Evaluation of a PPG-based algorithm for prediction of Neurally Mediated Syncope

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Abstract— **Syncope is a transient and self-limited loss of consciousness that affects mostly elderly people. Although it is not lethal it can lead to serious injuries and the appearance of severe medical complications. With a high socioeconomic and medical impact, it is highly pertinent to develop personalized health systems that are capable of predicting impending syncope events and avoid major complications. In the later years we have been assisting to a rising interest on wearable monitoring systems and in several devices (e.g. sports watches) the photoplethysmogram (PPG) is already being used due to the easy applicability, cost effectiveness and unobtrusiveness. Thus, the development of an algorithm for syncope prediction that can be integrated on such systems would be of huge interest. In this paper we evaluate an algorithm for syncope prediction based on the analysis of the PPG signal alone and we compare it to our former algorithm based on the joint analysis of the electrocardiogram (ECG) and PPG signals.**

I. Introduction

Neurally mediated syncope (NMS) is thought to be the consequence of an over-response of the autonomic nervous system to the over stimulation of the left ventricle walls, wich can be triggered by factors such as blood shift and pooling in the lower body. The result is a paradoxical suppression of the sympathetic activity and an increase of the parasympathetic tone, which leads to the bradycardia, vasodilation, and consequently hypotension and syncope [1].

Several studies have been proposed in literature aiming the prediction of neurally mediate syncope. While some authors focus of the early prediction of the head-up tilt table test (HUTT) outcome based on the evaluation and comparison of heart rate and blood pressure parameters extracted during specific phases of the HUTT test (e.g. [2-4]), others concentrate on the real time prediction problem, where the risk of an impending syncope episode is continuously assessed from the monitored hemodynamic parameters [5-9].

In a previous work [10] we characterized this mechanisms using the joint analysis of the electrocardiogram (ECG) and the photoplethysmogram (PPG) signals and proposed an algorithm for the prediction of syncope based on these two modalities. However, the requirement of the ECG signal can difficult its translation to real life scenarios where this modality is not accessible. Additionally, the rising interest on modalities such as the PPG that can be easily applied to p-health (personalized-health) systems, highlight the importance of the development of an algorithm based on the PPG alone. Such algorithm could be easily applied to the emerging PPG-based monitoring devices, such as pulse rate monitoring watches. In this paper we propose an algorithm that does not require the analysis of the ECG signal and we compare it to our previously proposed ECG/PPG-based algorithm.

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II. Methods

The proposed algorithm consists of four main steps. The first step is the detection of motion artefacts, which is performed based on the analysis of the PPG signal using the algorithm proposed in [11]. The following steps are the extraction of hemodynamic parameters from the PPG signal and consequent pre-processing, the extraction of features and finally, the prediction of syncope events.

In the parameter extraction step, our algorithm focuses on the three main mechanisms that characterize the development of syncope. The chronotropic changes are assessed by the pulse rate (PA_1 - PR), while the inotropic changes are assessed by the left ventricular ejection time (PA_2 - LVET). The PR was defined as the time span between consecutive PPG pulses, while the LVET was assessed using an algorithm based on the modelling of the PPG pulse, proposed in [12]. To assess the vascular tone and blood pressure changes two highly pressure dependent parameters were extracted: 1) the stiffness index (PA_3 - SI), was defined by the time span between the forward and reflected waves, while; 2) the reflection index (PA_4 - RI), was defined by the amplitude ratio between both waves.

Finally, the parameter outliers were detected using an approach similar to [13], where a box plot analysis over a sliding window was adopted to detect sporadic parameters values that greatly differ from the parameter main trend. The high frequency noise was suppressed by applying a 0.05Hz Butterworth filter to the interpolated (2Hz) parameters time series.

In order to extract features that are independent from each patient physiological and hemodynamic characteristic, the extracted parameters were normalized using equations (1) and (2), leading to the definition of 8 features.

$$n[PA_i(t)] = \frac{PA_i(t)}{PAref_i}, i = 1, \dots, 4 \quad (1)$$

TABLE I. RESULTS ACHIEVED BY THE CURRENT PPG-PBASED ALGORITHM AND BY THE PREVIOUSLY PROPOSED ECG/PPG –BASED ALGORITHM

Algorithm	Phase	SE (%)	SP (%)	PPV (%)	FPRh (h^{-1})	PreTime (s)
ECG/PPG-based	*Train/Validation*	93.3	96.7	94.8	0.15	61.0±38.6
	Test	100	92.3	85.7	0.15	243.3±242.5
PPG-based	*Train/Validation*	65.3	94	88.3	0.14	82.6±44.9
	Test	83.3	76.9	62.5	1.03	238.6±185.1

$$n\Delta[PA_i(t)] = \frac{PA_i(t) - PA_i(t-1.5)}{PAref_i}, i = 1, \dots, 4 \qquad (2)$$

where , PA_i is the ith parameter, $PAref_i$ is the average of each parameter during the second minute (reference window) after the patient was tilted to the upright position and t is the time instant.

The abrupt changes of the previously defined features were assessed by the Minkowski distance ($p=2^{-0.5}$) to the stable orthostatic state, i.e. the reference point at the beginning of the standing period, and the risk of an impending syncope event was identified if the distance to the stable orthostatic state exceeds a predefined optimal threshold.

III. RESULTS AND DISCUSSION

The proposed algorithm was validated on a database consisting of ECG-II lead and PPG signals collected using a Philips MP50 patient monitor from 43 subjects scheduled for diagnostic HUTT. The PPG signals where collected with a standard SpO2 sensor attached to the index finger.

In the adopted three-way data split validation approach, a subset of 30 patients was used to train/validate the algorithm, using a 5-fold cross validation scheme, and an independent subset of 13 patients was used to test the algorithm. The optimal threshold used during the test phase was defined as the average of the thresholds computed during the train/validation phase.

The results achieved by current PPG-based algorithm and the previously proposed ECG/PPG-based algorithms are presented in Table 1. As it is possible to observe, the current algorithm achieved a better performance during the training/validation phase than in the test phase. Although a high specificity was achieved (SP: 94%), the ability of the algorithm to predict syncope events was low, shown by the low sensitivity (SE: 65.3%). However, the number of false alarms remained low (FPRh: 0.14 h^{-1}) and a good prediction time was achieved in this phase (82.6 s). The results achieved during the test phase were considerably lower, shown by the lower specificity (SP: 76.9%) and a higher false alarm rate (FPRh: 1.03 h^{-1}). Contrarily, the sensitivity and the prediction time of the algorithm were higher at this phase. Comparing the currently PPG-based algorithm with the previously proposed ECG/PPG-based algorithm, it is shown that the current algorithm was not able to outperform the ECG/PPG-based algorithm in none of the performance metrics, with an exception to the FPRh (0.15 vs 0.14 h^{-1}) and the PreTime (61.0±38.6 vs 82.6±44.9 s) during the train/validation phase.

These results show the importance of the heart rate (HR) and especially the pulse arrival time (PAT) extracted from the analysis of the ECG signal, as measures of chronotropic and blood pressure changes. Although the PR can be used as a surrogate for the HR, the PAT was not included in the current algorithm due to the impossibility of capturing the onset of the ventricular depolarization using only the PPG signal. The absence of this feature, which has been shown to be an important marker of blood pressure changes and the most important parameter of the previously proposed ECG/PPG-based algorithm, showed to have a major impact on the performance of the current algorithm.

IV. CONCLUSIONS AND FUTURE WORK

In the later decades the PPG signal has been increasingly used in personal health devices, such as sport watches, due to its easy applicability, cost effectiveness and non-obtrusiveness. It would be of great interest to develop an algorithm resorting on the analysis of the PPG signal alone, capable of being integrated in such devices and deployed in real life scenarios. To this end, we propose in the present study an algorithm for syncope prediction that based on the analysis of the PPG signal alone and we compare it to our previously proposed ECG/PPG-based version.

The current algorithm resorts on the extraction of features associated with the main mechanisms leading to development of syncope, namely by assessing the chronotropic (PR), inotropic (LVET), vascular tone and blood pressure (SI and RI) changes relative to the orthostatic stable state. The risk of impending syncope was assed using a threshold-based approach, where alarms are generated if the distance to the reference stable surpasses a predefined threshold.

Our results highlight the importance of the PAT parameter as a measure of abrupt blood pressure changes for the prediction of impending syncope. The exclusion of the ECG analysis from the current algorithm, lead to the impossibility of determining the reference point corresponding to the onset ventricular depolarization and consequently the exclusion of the PAT from the parameter set. In fact, the absence of PAT related features in the current algorithm showed to have a negative impact on the prediction capability, in the train/validation and more prominently in the test phases. These results show that in order to develop a robust algorithm for syncope prediction, based exclusively on the analysis of the PPG signal, it is essential to integrate novel features that can counteract the absence of such a critical feature.

Our future work will focus on the investigation of the PPG pulse characteristic points that better suit the assessment of PR as a surrogate of HR. Additionally, this work will also enable to assess which characteristic points can be used to assess accurate heart rate variability indexes (in this case pulse rate variability - PRV) and consequently on the inclusion of PRV indexes capable of increasing the algorithms performance.

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