Cardiorespiratory Coupling During Spinal Anesthesia Assessed via Causal Squared Coherence

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Abstract

Spinal anesthesia is an alternative to general anesthesia in lower abdominal surgery. Despite its impact on sympathetic control, little is known on the influence of spinal anesthesia on cardiorespiratory coupling (CRC) as evaluated from the concomitant analysis of heart period (HP) variability and respiration (RESP). The study aims to assess CRC before (PRE) and after (POST) spinal anesthesia in 14 patients (age: 59 ± 12 yrs, 3 females, 11 males, ASA physical status I-II) undergoing lower abdominal surgery. Anesthetic was injected below T8. In POST fluids were administered to the patient to prevent hypotension. CRC was assessed via the computation of model-based causal squared coherence assessing the strength of interactions from RESP to HP and vice versa. HP mean, variance, the power of HP series at the respiratory rate, and the breathing frequency remained stable in POST compared to PRE. Regardless of the directionality of the interactions, CRC did not vary in POST and this result held regardless of the direction of the interactions. The steady values of HP variability and CRC markers suggest that spinal anesthesia performed at a relatively low level (i.e., below T8) and associated with fluid administration might have minimal impact on the cardiac control.

1. Introduction

Spinal anesthesia is a commonly used and well-tolerated anesthetic technique for lower abdominal surgery. A common adverse event related to spinal anesthesia is systemic hypotension, occurring in 30% of cases [1-3]. This event is caused by the arteriolar and venous dilation in the body regions innervated by sympathetic fibers originating from the spinal cord below the level of injection of the anesthetic [4]. The impact of spinal anesthesia on cardiac control is commonly studied via the analysis of heart period (HP) variability [5-7]. Results depends on the level of the blockade given that in humans cardiac preganglionic cell bodies are positioned in the grey matter of the first six segments (T1–T6) of the thoracic spinal cord [8]. As the blockade progresses toward T1 the magnitude of heart period (HP) changes decreased [5]. When the block is performed at intermediate thoracic level the decline of HP variability is evident in the high frequency band as well, thus indicating an impact on vagal modulation [5,6]. The ratio of the low frequency to the high frequency power suggested a shift toward a more powerful sympathetic inhibition [6]. However, even the opposite result was detected when the blockade is carried out at a high thoracic level (T1–T5), thus suggesting a physiological adjustment to venous pooling in the lower part of the body [7]. Analysis of the impact of spinal anesthesia is commonly carried out considering separately HP variability [5-7] and respiratory signal (RESP) [9], while disregarding their dynamic interactions.

Cardiorespiratory coupling (CRC) reflects the reciprocal interactions between heart and respiratory system [10,11]. CRC analysis is based on the concurrent analysis of HP variability and RESP. Specifically, causality methods in the frequency domain, such as causal squared coherence (CK^2) [12,13], have proven to be effective in investigating HP-RESP directional interactions [14]. No studies explored the effects of spinal anesthesia on CRC, despite the significant clinical implications of assessing the link between respiratory activity and autonomic modulation, as derived from HP

fluctuations.

Thus, the aim of this study is to investigate CRC before (PRE) and after (POST) the induction of spinal anesthesia. We hypothesize that blocking sympathetic control at a level that negligibly affects cardiac sympathetic does not affect CRC, especially whether hypotension is prevented via fluid administration. CK^2 was applied to elucidate both the strength of the interactions from RESP to HP and *vice versa* at the respiratory rate [12,13].

2. Methods

2.1. Experimental protocol

Fourteen patients (age: 59 ± 12 yrs, 3 females, 11 males, body mass index: 24 ± 2) scheduled for lower abdominal surgery undergoing subarachnoid spinal anesthesia were enrolled at "L. Sacco" Hospital, Milan, Italy. Patients underwent surgery for inguinal hernioplasty (n=12) and hemorrhoidectomy (n=2). All patients had American Society of Anesthesiologist (ASA) physical status I (n=5) or II (n=9), indicating a low and mild risk during anesthesia. The study was performed according to the Declaration of Helsinki and was approved by the ethical review board, namely Comitato Etico Interaziendale Area 1, Milan, Italy, approved the protocol (approval number 3712013). All patients gave their written informed consent.

With the patient in supine resting position on the surgery bed, electrocardiogram (ECG) was acquired from the patient's monitor (IntelliVue MX800, Philips, Best, The Netherlands) in PRE and POST conditions. The ECG signal was sampled at 400 Hz. Spinal anesthesia was accomplished below T8 and it was checked that no block ascended above T6. Five patients required mild sedation to cope with surgery anxiety. No adverse events were reported.

2.2. Series extraction and markers

After detecting the R-wave peaks on the ECG, HP was computed as the time interval between two consecutive R-wave peaks. The RESP value was derived from the respiratory-related amplitude modulations of the ECG, as the amplitude of the first R-wave peak delimiting HP and measured from the isoelectric line. The resulting series were manually corrected via linear interpolation in the case of missing beats or misdetections. Corrections did not exceed 5% of the total sequence length. Sequences of 256 consecutive values were selected.

In the time domain, we computed the mean and variance of HP series, namely μ_{HP} and σ^2_{HP}, expressed in ms and ms^2, respectively. In the frequency domain, indexes were computed via autoregressive parametric power spectral analysis. The power of the HP series whose central frequencies fell into the high frequency (HF) band (0.15-0.4 Hz) was taken as a marker of vagal modulation directed to the heart, indicated as HF_{HP} and expressed in ms^2. The frequency of the dominant component of the RESP series in the HF band was taken as an estimate of the respiratory frequency (RF) expressed in breaths per minute (bpm).

2.3. Causal spectral CRC indexes

CK^2 was computed to assess the strength of the link from RESP to HP and *vice versa* [12,13], labelled as $CK^2_{RESP\rightarrow HP}$ and $CK^2_{HP\rightarrow RESP}$ respectively. The computation of the CK^2 was grounded on the assessment of traditional squared coherence (K^2) via bivariate autoregressive (BAR) model. $CK^2_{RESP\rightarrow HP}$ was computed from K^2 between RESP and HP by imposing to 0 the coefficients of the model in the reverse causal direction (i.e., from HP to RESP). Reversing the role between RESP and HP allowed us to compute $CK^2_{HP\rightarrow RESP}$. Coefficients of the BAR model were calculated via traditional least squares technique solved through Cholesky decomposition method [15] and model order optimized via the Akaike information criterion within the range of 5 to 12 [13]. The delay from RESP to HP was set to 0 beats and from HP to RESP to 1 beat. CK^2 functions were sampled in correspondence of the peak in the HF band [13].

2.4. Surrogate data approach

Surrogate data approach was employed to test the null hypothesis of uncoupling. From the original HP and RESP series one-hundred surrogate pairs were constructed via iteratively refined amplitude-adjusted Fourier transform method. The method preserved the distribution and the power spectral density of the original series, but phases were randomized with two different realizations of white noise with uniform distribution between 0 to 2π. The null hypothesis of uncoupling was rejected if CK^2 marker computed over the original series exceeded the 95^{th} percentile of the CK^2 indexes computed from surrogate pairs. The percentages of subjects featuring the rejection of the null hypothesis of uncoupling were indicated as $\%CK^2_{RESP\rightarrow HP}$ and $\%CK^2_{HP\rightarrow RESP}$ respectively.

2.5. Statistical analysis

Paired t-test, or Wilcoxon signed rank test when appropriate, was used to check the significance of the differences between markers computed in PRE and POST conditions. The χ^2 test was exploited to verify the significance of the difference between the proportions of

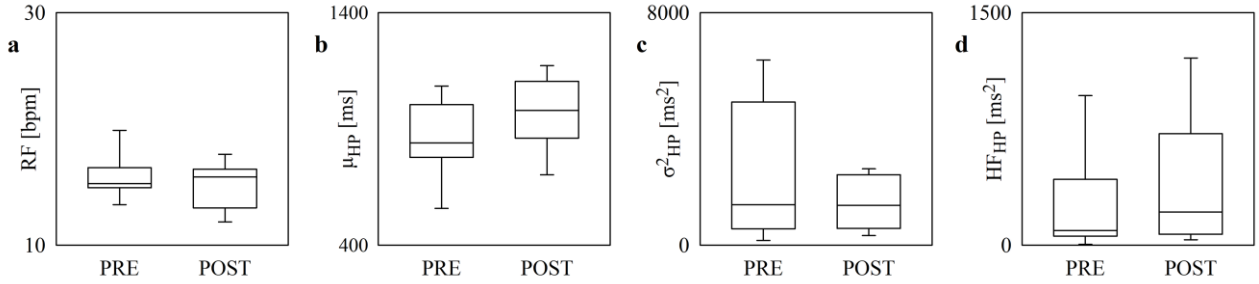

Figure 1. The boxplots show RF (a), μ_{HP} (b), σ^2_{HP} (c) and HF_{HP} (d) as a function of the experimental condition (*i.e.*, PRE and POST).

rejection of the null hypothesis of uncoupling in PRE and POST. Results are reported as mean ± standard deviation. A $p<0.05$ was always considered as significant.

3. Results

Markers were not computed over 2 subjects due to poor registration quality or missing ECG sinus rhythm, while they were computed in 12 subjects in both PRE and POST conditions.

The box plots in Figure 1 show 10th, 25th, 50th, 75th, and 90th percentiles of RF (Fig.1a), μ_{HP} (Fig.1b), σ^2_{HP} (Fig.1c) and HF_{HP} (Fig.1d) as a function of the experimental condition (*i.e.*, PRE and POST). None of the markers varied in POST compared to PRE.

Figures 2a,b feature the same structure as Figs.1 but they show $CK^2_{RESP\rightarrow HP}$ (Fig.2a) and $CK^2_{HP\rightarrow RESP}$ (Fig.2b). Spectral causality markers did not change in POST compared to PRE. The bar graphs in Figs.2c,d show the percentage of subjects featuring the rejection of the null hypothesis of uncoupling in PRE and POST along the time direction from RESP to HP, namely $\%CK^2_{RESP\rightarrow HP}$ (Fig.2c), and from HP to RESP, namely $\%CK^2_{HP\rightarrow RESP}$ (Fig.2d), in PRE and POST. No significant differences were detected between PRE and POST.

4. Discussion

The study suggests that both autonomic and CRC markers did not vary after spinal anesthesia. This result might be related to the level of anesthetic injection and to the administration of fluids in POST.

4.1. Cardiac control markers are stable during spinal anesthesia

During spinal anesthesia, a blood pooling towards the body regions innervated by sympathetic endings originating from segments of the spinal cord below the level of anesthetic blockage is expected [4]. This pooling is known to induce a decrease of the venous return to the heart, leading to hypotension and activation of the baroreflex in the attempt to trigger a reflex sympathetic activation and vasoconstriction [16]. Sympathetic activation should lead to modifications of HP variability markers in POST compared to PRE given that in our experimental setup the blockade, being below T8, did not affect preganglionic sympathetic activity directed to the heart originating from the segments of the spinal cord from T1 to T6. However, to counteract hypotension resulting from venous return decline, it is a common practice to administer fluids and this administration might be responsible for preventing reflex sympathetic activation. In our experimental setup fluid administration might be responsible for the stability of σ^2_{HP} and HF_{HP} in POST compared to PRE.

4.2. CRC is unaffected by spinal anesthesia

CRC assessed via CK^2 did not vary in POST. Remarkably this result held regardless of the time direction of the interactions, namely from RESP to HP and *vice versa*. This result corroborates at the level of markers of CRC the limited impact of spinal anesthesia

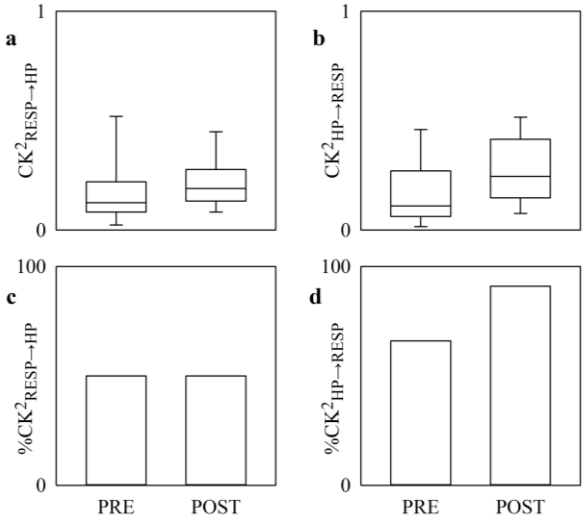

Figure 2. The box plots show $CK^2_{RESP\rightarrow HP}$ (a) and $CK^2_{HP\rightarrow RESP}$ (b) as a function of the experimental condition (*i.e.*, PRE and POST), while the bar graphs show $\%CK^2_{RESP\rightarrow HP}$ (c) and $\%CK^2_{HP\rightarrow RESP}$ (d).

on cardiac autonomic control likely due to the level of the spinal blockade and fluid administration. However, given that CRC indexes are computed while considering concomitantly both RESP and HP variability, CRC markers should not be considered redundant compared to autonomic indexes derived from HP variability and indexes describing respiratory activity. Indeed, CRC indexes are inherently normalized by the amplitude of variations of RESP and HP series. In addition, the use of a directional metric, such as CK^2, allowed the separation of the actions from R to HP from those in the reverse causal direction. Indeed, CRC might be the result of the activity of respiratory centers modulating vagal and sympathetic activity directed to the sinus node [17] as well as due to the possibility that the heart could contribute to facilitate the onset of respiratory activity via baroreflex [18].

5. Conclusions

The main finding of our study indicates that indexes of cardiac autonomic control and CRC did not vary after spinal anesthesia. This result is the likely consequence of the site of anesthetic injection and of the fluid administration preventing hypotension during spinal anesthesia. Future studies should incorporate an analysis of blood pressure oscillations and calculation of baroreflex indexes. In addition, a larger sample size is recommended. Increasing the number of subjects would allow for the examination of potential confounding factors such as age and body mass index. Furthermore, specific studies should be conducted on the impact of type of anesthetic, time onset of POST session after induction of the anesthesia, and site of injection.

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