Arterial Blood Pressure Variability before and after Chronic Pacing Induced Heart Failure in Conscious Dogs

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Abstract

To examine the effects of heart failure on beat-to beat arterial blood pressure (ABP) variability, four adult mongrel dogs (20-25 kg) were chronically instrumented for ventricular pacing and continuous measurements of central ABP and cardiac output (CO). Five minutes recordings with the dogs conscious and at rest took place after recovery from surgery (control) and after a 30 days long period of pacing at 240 bpm (heart failure).

Autoregressive spectral analysis of the beat-to-beat ABP fluctuations was performed and paired t-test revealed that ABP total, low frequency (LF) and high frequency (HF) power all significantly decreased following chronic pacing induced heart failure. No significant difference was found in the contribution of CO to ABP variability.

Our results suggest that heart failure induces changes in autonomic reflexes and hemodynamics that dampen the mechanisms responsible for generating ABP variability.

1. Introduction

Heart failure has been deeply investigated in its etiology, pathophysiological mechanisms and clinical implications and treatments. From the point of view of cardiovascular parameters monitoring, in literature there is a significant amount of works dedicated to the analysis of the impairment of heart rate variability (HRV) during heart failure, both in human patients and animal models. Nevertheless, to our knowledge, very few papers have looked at arterial blood pressure (ABP) variability in comparison with HRV analysis findings [1] and none has proposed any modeling interpretation of the effect of heart failure on ABP fluctuations and its hemodynamic implications.

Also, very few studies have examined the effects of heart failure on beat-to-beat ABP variability with the same subject serving as the control. These studies were typically carried out using animal models and monitoring the ECG of the animals before (control) and after inducing heart failure, usually by means of chronic ventricular pacing.

It was demonstrated that HRV is severely impaired in heart failure, as a consequence of strong alterations in neurohormonal responses. Notably, heart failure is characterized by a marked increase in central sympathetic nerve activity (SNA), as demonstrated by several papers on muscle sympathetic nerve activity [2,3] and cardiac sympathetic nerve activity [4,5] in heart failure. This sympathetic overactivity is accompanied by a strong blunting of the arterial baroreflex [6] and by peripheral vasoconstriction [2,6,7]. Blunted arterial baroreflex is associated to a reduced or missing modulation of SNA, even if this aspect was shown not to be the sole responsible of this phenomenon [5,8,9].

Analysis of HRV in heart failure patients showed that, contrarily to expectations, SNA overactivity and blunting of arterial baroreflex modulation and sympathoinhibitory reflexes do not reflect on increased low frequency (LF) oscillations in heart rate [7] and that a low or absent LF power can be a strong predictor of mortality in heart failure patients [10]. More in general, in the clinical study reported in [1], both HRV and ABP variability appeared lower in heart failure patients compared to control subjects.

Increased peripheral resistances were interpreted as the combined effect of increased SNA activation, tonic baroreflex component reduction [6], enhancement of neurohormonal responses [2], but no systematic analysis of the subsequent effect on short-term beat-to-beat ABP variability has been performed. In addition to these observations, another experimental study [11] pointed out that mechanisms other than SNA activity and arterial baroreflex play a role in the peripheral responses during heart failure. This study showed that peripheral

chemoreceptive stimuli also contribute and that regional blood flows distribution are clearly affected by their action.

Quite surprisingly, given the high number of factors concurring to heart failure, including peripheral responses and the impact of autonomic alterations on them, an in depth analysis of blood pressure was often neglected, even if hypertension is often associated to heart failure.

Nevertheless, its investigation could bring new knowledge to the mechanisms of heart failure and could allow to better understand the changes affecting the peripheral circulation, besides the well studied alterations of heart rhythm.

In this study, we tried to mathematically analyze the short term beat-to-beat ABP variability in the same group of dogs, after inducing heart failure by means of chronic ventricular pacing, in order to assess how heart failure affects autonomic and hemodynamic responses.

2. Methods

2.1. Experimental protocol

Four adult mongrel dogs (20-25 kg) were chronically instrumented with a fluid-filled catheter in the abdominal aorta for beat-to-beat ABP, an ultrasonic flow probe around the ascending aorta for beat-to-beat cardiac output (CO) and stainless steel electrodes on the right ventricular free wall for chronic pacing.

After recovery from major surgeries necessary to implant the instrumentation, baseline continuous recordings of ABP and CO took place with the dogs at rest and fully awake and these recordings represented the control condition of the experiment.

We then instituted ventricular pacing at 240 bpm for ~30 days. After discontinuing the pacing, we likewise recorded the same hemodynamic measurements.

Data were recorded continuously from Gould 4600 series signal conditioners connected to a Dataq Instruments DI-710 a/d conversion device with Windaq software. Sampling frequency of the recordings was 300 Hz.

2.2. Signal processing and modeling

We picked segments approximately five minutes long and artifact free in ABP and CO recordings before and after chronic pacing induced heart failure.

ABP and CO raw signals were preprocessed first by averaging their values over every cardiac cycle, in order to obtain a stepwise continuous signal which was then resampled to 2 Hz. This procedure was equivalent to low pass filtering of the original signals; their fast dynamics were thus cut off and only their slow dynamics, characteristic of beat-by-beat variability analysis, were maintained. Zero-mean time series of beat-to-beat ABP and CO fluctuations, normalized with respect to their mean values, were derived according to (1) and (2):

$$ABP(t) = \frac{ABP_r(t) - \overline{ABP_r}}{\overline{ABP_r}} \quad (1)$$

$$CO(t) = \frac{CO_r(t) - \overline{CO_r}}{\overline{CO_r}} \quad (2)$$

In Eqs. 1 and 2 ABP(t) and CO(t) are the zero-mean time series resulting from preprocessing, $ABP_r(t)$ and $CO_r(t)$ are the time series obtained after resampling to 2 Hz and $\overline{ABP_r}$ and $\overline{CO_r}$ and their respective mean values.

Auto-regressive (AR) spectral analysis of ABP time series obtained for the two experimental conditions was carried out and two spectral bands were investigated. For our purposes, we defined a low frequency (LF) band ($f < 0.1$ Hz) and a high frequency (HF) band ($0.1 < f < 0.5$ Hz).

We also tried to identify the contribution of CO beat-to-beat fluctuations to ABP variability and to verify whether heart failure induced any significant change. To do that, we applied a linear model for ABP prediction [12] in order to disentangle the contributions of CO and uncorrelated components of total peripheral resistance (TPR) to ABP beat-by-beat oscillations and we focused, for the purposes of this study, on the contributions brought by CO variability alone. The mathematical formalization of the model proposed in [12] is shown by Eq. 3, in which ABP variability is predicted by CO variability and noise is interpreted as TPR variability:

$$ABP(t) = \sum_{i=0}^{n} b_i \cdot CO(t-i) + n(t) \quad (3)$$

By means of this modeling approach, we also tried to quantify the role of CO variability in mediating ABP beat-by-beat oscillations in the HF band.

2.3. Data analysis.

After the computation of AR spectra and the model identification, a few indices relevant to our analysis and to the assessment of autonomic changes were extracted and we tested the statistical significance of the differences in their mean values across the population between control and heart failure by means of paired t-test.

In particular, we investigated the effect of heart failure

on ABP total power or variability, ABP absolute LF power and ABP absolute HF power.

As to the modeling interpretation of the role of CO in mediating ABP oscillations, we took two ratios between spectral indices into considerations. We computed the ratio between CO HF absolute power and ABP HF absolute power to evaluate the contribution of CO to fast fluctuations and we computed the ratio between the variance of ABP estimated by the model and the variance of measured ABP to evaluate the overall contribution of CO in predicting ABP variability.

3. Results

Figure 1 shows typical spectra of ABP and CO measurements and noise from model identification, for one dog during baseline. In figure 2, the same spectra are shown for the same dog after chronic pacing induced heart failure.

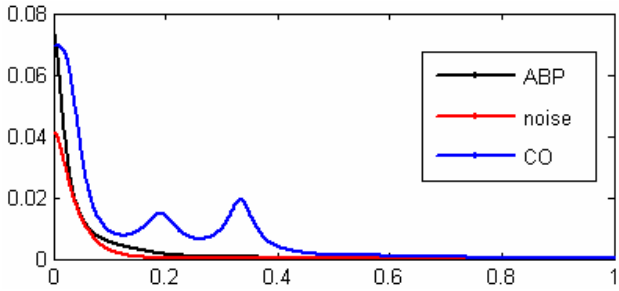

Fig.1: Power spectra of ABP (black), CO (blue) and noise (red) after AR spectral analysis of ABP and CO measurements and system identification and computation of noise from the model, for one dog during baseline.

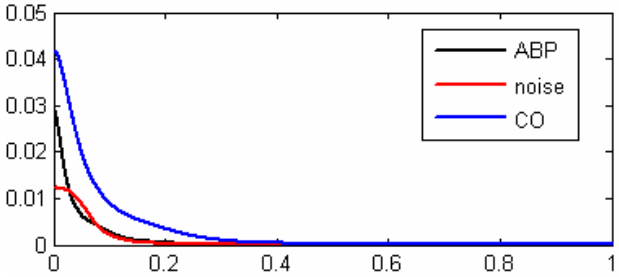

Fig.2: Power spectra of ABP (black), CO (blue) and noise (red) after AR spectral analysis of ABP and CO measurements and system identification and computation of noise from the model, for one dog after heart failure.

Paired t-test revealed that, after chronic pacing induced heart failure, ABP overall variability, ABP LF power and ABP HF power all significantly varied (table 1). In particular, ABP total power decreased to about half the control value (0.00425±0.00072 unitless during baseline, 0.00185±0.00021, p-value<0.05) ABP LF power showed a decrease to about 10% of the control value (from 0.00188±0.00035 to 0.00070±0.00011, p-value<0.05) and ABP HF power decreased to about half of the initial value (from 0.00035±0.00006 to 0.00016±0.00004, p-value <0.05).

As regards the quantitative assessment of the role of CO in mediating ABP variability by means of the linear prediction model described in (3), no significant differences in the mean values of the ratios between CO HF power and ABP power and between the variances of ABP estimate and ABP recordings were found between control and heart failure by statistical analysis.

Table 1. Mean values of BP and CO spectral indices from measurements (BP total power, BP LF power, BP HF power, ratio between CO and ABP HF power) and model analysis (ratio between the variance of ABP estimate (ABP est) from model identification and measured ABP) during baseline and after heart failure. *=p-value<0.05

	Baseline	Heart failure
ABP power*	0.00425±0.00072	0.00185±0.00021
ABP LF power*	0.00188±0.00035	0.00070±0.00011
ABP HF power*	0.00035±0.00006	0.00016±0.00004
CO HF / ABP HF	4.796±0.623	7.375±3.268
Var (ABP(est)) / Var (ABP)	0.341±0.144	0.145±0.0375

4. Discussion and conclusions

ABP variability, LF power and HF power all decreased after chronic pacing induced heart failure. These results were consistent with the findings in [1,7,10]. In particular, the decrease in LF variability was remarkable and this should be explained by the same considerations that were proposed in those studies as the reason for the reduction in LF oscillations of HRV. It may be supposed that increased SNA produces vasoconstriction together with neurohormonal factors, but the blunting of arterial baroreflex reduces overall variability because of the absence of its modulating action.

As to our modelling analysis for the separation of the uncorrelated sources of beat-to-beat ABP fluctuations, CO explained only 34.1%±14.4% of ABP oscillations at baseline and 14.5%±3.75% after chronic-pacing induced heart failure. This trend was not statistically significant,

maybe because of the low number of subjects included in the study, but it could represent an interesting preliminary result to better analyze in future studies.

One of the most relevant aspects to consider was the low power of ABP in the HF band, both at control and after heart failure. Respiration effects on ABP variability did not influence ABP oscillations, as shown in fig. 1 and fig. 2. However, the HF oscillations of CO interestingly decreased with heart failure.

We found that most of the reduction in LF oscillations was due to a decrease in power around 0.1 Hz. Consistently with [7], after heart failure ABP spectra still showed a relevant amount of power in the very low frequencies (VLF, f <0.04 HZ), that Van den Borne and co-workers identified but did not explain.

Based upon our model and to the meaning we attributed to the noise in the prediction, this VLF power may be due to non-neural modulations of TPR that are eventually buffered by CO [12,13]. These phenomena may affect vascular resistance, which is increased under heart failure [2,3,4,5,6,7,8,9,11] and their origin may be either hormonal or related to local mechanisms [11] which determine blood flow redistribution between tissues.

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