Heart Rate Variability Analysis a Non-invasive Clinical Screening Tool to Detect Functional Ability of Diabetic Cardiac Autonomic Neuropathy

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ABSTRACT
Cardiovascular complications are the main cause of death in people with diabetes, which if identified can lead to improved health. A non-invasive, clinical system for low-cost screening of diabetes mellitus (DM) is introduced and tested on patients with some known conditions. Data recorded on 20 Normal Control (NC) and 20 Diabetic mellitus. Lead II electrocardiogram (ECG) was recorded in three modes, supine, sitting to standing and deep breath. The heart rate variability (HRV) signal is extracted from ECG recording. The HRV signal is then characterized using time domain and frequency domain analysis method which is subsequently used as a basis for detection of percentage functional ability of sympathetic, parasympathetic and autonomic nervous system of diabetes mellitus. Almost 20 time domain and frequency domain parameters have significance *p*-value less than 0.05.Poor heart rate variability is seen in diabetes patients in all three modes. In patients with type 2 DM significant reduction of spectral power in HF band of the heart rate variability was found for orthostatic stress and respiratory stress. Decreased values of Dynamic Orthostatic Stress (DOS) index, Dynamic Respiratory Stress (DRS) index and Ortho-Respiratory Stress (ROR) Index for DM compared to NC indicates damage to sympathetic, parasympathetic and autonomic nervous system of DM as an effect of diabetes.

Keywords

Heart Rate Variability, Diabetes Mellitus, Time Domain Analysis, Frequency Domain Analysis.

1. INTRODUCTION
A well known relation exit between autonomous neural system alterations and cardiovascular mortality [1]. Many studies show that an increment in the sympathetic activity and/or reduction of the vagal activity provokes a grater lethal arrhythmia incidence [2]. Heart rate variability (HRV) analysis has proven to be a good quantitative index for the autonomous cardiovascular activity. Thus, it is used as prognostic marker in many different pathologies [3], as a chronic side effect, Diabetes Mellitus (DM) affects both peripheral and autonomous neural system[4]. Autonomous diabetes neuropathy (NAD) affection foresees an uncertain future to these patients; the mortality index after 5 years ranges from 25% to 50% with sudden death as a quarter of the total death incidence [5,6,7,8]. This is a high ratio even considering that patients with advanced neuropathy or cardiopathy are excluded from this study. The frequency domain parameters of HRV signal, computed during supine, sitting to standing and the deep-breathing state, have a resulted in an understanding of the effect of the ANS on the HRV signal [1].The approach consist of studying and analyzing the variations of the heart rate, which are controlled almost entirely by the two branches of the nervous system namely, sympathetic nervous system and para-sympathetic nervous system [9]. In the frequency domain the HRV spectrum has been found to have two bands of interest namely i) Sympathetic (S) band (0.025-0.125) Hz and (ii) Para-Sympathetic (PS) band (0.125-0.400) Hz power spectrum of HRV signal, estimated using the Fast Fourier Transform algorithms, show an appreciable variation in the two states of recording [10]. Currently, Ewing's battery of tests is used for clinical assessment of cardiac neuropathy. These tests measure the variations of Blood Pressures (BP) and the Heart Rate (HR) during stressed conditions like deep breathing, standing, etc [11]. The tests usually take around half-an-hour to perform and another half an hour to analyze the result in order to identify the type of neuropathy. These delays and resultant strain for the subjects necessitated the development of an alternative approach to detect DCAN, in the form of signal processing methodology. Due to the application of computers in signal processing calculation [12-20], which includes extraction of heart rate signal from ECG, fast and accurate HRV analysis in detection of DCAN is used further for classification of the neuropathy. These estimated parameters are used by the cardiologists to identify the neuropathy in subject and next possible logical development in the system is the ability to identify the percentage of functional ability of the sympathetic, para-sympathetic, and autonomic nervous system [21]. The present expert system is designed with the aim of being used by nurses and other paramedical personnel as the end-users. The result sheet derived as the output from the signal processing algorithms can be utilized for detection of DM and heart deices prior to clinical events, coupled with implementation of preventive management strategies, to delay the progression of these diseases.

2. METHODOLOGY
The subject population including 20 DM and 20 NC subjects for comparison purpose, 5 minuets ECG data recording was done on all the subjects under supine, sitting to standing and deep breath state. The data acquisition system is also developed by us, includes an II lead ECG, low pass filter, and amplifier and 10 bit ADC. The software chosen as reference for development of our system is Software for advanced HRV analysis made by the

Department of Applied Physics, University of Kupio, and Finland. We verified the developed data base first processing on this software and found similar results when compared with the previous work on same area. The software developed by us is using Matlab v 7.5 is dived in five stages,
1) To call all three mode (supine, sitting to standing, deep breath) data recordings.
2) Preprocessing by removing the artifacts in raw ECG.
3) R-R interval detection, by modified derivative based 'Variable threshold input method' for accurate extraction of HRV signal from raw ECG.
4) Evaluation of time-domain parameters.
5) Detection of functional ability of DM autonomic nervous system.
Time domain analysis can be applied directly onto the successive R-R interval values. Time domain parameters are associated mostly with the overall variability of the R-R intervals over the time of recording. They are Mean R-R; mean HR, Standard deviation of all NN intervals (SDNN), defined as follows,

$$\text{SDNN}= \sqrt{\frac{1}{N-1}\sum_{j=1}^{N}\left(RR_j - \overline{RR}\right)^2}$$

Here, N is the total number of successive intervals and $R\text{-}R_j$ represents the value of the j^{th} R-R interval. And we then take the square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD). The number of adjacent NN intervals differing by more than 50 m sec (NN50 count) is calculated. The percentage of differences between adjacent NN intervals differing by more than 50 m sec (pNN50 %) is calculated as,

$$\text{pNN50} = \frac{NN\ 50}{N-1} \times 100\ \%\ ,$$

Standard deviation (STD) of the mean heart rate per minute and a number of other parameters can be calculated from the original R-R intervals.

The spectral analysis of the HRV signal allows one to separate in bands, the frequencies related to the sympathetic and parasympathetic activities of the nervous system [5]. The most popular techniques for the spectral analysis of HRV are the Fast Fourier Transform (FFT) and the Autoregressive modeling. These techniques require samples of the signal being analyzed to be evenly spaced in time. This is not the case with the HRV signal because its samples are spaced according to the heart beat intervals. Since the sampling of the HRV signal is non uniform, in order to use the techniques proposed here, some preprocessing is required. A solution for this problem is to reconstruct the signal at a higher sampling rate [6]. The power spectrum density of the signal is calculated as follows.

- The series of R-R interval is interpolated by cubic splines and the interpolated signal is re-sampled at a higher, uniform rate (2-4Hz).
- The reconstructed signal is multiplied by the Hanning window. The DC component of the signal is removed.
- The spectrum is calculated, using the absolute value of the FFT.
- The amplitude spectrum is squared and multiplied by the sampling periods.
- In FFT, the result is divided by the number of samples in the window.

The power spectrum is divided into three bands. First, VLF (0 to 0.04 Hz) second, LF (0.04 to 0.15 Hz) and third is HF (0.15 to 0.5 Hz). The energy contained in the LF band is related to the sympathetic activity of the signal and the HF band is related to parasympathetic activity [5, 7]. The power in these bands is calculated based on the area under the curve, and the ratio between them indicates the sympathetic-parasympathetic balance in the segment of the signal. The absolute power contained in the LF and HF bands and the LF/HF ratio is a good indicator for detecting alterations in the nervous system behavior.

The most important part of the system is to detect the functional ability of the sympathetic, para-sympathetic, and autonomic nervous system by calculating the sympathetic and parasympathetic indices. The method as follows,

*BIst-Balance Index sitting=LF/HF sitting mode
*BIslp-Balance Index slipping=LF/HF slipping mode
*BIdb-Balance Index deep breath =LF/HF deep breath mode.

From these index values,
*Dynamic Orthostatic Stress Index, which is the difference between sympathetic and parasympathetic balance index during sitting and supine referred to supine is calculated as
1) DOS=(BI st-BI slp)/BI slp

*Dynamic Respiratory Stress Index, is a difference between inverse of sympathetic and para sympathetic balance indices during deep breathing and supine referred to supine mode is calculated as
2) DRS=((1/BI db)-(1/BI slp))/(1/BI slp)

*Ortho-Respiratory Stress Index i.e. the balance during sitting to Balance, during Deep Respiration
3) ROR=BI st/BI db These indices are calculated to detect diabetic autonomic dysfunctions

3. RESULTS AND DISCUSSION

Sl.no.	Parameter	Symbol	NC Mean Index	DM Mean Index	p-Value
1	MEAN-RR- slp (ms)	MEAN-RR- slp	889.77 ±119	723.79 ±70	<0.009
2	MEAN-RR- st (ms)	MEAN-RR- st	831.65 ±203	721.932 ±77	<0.01
3	MEAN-RR-db (ms)	MEAN-RR- db	883.0 ±113	730.29 ±58	<0.001
4	SDNN- slp (ms)	SDNN- slp	49.40 ±21	26.0 ±25	<0.001
5	SDNN-st (ms)	SDNN- st	49.68 ±25	26.28 ±26	<0.001
6	SDNN-db (ms)	SDNN- db	47.66 ±16	23.90 ±24	<0.001
7	RMSSD- slp (ms)	RMSSD- slp	0.056 ±0.02	0.029 ±0.005	<0.001
8	RMSSD-st (ms)	RMSSD- st	0.041 ±0.014	0.031 ±0.011	<0.006
9	RMSSD-dp (ms)	RMSSD-- db	0.073 ±0.038	0.035 ±0.018	<0.001
10	NN50- slp	NN50- slp	13.6 ±15	4.52 ±8.9	<0.001
11	NN50- st	NN50- st	13.0 ±14	3.25 ±9.2	<0.008
12	NN50- db	NN50- db	11.95 ±13	3.5 ±7.9	<0.001
13	pNN50- slp	pNN50- slp	6.8 ±7.3	2.26 ±4.4	<0.001
14	pNN50- st	pNN50- st	6.5 ±7.0	1.6 ±0.8	<0.005
15	pNN50- db	pNN50- db	6.5 ±6.5	1.79 ±3.9	<0.001
16	Sympathetic to parasympathetic Balance index- slp	BI- slp	1.684 ±0.43	3.86 ±1.5	<0.001
17	Sympathetic to parasympathetic Balance index- st	BI- st	4.604 ±1.45	5.51 ±1.7	0.683
18	Sympathetic to parasympathetic Balance index-db	BI- db	0.3635 ±0.16	2.06 ±0.088	<0.001
19	Dynamic Orthostatic Stress Index	DOS	2.01 ±1.56	0.800 ±0.95	<0.001
20	Dynamic Respiratory Stress Index	DRS	4.95 ±4.5	1.672 ±2.18	<0.001
21	Ratio of Balance during Sitting to Balance during Deep breathing	ROR	14.30 ±19	4.05 ±2.83	<0.001

Table.1. Profile of Time domain, Frequency domain analysis parameters, orthostatic stress index and respiratory stress index evaluation result.

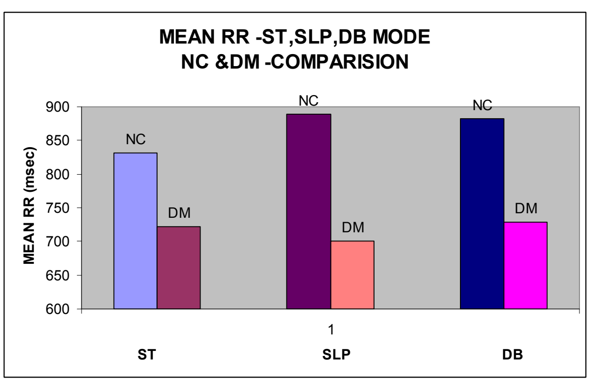

Fig.1 MEAN RR NC &DM in sitting, supine, deep breath Mode.

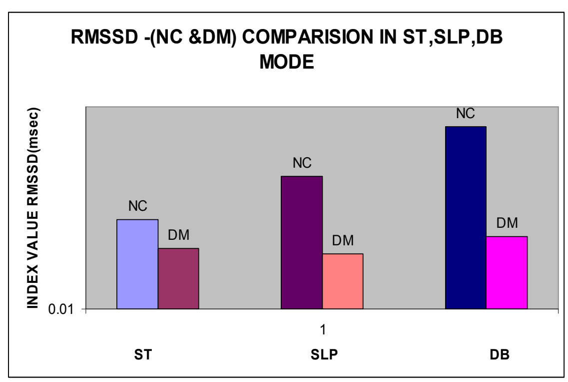

Fig.2 RMSSD NC &DB in sitting, supine, deep breath Mode.

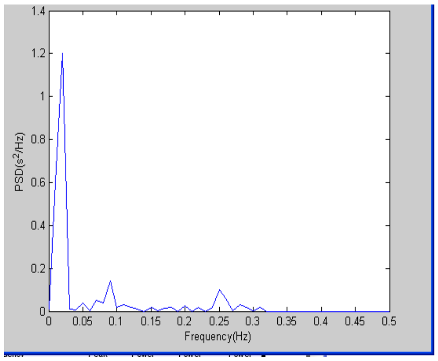

Fig.3. PSD of the HRV Data of 62 year old DM

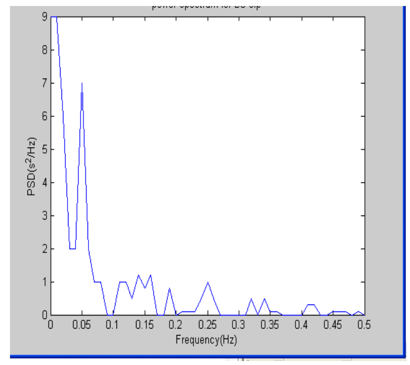

Fig.4. PSD of the HRV Data of 50 year old NC

In this study, it has found from table 1 that out of 21 indices calculated 20 indices have p-value less than 0.05. There is a significant variation in both the group. It is clearly seen in the fig 1, 2 that, the diabetes mellitus subjects have prominent Sympathetic activity at all conditions compared to normal subjects. As shown in table 1, fig.1 and 2, Time domain parameters that, for diabetes mellitus group there is a very low variation in R-R interval during orthro static stress and respiratory stress due to improper sympatho vagal balance. Indices derived from frequency domain analysis from table 1 and fig.3 and 4 indicates that power in HF band is significantly decreased for DM compared to NC. As a loss of parasympathetic control. DOS index draws maximum response from sympathetic activity; DRS from parasympathetic activity and ROR which is the result of these two activities represent status of the autonomic nervous system. Result shows reduction in index values of these indices in diabetes mellitus compare to the normal group. DOS 2.1 for NC to 0.8 for DM indicate damage to sympathetic to parasympathetic system. Similarly DRS, and ROR indices for NC and DM indicates functional damage to autonomic nervous system of DM. Non-invasive clinical screening not only lowers the risk and stress to the subjects, but is low cost effective when implemented with a personal computer and acquisition system for ECG and thus HRV time domain and frequency domain analysis. Therefore the clinical system is able to screen for diabetic cardiac autonomic neuropathy.

4. DISCUSSION

In the recent years, it has been proved that the HRV time domain and frequency domain analysis is an important method for identifying different pathological conditions. In neuropathy associated with diabetes mellitus characterized by the alteration of small nerve fibers, the heart rate variations decrease. This system has the advantage of reducing the time interval necessary to perform the diagnostic procedure and of increasing the reliability and accuracy of the diagnosis.

5. CONCLUSION

Considering the increased frequency of DM and its progression in countries like India there is a need that every Diabetologists must be provided with inexpensive ECG data acquisition system and analysis software in order to keep the record of DM ECG and its progression as regular screening procedure. This motivation was our main objective and we developed a tool for detection of DCAN which found a successful step towards it, Non-invasive clinical screening not only lowers the risk and stress to the subjects, but is low cost effective when implemented with a personal computer and acquisition system for ECG and thus HRV time domain and frequency domain analysis. Therefore the clinical system is able to screen for diabetic cardiac autonomic neuropathy.

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7. REFERENCES

[1] Task Force of the European Society of Cardiology the North American Society of Pacing and Electrophysiology "Heart rate variability: standards of measurement, physiological interpretation and clinical use". Circulation, 1996; 93:1043–1065.

[2] Juha-Pekka Niskanen, Mika P Tarvainen, Perttu O Ranta-aho, Pasi A Karjalainen, "Software for advanced HRV analysis". Computer Methods and Programs in Biomedicine, 2004; 76, 73-81.

[3] Yonglin Shen, Ke Jiang et.al., " HRV analyses system based on Windows 95 and its Preliminary exploration for analyzing Diabetics". In Proc. of the 20th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 1998; vol. 20, No.1.

[4] M. L. Jacobson, "Non-invasive clinical screening of diabetes and coronary heart disease". In Proc. of the 4th Annual IEEE Conference on Information Technology applications in Biomedicine, UK. 2003. Vol 32, 226-229.

[5] Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati F L, Powe N R. "Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus". Ann Intern Med, 2004; 141:421-31.

[6] Gerstein H C, Pogue J, Mann J F, Lonn E, Dagenais G R, McQueen M. "The relationship between dysglycaemia and cardiovascular and renal risk in diabetic and non-diabetic participants in the HOPE study: a prospective epidemiological analysis". Diabetologia, 2005; 48:1749-55.

[7] Stratton I M, Adler A I, Neil H A, Matthews D R, Manley S E, Cull C A. “Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study”. BMJ, 2000; 321:405-12.

[8] Goff D C, Gerstein H C, Ginsberg H N, Cushman W C, Margolis K L, Byington R P. “Prevention of cardiovascular disease in persons with type 2 diabetes mellitus: current knowledge and rationale for the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial”. Am J Cardiol, 2007; 99:4i-20i.

[9] Dipali Bansal. et.al., “A Review of Measurement and Analysis of Heart Rate Variability”. In Proc. International Conference on Computer and Automation Engineering, 2009.

[10] A Heitmann, T Huebner, R Schroeder, S Perz and A Voss. “Ability of Heart Rate Variability as Screening Tool for Heart Diseases in Man”. Computers in Cardiology, 2009; 36:825−828.

[11] Chengyu Liu, Changchun Liu, Liping Li, Qingguang Zhang, Bin Li. “Systolic and Diastolic Time Interval Variability Analysis and Their Relations with Heart Rate Variability”. IEEE, 2009; 978-1-4244-2902-8:1-4.

[12] Bert-Uwe Kohler, Carsten Henning, Reinhold Orglmeister, “The Principles of Software QRS detection”. In IEEE Engineering in Medicine and Biology magazine, 2002.

[13] S S Mehta et al. “Computer-aided interpretation of ECG for diagnostics”. Int. Journal of System Science, 1996; 43-58.

[14] D Benitez. et al. “The use of Hilbert transform in ECG signal analysis”. Comp. in Bio. and Med, 2001; 31:399-406.

[15] S C Saxena. et al. “Feature extraction from ECG signals using wavelet transform for disease diagnostics”. Int. Journal of System Science, 2002; 33:1073- 1085.

[16] M. Engin. “ECG beat classification using neuro-fuzzy network”. Pat. Rec. Letters, 2004; 25:1715-1722.

[17] N M Arzeno, Z D Deng and C S Poon. “Analysis of first derivative based QRS detection algorithms,” IEEE Transactions on Biomedical Engineering, 2008; vol. 55, 478-484.

[18] Mel M S Ho, Tor S. Lande and Christopher Toumazou. “Efficient Computation of the LF/HF Ratio in Heart Rate Variability Analysis Based on Bitstream Filtering.” IEEE, 2007; 1-4244-1525: 17-20.

[19] Tran Thong. “Real-time Evaluation of Spectral Heart Rate Variability.” IEEE, 2006; 1-4244-0033-3:1768-1771.

[20] E. Jovanov. On Spectral Analysis of Heart Rate Variability during Very Slow Yogic Breathing. IEEE, 2005; 0-7803-8740-6: 2467-2470.

[21] Alam M K, Begum N, Begum S. “Parasympathetic Nerve Functions in Type 2 Diabetes Mellitus: Relation to Glycemic Status and Duration of Diabetes “, Jour Bangladesh Soc Physiol, 2008; (3):42-49.