

Heart Rate Turbulence Modeling using Boosted Regression Trees

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Abstract

Heart Rate Turbulence (HRT) is a relevant cardiac risk stratification criterion. It is accepted the baroreflex hypothesis as a source of the HRT. However, several studies showed different results about the relationship between coupling interval (CI) and HRT turbulence slope (TS) parameter. Our aim was to propose a nonparametric model based on Boosted Regression Trees (BRT) of TS as a function of CI, heart rate (quantified by sinus cardiac length SCL in ms), Age and Sex. We used a set of 11 patients with normal heart undergoing electrophysiological study (EPS) and 61 holters from acute myocardial infarction (AMI) patients (Hospital Arrixaca de Murcia). The AMI set was split into: AMI low-risk, and AMI high-risk according to HRT. We propose to model TS using BRT, which is an ensemble approach to build a regression model using several trees. SCL was the explicative variable with the highest importance both in EPS and AMI low-risk. TS correlated nonlinearly with SCL, and negatively with CI both in EPS and AMI low-risk. The model was completely different for AMI-HR. R^2 was higher for EPS (0.63) and AMI-LR (0.38) than for AMI-HR (0.28). The model was in agreement with the baroreflex hypothesis, and the role of age and sex agrees with previous results for EPS and AMI-LR. CI was the most important variable and positively correlated with TS in AMI-HR.

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]. It has been studied in the literature some interaction effect between sex and hear rate on HRT [11]. Also, it has been documented a decrease in HRT with increasing age in men [12].

In this work, we propose to use a nonparametric model of the HRT using a boosted regression tree (BRT). The explanatory variables of the model are the previous heart rate, the CI , Age and Sex. The response variable, assessing the HRT, is TS . The aim is to study dynamics of HRT as explained by hear rate, CI , Age and Sex. Data from a database of 11 patients with structurally normal heart undergoing electrophysiological study (EPS) is gathered. In those patients, VPC are delivered according to a protocol. Also a database of patients with acute myocardial infarction (AMI) is used.

The structure of the paper is as follow. In Section 2, BRT model is explained. In Section 3 datasets are detailed. In Section 4 results are reported. Finally, in Section 5, conclusions are presented.

2. Boosted Tree Regression Model

We propose to model the HRT, as assessed by a parameter T , as a function of the following explanatory variables: S_{cl} (sinus cardiac length, instead of heart rate), C_i (coupling interval), A (age), and S (sex):

$$T = f(S_{cl}, C_i, A, S) \quad (1)$$

In this work, we propose to learn the function, f , from the data using BRT as regression method. BRTs are based on the idea of adaptively combining large numbers of relatively simple tree models. The goal is to optimize predictive performance [13]. This method has been widely used to generate predictive models in ecological and biological studies [14]. The BRT estimation, $\hat{f}(x)$, where, $x = [S_{cl}, C_i, A, S]^T$, is obtained sequentially as follows

1. Set $\hat{f}(x) = 0$ and $r_n = T_n$ for all the n VPC tachograms available, where r_n are the residuals.

2. For $b = 1, 2, \dots, B$, repeat

(a) Fit a small tree, \hat{f}^b to the training data $\{x_n, r_n\}$, where explicative variables are in vector x_n and response variable is r_n .

(b) Update \hat{f} by adding a shrunk version of the new small tree \hat{f}^b :

$$\hat{f} \leftarrow \hat{f} + \lambda \hat{f}^b \quad (2)$$

(c) Update the residuals, r_n ,

$$r_n \leftarrow r_n - \lambda \hat{f}^b \quad (3)$$

3. Finally, output the *BRT* model:

$$\hat{f} = \sum_{b=1}^B \lambda \hat{f}^b \quad (4)$$

The main idea is to *learn slowly*. A new small tree (with few terminal nodes) is fit using the current residuals and then added to \hat{f} , so that \hat{f} is slowly improved in areas where it does not perform well [15].

BRT has three tuning parameters namely, the number of trees B , the shrinkage parameter λ that controls the rate at which BRT learns, and the number of splits (number of terminal nodes) in each tree, which controls the complexity of the boosted ensemble, it also controls the interaction order between explanatory variables in the model. Note that this feature allows to explore the interaction between *SCL* and *CI*, which is argued as an explanation to conflicting results when studying relationship between HRT and *CI* [8–10]. Parameters were tuned using 10-fold cross-validation, which is a usual procedure [15].

Unlike simple regression trees, BRT models can be more difficult to interpret. However, they can provide some summary statistics that allow a better understanding of the final model and assess the feature importance. The

relative importance and the *partial dependence plots*, PDP, are two such statistics. The *relative importance* measures the contribution of each explanatory variable to the final model, scaled such that the total sum reaches 100, with higher numbers for more important variables [13,14]. PDP are graphical tools to quantify the effect of one variable on the response after accounting for the average effects of the remaining variables in the model (Elith et al., 2008). There exists one-way PDP accounting for the interaction between the response variable (TS) and one explanatory variable, and two-way PDP among two features [14].

3. Data sets

Eleven patients (50 ± 15 years, 7 women) with structurally normal hearts were included in the study, all of them referred for EPS in the Hospital Universitario Virgen de la Arrixaca (Murcia, Spain). The study was approved by the local Ethics Committee and all participants granted a signed informed consent. The EPS was performed during sinus rhythm after ablation procedures, and sequences of 10 single induced VPCs were delivered every 20 s from the right ventricular apex.

The study was designed to investigate the influence of HR on HRT, and the combined influence of HR and CI on HRT, respectively. The HR was increased with isoproterenol, which activates beta-1 receptors in the heart inducing positive chronotropic effects [16], whereas the CI was controlled by modifying the VPC prematurity at the pacing trains.

We used a data set with 61 post-myocardial infarction patients (64 ± 9 years, 18 women) who underwent emergency coronary angiography, and, when appropriate, percutaneous infarction revascularization. These data were collected in a prospective study at University Hospital Virgen de la Arrixaca [17] in order to evaluate the impact of primary angioplasty on the indication for implantable defibrillator in patients with AMI. 24-h ambulatory electrocardiographic monitoring was done in patients with stable sinus rhythm between 2 and 6 weeks after the infarction, and patients with at least 1 VPC during the monitoring period were included in the study.

This dataset was split into two different subsets, namely, the AMI low-risk subset, which comprised 17 patients (63 ± 12 years, 5 women) with $TS \geq 2.5$ ms/RR-Interval and $TO \leq 0$, and the AMI high-risk subset, which comprised 6 patients (70 ± 6 years, 1 woman) with $TS < 2.5$ ms/RR and $TO > 0$ %. These TS and TO cutoff values are commonly used in most clinical studies, where $TS > 2.5$ ms/RR and $TO < 0$ % are considered as normal, and they were proposed using data from different post-infarction studies [2].

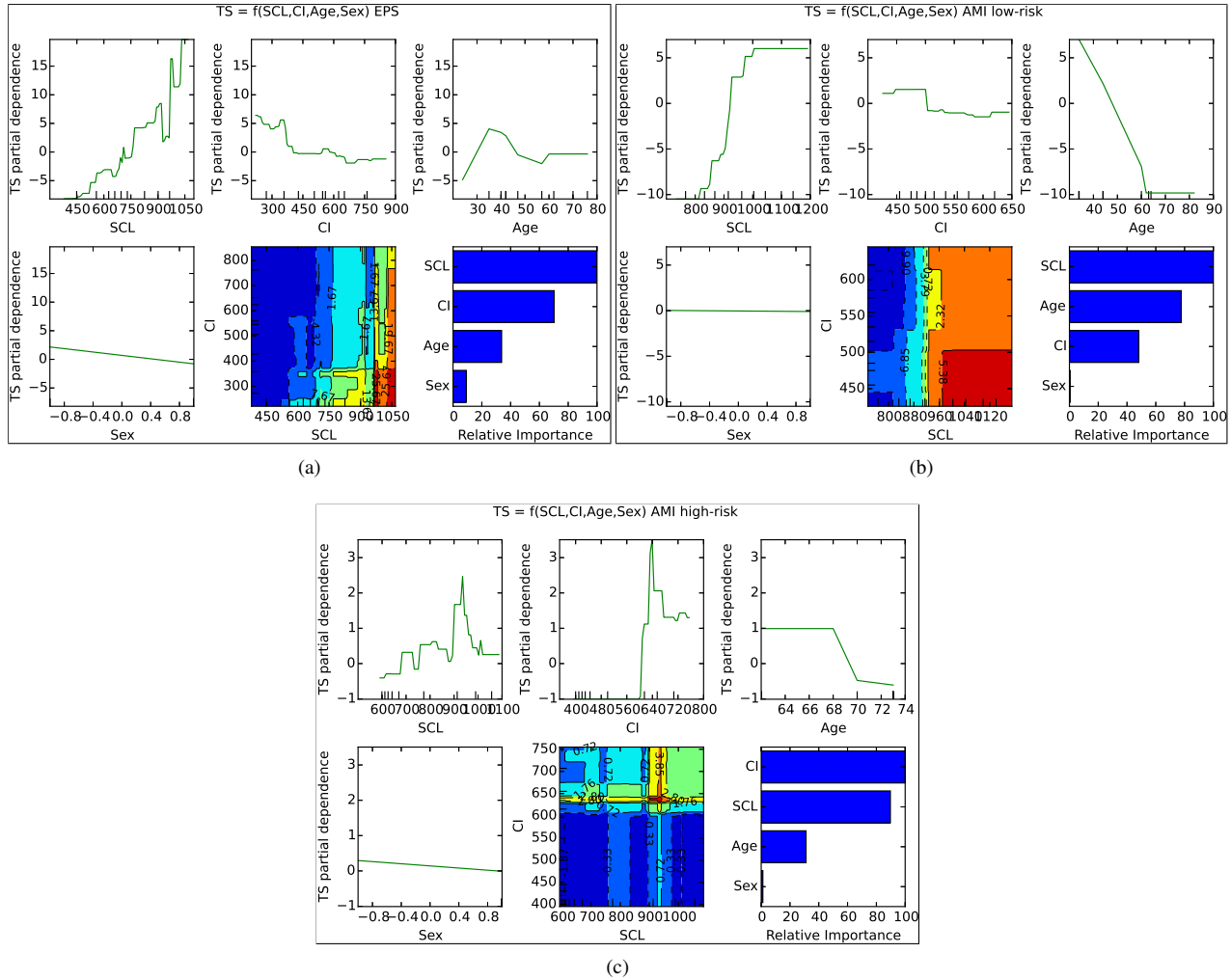


Figure 1. Summary of results, PDP (one-way and two-way) and feature relative importance of modeling HRT using BRT for EPS(a), AMI low-risk (b) and AMI high-risk (c).

4. Results

Figures 1(a), 1(b), and 1(c) show one-way, two-way PDP and feature relative importance obtaining modeling HRT using BRT for EPS, AMI low-risk and AMI high-risk patients respectively.

The most important feature in EPS and AMI low-risk groups was *SCL*, whereas in AMI high-risk group was *CI*. It is clear the nonlinear positive relationship between *TS* and *SCL*, especially in EPS and AMI low-risk. The relationship between *TS* and *CI* is negative, as suggested by the baroreflex hypothesis, both in EPS and AMI low-risk. In contrast, in AMI high-risk, *CI* and *TS* had a positive relationship. Two-way PDP shows a similar HRT dynamics as a function of *SCL* and *CI*, both in EPS and AMI low-risk, in contrast to the behaviour exhibited by AMI high-risk group.

The coefficient of determination, R^2 was obtained to evaluate how well the model predicts. R^2 was obtained using cross-validation 10-fold. R^2 was higher for EPS (0.63) and AMI low-risk (0.38) groups than for AMI high-risk group (0.28).

5. Conclusions

In this work we propose to use BRT to model the relationship between HRT parameter *TS* and variables *SCL*, *CI*, *Age*, and *Sex*. The model was fitted using data from three different groups, namely, a healthy group obtained from EPS, a low-risk and a high-risk groups from AMI patients.

R^2 results suggested that the explanatory variables used are good predictors of the value of *TS* in healthy conditions (EPS group). R^2 lower values in the high risk group

may suggest a loss of heart rhythm control by the baroreflex and autonomic nervous system.

This loss of control seems to be confirmed by the change in the relationship between TS and the explanatory variables according to the one-way PDP, which are similar in EPS and AMI low-risk, but different in AMI high-risk.

Further work should be directed to incorporate all the available information about physiological variables when assessing HRT on patients. Also, comparing HRT dynamics, regarding the proposed explanatory variables, between different patient groups may give some insight on cardiovascular risk stratification.

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