Heart Rate Variability in Pregnant Women before Programmed Cesarean Intervention

Juan Bolea[1], Raquel Bailón[1], Eva Rovira[2], Jose María Remartínez[2], Pablo Laguna[1], and Augusto Navarro[2]

[1] GTC, I3A, IIS Aragón, University of Zaragoza, Zaragoza, Spain, CIBER de Bioingeniería, Biomateriales y Nanomedicina, Spain
[2] Anaesthesia Service, Hospital Miguel Servet, Zaragoza, Spain, Faculty of Medicine, University of Zaragoza, Zaragoza, Spain

Abstract—**Background: Heart rate variability (HRV) indices have shown ability for hypotension prediction during spinal anaesthesia in pregnant women programmed for cesarean only the same day of the surgery but not the previous day. Objective: To study changes in linear and nonlinear HRV indices of pregnant women programmed for cesarean between the previous day and the surgery day. Methods: Previous day recordings (PDR) and surgery day recordings (SDR) of 71 pregnant women programmed for cesarean have been studied during the following conditions: lateral decubitus (LD), supine decubitus (SD) and Valsalva maneuver recovery (VR). Linear HRV indices include classical temporal and spectral indices. Nonlinear HRV indices consist of sample and approximate entropy and correlation dimension (D_2). Results: Some linear HRV indices show very significant increases ($p < 0.01$) in SDR with respect to PDR: HRM in VR, SDNN in LD and SD, power in the very low frequency band in LD, power in the low frequency band in LD and SD. On the contrary, nonlinear HRV indices show a decrease in almost every condition and index in SDR with respect to PDR, being only statistically significant for D_2 in SD ($p < 0.01$). Conclusions: The increase in the former linear indices and the decrease in nonlinear indices the surgery day with respect to the previous day can be attributable to the stress induced by the imminent surgery.**

Keywords—**heart rate variability, pregnancy, spinal anaesthesia, prospective studies, human**

I. Introduction

Heart rate variability (HRV) allows noninvasive assessment of autonomic nervous system (ANS) [1], although the exact contribution of its two branches (sympathetic and parasympathetic) is a matter of debate and research [2]. Several HRV indices allow the assessment of the impact that some pathologies have on ANS (diabetes, obesity), medium and long term risk stratification (mortality after AMI), and short term response to drugs (hypotension and hemodynamical instability with general or spinal anaesthesia [3, 4]). The former applications, as well as its potential clinical use, make analysis of HRV specially interesting.

Spinal anaesthesia is the elective technique in cesarean intervention due to its lower maternal risk and lower fetal exposition to depressant drugs than general anaesthesia, despite its high rate of hemodynamic instability and clinical hypotension (>60%) in habitual practice without pharmacological prevention [5]. Repercussion of these hypotension events on the mother and the fetus makes the prediction of this clinical situation specially relevant.

HRV has been studied in pregnant women for hypotension risk prediction after spinal anaesthesia for cesarean intervention. Predictive value has been reported for linear (ratio between power in low frequency (P_{LF}) and high frequency (P_{HF}) bands, LF/HF [6]) and nonlinear (peak correlation dimension [7] and approximate entropy [8]) parameters. In Hans et al work [6] the LF/HF index predictive value is limited to the analysis of ECGs recorded the surgery day, and not the previous day. This fact motivates the study of the differences in HRV between surgery day and the previous day.

Our hypothesis is that these hypotension events may be caused by some disorders of ANS, which can be induced by stress of the imminent surgery.

This work is designed to describe changes in different linear and nonlinear HRV indices, obtained from ECGs recorded the surgery day (SDR) and the previous day (PDR) in pregnant women programmed for elective cesarean. Recordings are made in lateral decubitus rest, in supine decubitus or hemodynamic stress test, and in the recovery period after Valsalva maneuver in sitting position.

II. Database

The database consists of the ECGs of 71 pregnant women programmed for cesarean intervention with inclusion criteria, recorded in the University Hospital Miguel Servet, Zaragoza, Spain, after giving their informed consent.

Three subjects were removed from the study, one due to sinus rhythm disruption, and the other two due to technical problems during the recording.

Study population characteristics (mean±standard deviation) of the 68 valid subjects are: gestational age 38.15±0.95 weeks; age 33.65±4.78 years; body mass index 27.95±4.37 kg/m^2; and height 162.92±6.20 cm. Indications for cesarean were: 27 for iterative cesarean; 20 breech presentation; 6 feet presentation; 2 transversal presentation; 8 placenta praevia; 1 previous uterotomy; and 4 for other causes.

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Two-lead ECGs were acquired for each subject the evening before the surgery (PDR), after admission (between 19-20 pm), and just before the surgery (SDR), first thing in the morning (during 8 to 10 am) and patient fasting, in the Surgery Area, with a sampling frequency of 1000 Hz (Biopac Data Acquisition MP System). A protocol was designed which submits the pregnant women to physiological stress in order to enhance ANS alterations. Firstly, the subject was at lateral decubitus (relaxed position, minimum stress) for 7 minutes (LD); then at supine decubitus (hemodynamic stress caused by aorto-cava compression) for other 7 minutes (SD); finally, a Valsalva maneuver of 15 s is performed, and the ECG is recorded during at least one minute of the recovery (RV).

III. Methods

Linear (temporal and spectral) and nonlinear HRV indices have been studied. First, beat occurrence time series are detected from the ECG using a wavelet-based detector [9]. Ectopic beats and misdetections are corrected applying the integral pulse frequency modulation (IPFM) model [10]. Then, two representations of HRV have been considered: the unevenly sampled RR interval series [1] and the HRV signal obtained from the IPFM model [10], sampled at 4 Hz.

Linear indices Temporal indices, namely, HRM, SDNN, RMSSD, SDSD and pNN50 are measured over RR interval series. Spectral indices are obtained from the power spectral density of the HRV signal obtained from IPFM model. Absolute and normalized powers are computed in the classical bands [1]: very low frequency (P_{VLF}, 0.015-0.04), low frequency (P_{LF}, 0.04-0.15 Hz) and high frequency (P_{HF}, 0.15-0.4 Hz) and also the ratio LF/HF. Normalized P_{LF} is also considered: $P^n_{LF} = \frac{P_{LF}}{P_{LF}+P_{HF}}$.

Nonlinear indices. Nonlinear indices include sample and approximate entropy [11, 12], SampEn and ApEn, respectively, which quantify the irregularity of a time series. Correlation dimension (D_2), which is an estimator of fractal dimension, related to the minimum number of variables needed to model the dynamics of the time series in the phase space [13] is also considered. Larger D_2 values are associated with more complex systems generating the time series. The former nonlinear indices are estimated on RR series. Their computation are based on correlation integrals, which depend on the number of points N and the threshold value/s r used [14]. In this work, $N = 300$ and , $r = 0.1$ for SampEn and ApEn and $r \in [0.01\ 1.2]$ in steps of 0.01 for D_2 are used applied on normalized to unity amplitude signal.

IV. Results

Mean and standard deviation ($\mu \pm \sigma$) of HRV indices from PDR and SDR in LD, SD and VR conditions are shown in Table 1. Paired T test statistical analysis over the results obtained are made with SPSS© software (PDR vs SDR), considering a p value lower than 0.05 as significant.

In the comparison of temporal indices in SDR with respect to PDR, HRM shows no statistical differences in LD and SD, and significant increase in VR ($p < 0.01$); SDNN presents significant increase in LD ($p < 0.001$) and SD ($p < 0.01$); SDSD, RMSSD and pNN50 show significant increase ($p < 0.05$) in LD and SD.

All spectral indices display increases the surgery day with respect to the previous day in all conditions. Parameter P_{LF} shows increases highly significant ($p < 0.001$) in LD and SD, and very significant ($p < 0.01$) in VR; P_{VLF} show highly significant ($p < 0.001$) increase in LD and very significant ($p < 0.01$) in SD, while P_{HF} only shows highly significant differences ($p < 0.001$) in SD. The ratio LF/HF increases in all the conditions but with very significant differences ($p < 0.01$) only in LD and VR.

Entropy indices do not show meaningful differences between SDR and PDR in neither condition. Among nonlinear indices only D_2 shows significant differences in SD ($p < 0.01$), being lower in SDR than in PDR in all conditions.

Figure 1 displays indices P_{VLF}, P_{LF} and the ratio LF/HF and D_2 during the three studied conditions in SDR and PDR.

V. Discussion

Previous day ECG recordings (PDR), made the admission evening, can be considered as basal recordings of term pregnant women, both in LD, SD and VR. Surgery day recordings (SDR), made just before the cesarean, with the patient in the surgical area, and very close in time to PDR, may reflect changes in ANS regulation induced by the stress of the imminent surgery, biological conditions due to the fasting and/or circadian fluctuations in autonomic function.

Comparing SDR with PDR, linear indices (temporal and spectral) show significant and highly significant increases in nearly all positions, reflecting a global increase in variability. Among temporal indices only HRM increases significantly ($p < 0.01$) with respect to the previous day in VR, with a notable increment with respect to LD the same day ($p < 0.001$). The other parameters (SDNN, SDSD, RMSSD, and pNN50) present significantly higher values in LD and SD with respect to the previous day, while lower values in VR (without statistical significance), attributable to the heart rate increase in this

Table 1 HRV indices represented as mean (μ), standard deviation (σ), and p-value (PDR vs SDR), those lower than 0.05 (significant) are marked in bold.

		Lateral Decubitus			Supine Decubitus			Valsalva Recovery		
		μ	σ	p_{value}	μ	σ	p_{value}	μ	σ	p_{value}
HRM [bpm]	PDR	80.20	1.10	0.574	79.93	1.20	0.359	82.48	1.21	**0.007**
	SDR	79.99	1.36		81.61	1.55		85.42	1.36	
SDNN [s]	PDR	39.55	2.46	**1e-04**	44.18	2.04	1e-04	49.10	2.17	0.549
	SDR	47.41	2.62		52.59	2.95		49.03	2.03	
SDSD [s]	PDR	29.66	2.50	**0.018**	27.40	1.99	**0.043**	35.02	2.44	0.222
	SDR	34.42	3.13		32.25	2.86		32.01	1.98	
RMSSD [s]	PDR	29.63	2.50	**0.018**	27.37	1.99	**0.043**	34.96	2.43	0.219
	SDR	34.38	3.13		32.22	2.86		31.96	1.97	
pNN50 [%]	PDR	9.89	1.66	**0.012**	8.04	1.26	**0.019**	14.93	1.82	0.200
	SDR	13.62	2.07		11.85	1.97		12.41	1.60	
P_{VLF} $[ms^{-2}]$	PDR	225.92	25.45	**1e-04**	361.09	43.19	**0.001**	405.57	51.38	0.340
	SDR	342.99	34.28		500.24	51.26		443.09	59.80	
P_{LF} $[ms^{-2}]$	PDR	141.70	22.39	**1e-04**	160.54	14.96	**1e-04**	242.83	22.36	**0.002**
	SDR	207.08	34.61		235.24	21.19		322.55	29.12	
P_{HF} $[ms^{-2}]$	PDR	147.80	25.06	0.130	110.11	13.80	**1e-04**	205.19	21.80	0.956
	SDR	179.88	36.02		141.99	17.83		218.93	24.95	
P^n_{LF} (%)	PDR	52.89	2.13	**0.023**	61.52	1.88	0.275	54.68	2.19	**0.008**
	SDR	57.72	2.06		63.43	1.92		60.20	2.02	
LF/HF	PDR	1.49	0.13	**0.009**	2.12	0.18	0.256	1.67	0.17	**0.003**
	SDR	1.94	0.19		2.46	0.23		2.08	0.19	
SampEn	PDR	1.06	0.03	0.969	0.94	0.03	0.369	0.88	0.04	0.347
	SDR	1.07	0.04		0.92	0.04		0.85	0.04	
ApEn	PDR	1.00	0.02	0.547	0.91	0.02	0.291	0.86	0.03	0.273
	SDR	0.99	0.02		0.89	0.03		0.83	0.03	
D_2	PDR	5.30	0.10	0.231	4.99	0.13	**0.006**	4.53	0.14	0.122
	SDR	5.18	0.14		4.48	0.14		4.38	0.14	

position. The increase in frequency domain indices appears in all bands (VLF, LF and HF), and shows a predominant sympathetic activity in autonomic balance, with significant increase in LF/HF ratio both in LD and VR.

Regarding nonlinear parameters, both entropies and D_2 show in SDR systematically lower values than in PDR in all conditions, only reaching statistical significance the decrease in SD (p <0.01).

In situations of stress stimulus in pregnant women, an increase in LF/HF ratio has been reported [15] due to HF power decrease. However, our patients present, the day of the surgery, an increase in both bands at SDR, even though the higher increase in LF determines sympathetic predominance, as revealed by the LF/HF ratio. This difference may be explained by the fact that in Klinkenberg [15] pregnant women are submitted to a psychosocial stress, which can be considered as an isolated stress, while anxiety or fear for the imminent surgery in our work is an intangible stimulus which may last in time [16].

It has also been reported that patients with two or more anxiety symptoms present a higher basal LF/HF ratio, with less reactivity to tilt stimulus [17], while our patients present higher LF/HF ratio the day of the surgery and keep their reactivity with similar increments in SD and VR regarding LD.

Prolongued fasting (48 h.) decreases linear HRV indices during resting and during a tilt test a meaninful decrease of P_{HF}, SDNN and RMSSD have been reported by Mazurak and co-workers [18]. Besides HRV indices from circadian fluctuacion studies, as reported by Nakagawa et. al. [19], show a sinusoidal daily rhythm with acrophase or maximum values, in the middle of the night or of the day. In addition, HRM and P_{LF} fluctuations have inverse phases respect to P_{HF}. Nevertheless, the results obtained show a significant increase in basal conditions (LD) as well as during hemodynamic stress(SD), and the fact of the timing recordings (19-21 pm at PDR and 8-10 am at SDR) suggest that possible fasting and circadian fluctuations effects are masked by physicosocial stress.

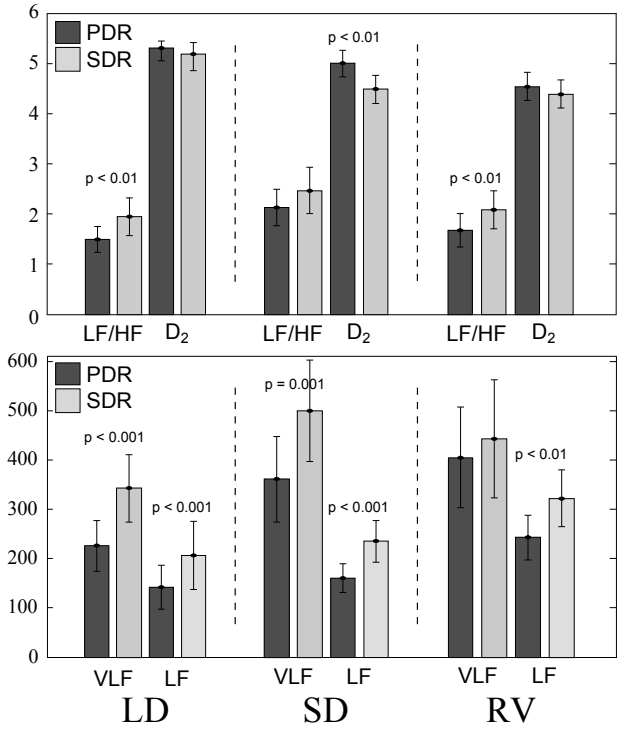

Fig. 1 Significant differences of the computed parameters at three positions (**LD**: Lateral decubitus; **SD**: Supine decubitus; **RV**: Valsalva maneuver recovery). Top panel shows LF/HF ratio and D_2 [adim]; Bottom panel shows VLF and LF [ms^{-2}].

VI. Conclusion

In this study HRV variability was evaluated before programmed cesarean section by non-linear and linear methods. The hypotension events that can suffer the women during surgery under spinal anesthesia was hypothesized due to disturbances in the ANS that could be detected previous hours to the surgery. In terms of pregnant women programmed for cesarean delivery there is a significant increase in linear HRV indices the day of the surgery with respect to the previous day, both in temporal indices and spectral indices with sympathetic predominance (HRM, LF/HF), as well as a decrease in nonlinear HRV indices (sample and approximate entropies and D_2), which is only statistically significant for D_2 in SD. Reported changes in the ANS that can cause hypotension episodes may be attributable to the stress of the imminent surgery.

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Author: Juan Bolea
Institute: University of Zaragoza; Street: Mariano Esquillor S/N
Email: jbolea@unizar.es