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Blood Pressure Drop Prediction by using HRV measurements in the Orthostatic Hypotension

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Abstract This paper presents a model to predict the systolic blood pressure drop due to postural hypotension, relying on heart rate variability measurements extracted from 5 minute ECGs recorded before standing. This model was developed and tested with the leave-one-out cross-validation technique enrolling 10 healthy subjects and finally validated with additional 5 healthy subjects, whose data were not used during the training and testing cross-validation process. The results show that the model predicts correctly the systolic blood pressure drop in 80% of whole experiments, with an error below the measurement error of a sphygmomanometer digital device.

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1 Introduction

Postural hypotension is a reduction of blood pressure due to gravitational force, which may cause dizziness and loss of balance when changing position (i.e. rising form bed or chairs). Those symptoms occur when the system fail to recover those drops with a prompt reaction. Severe cases of postural hypotension are known as Orthostatic Hypotension (OH) and occur when a drop in systolic blood pressure of at least 20 mm Hg or in diastolic blood pressure of at least 10 mmHg Is observed within 3 minutes after that a person assumes a standing position.

This phenomenon is more prevalent in elderly people [2, 3], for which OH is significantly associated with falls, fractures and potential serious morbidity. In fact, OH has been considered an important risk factor for falls since 1960. Sheldon reported in [4] that 4% of 500 falls in 202 elderly people were attributed to abnormal blood pressure homeostasis. Also Ooi et al. [5] identified OH as a risk factor for recurrent falls in a subset of people who had previously fallen. In addition, increased mortality and incidence of cardiovascular disease (CVD) related to prevalent OH has been reported in different people [6-8].

For those reasons, several study have been conducted aiming to detect or predict OH events as it can cause fall-related injuries [9] and consequently compromise quality of life and mobility[10].

This paper presents the preliminary results obtained with a model aiming to predict drops in blood pressure using Heart Rate Variability (HRV) features registered 5 minutes before standing.

2 Background

Gravity causes blood to pool in the veins of the legs and trunk, when standing. This pooling lowers the blood pressure and the amount of blood the heart pumps to the brain, causing in some cases dizziness and other symptoms. To compensate these drops, the Autonomous Nervous System (ANS) quickly increases the heart rate and constricts blood vessels, in order to restore blood pressure homeostasis. One of the most studied non-invasive biomarkers of ANS activities is HRV [14-16].

Even if OH is more prevalent in elderly people, the phenomena of an huge drop down in blood pressure due to standing hypotension can be observed also in healthy young subjects [17] when they undergo on an orthostatic stress.

Therefore, this study focused on healthy young subjects, considered as control group for future study focusing on elderly. Since HRV is one of non-invasive estimator of the ANS, which is the controller of blood pressure homeostasis, this study investigated the relationship between Heart Rate Variability (HRV) and the drop in Blood Pressure (ΔBP) that occurs when a person stands up from a bed or couch. The underlying hypothesis of this study is that the BP drop (ΔBP) due to standing is not independent of the HRV features measured in the 5 minutes before standing. The study is a first attempt to understand the potential of HRV to predict the OH and than to predict falls.

3 Method

According to [18], 15 healthy subjects were enrolled. The inclusion criteria were:

- no pathological cardiovascular conditions, neurological or psychiatric disorders [19, 20] or other severe diseases;
- not taking any medication at the time of the study;
- not professional athletes or high-level sport participants;
- not caffeine or alcohol in the 12 hours prior to the measurements.

The experimental protocol was defined to maximize repeatability and reproducibility of experiments and aiming to reproduce at best the real life standing from a couch. It was composed by three phases as described in figure 1, namely that they:

- Phase 1 -Sitting: During this phase the volunteers were invited to seat in a comfortable position for a baseline recording of the systolic BP (BP1 measurement) and ECG. This phase has a duration of 2 minutes, from time 0 until time 2min.
- Phase 2 -Lying: In this phase the volunteers were invited to lay down in supine position for 10 minutes. The first 5 minutes (from time 2 until time 7) are resting times. During the last 5 minutes (from time 7 until time 13), ECG was recorded continuously using a commercial wearable devices and systolic BPs was recorded 4 times: BP2, BP3, BP4, and BP5, once each 60 seconds.
- Phase 3 -Standing: in this phase the volunteers were invited to stand up actively and to stay in upright position for 5 minutes (from time 13 until time 18). Once standing, systolic BPs was recorded 4 times: BP6, BP7, BP8 and BP9, once each 60 seconds, and ECG was recorded for 5 minutes. Phases 2 and 3 were repeated 4 times.

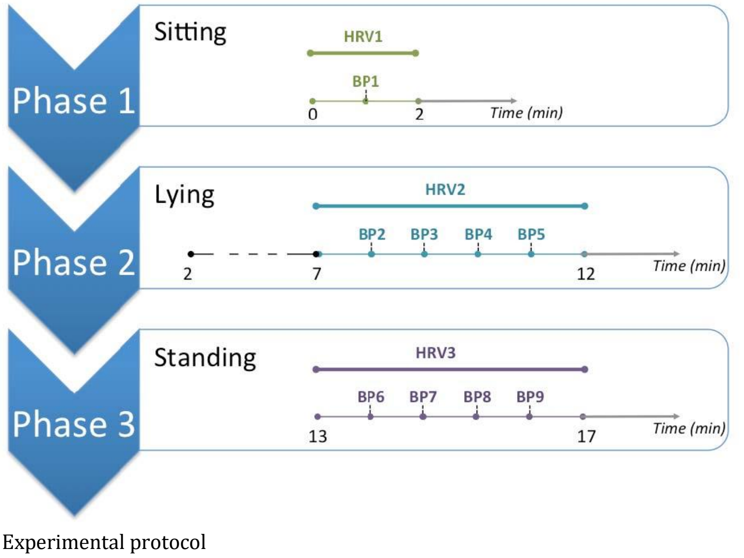

Fig. 1 Experimental protocol

The experimental protocol has been approved by the Biomedical and Scientific Research Ethics Committee (BSREC) of the University of Warwick and each subject was given detailed information about the study and gave her/his informed consent before starting the measurements.

During the experiments, 1 lead ECG signal was monitored using a one-lead wearable electrocardiogram sensor, the BH3-M1 (Zhephyr Ltd). Blood Pressure values were measured with a digital sphygmomanometer, the M2 basic (OMRON Ltd).

4 Mathematical Model Extraction

The ECG recordings from phase 2 were pre-processed by using Kubios [21] a Matlab based software package for event-related bio-signal analysis developed by the University of Kuopio, Finland, and they were associated with BP drop-down calculated as:

$$\Delta BP = BP\,7 - \text{mean}(BP\,2, BP\,3, BP\,4, BP\,5) \quad (1)$$

From the ECG, 34 HRV features were extracted in linear [14] and non-linear domain [22], as shown in the table 1. Details about HRV features extraction and convention can be seen in [23]. In order to develop and test a model to predict the magnitude of BP drop, we have generated a dataset. This dataset contains four instances for each subject, one for each experiment repetition. Each instance is defined as follow:

$$i = sub_{id}; test_{id}; \Delta SYS_{BP}; f(HRV) \quad (2)$$

where:

- sub_{id}: is a number value from 1 to 15 to univocally identify each subject;
- $test_{id}$: is a number value from 1 to 4 indicating the experiment repetition;
- ΔSYS_{BP} : is the blood pressure drop calculed by using the equation 1;
- F(HRV) : is a vector containing the 34 HRV measurements reported in Table 1 related to the phase 2, the Lying phase before standing

The mathematical model to predict BP using the HRV registered in the 5 minutes before standing was developed using a robust multi-linear regression [24]. An exhaustive search method was performed to select the best 5 HRV features to use in the model.

Particularly, the dataset was divided into two sets:

- a training/testing set composed by 2/3 of the whole dataset (10 subjects);
- a validation set composed by the remaining 1/3 of the whole dataset (5 subjects).

The model was computed with the leave-one-out cross-validation technique [25] by using only the training/testing set. Therefore, the robust regression was performed ten times, each time using 9 subjects to develop the model and one to validate it. This process was repeated 10 times, leaving out in turn all the subjects. Consequently, 10 models were computed and the final model was then selected evaluating the percentage of errors on the validation set. This selection was performed in order to give more generalization capacity to the model on new unknown data. Instead, the testing set was used to test the final model on totally unknown data.

5 Results

The best combination of HRV features resulted to be the following:

- Root Mean Square of the Successive Differences,the square root of the mean of the squares of the successive differences between adjacent NNs (RMSSD);
- The number of pairs of successive NNs that differ by more than 50 ms (NN50);
- The triangular interpolation of NN interval histogram (TINN);
- The absolute powers of high frequency band (HF);
- The standard deviation of the Poincar plot alond to the line of identity and the Deteminism (DET).

The mathematical model based on those HRV features was:

$$\Delta BP_{predicted} = -25.67 - 0.45 * RMSSD + 0.05 * NN50 + - 0.02 * TINN + 0.01 * HF + 0.3 * DET \quad (3)$$

The results shown a correct prediction of 80% validation set, confirming the results obtained with the training/testing dataset and reported in [26]. This value was calculated as the % of prediction that differ from the measured ΔBP less than the measurement error (4.5 mmHg) of the sphygmomanometer. The histogram of errors is reported in Figure 2. Figure 3 shows the values of the ΔBP predicted by the developed model (red crosses) against the measured values (blue circles) and the measurement error (vertical blue error bars) for the 5 subjects of the testing set.

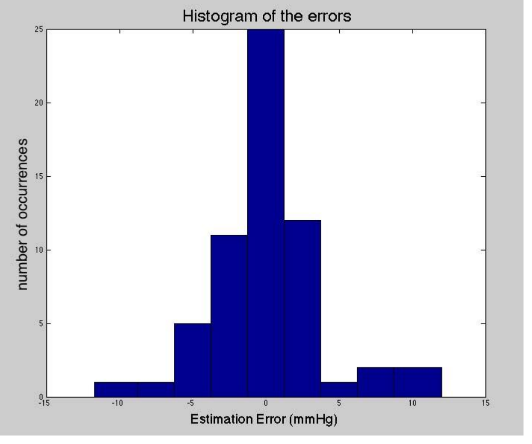

Fig. 2 Histogram of errors, which represents the distribution of the prediction errors.

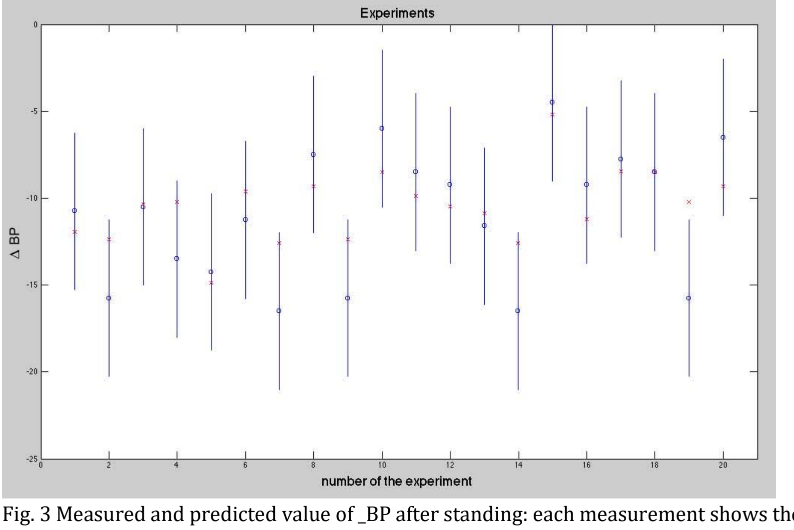

Fig. 3 Measured and predicted value of _BP after standing: each measurement shows the measured _BPs (blue circles) with the measurement errors (vertical blue bars) and the predicted _BPs (red crosses) using the model described here

6 Discussion

This paper presented the design and the preliminary result of a prof-of-concept study investigating if it is possible to predict systolic ΔBP due to standing using short term HRV measures extracted from ECG recorded 5 minutes before the standing. The preliminary results show that ΔBP magnitude is predictable with the HRV features almost in the 80% of cases. This results, although preliminary demonstrated that it is possible to predict BP drop-down due to postural hypotension using HRV. A recent retrospective study [13] demonstrated that there is a significant association between a depressed HRV and the risk of falling in elderly. The authors concluded that this was due to the fact that a depressed HRV reflects a reduced capability to react to risky situations. The preliminary results presented in this paper could explain this association. Other studies, [15] and [5], investigated the associations between SH and HRV. However, those papers focused on how HRV changes before and after standing, and mainly focusing on linear HRV measures. Differently, this pilot study aimed to understand how HRV changed before the BP drop-down and how it could be possible to predict the ΔBP from HRV measures.

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