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DECELERATION CAPACITY INDEX FOR TYPE 2 DIABETES MELLITUS CLASSIFICATION USING SUPPORT VECTOR MACHINES IN ELDERLY WOMEN

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ABSTRACT

The purpose of this study was to present study was to stratify the degree of type 2 diabetes mellitus (T2DM) in elderly women based on the phase-rectification signal averaged (PRSA) approach to HRV analysis using SVM and cross-validated by the k-Fold. This study was designed as a cross-sectional study of elderly women subjects 60 to 70 yrs of age were divided into two groups, twenty subjects each: diabetes group (DG) with a diagnosis of T2DM and control group (CG). All subjects were instructed to lie in the supine position for 5 min at rest while breathing normally with a heart rate monitor Polar V800 working at a sampling rate of 1000 Hz was used to record RR intervals (RRi), it was created a vector of the differences between successive elements of the RRi series; the cardiac-deceleration rate (CDR) index was defined as the mean of the positive values. A Gaussian SVM classifier trained on classifying the DG and healthy based on CDC index was tuned and validated using multiple runs of k-fold cross-validation. After ten runs of ten-fold cross-validation, our method using 10-fold cross validation obtains the highest classification accuracy, 97.5%, reported so far. In conclusion, CDC index of RR time series at rest was proposed and validated to stratify the degree of T2DM in elderly women using SVM, might be complementary to existing autonomic function assessment. Then, machine learning approaches offer new solutions and ways forward in biomedical, bioengineering and clinical applications, mainly, in diabetes research.

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INTRODUÇÃO

Diabetes Mellitus (DM) is a metabolic disease characterized by hyperglycemia which results from defects in insulin secretion, insulin action or both (American Diabetes Association, 2013). DM is associated with increased risk of multiple coexisting medical conditions in older adults, such as whether stringent glycemic control would be of net benefit (Kirkman *et al*., 2012). In the sense, type 2 diabetes mellitus (T2DM) was associated with an overall decrease in the HRV (Benichou *et al*., 2018; Tarvainen *et al*., 2014), but both sympathetic and parasympathetic activities were decreased, which can be explained by the deleterious effects of altered glucose metabolism on HRV, leading to cardiac autonomic neuropathy and associated with high cardiovascular mortality (Fakhrzadeh *et al*., 2012). As an alternative, the analysis of heart rate variability (HRV) is the physiological phenomenon of the variation in the time interval between consecutive heartbeats (Rosenwinkel *et al*., 2001) frequently used to assess the autonomic control of the heart rate fluctuations (Pomeranz *et al*., 1985).

used to assess the autonomic control of the heart rate fluctuations (Pomeranz *et al*., 1985). Despite the widespread application of HRV, linear approaches to HRV signals may introduce intrinsic computational errors (Lombardi, 2000). Moreover, since traditional linear HRV analyses cannot accurately distinguish the vagal and sympathetic activities of the autonomic nervous system and there is potential for incorrect conclusions and for excessive or unfounded extrapolations (Manor *et al*., 2010). Pan and colleagues (2016) introduced the phase-rectification signal averaged (PRSA) approach to HRV analysis that consists in separately assessing the accelerating and the decelerating phases of RR interval series in order to estimate the sympathetic and the parasympathetic contributions to heart rate control. Particularly the decelerating capacity index (DC) or sympathovagal imbalance is a common underlying disorder in patients with type 2 diabetics (Wang et., 2018). Therefore, the promotion of DC detection will bring the far-reaching influence on prevention and treatment of sudden cardiac death for the patients with type 2 diabetics (Wang *et al*., 2020). Artificial intelligence, machine learning, health care robots, and algorithms for clinical decision-making are currently being sought after in diverse fields of clinical medicine and bioengineering in cardiology (Johnson *et al*., 2018). The support vector machine (SVM) is a rising machine learning approach that offers robust classification of high-dimensional big data into small numbers of data points or support vectors, achieving differentiation of subgroups in a short amount of time (Turki; Wei, 2018). Then, the purpose of the present study was to stratify the degree of type 2 diabetes mellitus in elderly women based on the phase-rectification signal averaged (PRSA) approach to HRV analysis using SVM and cross-validated by the k-Fold.

METHODS AND MATERIALS

The study protocol was approved by a local Ethical Human Research Committee of Universidade Federal do Amapá (protocol: 89612818.2.0000.0003), and an informed written consent was obtained from all subjects. This study was conducted in accordance with the instructions of the Helsinki Declaration of 2008 and in accordance with Resolution 466/2012 of the National Health Council.

Subjects: This study was designed as a cross-sectional and forty elderly women, 60–85 years old, nonsmokers and with no history of cardiopulmonary disease were divided into two groups, twenty subjects each: diabetes group (DG) with a diagnosis of type 2 diabetes mellitus selected at random from the Project of the Health Promotion Program for People with Diabetes Mellitus (AMAP/UNIFAP) from the Federal University of Amapá located northwest of the North Region of Brazil, also known as the Amazon Region and the control group (CG).

Anthropometric Measurements: During an orientation session, testing procedures and time commitment required for participation in this study were verbally explained to potential participants. The data collection and the anthropometric variables were performed by the same and experienced evaluator throughout the study. The height was measured in centimeters and the body mass was measured in kilogram with certified and calibrated mechanics scale (Filizola, Brazil). Body mass index (BMI) was calculated as the quocient ratio of weight over squared height (kg/m2).

Experimental procedures: The tests were conducted in a quiet room with temperature maintained at 22ºC. All volunteers were instructed to avoid strenuous activity in the 24 hours prior to each testing session and to avoid alcohol, caffeine as well as the consumption of large meals for, at least, three hours prior testing. In the first visit to the lab, all subjects were instructed to lie in supine position for 5 min at rest while breathing normally. A heart rate monitor Polar V800 (Polar, Finland), working at a sampling rate of 1000 Hz was used to record R-R intervals (RRi), during this period. The tachograms of RRi were transferred using an infrared interface device to the Polar Precision Performance SW software v. 3.0 (Polar, Finland), which automatically corrects RRi based on moving average filter. All records of sample data showed less than 2% error, and were then saved to ".txt" files.

Cardiac-deceleration rate index: Following the original proposal of Bauer *et al*. (2006), the decreasing and increasing phases of heart rate were also analyzed separately, in order to better estimate the contributions of parasympathetic and sympathetic control, respectively. In the present study, a simplification was proposed. Firstly, it was created a vector of the differences between successive elements of the RRi series; then, the cardiac-deceleration rate (CDR) index was defined as the mean of the positive values.

Data analysis: Data were presented as the mean ± standard deviation (SD) for continuous variables. Gaussian distribution and homogeneity of variance tests were applied to determine the distribution and homoscedasticity of sample data. The Kolmogorov-Smirnov test confirmed the normality of distribution. Subsequently, the linear approach by support vector machines (SVM) as the separating the best hyperplane for an SVM means the one with the largest margin between the two classes was used to classify the T2DM and healthy based on CDC index and was cross-validated by the k-Fold. The data set is divided into k subsets, and the holdout method is repeated k times. Each time, one of the k subsets is used as the test set and the other k – 1 subsets are put together to form a training set. Then, the average error across all k trials is computed. After the implementation of the SVM algorithm and the identification of two groups, the difference in anthropometric and physical characteristics and CDC index between the groups was tested using the Student's t-test for independent variables. All procedures assumed $\alpha = 0.05$ for statistical significance and were processed in the Matlab v. 2020.b (The Mathworks, EUA).

RESULTS

Figure 1 illustrates a Gaussian SVM classifier trained on classifying the T2DM and healthy based on CDC index was tuned and validated using multiple runs of k-fold cross-validation. After ten runs of ten-fold cross-validation, our method using 10-fold cross validation obtains the highest classification accuracy, 97.5%, reported so far.

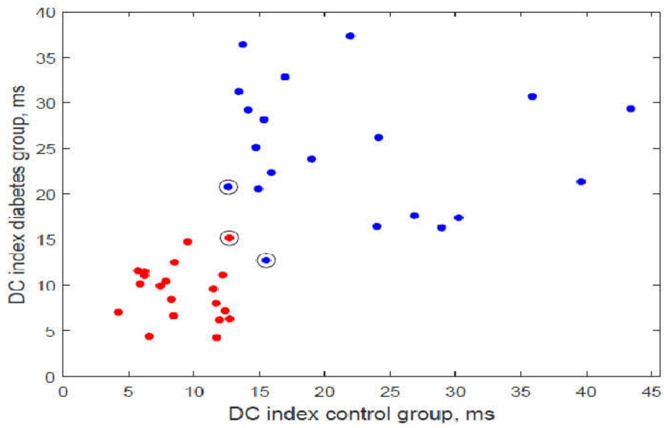

Figure 1. Classifying T2DM and healthy based on DC index using Support Vector Machine. Diabetes group diabetes represented by red and the control group by blue and the circles correspond to the Support Vector

After clusters analysis and groups separation, the anthropometric and physical characteristics of the subjects of the low CDC index in T2DM group were compared to those of the higher CDC index in control group (Table 1). The low dispersion of data in anthropometric and physical characteristics of subjects in both groups indicated the homogeneous of the sample with no significant difference ($P > 0.05$).

Table 1. Anthropometric and physical characteristics of subjects

Variables	DG	CG	P-value
Age (years)	64.0 ± 3.7	65.2 ± 2.1	0.26
Height (cm)	151.4 ± 7.3	150.5 ± 4.8	0.71
Body mass (kg)	65.5 ± 10.7	64.5 ± 8.5	0.78
BMI (kg/m^2)	28.8 ± 4.9	28.4 ± 3.6	0.83
CDC index (ms)	9.2 ± 2.9	23.4 ± 8.2	< 0.01

DISCUSSION

The purpose of the present paper was to stratify the degree of type 2 diabetes mellitus in elderly women based on the PRSA approach to HRV analysis using SVM and cross-validated by the k-Fold. Therefore, a Gaussian SVM classifier trained on classifying the T2DM and healthy based on CDC index was tuned and validated using multiple runs of k-fold cross-validation. In the original PRSA method proposed by Bauer *et al*. (2006), each positive change of RR time series was used as the anchor for the coherent average of the surrounding RR interval segment, and the resulting step was defined as the decelerating capacity index (DC). Similarly, the accelerating capacity index corresponded to the respective step obtained from the negative RR changes. Afterwards, enhancing the deceleration capacity index of heart rate by modified-phase-rectified signal averaging (Pan *et al*., 2010) and validity of the indices (Pan *et al*., 2016) and, recently, a refined method of qualifying deceleration capacity index for heart rate variability analysis (Liu *et al*., 2018). In the present study, a simplification was proposed. Firstly, it was created a vector of the differences between successive elements of the RRi series; the cardiac-deceleration rate (CDR) index was defined as the mean of the positive values (Materko *et al*., 2018).

The lower DC index have been associated in patients with dilated cardiomyopathy (Wang *et al*., 2017; Zou *et al*., 2016; Bas *et al*., 2015), after myocardial infarction (Rizas *et al*., 2018), predicts 1-year mortality of patients undergoing transcatheter aortic valve implantation (Duckheim *et al*., 2017), in acute hemispheric ischemic stroke (Xu *et al*., 2016), predicts arrhythmic and total mortality in heart failure patients (Arsenos *et al*., 2016) and in type 2 diabetes mellitus patients (Wang et., 2018). Despite the growing application of DC (Rizas *et al*., 2018; Wang *et al*., 2017; Duckheim *et al*., 2017; Xu *et al*., 2016; Arsenos *et al*., 2016) the method is affected by one shortcoming non-vagally mediated abnormal variants of sinus rhythms in heartbeat interval time series are used to quantify DC, thus confounding the evaluation of cardiac vagal modulation. (Liu *et al*., 2018), but DC was positively correlated to sympathetic activity and negatively correlated to vagal activity (Pan *et al*., 2016).

Diabetic autonomic neuropathy have been showing lower heart rate variability, consequently, vagus is the decelerating nerve of the heart, but DC declines, vagus excitability lowers, and the protection function for human body decreases (Wang *et al*., 2020). Thus, the risk of sudden death increases (Arsenos *et al*., 2016). Increased sympathetic activity of the autonomic vegetative system has already been described in patients with type 2 diabetes mellitus (Materko *et al*., 2020; Cardoso *et al*., 2020; Benichou *et al*., 2018), which can be explained by the deleterious effects of altered glucose metabolism on HRV (Fakhrzadeh *et al*., 2012). In concordance, the present study stratified the degree of type 2 diabetes mellitus in elderly women based on the PRSA approach to HRV analysis using SVM and cross-validated by the k-Fold.

The improvements in expert systems and machine learning tools, the effects of these innovations are entering to more application domains day-by-day and medical field is one of them. Classification systems that are used in medical decision making provide medical data to be examined in shorter time and more detailed (Johnson *et al*., 2018). Future research should address the limitations of the present study by employing a sample from different age and both sexes, and, mainly, compare the performance of the present SVM and other diagnostic and therapeutic prediction models across the data types in biomedicine.

CONCLUSION

The CDC index of RR time series at rest was proposed to stratify the degree of type 2 diabetes in elderly women using SVM and cross-validated by the k-Fold, might be complementary to existing autonomic function assessment. Then, machine learning approaches offer new solutions and ways forward in biomedical, bioengineering and clinical applications, mainly, in diabetes research.

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Conflict of interest: The authors declare that the research was conducted in the absence of any commercial or financial relations hips that could be construed as a potential conflict of interest.

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