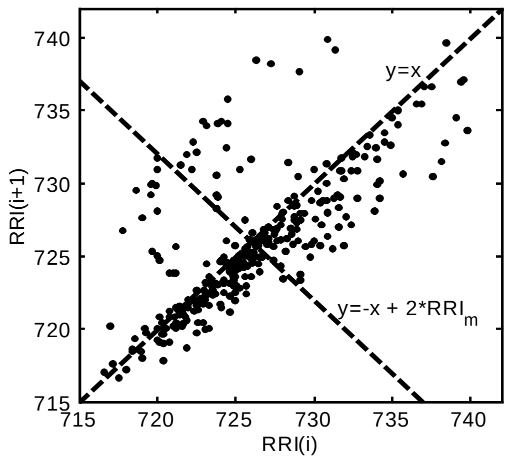

Fig. 1. Poincare plot of the RRI signal. SD1 and SD2 are defined as standard deviation of the distances of each RRI(i) from the lines $y = x$, and $y = -x + 2$*RRI$_m$, respectively. RRI$_m$ is the mean of all RRI(i).

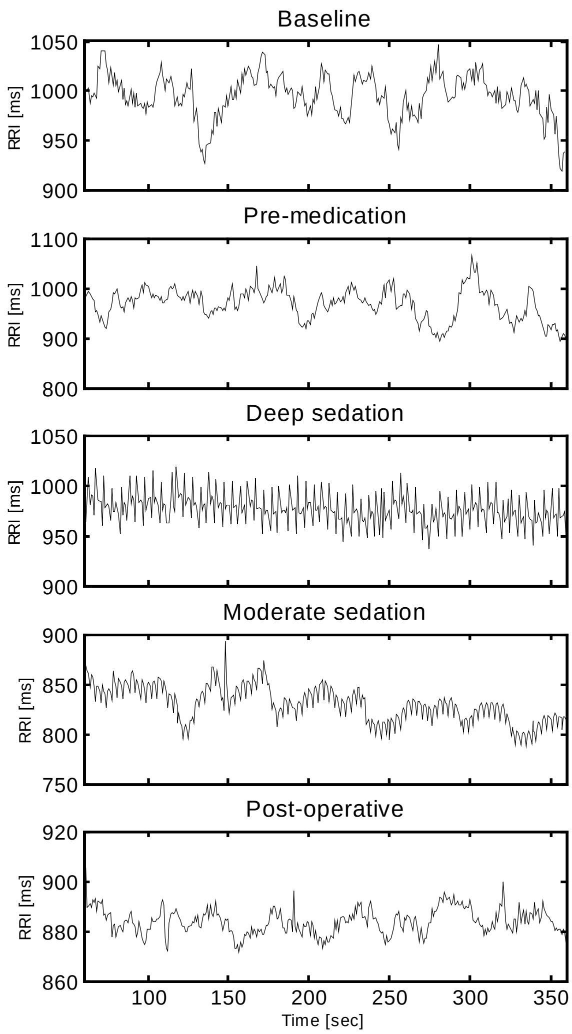

Fig. 2. Examples of RRI signals from different situations in one patient. Note the effect of mechanical ventilation during deep and moderate sedation.

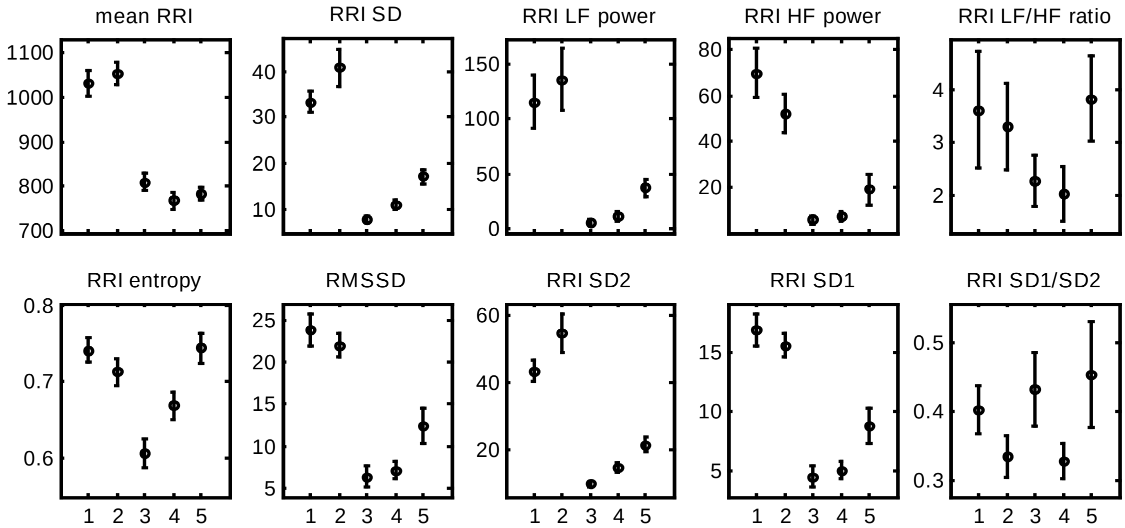

Fig. 3. HRV paremeters during baseline (1), pre-medication (2), deep sedation (3), light sedation (4) and post-operatively (5). Data are plotted as mean ± standard error of mean. Units are msec (RRI, RRI SD, RMSSD, SD1 and SD2) or msec^2 (LF, HF power).

TABLE 1
PEARSON'S CORRELATION COEFFICIENTS BETWEEN DIFFERENT HRV PARAMETERS

Pearson's R	SD	RMSSD	LF power	HF power	LF/HF	SD1	SD2	SD1/SD2	Entropy
RRI mean	0,56	0,53	0,35	0,47	ns	0,53	0,54	ns	0,22
SD		0,71	0,74	0,67	0,16	0,71	0,98	ns	0,23
RMSSD			0,44	0,87	ns	1,00	0,58	0,54	0,30
LF power				0,43	0,40	0,44	0,76	-0,14	ns
HF power					-0,19	0,87	0,58	0,29	0,31
LF/HF						ns	0,20	-0,37	0,31
SD1							0,58	0,54	0,30
SD2								-0,21	0,20
SD1/SD2									ns

III. RESULTS

An example of RRI signal in different situations in one patient is presented in Fig. 2. The transition from complex to more regular signal during sedation is easily recognised. The effect of mechanical ventilation gives rise to regular peak-like RSA especially during deep sedation. In deep sedation other rhythms are mostly absent. When patient is awake, RRI is characterised by increased complexity of the existing rhythms.

The mean±SEM of each parameter during different situations are shown in Fig. 3. Heart rate increased (mean RRI decreased) and overall HRV decreased in sedation (periods 3-4) compared to the pre-surgery values (periods 1-2). Almost all HRV parameters (mean RRI, SD, RMSSD, LF power, HF power, entropy, SD1 and SD2) evidenced this reduction. Only ratios (LF/HF ratio, SD1/SD2) could not discriminate these periods from each other. When comparing deep level of sedation (Ramsay 6, period 3) to moderate level (Ramsay 4, period 4), only SD, entropy and SD2 discriminated these levels.

The mean heart rate remained accelerated the day after surgery (Fig. 3). HRV, in turn, as measured by the most of the parameters, started to recover from the values during sedation but remained attenuated compared to the pre-surgery values. Among the parameters capable of discriminating the periods of sedation from the pre-surgery periods, only RRI entropy was fully recovered by the next day.

Different HRV parameters were highly correlated despite their different theoretical background (Table 1). Especially, SD1 was strongly related to RMSSD (R=1.00) and HF power (R=0.87), as were RMSSD and HF power (R=0.87). Also, SD and SD2 were strongly correlated (R=0.98). All the parameters except the ratios (LF/HF and SD1/SD2) correlated significantly with the mean RRI. Among the parameters with discriminative power in respect to the level of sedation, the RRI entropy was the least correlated with the other parameters, including mean RRI.

IV. DISCUSSION

The results show that HRV is modified by different levels of sedation, and by cardiac surgery. In sedated patients after cardiac surgery heart rate was higher and HRV lower than in baseline, suggesting increased sympathetic tone and decreased parasympathetic tone. By the next day after the surgery, heart rate remained at the same level than during the sedation but HRV had started to recover. This suggests at least partial recovery of the ANS control mechanisms from the sedation and surgery despite the different sympathetic and parasympathetic tones compared to the pre-surgery states.

The changes in HRV during sedation were successfully detected both by linear and non-linear methods. Among the parameters studied, the linear time domain methods (SD, RMSSD) and the non-linear methods based on the analysis of Poincare plot (SD1, SD2) or complexity of the RRI signal (RRI entropy) provided the best performance in terms of discriminative power.

Many of the parameters studied were found closely correlated. In addition, all the other parameters but the ratios (LF/HF, SD1/SD2) correlated significantly with the mean RRI. This is natural since the mean RRI is set by the parasympathetic and sympathetic tones, while HRV is a result of the modulation of these tones. This correlation emphasises that HRV should never be interpreted without knowledge of the changes in heart rate.

Since different HRV parameters provide partially redundant information as evidenced by their strong correlation, a sub-set of the parameters could be sufficient to depict the relevant changes in HRV during sedation. The parameters mostly related to RSA are RMSSD, HF power and SD1, while SD, SD2 and LF power all measure slower HRV rhythms such as the 10-sec rhythm. Hence, it might be sufficient to use only one parameter from each of these two groups. Based on the preliminary analysis presented in this study, the optimal sub-set would be mean RRI, SD1, SD2 and RRI entropy. One advantage of this selection is that the quantitative Poincare plot analysis does not require pre-processing or stationarity of the signal [10], and the parameters SD1 and SD2 are very fast to compute. However, more thorough statistical analysis would be needed to make the final selection for the optimal sub-set.

A possible confounding factor in this study was that the ventilation mode of the patients was different between the different periods. In periods 1, 2 and 5 the patients were awake and breathing spontaneously. After cardiac surgery in deep sedation (period 3) they were ventilated by forced ventilation mode, meaning that both the rate and depth of the ventilation were controlled by the ventilator. In moderate sedation (period 4) the ventilation mode was changed to supported ventilation, i.e. the rate and phase of ventilation were controlled by the patient and only the depth (minute volume) of the ventilation was controlled by the ventilator. These three modes of ventilation are physiologically very different, and hence some changes in HRV may be contributed to this factor. Especially, characteristic for the spontaneous respiration is relatively complex respiratory waveform, while in forced mechanical ventilation the respiratory input to the ANS is very monotonic with a single carrier frequency. Hence, especially the changes in RRI entropy may be partially attributed to this fact.

V. CONCLUSIONS

The results of this study confirm that the level of sedation modifies the HRV, and hence HRV is a potential tool for the assessment of the level of sedation in critical care. The changes in HRV may be measured both by linear time and frequency domain parameters, and non-linear parameters based on the complexity analysis or quantification of the Poincare plot of the RRI signal. Different HRV parameters are strongly correlated with mean heart rate and each other, and hence they provide partially redundant information. Among the parameters studied, the optimal sub-set to pick up relevant changes in HRV during sedation would be mean RRI, SD1, SD2 and RRI entropy.

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