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The effects of general anaesthesia on heart rate variability during abdominal surgery

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Abstract:
We aimed to realized a pilot study that investigated heart rate variability (HRV) during anesthesia to study of alterations in the autonomous function and study the effects of anesthetic drugs with a not invasive test. We studied 15 subjects of both sexes (9 women and 6 men) with a mean
age of 53.6 ± 14.3 years.
ECG signal recording, lasting 5 minutes each, in three times: First time, the registration before anaesthesia. The second was performed after anaesthesia induction and after 5 minutes after the start of maintenance.
The third measurement was performed 24 hours after surgery.
The mean heart rate did not show significant alterations during anesthesia and after 24 hours of surgery compared with baseline.
On the contrary, the indices of heart rate variability in the frequency domain showed significant variations during general anesthesia. In fact there was a significant decrease in LF, expressed in normalized units and at the same time a significant increase in HF, always expressed in normalized units. It follows that the LF / HF ratio has been significantly reduced during the period of anesthesia. All indices are nearly returned to baseline after 24 hours of surgery.
The analysis of anesthetic effects on HRV may provide a more valuable noninvasive tool for investigating alterations in autonomic function.
Anesthetics used in general anesthesia suppress the autonomic nervous system and contribute to the safety of general anesthesia not only because suppress the excessive sympathetic activity caused by the operation but also because suppress parasympathetic reactions. The attenuation of sympathetic activity during general anesthesia is usually assessed by measuring changes in blood pressure or heart rate. In all cases, because of these antagonistic effects, evaluation becomes problematic when parasympathetic activity is simultaneously depressed.

Keywords:
HRV; heart rate variability; general anaesthesia; autonomic nervous system.

1. Background

Heart rate variability (HRV) is used to estimate the ANS activities of human traditionally, because of its meaningful and non-invasive characteristics [1-2-3]. The HRV is measured based on the beat-to-beat variations in RR intervals, which is from electrocardiogram (ECG). Furthermore, this calculation method has been widely accepted in the analysis of ECG signal, and can traditionally be subdivided into time domain and frequency domain [4].

There are currently several methods to assess heart rate variability.

The analysis performed in the time domain is a quantitative estimate of the magnitude of change in the cardiac cycle. The easiest way in this area is to calculate the standard deviation of the average of all successive RR and its derived parameters SDANN, r-MSSD1; the last two indices are considered as measures which reflect mainly the parasympathetic component of heart rate variability [5].

The SD of the R-R sequence was shown to be a predictor of important pathophysiological states. A heart attack is preceded by a sharp reduction of SD; aging causes a slight, but significant, reduction of SD of R-R intervals at rest [5].

The analysis performed in the frequency domain is based on Fourier analysis of the variability of R-R intervals and allows the expression of the sequence of R-R intervals as a sum of regular patterns with different frequencies (periodicity). The relative weight of these different frequencies in determining the signal, and what their weight distribution is in that signal spectrum are calculated. In 1981 Akselrod stated in Science that spectral analysis (spectral density analysis) non-invasively provided information on sympathetic-vagal control of heart, demonstrating the possibility of a direct relationship between fluctuations in heart rate and neurogenic modulation of the heart [2]. This method is the traditional analysis method and had been used to analyze ECG data to evaluate ANS previously.

It uses Fast Fourier Transform (FFT) to estimate power spectrum density (PSD), and divided to three regions, which are high frequency (HF) 0.15~0.4 Hz, low frequency (LF) 0.04~0.15 Hz and very low frequency (VLF) 0.003~0.04 Hz. The sum of area under power spectrum means total power (TP), and the area in each frequency region represents the region's power. Generally, the individual power is divided by TP to normalization.

On the significance of physiological, the ratio of the high frequency power (HFP) and TP were used as the index of parasympathetic nervous system, and the ratio of the low frequency power (LFP) and TP were used as the index of sympathetic nervous system. Moreover, the ratio of LFP and HFP were used as the index of parasympathetic – sympathetic nervous system balance [6-7-8].

2. Objective

Previous studies in anaesthetized patients have linked some alterations in spectral analysis of HRV to several mechanisms: alterations in sympathetic and parasympathetic activities, changes in sensitivity of baroreceptors, disruption of autonomic reflex pathways**,** reductions of brain functions and neuropathies.

During anesthesia, it was observed that altered HRV correlated to both, the depth of anesthesia and the level of sedation [9-10-11].

If alterations in baroreceptor sensitivity and / or in the activity of the autonomic system also play a role in the effect of anesthetics on HRV then different anesthetics should have different effects on HRV [12-13].

So the analysis of the effects of anesthetics on HRV may be a better tool for noninvasive evaluation for the study of alterations in the autonomous function.

Therefore the aim of this work was to evaluate the effects of general anesthesia deep, carried out with the simultaneous co-administration of different anesthetics both inhaled and parenteral on major cardiovascular parameters that explore the heart rate variability both in the time domain and in the frequency domain.

3. Materials and methods

We studied 15 subjects of both sexes (9 women and 6 men) with a mean age of 53.6 ± 14.3 years with digestive diseases with a prevalence of gallbladder disease. None of the patients used drugs or was suffering from

cardiovascular disease or diabetes. ECG signal recording, lasting 5 minutes each, were made using a hand held digital ECG with dedicated software (Xai-Medica) and then transferred to a PC for subsequent analysis performed by the program Cardiolab.

3.1 Protocol

The day of the procedure the basic registration was made in the anaesthesia room adjacent to the operating room. The patient was then anesthetized after endotracheal intubation. The recording was performed after anaesthesia induction and after 5 minutes after the start of maintenance. The third measurement was performed 24 hours after surgery.

3.2 Anaesthesia

All the patients underwent general anaesthesia [11-12-13-14-15-20] using the scheme in Table 1.

Table1. Suministración anesthetic in the different phases of anaesthesia.

Phases	Drugs
Pre-anesthetic	Midazolam 0,04mg/Kg + Fentanil 1,4 g/Kg
Induction	Propofol 1,8-2,5 mg/Kg
Curarization	Cisatracurium 0,2 mg/Kg
Maintenance	Desflurano 4-7% in aria e O2 al 50% o Sevoflurano 1-2% in aria e O2 al 50% Fentanil 0,7µg/Kg ogni 30'-45'
Curarization reversal mixture	Prostigmina 35µg/Kg+ Atropina 20µg/Kg

3.3 Analysis of heart rate in the time domain

The following measures in the time domain [16] were taken into consideration:
1. Mean of all normal RR intervals expressed in ms and its standard deviation expressed in ms (SDNN);
2. Square root of average squared differences between each successive RR interval in ms (rMSSD);
3. Percentage of successive RR intervals differing by more than 50 ms compared to the total RR intervals (pNN50%).

3.4 Analysis of heart rate variability in the frequency domain:

The spectral analysis of RR interval variability enables the identification of oscillatory components hidden in it, the sum of which is the total Heart Rate Variability (HRV). This type of analysis allows the bundling of oscillations in heart rate in two main frequency bands: a low frequency band, known as LF (Low Frequency), about 0.10 Hz correlated with the sympathetic nerve activity, and a high frequency, called HF (High Frequency), synchronous with the breath between 0.15 and 0.30 Hz, whose output provides a quantitative estimate of vagal activity (figure1). [17]
The relative importance of these two components, expressed by the ratio between the powers (LF / HF), provides an estimate of the state of sympathetic-vagal balance. The data are expressed in standard units.

Figure1.

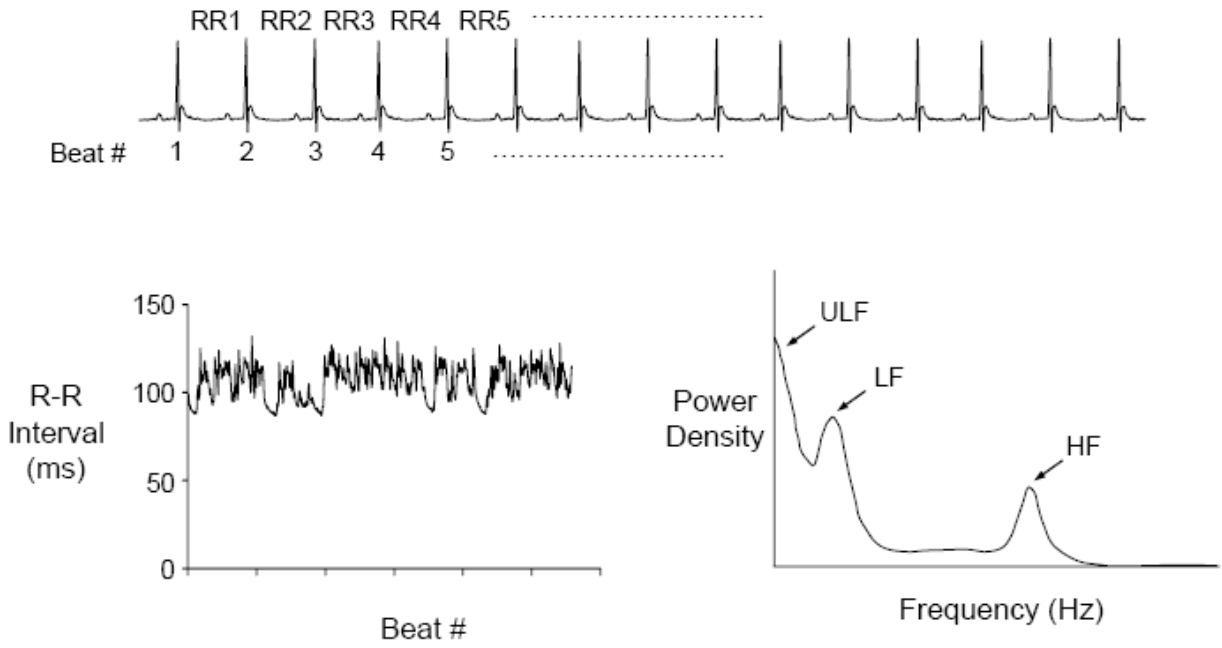

Figure1. Schematic representation of the method used to calculate the autospectra of RR interval variability. From surface ECG (upper box), the program calculates successive RR intervals (RR1-RR2, etc.) and stores them as a tachogram (lower left box). We apply the Fourier transform and subsequently the autoregressive method. Generally we recognize two main components: low-frequency component (LF) and high frequency (HF); in addition a large fraction of the power, due to very slow oscillations (below 0.03 Hz) can be recognized around 0 Hz (ULF). The latter component is not considered in the analysis (from Malliani Group).

3.5 Statistics

All variables were tested to verify the normality of their distribution using the Kolmogorov-Smirnov test. When data exceeded the test we applied a statistical analysis by repeated measures ANOVA. Values are presented as mean ± SD**.** Alterations of $p < 0.05$ were considered statistically significant.

4. Results

All patients were normotensive with a mean systolic blood pressure of 128.6 ± 10.59 mmHg and a mean diastolic pressure of 77.86 ± 6.74 mmHg. The mean heart rate did not show significant alterations during anesthesia and after 24 hours of surgery compared with baseline (Table 2). The indices of heart rate variability in the time domain did not show significant changes in the three experimental phases studied.

On the contrary, the indices of heart rate variability in the frequency domain showed significant variations during general anesthesia. In fact there was a significant decrease in LF, expressed in normalized units and at the same time a significant increase in HF, always expressed in normalized units. It follows that the LF / HF ratio has been significantly reduced during the period of anesthesia (Figure2). All indices are nearly returned to baseline after 24 hours of surgery (Table 2).

Table2.

		BASE			ANESTHESIA			24 hours		
R-R	msec	777.00	±	82.66	776.13	±	99.32	807.47	±	109.52
SDNN	msec	37.79	±	95.26	56.33	±	33.58	41.03	±	22.21
RMSDD	msec	20.90	±	17.70	33.85	±	32.40	30.85	±	29.47
pNN50	%	3.18	±	11.55	6.03	±	10.64	7.89	±	12.85
LFnorm	un	71.57	±	14.79	52.66	±	20.15*	63.36	±	20.77
HFnorm	un	28.43	±	14.79	47.34	±	20.1*	36.64	±	20.77
LF/HF		4.15	±	3.68	1.78	±	2.06*	3.06	±	2.94

Data are presented as means ± SD. * = P <0.05;

Figure 2.

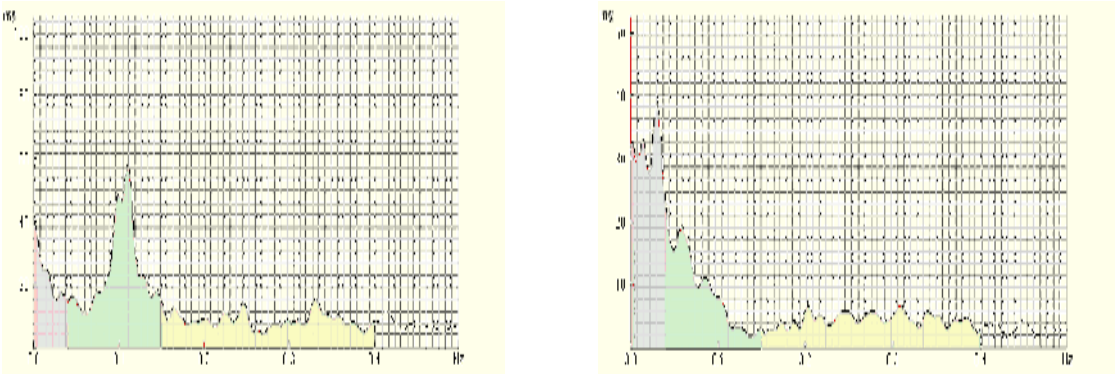

Figure 2. Example of spectral analysis of a patient before and during general anesthesia using both the Fourier transform and the autoregressive method.

5. Discussion and conclusion

Spectral analysis of the RR interval in the frequency domain provides information on the distribution of variability as a function of frequency. We can identify up to three peaks:

1) Very-Low-Frequency (VLF) band (0.003Hz - 0.04Hz);

2) Low Frequency (LF) band, (0.04Hz- 0.15Hz);

3) High Frequency (HF) band (0.15Hz - 0.4Hz)

The HF component of HRV is an index of vagal activity synchronous with the respiratory rhythm, and is in fact reduced by more than 90% by administration of atropine, but not feeling the effects of sympathetic blockade with propranolol; the LF and VLF components reflect variability secondary to a more subtle sympathetic-vagal modulation [18].

The assumption that non-linear HRV indices can provide a prognostic information better than that obtained by traditional indices has been successfully tested in patients with heart disease, especially those with a previous myocardial infarction and heart failure [19].

Preliminary results of our pilot study indicate significant interactions of anesthetic conduction on HRV and in particular we highlighted a reduction in the LF component and a simultaneous increase in the HF component. The LF / HF ratio is considerably and significantly reduced from general anesthesia.

A careful pre-operative evaluation of risk factors for autonomic dysfunction, with the knowledge of the possible pharmacological interferences, is of considerable importance in order to prepare adequate preventive or corrective measures to reduce the incidence of complications in the perioperative period.

Anesthetics used in general anesthesia suppress the autonomic nervous system and contribute to the safety of general anesthesia not only because suppress the excessive sympathetic activity caused by the operation but also because suppress parasympathetic reactions. The attenuation of sympathetic activity during general anesthesia is usually assessed by measuring changes in blood pressure or heart rate. In all cases, because of these antagonistic effects, evaluation becomes problematic when parasympathetic activity is simultaneously depressed.

Therefore, the analysis of anesthetic effects on HRV may provide a more valuable noninvasive tool for investigating alterations in autonomic function.

Despite these promising results, there are still important issues that must be explored before the non-linear techniques reach a large audience of researchers and clinicians and can be considered a useful tool for diagnosis and management of patients.

Moreover It would be interesting to study the autonomic nervous system with HRV during the operation or under pain stimulation as well as help in improving the use of medicines with an optimal balance between opioid drugs and anesthetics during deep anesthesia.

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