Physiological Feature Analysis in Heart Rate Turbulence using LASSO Model

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Abstract

Heart Rate Turbulence (HRT) is a relevant cardiac risk stratification criterion. It is usually assess by means of turbulence slope (TS) and turbulence onset (TO) parameters. HRT is known to be affected by several physiological factors, mainly heart rate (HR) and coupling interval (CI). The physiological hypothesis accepted is the baroreflex source of the HRT. However, several studies showed different results about the relationship between CI and HRT parameters. Our aim was to propose a complete LASSO model using CI and sinus cardiac length (SCL), their powers and an interaction term as explanatory variables to account for the physiological dynamic of the TS parameter.

We used a database of 61 recording holters from acute myocardial infarction (AMI) patients. The database was split into two groups; low-risk patients ($TS > 2.5$ & $TO < 0$), and high-risk patients ($TS < 2.5$ & $TO > 0$). We performed a feature analysis by means of the LASSO paths, in which the regularization parameter is changed from very high values, where all weights of the explanatory variables are zero, to small values were all the weights are different from zero.

The first variable activated, with a coefficient different from zero, was SCL on low-risk patients and the two following where related to CI. Whereas the first variable activated on high-risk patient was CI and the two following were relate to SCL. Results from LASSO paths suggest that the influence of physiological variables on HRT is broken on AMI high-risk and completely different from low-risk. Also, the features selected by LASSO model on AMI low-risk are in agreement with the hypothesis of a baroreflex source of the HRT, in which SCL is the most important variable, and CI has a negative correlation with TS.

1. Introduction

Heart Rate Turbulence (HRT) is the physiological response to a spontaneous ventricular premature complex (VPC). In normal subjects consists of an initial acceleration and subsequent deceleration of the sinus heart rate. It has been shown to be a strong risk stratification predictor in patients with high-risk of cardiac disease [1, 2].

HRT is usually assessed by two parameters, Turbulence Onset (TO) and Turbulence Slope (TS), computed on an averaged VPC, even though there exist some other approaches to quantify HRT [3, 4]. TO assesses the amount of sinus acceleration following a VPC, and it is defined as the percentage difference between the heart rate immediately following the VPC and the heart rate immediately preceding the VPC. TS represents the rate of sinus deceleration that follows sinus acceleration, and it is defined as the maximum positive regression slope assessed over any 5 consecutive sinus rhythm RR-intervals within the first 15 sinus rhythm RR-intervals after the VPC [2].

It has been documented in the literature the influence of several physiological factors on the HRT [2]. The heart rate affects the strength of the HRT response, in a way that HRT is reduced at high heart rate. VPC prematurity also influences the HRT response. So, in agreement with the baroreflex source of HRT, the more premature the VPC, the stronger the HRT response should be. Nevertheless, the effects of VPC prematurity on HRT were analyzed in different studies, but with contradictory results and even contrary to the physiological hypothesis of the HRT [5–7]. Conflicting results between different studies about correlations between HRT parameters and coupling interval (CI) are usually explained by the effect of baseline HR. Since HRT is blunted at high HR it is unlikely to be correlated with CI [8–10].

In this work, we propose to use a LASSO model using the sinus cardiac length (SCL) and CI, and their powers up to the cubic and an interaction term, as explanatory variables. TS parameter is the dependent variable. The aim is to study dynamics of HRT as explained by SCL and CI using sparsity of LASSO approach in order to select features in the proposed model. Data from a database of patients with acute myocardial infarction is used. Only patients at low risk of sudden cardiac death ($TS > 2.5$ and $TO < 0$) are selected.
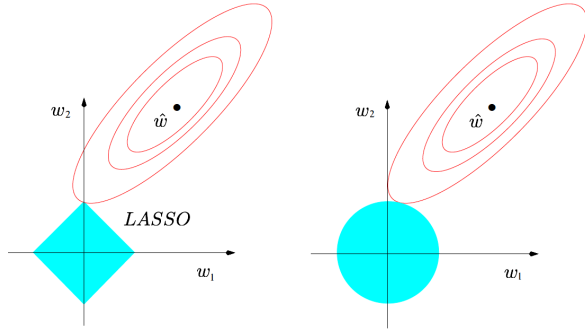
Figure 1. Comparison of estimation weights constraints between LASSO (left) and regularized regression (right). Adapted from [11].Adapted from [11].

The structure of the paper is as follow. In Section 2, LASSO model is explained, and dataset and model analysis are explained. In Section 3 results are reported. Finally, in Section 4, conclusions are presented.

2. Methods and data

2.1. HRT LASSO model

We propose the following model for TS parameter as a function of SCL and CI physiological variables:

$$TS_i = f(SCL_i, CI_i; \boldsymbol{w}) + \varepsilon_i; \ i = 1, \ldots, N \quad (1)$$

where i refers to the i-th individual VPC tachogram, ε_i is the residual of the i-th term, $\boldsymbol{w}$ are the parameters of the model, and N is the total number of available VPCs. The model that we propose take into account powers of SCL and CI up to the cubic element and also incorporates an interaction term:

$$\widehat{TS} = w_0 + w_1 \varphi_1 + w_2 \varphi_2 + w_3 \varphi_3 + w_4 \varphi_4$$
$$+ w_5 \varphi_5 + w_6 \varphi_6 + w_7 \varphi_7 \quad (2)$$

where the terms in the model are

$$\boldsymbol{\varphi} = \left[1, SCL, CI, SCL^2, SCL^3, CI^2, CI^3, SCL \cdot CI \right]^T \quad (3)$$

Nonlinear terms aim to capture possible nonlinear relationship between the HRT pattern and the physiological variables, whereas the interaction term aims to capture coupling effects between HR and prematurity of VPC. whereas the interaction term aims to capture coupling effects between HR and prematurity of VPC. This interaction is argued as an explanation to conflicting results when studying relationship between HRT and CI [8–10].

Re-writing the model in compact matrix notation:

$$\boldsymbol{TS} = \boldsymbol{\Phi w} + \boldsymbol{\varepsilon} \quad (4)$$

where $\boldsymbol{\Phi}$ is the matrix with all the physiological terms defined as:

$$\boldsymbol{\Phi} = \left[\mathbf{1}, \boldsymbol{\varphi}_1, \boldsymbol{\varphi}_2, \ldots \boldsymbol{\varphi}_N \right]^T \quad (5)$$

Weights of the model, $\boldsymbol{w}$, can be estimated minimizing the mean square error including a regularization term to avoid overfitting:

$$\hat{\boldsymbol{w}} = \underset{\boldsymbol{w}}{\operatorname{argmin}} \|\boldsymbol{TS} - \boldsymbol{\Phi w}\|_2^2 + \lambda \|\boldsymbol{w}\|_2^2 \quad (6)$$

The LASSO approach is shrinkage method like the previous one, but substituing L_2 norm in the regularization penalty on weights by L_1 norm [11]:

$$\hat{\boldsymbol{w}}_{lasso} = \underset{\boldsymbol{w}}{\operatorname{argmin}} \|\boldsymbol{TS} - \boldsymbol{\Phi w}\|_2^2 + \lambda \|\boldsymbol{w}\|_1 \quad (7)$$

where $\|\boldsymbol{w}\|_1 = \sum_{j=1}^N |w_j|$.

The nature of LASSO constraint allows to control the number of weights actives ($\neq 0$), so that, making λ sufficiently large will cause some of the weights to be exactly zero, see Figure 1.

Linear models penalized with the L_1 norm have sparse solutions, so that many of their estimated weights are zero. Accordingly, it is possible to use LASSO regression models to report the more important variables (features) of the model in the sense of mean squared error [12].

It is possible to perform a search on the regularization parameter λ. This is the so called LASSO path, in which starting at high values of λ assures that all weights are equal to zero. Then we give smaller values for λ up to zero. The idea is to register the event when a weight actives, that is, when $w_i \neq 0$, meaning that the associated feature represent an important variable to explain the TS values in the sense of minimum squared error [11].

2.2. Data set and analysis

We used a data set with 61 post-myocardial infarction patients included in a prospective study at a tertiary University Hospital [13]. A 24-hour ambulatory electrocardiographic monitoring was performed in patients with stable sinus rhythm between 2 and 6 weeks after infarction and 61 with at least 1 VPC during the monitoring period were included in the analysis (age 64.3 +/- 9.0 years, 26 men). The average number of VPCs per patient was 50.7.

We split the data set into two different subsets: one selected from patients with $TS > 2.5 \ \& \ TO < 0$, called Low-Risk AMI. $TS < 2.5 \ \& \ TO > 0$, called High-Risk AMI [2]. The goal of this division was to be able to study the difference in the dynamics of HRT, as explained by physiological factors SCL and CI, between AMI patients with high and low cardiovascular risk.

We performed a complete LASSO path analysis in order to evaluate the activation dynamic of the weights for the two AMI groups.
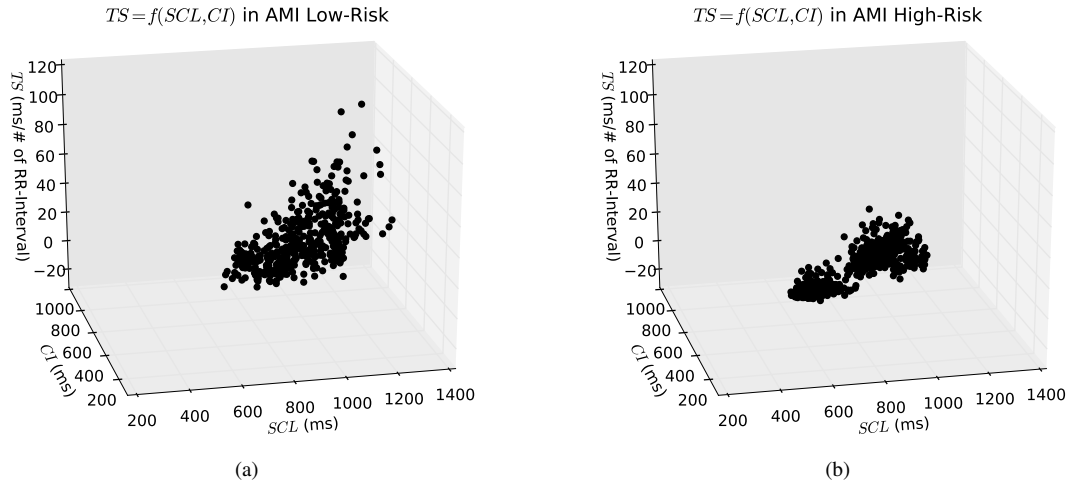
Figure 2. Scatter 3D plot of TS vs SCL and CI AMI low-risk patients (a) and AMI high-risk patiens (b).

3. Results

Figure 2 shows a 3D scatterplot of TS vs. SCL and CI for both low-risk (a) and high-risk (b) AMI patients. Every point corresponds to a TS parameter computed on individual VPC tachogram. Figure 3 shows LASSO paths from AMI high and low risk. Complete paths are shown in Figures 3(a), and 3(c), whereas Figures 3(b) and 3(d) shows LASSO path to observe with greater detail the activation of the three first weights.

Complete LASSO paths suggested a more complex dynamic in AMI low-risk patients, since weights showed a more dispersed pattern along the path, with several coefficients far from zero. Whereas LASSO path for AMI high-risk showed only three weights very different from zero. The remaining coefficients remain near zero along the complete path.

Analysis of the three activated weights allowed to compare the differences in the HRT dynamics between high and low risk. The first weight activated on low-risk was SCL, suggesting that the main factor affecting TS is the heart rate. The following two weights were associated with CI, and with negative values, in agreement with baroreflex hypothesis of HRT. Whereas on high-risk, the first weight activated was CI, but with positive value, meaning a completely different dynamic. The remaining weights to be activated were those corresponding to SCL and SCL^3.

4. Conclusions

We proposed a LASSO model based on the assumption that TS HRT parameter is a function of the physiological variables SCL and CI, which are the explanatory variables along with their powers to the cubic with an interaction term. We fit this model using data from AMI patients split into two subgroups, one with low-risk and one with high-risk. The model allowed to study the dynamics of TS as a function of physiological variables.

Results from LASSO paths suggest that the influence of physiological variables on HRT is broken on AMI high-risk, leading to small TS values regardless the values of SCL and CI. Also, the features selected by LASSO model on AMI low-risk are in agreement with baroreflex hypothesis as source of the HRT, in which SCL is the most important variable, and CI has a negative correlation with TS, so that premature VPC implies higher TS values.

Further work should be directed to incorporate all the available information about physiological variables when assessing HRT on patients. Also, searching for broken dynamics may give some insight on cardiovascular risk stratification.

Acknowledgements

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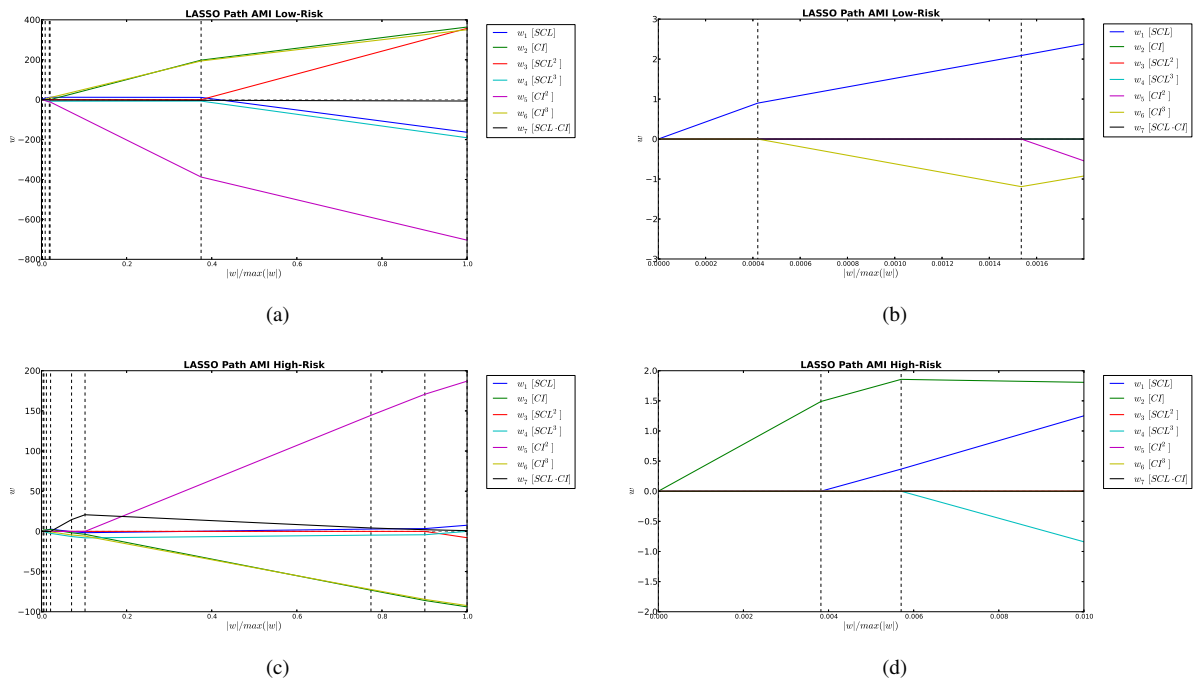
Figure 3. Activation of weights according to LASSO AMI low-risk patients (a)(b) and AMI high-risk patiens (c)(d).

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