Heart Rate Variability towards Noninvasive Glucose Measurement

Subjects: Statistics & Probability

Contributor: Aleksandar Stojmenski, Marjan Gusev, Ivan Chorbev, Stojancho Tudjarski, Lidija Poposka, Marija Vavlukis

Heart rate variability (HRV) is defined by the heart rate variations caused by the periodic change of heart rhythm over time in the absence of physiological activity, postural changes, and emotional stimuli. This labels HRV as a noninvasive marker of the autonomic nervous system (ANS) function. Heart rate variability (HRV) parameters can reveal the performance of the autonomic nervous system and possibly estimate the type of its malfunction, such as that of detecting the blood glucose level.

Keywords: heart rate variability ; machine learning ; age and gender ; glucose levels ; noninvasive glucose monitoring

1. Introduction

Several papers presented work on the relation between ANS and HRV [1][2]. Since ANS influences cardiac control, changes in HRV are expected due to an inflammatory response (protection against infection) or ANS blockade. Additionally, increased physical activity [3] or excitement reflects increased heartbeats while oxygen is delivered to the body. Dependencies of ANS on gender are also reported [4]. It has so far been concluded that [5], with aging, ANS responds slower to heartbeat-increasing stimuli (e.g., physical activity), which is one possible reason for the negative correlation between HRV and age.

It has previously been shown that HRV parameters can predict glucose levels by noninvasive methods [6]. This has brought the concept one step closer to reality and has once more established point-of-care (POC) HRV measurements as one of the most promising candidates for noninvasive glucose testing. Nevertheless, the actual applicability of the technique depends on the degree to which other influences on HRV, such as age and gender, can be systematically eliminated.

HRV is associated with a high risk of heart disease and death in different age groups [7], and it is exciting to understand its variability to increase its applicability as a diagnostics/prevention tool. HRV parameters vary by multiple factors, including gender and age.

2. Heart Rate Variability

Several research papers address the HRV relation to a combination of age and gender. Age has been consistently shown to be negatively correlated with HRV, albeit minor differences in the amount and persistence of this correlation with age can still be found.

Umetani et al. [8] present a significant negative correlation between aging and HRV parameters (pNN50, SDNN, and rMSSD particularly) with 95% confidence. The authors explain an HRV decline with aging, showing pNN50 as the primary contributor with a rapid decline, while rMSSD and SDNN decline gradually. This study also indicates that HRV decreases slowly with aging and at a different rate in male and female subjects.

A similar pattern of HRV decreases with aging was found to be steeper for men (1.07/year) than for women (0.68/year) ($p < 0.05$) [9] without significant gender difference in the association of heart rate to BMI. Supporting these two works is the research by Jensen et al. [10], who also concludes that HRV parameters are negatively correlated with age.

A cross-sectional survey of 4580 healthy Chinese men and women aged 20–85 years was performed to detect correlations of age, gender, and BMI with HbA1c, which can be derived from and is correlated with HRV [11]. The study shows that glycohemoglobin levels (HbA1c) increased with age among all groups divided into quartiles.

HRV predictability was the focus of research realized by Voss et al. [12]. They show that HRV increases in the elderly subject group (age 50–74 years) compared to the younger subject group (25–49 years) and discuss that significant modifications of the HRV indices in terms of age disappeared within the last two age decades (age range 55–74 years). General dependence on gender for many HRV indices, particularly from FD, STSD, SPPA, IA, ACOR, and AMI (highly significant), was proven in young subjects. It is shown that those dependencies disappear with increasing age. According to HRV analysis methods, the influences of age and gender on HRV indices differed partly, whereas in general, the gender influences were considerably weaker than the age influences.

3. Correlation Analysis

Several research studies analyze the correlation of HRV between men and women. This was usually conducted based on a subset of the parameters with the highest influence on HRV (SDNN, SDANN, ASDNN, RMSSD, NN50, pNN50, SDNNi, HF, LF). Ramaekers et al. [13] explain that cardiac autonomic modulation, as determined by HRV, is significantly lower in healthy women than in healthy men. HRV difference by gender was also concluded by Antelmi et al. [9], finding that HF, rMSSD, and pNN50 measures were more significant among women compared with men ($p < 0.05$) in all age groups.

Jensen et al. [10] found that women had lower HRV than men, addressing that the SDNN time-domain parameter was lower in women than in men. Although lower HRV was concluded among women compared with men, analyzing all time-domain parameters, only SDNNi decreased significantly ($p < 0.05$) in females. They also took into account frequency-domain parameters, showing that only LF was especially ($p< 0.05$) decreased in females [14]. Interestingly, these gender differences have been shown to diminish after the age of 50 [8].

HRV was also shown to be susceptible to other other factors, both innate and acquired. Obesity and weight loss in correlation with HRV parameters were analyzed by Karason et al. [15]. The study showed that obese subjects had significantly lower overall HRV (SDNN), which was due to a reduction in both long-term HRV (SDANN) and, in particular, short-term HRV (SDNN index). The study covered a weight loss group, showing a significant decrease in heart rate (8% prolongation of mean RR) and an increase in overall HRV (SDNN).

HRV was also analyzed concerning race, and initial research concludes racial differences that show Afro-Caribbean subjects having a lower sympathetic drive than age-matched Caucasians [16][17].

Several studies show an inverse correlation of HRV with heart rate itself [9]. A similar influence of heart rate on HRV has already been demonstrated [18][19].

All studies focus their research on healthy patients. Most of the studies focus solely on long-term measurements, and to our knowledge, only two studies [12][15] analyze the impact of short-term HRV, measuring over periods of less than or equal to 30 min.

4. Machine Learning Methods for Glucose Measurement

ML techniques have gained significant traction in healthcare, offering powerful tools for analyzing complex medical data. In the HRV analysis context, ML algorithms have been employed to extract meaningful insights from HRV data and improve predictive models. Several studies have demonstrated the effectiveness of ML methods in HRV-based risk assessment and disease diagnosis [20][21].

Several recent studies have investigated using HRV for noninvasive glucose monitoring. Gusev and Poposka [22] used ML and neural network methods to correlate HRV with glucose levels, achieving a mean absolute error of 10.5 mg/dL. This means that the average difference between the predicted and actual glucose levels was 10.5 mg/dL. A mean absolute error (MAE) of 10.5 mg/dL is considered acceptable for noninvasive glucose monitoring.

Avci et al. [23] also used ML techniques to develop a noninvasive glucose monitoring system based on HRV, achieving a mean absolute error of 12.3 mg/dL. This is slightly higher than the error achieved by Gusev and Poposka, but it is still within an acceptable range. Wang et al. [24] used a combination of HRV and ML to develop a system with a mean absolute error of 11.4 mg/dL. This is closer to the error achieved by Gusev and Poposka, and it suggests that combining HRV with ML can improve the performance of noninvasive glucose monitoring. Zhang et al. [25] used deep learning to develop a system with a mean absolute error (MAE) of 10.8 mg/dL. This is the lowest error reported in any of the studies, and it suggests that deep learning is a promising approach for noninvasive glucose monitoring.

The golden standard for glucose monitoring is a blood test, which has an MAE of about 5 mg/dL. However, blood tests are invasive and inconvenient, so there is a need for more accurate and convenient methods of glucose monitoring. Noninvasive glucose monitoring systems with an MAE of 10.5 mg/dL could be a valuable tool for people with diabetes or other conditions that require frequent glucose monitoring. It is important to note that the MAE of a noninvasive glucose monitoring system can vary depending on the individual and the conditions under which the system is used. For example, the MAE may be higher if the person exercises or has certain medical conditions. Additionally, the MAE may improve over time as the system is further developed and refined.

Given the different dependencies of HRV, its use for predictive purposes requires a more profound understanding to determine its baseline to varying ages for both genders. This implies that all parameters must be considered to understand the parameter landscape and the different influences fully. Moreover, focusing on the short- and medium-term measurements is crucial to integrate this technique into POC measurement devices. The practical applicability of this technique for glucose prediction will strongly depend on its relevance not only in healthy individuals but also in those with arrhythmia and diabetes as the most prevalent chronic diseases in concerned patients. It is, therefore, necessary to include data on such patients in this research.

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