

# Spectral Analysis of Blood Pressure Variability in Atrial Fibrillation: the Effect of Tilting

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## Abstract

*Aim of this study was to assess changes of blood pressure (BP) variability spectrum in response to a sympathetic stimulation during a tilt-up stress test. Thirty patients (21 males,  $69 \pm 10$  years) with AF were included in the study. Surface ECG and non-invasive beat-to-beat BP were recorded for 10 minutes at rest and during tilt (in 19 patients). The systolic and diastolic BP series were resampled at 1Hz using cubic spline interpolation and spectral analysis was performed using autoregressive (AR) models. The total power was decomposed into  $M$  contributions, one for each pole. The poles whose frequency was in the Low Frequency (LF, 0.03-0.15 Hz) or High Frequency (HF, 0.15-0.4 Hz) were selected. LF component power increased during tilt in both systolic and diastolic BP (rest vs. tilt: systolic BP:  $6.5 \pm 5.3$  vs.  $13.0 \pm 13.4$   $p < 0.05$ ; diastolic BP:  $8.6 \pm 4.5$  vs.  $10.9 \pm 9.2$  ns). HF component power also increased during tilt, and the HF peak was shifted towards lower frequency values during tilt. Thus, BP spectrum shows LF and HF components even in patient with AF and these components are influenced by a sympathetic stimulus, such as the one induced by a tilt-up stress test. This finding highlights the capability of the autonomic nervous system to modulate periodic LF and HF oscillations in BP variability even in presence of an irregular ventricular electrical and mechanical activity.*

## 1. Introduction

Atrial fibrillation (AF) is a common arrhythmia characterized by an irregular ventricular rhythm [1], which precludes the spectral analysis of heart rate (HR). Therefore, very few studies evaluated whether rhythmical components could be identified in HR and systolic arterial pressure (SAP) variability in patients with AF. However, a first study [2] reported that a respiratory related HF component of SAP variability could be observed during AF even in absence of a respiratory sinus arrhythmia. In the same study, no attempt was made to evaluate whether the existence of

LF oscillations could also be detected. A few years ago, we analyzed the short-term arterial pressure variability before and immediately after restoration of sinus rhythm in patients with persistent AF [3]. The main findings of the study were the observation of a low frequency (LF) component of arterial pressure variability during AF and the independence of this component from the presence of a correspondent component in HR variability.

With our previous study as starting point, aim of this study was to assess changes of blood pressure variability spectrum due to a sympathetic stimulation during a tilt-up stress test in patients with AF.

## 2. Methods

### 2.1. Study patients

We analyzed 30 consecutive patients ( $67 \pm 7$  years, 70% male gender) who underwent electrical cardioversion (EC) for persistent AF according to international guideline indication. The mean duration of arrhythmia was 61 months. All patients had a history of hypertension with a preserved ventricular function (defined as a LVEF  $> 45\%$ ) and were on oral anticoagulant therapy. No patient was on beta-blocker or digoxin therapy. ACE inhibitors were given to all subjects. The study was approved by the Ethics Committee of San Paolo Hospital in Milan (Italy). All patients gave their written informed consent for the procedures related to the study.

### 2.2. Study design

Three orthogonal leads, a periodic reference AP measurement and a continuous beat-to-beat non-invasive recordings of AP were obtained with a Task Force Monitor (CNSystem; Austria) recording system. Surface ECG and blood pressure signals were acquired at rest in all patients, and during a passive orthostatic stimulus (75 degree tilting) in the last consecutive 19 patients of the study group. The sampling frequency was 1 kHz for the ECG signal and 100 Hz for continuous AP recording. Raw data were exported

as ASCII text files for off-line analysis. Biphasic DC shock (Life Pack 12 defibrillator, Medtronic Inc., Minneapolis, USA) was delivered with rising energies when needed, starting from 100 J (single shock in almost all cases). Patients follow-up was planned with weekly phone contacts to investigate patients symptoms in the first two weeks after EC and an ambulatory visit with ECG recording, three weeks after cardioversion. Recurrences within this time frame were considered as sub-acute recurrences. All patients were also advised to contact our outpatient clinic when experiencing palpitations or shortness of breath during the three weeks follow-up period.

### 3. Methods

#### 3.1. Series extraction

An automatic QRS detection algorithm was used to locate R waves on the ECG and the RR intervals measured as the distance between two consecutive R waves.

During normal sinus rhythm, the extraction of beat-to-beat systolic pressure series is commonly performed by searching for a local maximum in the BP signal following each R-waves. This approach is inappropriate during AF as R waves may not be coupled with an adequate left ventricular output to generate discrete pulses in AP and the QRS's are not necessarily followed by a AP pulse, as shown in Fig.1. For measuring the beat-to-beat systolic values, we applied a method not relying on the information about QRS location [3]. It first coarsely localizes AP systolic peaks and then refines their positions, thus obtaining the systolic values.

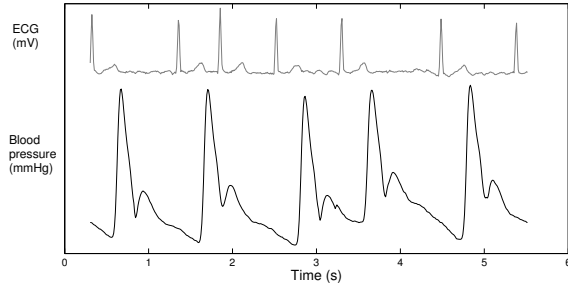


Figure 1. Blood pressure signal (black line) and ECG signal (grey line) of a patient during AF. The third QRS complex is not followed by a pressure pulse.

An interactive graphic interface allowed the operator to visually identify and correct misdeteected AP pulse events. We also extracted and analysed DAP series, whose values were defined as the local minimum preceding the detected valid systolic value. Finally, SAP and DAP series were interpolated (using cubic splines) and re-sampled at 1 Hz to obtain series with the same length.

#### 3.2. Spectral analysis

Power spectral analysis was performed on SAP and DAP series by means of an autoregressive (AR) model:

$$y(n) = \sum_{k=1}^p a_k y(n-k) + w(n) \quad (1)$$

where  $w(n)$  is a gaussian white noise process,  $n$  is the discrete time index,  $p$  is the model order and the  $a_k$ 's are the AR model coefficients. In the  $z$ -domain, the model transfer function become

$$H(z) = \frac{1}{A(z)} = \frac{1}{1 - \sum_{k=1}^p a_k z^{-k}} = \frac{z^p}{\prod_{i=1}^p (z - z_i)} \quad (2)$$

where the  $z_i$  are the model poles.

In this study, the model coefficients were estimated using the Levinson Durbin algorithm and the Andersons test [4] was used to check the validity of the model. The model order was selected by Akaike information criterion [5], starting from a minimum order of 7 up to a maximum order of 20.

Using Cauchy's residue theorem, the AR spectrum,  $P(\omega)$ , can be divided into a sum of  $p$  components [6]

$$P(\omega) = \frac{\sigma_e^2}{f_s} \sum_{i=1}^p \gamma(z_i) \left\{ \frac{z_i}{z - z_i} + 1 + \frac{z_i}{1/z - z_i} \right\}_{z=e^{j\omega}} \quad (3)$$

where  $\sigma_e^2$  is the prediction error variance,  $f_s$  is the sampling frequency and the quantity

$$\gamma(z_i) = \frac{z^{-1}(z - z_i(t))}{A(z, t)A(1/z, t)} \Big|_{z=z_i(t)} \quad (4)$$

is the pole residue. Equation 3 evidences the relationship between spectral components and model poles, which control both the component profile (the term in parentheses) and its power (the residue  $\gamma$ ). In general, the closer the pole module is to one, the sharper the spectral peak is.

Consequently, the spectrum can be decomposed into bell-shaped curves, named the spectral components. The center frequency  $f_i$  and the power  $P_i$  of the  $i$ -th spectral component can be computed as [7]

$$f_i(t) \approx f_s \frac{\mathcal{L}(z_i(t))}{2\pi} \quad P_i(t) = \mu \frac{\sigma_e^2(t)}{f_s} \text{Re} \{ \gamma(z_i(t)) \} \quad (5)$$

where  $\mathcal{L}(\cdot)$  is the phase expressed in radians, and  $\mu = 2$  for complex pole pairs and  $\mu = 1$  for real ones.

The spectral decomposition algorithm [7,8] was used to measure the central frequency and the power of the spectral components falling in the low frequency (LF, 0.03 - 0.15)

Table 1. Pressure and RR values during AF.

		Rest	Tilt
SAP (mmHg)	mean	104 ± 18	107 ± 21
	min	88 ± 17	90 ± 20
	max	118 ± 19	121 ± 22
DAP (mmHg)	mean	75 ± 18	82 ± 19 *
	min	62 ± 17	68 ± 18 *
	max	91 ± 22	98 ± 23
RR (ms)	mean	748 ± 159	700 ± 141 **
	min	435 ± 152	421 ± 155
	max	1313 ± 323	1256 ± 300

\*  $p < 0.05$ , \*\*  $p < 0.001$

and high frequency (HF, 0.15 - 0.40 Hz) bands. An LF (or HF) rhythm is detected if at least one spectral component has its center frequency (related to AR poles position) lying in the band.

### 3.3. Statistical analysis

The data are given as mean values ± one SD. A Students t test for paired data was used to evaluate the differences between parameters before and after electrical cardioversion. A value of  $p < 0.05$  was considered significant.

## 4. Results

Table 1 shows blood pressure and HR parameters as mean ± one SD for all the patients, during rest and tilt. It can be observed that heart rate significantly increased (mean RR decreased) during tilt, as it occurs in normal subjects. No significant changes can be observed in SAP variables, whereas a significant increase was found in DAP variables.

Regarding spectral analysis, an LF component of arterial pressure variability was evident in almost all the patients during AF. In particular, during rest this component was detectable in 22 out of 30 patients in SAP variability and in 21 out of 30 patients in DAP variability. During tilt the LF component was detectable in 14 out of 19 patients in SAP variability and in 13 out of 19 patients in DAP variability.

Figure 2 shows an example of one patient SAP spectral analysis during rest and tilt phases. An increase in the low frequency power can be observed during tilt.

These results are confirmed by the analysis of the whole database, as shown in Fig.3.

## 5. Discussion and conclusion

AF is a condition characterized by an irregularity of the RR interval time series that has always precluded the spec-

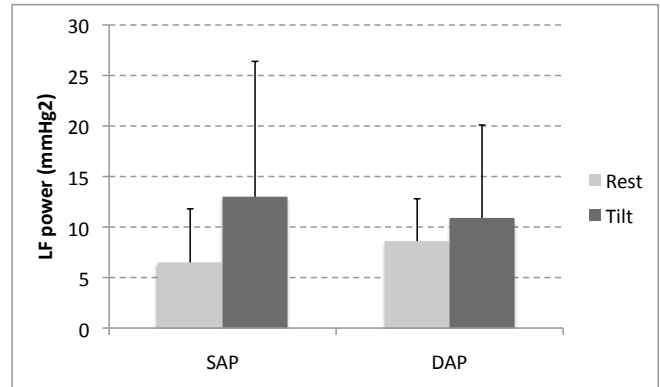


Figure 3. Mean and standard deviation of systolic (SAP) and diastolic (DAP) arterial pressure low frequency (LF) power during rest and tilt phases. In both pressure series, a significant increase in the low frequency power can be observed during tilt.

tral analysis of the series itself. In fact, during AF when the variability of the RR series is analyzed with spectral techniques, a white noise pattern without any identifiable discrete components along the frequency axis becomes evident. However, we have recently shown [3] the presence of an LF component of systolic blood pressure variability in patients with AF, confirming that the 0.1 Hz oscillatory component of systolic blood pressure variability may be present in absence of a correspondent fluctuation in the RR interval time series. That finding reflected, in our opinion, the capability of autonomic nervous system in generating LF oscillations in BP even in presence of an irregular ventricular electrical and mechanical activity.

In the present study, we reported for the first time the spectral analysis of blood pressure variability in patients with AF during a tilt-up test, i.e., a sympathetic stimulus. Using the results in [3] as starting point, we assessed the changes of blood pressure variability spectrum due to a sympathetic stimulation during a tilt-up stress test in patients with AF.

Although these results are preliminary, they may contribute to a better description of blood pressure characteristics during AF and of the mechanisms responsible of 0.1 Hz oscillations of systolic and diastolic arterial pressure variabilities during AF. In particular, it could be interesting to investigate if either the power or the center frequency of this rhythm could be modified after restoration of sinus rhythm (i.e., as the one obtained by electrical cardioversion) or if these 0.1 Hz oscillations mainly reflect the major oscillatory component of sympathetic discharge in the brain, which may be also modulated by autonomic stimulus such as head up tilt. In conclusion, this result paves the way to a better understanding of cardiovascular control mechanisms during non-sinusal rhythms.

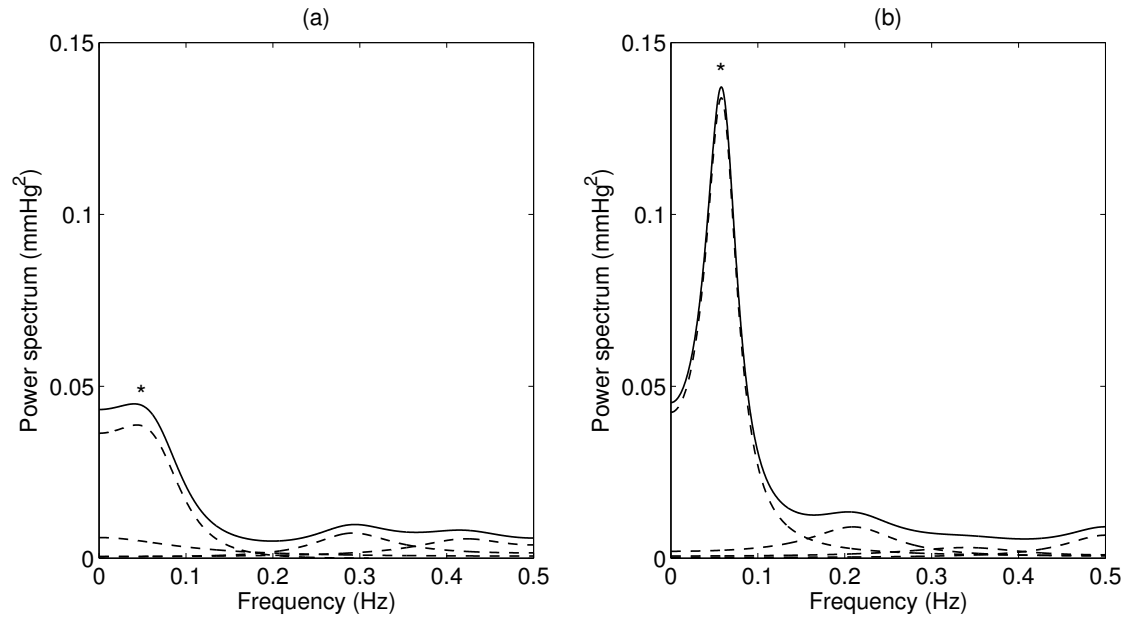


Figure 2. Example of one patient systolic arterial pressure (SAP) spectral analysis during (a) rest and (b) tilt phases. In both panels solid line represents the total power, whereas dashed lines represent the autoregressive decomposition of the spectrum. An increase in the low frequency peak (identified by an \*) can be observed during tilt in panel (b).

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