ECG analysis during continuous-flow LVAD

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Abstract

Nowadays, left continuous-flow assist devices (LVAD) are used for the treatment of end-stage heart failure not only as bridge to transplantation but also as a destination therapy. For this reason, LVAD patients monitoring is of large interest, especially for the understanding of ventricular loading condition and its interaction with the assist device. Aim of this work is the investigation of possible relationships between the ventricular mechanical status (volume) and the electrical myocardial activity. To this aim, 6 pigs undergoing LVAD implantation were studied and analyzed. Different levels of support were investigated by changing LVAD speed with stepwise increments. The analysis revealed that there is a consistent relationship between ventricular volume and R wave peak amplitude. In addition, parameters from shape analysis of the QRS complex, during the changes of the pump speed were studied and did not exhibit any correlation with the left ventricular volume. In conclusion, the correlation found between the R wave peak and the ventricular volume can be further investigated for future non-invasive LVAD patient monitoring strategies.

1. Introduction

Continuous-flow assist devices (VAD) are becoming nowadays a valuable alternative for the treatment of end stage heart failure patients. Several studies report the use of continuous flowLVAD as a long-term therapy other than a bridge to transplantation, able to assure a better quality life to patients [1][2]. Important issues in the management of LVAD patients are the selection of the proper LVAD speed in order to assure the propel level of ventricular unloading, and the possibility to detect adverse events like suction, obstruction etc. At the moment, LVAD variables such as power or current are commonly used to check LVAD working condition and to get an estimation of the flow provided by the device. The monitoring of ventricular status is still an open issue, especially because it should be ideally non invasive and continuous. The present work is just focused on investigating the possibility to provide a ventricular monitoring during LVAD assistance using ECG signal. ECG signal has the big advantage of being non invasive and easily accessible. Although it provides a measurement of ventricular electrical activity it is well known that electrical and mechanical activities in the myocardial muscle are strictly correlated [3–5] . In particular it is well known that a higher preload induces a higher mechanical stretching of the ventricular walls that in turn provokes an early after depolarization, a shortening of the action potential duration and a reduction of its amplitude. Starting from these observations, the hypothesis of this study is that the mechanical unloading of the left ventricle, provoked by the LVAD, may induce some changes of ventricular electrical activity as well. The aim of the present work therefore is to detect any change of ventricular electrical activity due to LVAD that can be used to infer any useful information about ventricular mechanical status. Ventricular volume, R wave peak value (RWP) and shape analysis of the QRS complex were investigated in 6 animals undergoing LVAD implantation surgery. The paper is organized as follows. The methods and materials are presented in Section 2, where the signal processing analysis and a method extended from a proposed T wave analysis are fully developed according to a specific model. Section 3 contains the results and Section 4 the conclusion.

2. Materials and Methods

2.1. Experimental data collection

Experiments refer to 6 pigs that underwent LVAD implantation. Five of them (labeled 1-5) were treated with a Gyro Centrifugal Pump 2 and one (labeled 6) with CircuLite Synergy Micropump (see figure 1). Both types of devices were implanted between the left atrium and the aorta. Animals 1-5 were two females and three males with an average weight of 47 ±8 Kg, animal 6 was a male of

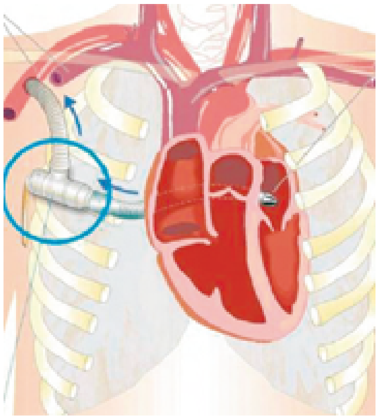

Figure 1. Example of CircuLite Synergy Micropump.

80 Kg. During the surgery the LVAD speed was increased step wise from a minimum of 1300 rpm to 1700 rpm for the Gyro Centrifugal Pump 2 and from a minimum of 12000 rpm to a maximum of 18000 rpm for the Circulite Synergy Micropump. An ECG (DII and AVR lead) was connected to the animal and the systemic arterial pressure was measured using a fluid-filled catheter in the carotid artery. A transducer catheter was inserted in the left ventricle to measure volume and pressure inside the chamber.

2.2. Data analysis

Data analysis was conducted using ECG (DII) and left ventricular volume (LVV) waveforms acquired during LVAD assistance. At first the QRS complex was detected by using a typical detector and the R wave peak magnitude (RWP) was measured for each heart cycle. The ECG was normalized dividing the signal by the average RWP. The LVV was calibrated using the cardiac output (CO) measured with the thermodilution method before LVAD onset. The LVV values measured at the times of RWP (LVV$_{RWP}$) were included in the analysis as well. These volumes provide a measurement of the ventricular preload as they correspond to the ventricular volume at the end of the diastole, just before the mechanical contraction driven by electrical depolarization occurs. The parameters mentioned above (RWP and LVV$_{RWP}$) are very dependent on ventilation. In this case the animals were under assisted ventilation with a constant frequency (15 cycles per minute for each animal) and with a constant ventilation volume. Therefore the influence of ventilation on both electrical and mechanical activities has the same cyclical shape over time. To reduce the effect of ventilation, 20 consecutive RWP and LVV$_{RWP}$ values were averaged over time, thus obtaining RWP$_p$ and LVV$_{RWP_p}$. In order to get rid of possible artificial correlations due this averaging, sliding window technique has been rejected. The number of cycles chosen to compute the average was enough to cover at least one full ventilation period. A linear regression analysis was then performed between RWP$_p$ and its corresponding LVV$_{RWP_p}$ for each animal, and the correlation coefficient was also calculated.

2.3. QRS shape analysis

In addition to RWP analysis, QRS shape changes were evaluated using a difference shape index (DSI) coming from an extension of the shape analysis method previously developed for the T wave [9,10]. It as been shown in [9,10] that QRS complex from ECG can be characterized by a set of parameters that can be estimated in the normalized integral domain. Each observation, indexed by i, of the QRS complex set has been modeled as:

$$x_i(t) = k_i s(\frac{t-d_i}{\alpha_i}) + n_i(t) \;\; with \;\; \alpha_i > 0; k_i > 0 \quad (1)$$

with k_i, α_i, d_i the amplitude coefficient, the scaling factor and the delay or shift, respectively. $s(t)$ is assumed to be a deterministic unknown signal and the noise $n(t)$ will be omitted in the following for the sake of clarity. This mathematical model allows the definition of a shape equality considering that all the $x_i(t)$ are the same shape if (1) is relevant.

Firstly, assume that $s(t)$ is positive and that the observations are noise free. The two normalized integrals namely $S(t)$ and $X_i(t)$, can be computed as:

$$S(t) = \left(\int_0^t s(u)du\right) / \left(\int_0^T s(u)du\right) \quad (2)$$

$$X_i(t) = \left(\int_0^t x_i(u)du\right) / \left(\int_0^T x_i(u)du\right) \quad (3)$$

These functions are strictly increasing assuming the positivity of the observations. If this assumption is not verified on the raw data, typically for QRS complexes, the absolute value can be applied.

From (1), $x_i(t)$ is related to $s(t)$ by the application of an increasing affine function called φ_i, that implies:

$$X_i = S \circ \varphi_i \Leftrightarrow X_i(t) = S(\varphi_i(t)) \;\; \text{with} \;\; 0 \leq t \leq T \quad (4)$$

The functions S and X_i being increasing, for any value of t we get:

$$y = S(t) = X_i(t_i) \Leftrightarrow t = S^{-1}(y) \;\; \text{with} \;\; t_i = \psi_i(t) \quad (5)$$

According to (1), we have the relation:

$$t_i = \alpha_i S^{-1}(y) + d_i \quad (6)$$

When the y axis is sampled with a sampling period δ_y, the values of t_i that correspond in the continuous case to $t_i = X_i^{-1}(y)$ are gathered in a vector $\mathbf{t}_i = [X_i^{-1}(0)\ X_i^{-1}(\delta_y) \cdots X_i^{-1}(1)]$. Using the vector formulation relation (6) is replaced by:

$$\mathbf{t}_i = \alpha_i \mathbf{t} + d_i \mathbb{1} \tag{7}$$

where $\mathbf{t}$ and $\mathbb{1}$ stand for the sampled $S^{-1}(y)$ that is unknown but common to all observations and the unit vector, respectively. Considering all the observations, not only the set of parameters (α_i,d_i) has to be estimated but also vector $\mathbf{t}$. In order to solve this problem we propose to decorrelate the estimation of the α_i's and d_i's by imposing orthogonality of $\mathbf{t}$ and $\mathbb{1}$. This is simply achieved by zeroing the mean of each $\mathbf{t}_i$. This leads to a two stage estimation: estimation of the α_i's and $\mathbf{t}$ followed by the estimation of the d_i's.

Using the entire set of observations, the first estimation solves the minimization:

$$\check{\mathbf{t}} = arg\ \min_{\mathbf{t}} (\sum_i \|\mathbf{t}_i - \alpha_i \mathbf{t}\|^2) \tag{8}$$

with theoretically unique α_i's. Imposing the constraint $\mathbf{t}^T\mathbf{t} = 1$ leads to the equivalent problem:

$$\check{\mathbf{t}} = arg\ \max_{\mathbf{t}} \mathbf{t}^T \mathbf{R} \mathbf{t} \tag{9}$$

where $\mathbf{R}$ stands for the correlation matrix of the observations $\mathbf{t}_i$'s. The solution is given by the eigenvector decomposition of the matrix $\mathbf{R}$ where the estimation $\check{\mathbf{t}}$ corresponds to the first eigenvector. In order to derive this decomposition as an equivalent Principal Component Analysis, a matrix $\mathbf{T}$ is defined as $\mathbf{T} = [\mathbf{t}_1 \cdots \mathbf{t}_N]$ and the SVD is computed such that $\mathbf{T} = \mathbf{V}\boldsymbol{\Sigma}\mathbf{U}'$. The first column of $\mathbf{V}$ is thus the normalized $\check{\mathbf{t}}$ waves with the proper leads. We consider the equation (7) without the mean of the signal, i.e. the second part of the equation. If the $\mathbf{t}_i$ are all of same shape, they are all generated by a single vector in $\mathbf{V}$ and only one non-zero singular value λ should therefore appear in the matrix of singular values resulted from the SVD decomposition of $\mathbf{T}$. Each scaling factor (SF) and delay are referred to the main singular vector in $\mathbf{V}$ and are directly computed from the derivation above. Each amplitude coefficient k_i (AMP) is then calculated by using the expression $\int_0^T x_i(u)du/\alpha_i$.

In order to take the first observation x_1 as the reference, the three parameters are corrected as α_i/α_1,k_i/k_1,$d_i - d_1$.

For this application, shape analysis is performed on each couple of observations $((1;2),(1;3),...)$, where the first is also the reference. Accordingly, the previous SVD decomposition is performed successively on 2xN matrices and gives two singular values λ_1 and λ_2 (with $\lambda_1 > \lambda_2$). We compute the difference shape index (DSI) as follows:

$$DSI = \frac{\lambda_1}{\lambda_1 + \lambda_2}. \tag{10}$$

DSI is an index ranging from 0.5 to 1. DSI equals to 1 if the two shapes are exactly the same, i.e. model equation (1) holds. Note that a shape difference could be also computed from the complete set $\mathbf{T}$ but more difficult to interpret.

3. Results

Results of the correlation coefficients between RWP_p and LVV_{RWPp} are reported in Table 1. Labels 1-5 indicate animals with Gyro Centrifugal Pump, label 6 indicates the animal with the CircuLite Synergy Micropump. Correlation coefficients between LVV_{RWPp} and QRS shape analysis indexes (difference shape index (DSI), amplitude coefficient (AMP) and the scale factor (SF)) are also reported in Table 1. As an example, also the RWP$_p$, LVV$_{RWPp}$ waveforms and DSI are reported: Figure 2 shows RWP$_p$, LVV$_{RWPp}$ and DSI of experiment 6 for different VAD speeds.

In Figure 2 the effects of LVAD in terms of ventricular unloading are evident. At LVAD onset a sudden decrement of LVV$_{RWPp}$ is observed. Then, as LVAD is increased, a further reduction of ventricular volume is detected. As the inflow catheter of the LVAD is placed in the left atrium, blood is drained from the left atrium and is ejected into the aorta bypassing the left ventricle. When LVAD speed is increased, the amount of flow drained and pumped by the LVAD increases thus reducing progressively the amount of blood flowing from the left atrium to the left ventricle during diastole.

The effect of ventricular unloading is reflected in the electrical signal very clearly: as LVV_{RWPp} decreases RWP$_p$ increases consistently both at LVAD onset and during LVAD speed increment.

For this type of analysis the ventilation can be considered as additional factor influencing both venous return both ECG signal. The analysis performed here permitted to reduce this effect in order to focus the analysis only on the ventricular volumes changes provoked by the LVAD.

While the R wave peak and the LVV are significantly correlated, other QRS shape analysis indexes (difference shape index, amplitude coefficient and the scale factor) do not exhibit any correlation with LVV changes on all animals (see Table 1).

Table 1. Correlation coefficients between left ventricular volume LVV$_{RWPp}$ and, R wave peak RWP$_p$, difference shape index (DSI), amplitude coefficient (AMP) and the scale factor (SF) for the 6 pigs. p-value $\dagger < 0.001$, $\S NS$

LVV	1	2	3	4	5	6
RWP$_p$	-0.94†	-0.96†	-0.86†	-0.84†	-0.86†	-0.84†
DSI	-0.02§	0.05§	0.43†	0.01§	-0.09§	-0.27§
AMP	-0.54†	-0.89†	0.71†	-0.48†	-0.46†	-0.89†
SF	0.03§	0.44†	-0.83†	-0.12§	0.08§	-0.29§

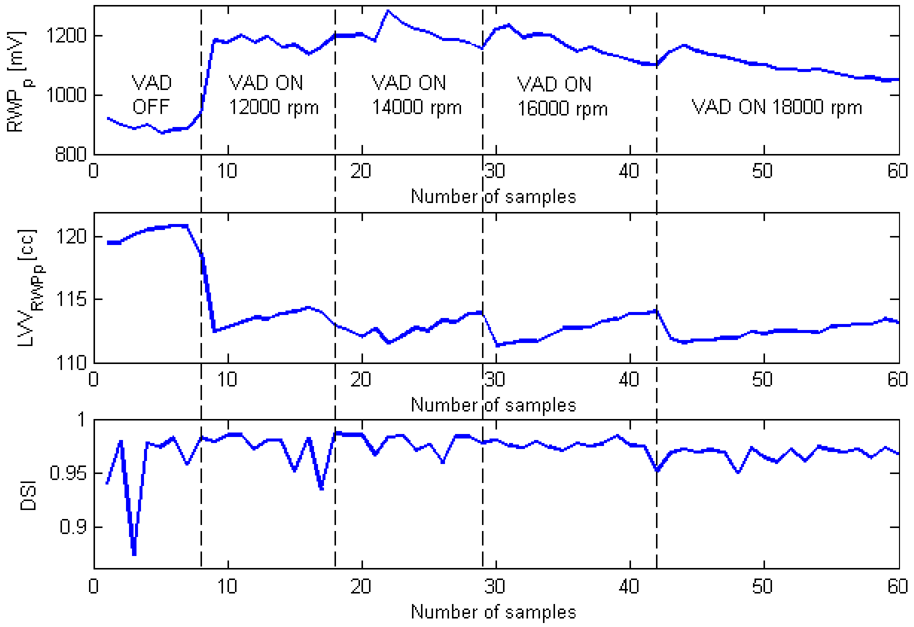

Figure 2. RWP$_p$, LVV$_{RWPp}$ and DSI profiles for experiment 6 before VAD activation and during VAD speed change.

4. Conclusion

The present study is an investigation of possible mutual relationships between ventricular volume and electrical ventricular parameters. To this aim, animals data were analyzed at different LVAD speeds in order to observe different levels of ventricular unloading. According to the results obtained we can conclude that RWP$_p$ and LVV$_{RWPp}$ are significantly correlated while QRS shape analysis indexes dont show any correlation with ventricular volume data. The present investigation can be a promising starting point in developing new strategies for ventricular continuous monitoring during LVAD therapy. As ECG can be acquired non invasively it can be an important input signal for the improvement of clinical managements of LVAD patients.

References

[1] Radovancevic B, Vrtovec B, Frazier OH. Left ventricular assist devices: an alternative to medical therapy for end-stage heart failure. Curr Opin Cardiol. 2003 May;18(3):210-4.
[2] Milano CA, Lodge AJ, Blue LJ, Smith PK, Felker GM, Hernandez AF, Rosenberg PB, Rogers JGN. Implantable left ventricular assist devices: new hope for patients with end-stage heart failure. C Med J. 2006 Mar-Apr;67(2):110-5.
[3] Franz MR, Burkhoff D, Yue DT, Sagawa K. Mechanically induced action potential changes and arrhythmia in isolated and in situ canine hearts. Cardiovascular Research, 1989, 23, 2 13-223.
[4] Franz MR. Mechano-electrical feedback in ventricular myocardium. Cardiovascular Research 32 (1996) IS-24.
[5] Taggart P. Mechano-electric feedback in the human heart. Cardiovascular Research 32 (1996) 38-43.
[6] Refaat M, Chemaly E, Lebeche D, Gwathmey JK, Hajjar RJ. Ventricular arrhythmias after left ventricular assist device implantation. Pacing ClinElectrophysiol. 2008 Oct;31(10):1246-52.
[7] Harding JD, Piacentino V, GaughanJP,Houser SR, Margulies KB. Electrophysiological Alterations After Mechanical Circulatory Support in Patients With Advanced Cardiac Failure. Circulation. 2001 Sep 11;104(11):1241-7.
[8] L. Fresiello, M. G. Trivella, A. Di Molfetta, G. Ferrari, F. Bernini, O. Meste. The relationship between R-Wave magnitude and Ventricular Volume During Continuous LVAD Assistance: Experimental Study. Artificial Organs, To appear, 2014.
[9] O. Meste, D. Janusek, M. Kania, R. Maniewski. T waves segmentation and analysis using inverse normalized integrals. EMBC, 2011, pp.4701-4.
[10] O. Meste, H. Rix, G. Dori. A new curve registration technique for the analysis of T waves shapes. EMBC, 2010, pp.6725-8.

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