# AN EXPERIMENTAL MODEL TO ASSESS MECHANISMS OF HEART RATE TURBULENCE

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**Abstract**

**Heart rate turbulence (HRT) is defined as the early acceleration (turbulence onset, TO) and subsequent deceleration (turbulence slope, TS) in sinus rhythm after a single premature beat (PB). In this study we design an experimental model to investigated the mechanisms involved in HRT from inside the heart. Aim of this study was to assess the autonomic responses to an ectopic beat on the SA node and on the AV conduction. One external lead (II) and two epicardial leads on left (L) and right (R) atrium were acquired during the 72 hours following the operation in 5 patients undergone coronary artery bypass grafting. TO and TS were computed on RR, $PP_L$, $PP_R$ and PR series. We found high correlations between $TO_{RR}$ (or $TS_{RR}$) and both $TO_{PPL}$ and $TO_{PPR}$ (or $TS_{PPL}$ and $TS_{PPR}$ ). No correlation has instead been found for $TO_{RR}$ and $TS_{RR}$ vs. $TO_{PR}$ and $TS_{PR}$. The similar HRT patterns found for RR and PP series suggest that the response to a PB is associated to the autonomic modulation of the SA and AV node. The poor correlations found for TO and TS between RR and PR series are consistent with the hypothesis that changes in cardiac cycle due to baroreceptors mask or avoid changes in AV conduction delay.**

## Introduction

Heart rate turbulence (HRT) is the phenomenon associated to the fluctuations of sinus rhythm cycle length after a single ventricular premature beat (VPB) [1]. HRT is defined as a short period of early acceleration and a subsequent longer period of deceleration of sinus rhythm after a single ventricular premature beat (Figure 1). This phenomenon was first described by Schmitt et al., who also introduced two descriptors [1]. The initial accelleration is quantified by

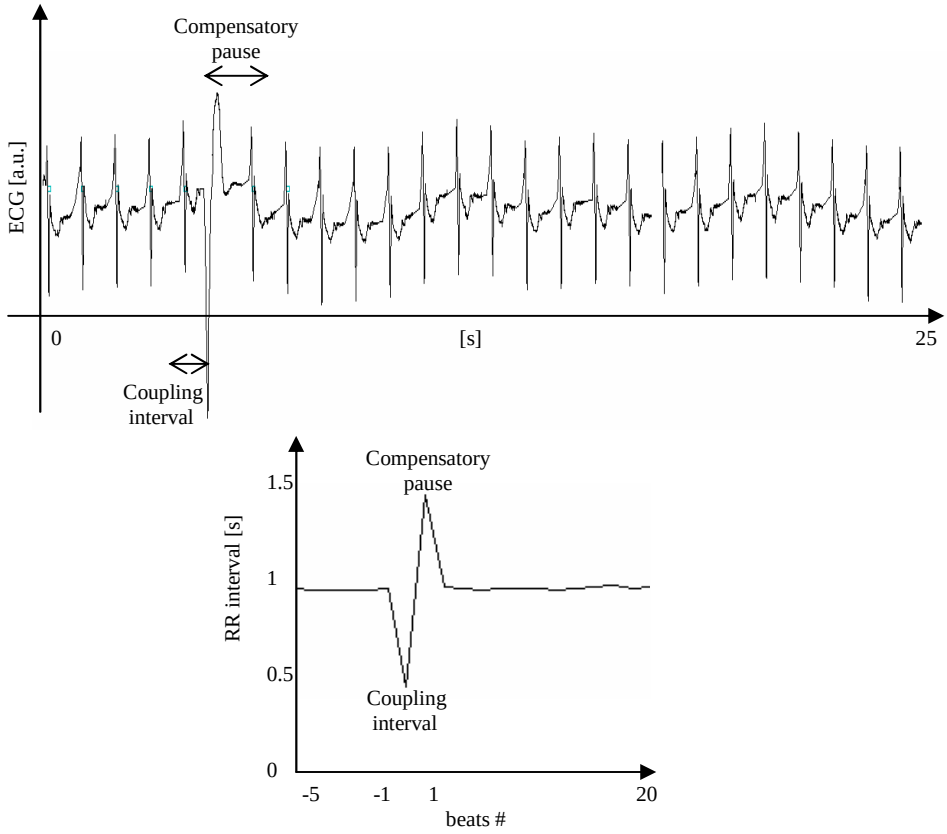


Figure 1. HRT phenomenon after a PB.


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the turbulence onset (TO) defined as the relative percentage change of RR intervals immediately after compared with immediately before a premature beat (PB). The subsequent deceleration is quantified by the turbulence slope (TS), defined as the maximum positive slope of a regression line assessed over any sequence of 5 subsequent sinus rhythm RR intervals within the first 20 sinus rhythm intervals after a VPB (expressed in ms per RR interval).

The first study on HRT showed that the absence of heart rate turbulence (HRT) after ventricular ectopic beats is a powerful stratifier for the risk of death after myocardial infarction [1]. The optimal dichitomy for TO was found to be 0%: negative turbulence onset (TO<0%) correspond to sinus rhythm accelleration after a VPB (normal behaviour); the otpimal dichotomy for TS was 2.5 ms per RR interval: TS higher than 2.5 ms/RR interval indicates normal pattern of HRT (sinus rhythm deceleration after a VPB).

The studies aimed at evaluating the underlying physiological mechanisms agree with the hypothesis that HRT is caused by a baroreflex mechanism [2-5]. Early acceleration is believed to results from a transient baroreflex-mediated inhibition of vagal activity [6]; subsequent deceleration could be associated with the compensatory increase in vagal tone triggered by the increase in stroke volume caused by the compensatory pause [7].

Major part of studies on HRT are based on Holter recordings of surface ECG. In this study we design an experimental model based on surface ECG and on left and right atrial electrogram recordings, to investigate the mechanisms involved in HRT from inside the heart. Particularly, the aim of this study was to assess the autonomic responses to premature beats (PB) on the SA node and on the atrioventricular conduction.

**Materials and methods**

One external lead (II) and two epicardial leads on left and right atrium were acquired by a digital Holter (PRIMA Holter, Cardioline, Como, Italy; 500 Hz, 12 bit) during the 72 hours following the operation in 5 patients (3 male, age 65.7±7.8) undergoing coronary artery bypass grafting.

The RR intervals were obtained from the surface ECG by detecting the QRS complexes; the series of intervals between two subsequent depolarisations in right and left atrium ($PP_L$ and $PP_R$, respectively) were defined from the epicardial leads.

The criterion of prematurity was shortening of the RR intervals or PP intervals by 15% or more.

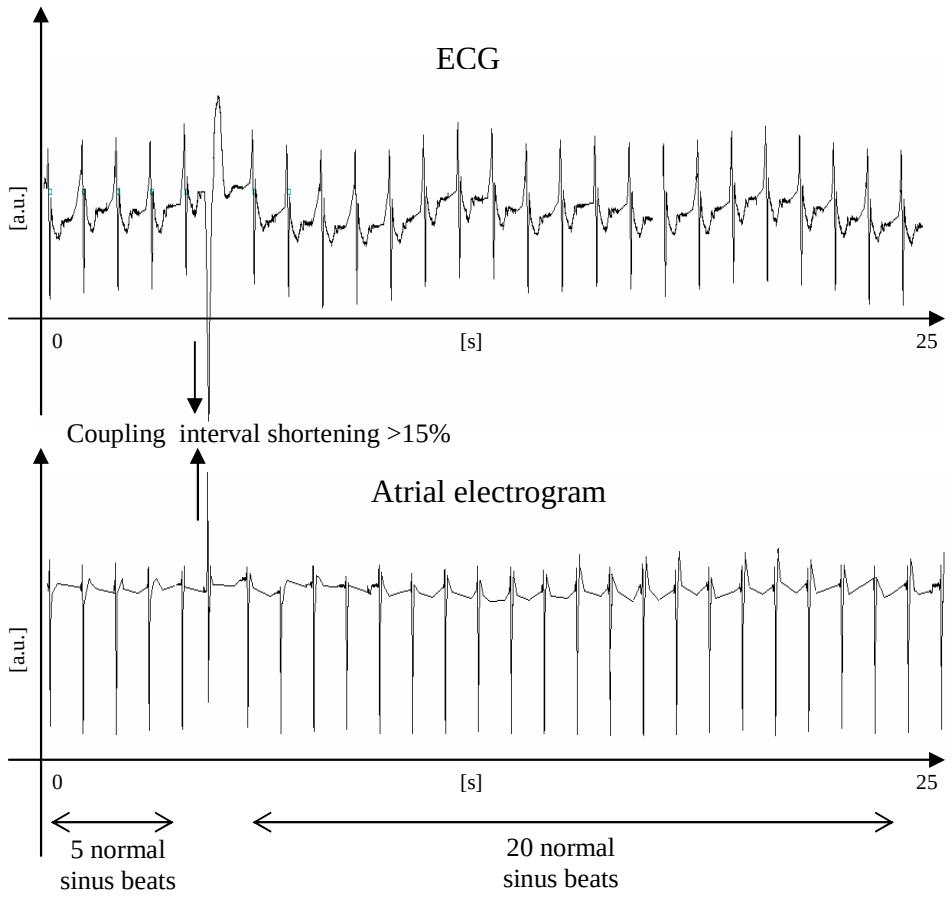


Figure 2. Criterion of prematurity and isolation to detect a PB on the surface ECG (top panel) and the atrial electrogram (bottom panel).


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All ectopic beats that occurred in isolation (preceded by al leats 5 and followed by at least 20 normal sinus beats, figure 2) were selected automatically by a computer algorithm and confirmed manually by visual inspection of surface ECG and electrograms.

Such further control was needed for a correct classification of premature beats (ventricular or atrial) and to eliminate ectopic beats corrupted or surrounded by wrong detections of atrial depolarizations or QRS complexes as well as by the presence of arrhythmia and atrifacts.

QRS complexes and atrial depolaritazions were detected from surface ECG and left atrial electrogram recordings, respectively, using a modified version of the algorithm proposed by Pan and Tompkins [8].

Parabolic interpolation was also used to improve the accuracy of the fiducial point estimation.

TO and TS were computed on RR, $PP_L$, $PP_R$ and PR series for each detected PB.

PR series is defined as the series of the intervals between each rigth atrial depolarization and the corresponding R wave (figure 3).

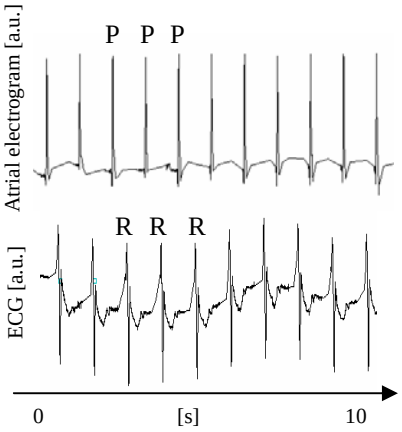


Figure 3. PR series definition.

## Results

A total of 1146 PB occurred in the population. Table 2 shows, for each patient, the total number of PB over the 72 h recording, and the TO and TS obtained from the RR series ($TO_{RR}$ and $TS_{RR}$), expressed as mean ± standard deviation.

Two out of 5 patients exhibited normal TO (negative) after a PB, while TS was normal (higher than 2.5 ms/RR interval) in 3 out of 5 patients.

Tables 3 and 4 shows the correlation coefficents between the TO and the TS values, respectively, obtained for RR series respect to those obtained for $PP_L$, $PP_R$ and PR series, for each patient, after a PB.

Figure 4 shows the regression lines and the correlation coefficents found for $TO_{RR}$ and $TS_{RR}$ vs TO and TS found for $PP_L$ and PR series, for one patient.

We found high correlations between $TO_{RR}$ (and $TS_{RR}$) and both $TO_{PPL}$ and $TO_{PPR}$ (and $TS_{PPL}$ and $TS_{PPR}$). No orrelation has instead been found for TO and TS obtained from RR series and those obtained from PR series.

Table 2: Total number of ectopic beats and TO and TS obtained from the RR series ($TO_{RR}$ and $TS_{RR}$, mean ± standard deviation).

| Patient | Number of ectopic beats | $TO_{RR}$ (%) | $TS_{RR}$ (ms/RR interval) |
|---|---|---|---|
| 1 | 482 | -0.01±0.16 | 1.90±0.32 |
| 2 | 381 | 0.75±0.87 | 3.27±0.52 |
| 3 | 79 | 0.67±0.24 | 7.53±0.41 |
| 4 | 122 | 0.20±0.18 | 6.23±0.85 |
| 5 | 82 | -0.41±0.36 | 2.44±0.57 |

Table 3: Correlation coefficents between the TO values obtained for RR series respect to those obtained for $PP_L$, $PP_R$ and PR series.

| Patient | $TO_{RR}$/ $TO_{PPL}$ | $TO_{RR}$/ $TO_{PPR}$ | $TO_{RR}$/ $TO_{PR}$ |
|---|---|---|---|
| 1 | 0.90 | 0.91 | 0.01 |
| 2 | 0.99 | 0.92 | 0.09 |
| 3 | 0.97 | 0.98 | 0.02 |
| 4 | 0.96 | 0.99 | 0.08 |
| 5 | 0.97 | 0.94 | 0.07 |

Table 4: Correlation coefficents between the TS values obtained for RR series respect to those obtained for $PP_L$, $PP_R$ and PR series.

| Patient | $TS_{RR}$/ $TS_{PPL}$ | $TS_{RR}$/ $TS_{PPR}$ | $TS_{RR}$/ $TS_{PR}$ |
|---|---|---|---|
| 1 | 0.93 | 0.96 | 0.01 |
| 2 | 0.99 | 0.99 | 0.2 |
| 3 | 0.97 | 0.98 | 0.03 |
| 4 | 0.92 | 0.96 | 0.1 |
| 5 | 0.95 | 0.96 | 0.06 |

## Discussion

The pathophysiological background of HRT is not fully defined. Since the definition of HRT in 1999 [1] many efforts have been made to identify its exact mechanisms [6-7], given the importance of such method as potent postinfarction risk stratified.


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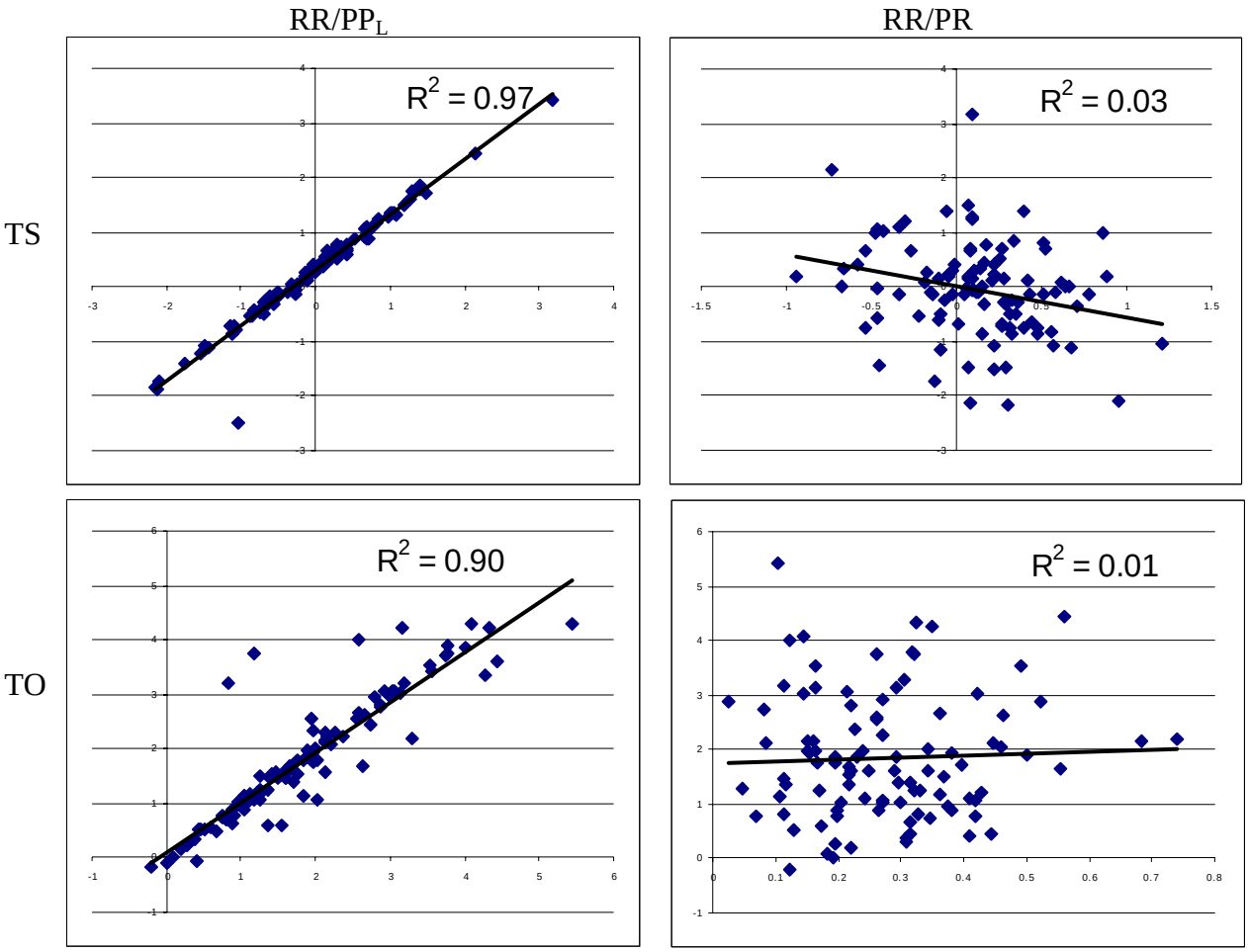


Figure 4 shows the regression lines and the correlation coefficients found for $TO_{RR}$ and $TS_{RR}$ vs TO and TS found for $PP_L$ and PR series, for one patient.

It is now believed that HRT is associated to the baroreflex mechanism [2-5].

According to this hypothesis the triggering event is the compensatory pause after the premature beat, which causes a transient fall of arterial pressure.

The induced haemodinamically inefficient ventricular contraction leads to a transient loss of vagal efferent activity, which causes the early acceleration of heart rate followed by a gradual deceleration.

In this study we designed experimental model based on left and right atrial electrogram recordings, to investigate the mechanisms involved in HRT from inside the heart.

We could therefore assess the autonomic responses to premature beats on both the SA node and the atrioventricular conduction, by introducing the HRT parameters of the PR series.

The designed experimental model guaranteed an accurate estimation of atrial depolarization instant.

The main findings of this study are twofold: (1) The similar HRT patterns found for RR and PP series suggest that the response to a PB is associated to the autonomic modulation of the SA and AV node. (2) The poor correlations found for TO and TS between RR and PR series are consistent with the hypothesis that changes in cardiac cycle due to baroreceptors mask or avoid changes in AV conduction delay.

Indeed, a physiological activation of baroreceptors due to changes in blood pressure seems to exert an inhibitory influence on atrioventricular conduction [9]. After a premature beat, the baroreceptors markedly alter the cardiac cycle, while maintaining atrioventricular conduction values close to normal.

In conclusion, the designed experimental model seems to confirm the accepted hypothesis that HRT is a phenomenon associated to the baroreflex mechanism.

It should be noted that, the finding that TO and TS values are abnormal in some patients is consistent with the worsening of HRT parameters after CABG, probably due to the mechanical damage of autonomic nervous fibers during aortic clamping [10].

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