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Original Research Article

Relationship between diabetes mellitus and heart rate variability in community-dwelling elders

Ícaro J.S. Ribeiro[a,b,*], *Rafael Pereira*[b,c], *Paulo F. Valença Neto*[d], *Ivna V. Freire*[a], *Cezar A. Casotti*[b,e], *Mitermayer Galvão dos Reis*[a]

[a] *Biotechnology in Health and Investigative Medicine Postgraduate Program, Gonçalo Moniz Research Center, Candeal – Salvador, BA, Brazil*
[b] *Nursing & Health Postgraduate Program, State University of Southwest Bahia (UESB), Jequie, BA, Brazil*
[c] *Department of Biological Sciences, State University of Southwest Bahia (UESB), Jequie, BA, Brazil*
[d] *Collective Health Institute, Federal University of Bahia, Canela, Salvador, Brazil*
[e] *Health Department, State University of Southwest Bahia (UESB), Jequie, BA, Brazil*

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ABSTRACT

Background and objective: Diabetes mellitus is one of the most common non-communicable diseases (NCDs) and may influence the autonomic nervous system. This study aims to analyze the autonomic control, through heart rate variability (HRV), from community-dwelling elders with (DM+) and without diabetes mellitus (DM−).

Materials and methods: This cross-sectional study, in which 205 elders (≥ 60 years old), from the urban area of Aiquara municipality gave their written consent to participate. HRV data was collected through a Polar RS800CX monitor with a 5-min initial record at rest, followed by the command to quickly stand up.

Results: The mean age was 71 years (SD, 7.32). The population was mostly made up of women 121 (59%), with low or no schooling 123 (60%), and low income 166 (81%). HRV analysis in a frequency domain showed no difference when comparing the two groups of DM + and DM−. Henceforth in a time domain, the rMSSD showed a median value of 16.09 (interquartile range, 9.91–30.68); pNN50 median of 0.79 (interquartile range, 0.00–6.62), with a statistical significance between the group of DM+ and DM−.

Conclusions: There is a difference between the studied groups principally in what concerns the time domain, which reflects the parasympathetic activity, suggesting that elders with diabetes mellitus may have a worse parasympathetic control.

* *Corresponding author at*: Nursing & Health Postgraduate Program, State University of Southwest Bahia (UESB), 45200-000 Jequie, BA, Brazil.

E-mail address: icaro.ribeiro29@gmail.com (Ícaro J.S. Ribeiro).

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1. Introduction

Non-communicable diseases (NCDs) have increased in recent decades, owing to changes in demographic profile, characterized by an increase in the elderly population [1,2]. Diabetes mellitus is one of the most common NCDs and, as well as the aging process, may influence the autonomic nervous system (ANS), leading to a poor autonomic control of heart [3,4].

The aging process brings a natural degeneration of the ANS. This has a direct impact on the autonomic function that has been observed in a number of different ways [5]. Some changes that may occur in ANS during aging include loss of neurons, loss of axon branches and alterations in neurotransmitters and other intra-cellular features [6,7]. Clinically, these events lead to a decline of the parasympathetic control of the heart with normal aging [8], and aging associated with NCDs, e.g., diabetes mellitus, may substantially impair the parasympathetic cardioprotection.

Autonomic dysfunction has been linked with a wide range of diabetic complications [9], and the early detection of subclinical autonomic disabilities through heart rate variability (HRV) analysis in people with diabetes mellitus may be important for risk stratification and subsequent therapeutic management, including pharmacological and lifestyle interventions [10,11]. Thus, we aimed to analyze the autonomic control, through heart rate variability, in community-dwelling elders with and without diabetes mellitus.

2. Materials and methods

A total of 205 elders (≥60-years-old) [12] from the urban area of Aiquara municipality gave their written informed consent to participate in the study. Aiquara is located in the central south region of Bahia, approximately 402 km from the state capital, with 4602 inhabitants, a Gini index of 0.5376, and a HDI value of 0.583 [13]. Elders were visited door to door and interviewed by trained interviewers; then, they were scheduled to attend the municipal hospital for carrying out the examinations. All procedures were approved by the local ethics committee according to the Declaration of Helsinki (#135\2008).

One week after the inclusion visit, the subjects reported to the hospital. The subjects were asked to abstain from smoking, alcoholic beverages, or caffeine-derived products 24 h before the data collection. Before resting for 10 min in an acclimatized and quiet room, the skin of the subject was cleaned and prepared for the attachment of the heart rate monitor (HRM) elastic electrode belt (RS800XC, Polar) [14]. The electrode belt was placed just below the chest muscles, using the xiphoid process as a reference. The procedures of data collection and analyses were according to the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [15].

After explaining the procedures and placement of the HRM, the elders were placed on a hammock in the supine position. After 5 min of resting the record was started. A 5-min record [15] was conducted on all subjects. Analyses of HRV were performed in time and frequency domain according to methods following previous recommendations [15]. For time domain analysis two parameters were used: the square root of the sum of the square of the differences between the R-R (rMSSD), an indirect measure of the parasympathetic activity, and the percentage of the total number of R-R that has a difference of more than 50 ms relative to the previous R-R (pNN50), both used as indirect measures of parasympathetic tone. Frequency domain analysis was carried out to determine the spectral power density, which was decomposed in a low frequency (LF) band (0.04–0.15 Hz) and a high frequency (HF) band (0.15–0.4 Hz). Normalized spectral power of the LF and HF bands (i.e., the power of these bands divided by the total spectrum power), as well as, the LF/HF ratio were used for statistical analysis [15–17].

Additionally, a lying-to-standing test was performed following recommendations from Ewing et al. [18]. After 5 min of bed rest, the subjects stood up as quickly as possible and remained standing for 2 min. The 30:15 ratio (i.e., the ratio of the longest R-R interval around the 30th beat to the shortest R-R interval around the 15th beat after posture change) was calculated as recommended by Ewing et al. [18]. This index (i.e., 30:15 ratio) reflects the activity of both parasympathetic and sympathetic autonomic nervous system activity, but, differently from other HRV-studied parameters, the 30:15 ratio reflects the parasympathetic modulation of the heart during a dynamic condition [18]. The studied population was stratified according to the results from the 30:15 ratio. For analysis, the criteria proposed by Boer et al. [19], which classifies the subjects as normal (≥1.01) and abnormal (≤1.00), was considered. The normality of the data distribution was verified by using the Kolmogorov–Smirnov test, and as the data were not normally distributed, the median and interquartile range of the studied variables were computed for the total population.

The indices obtained by time (rMSSD, pNN50) and frequency (LF, HF, LF/HF) domain from person with (DM+) and without (DM−) diabetes mellitus were compared using the Mann-Whitey test. The chi-square (χ^2) test was applied to compare the proportions between groups DM+ and DM− for the autonomic test outcomes (i.e., normal or abnormal response of 30:15 ratio). A significance level of $P < 0.05$ was used with all statistical procedures. Statistical analysis was completed using SPSS 21.0 (SPSS Inc., Chicago, IL).

3. Results

During the period from February to April 2013, a total of 205 individuals were interviewed and examined, including 37 DM+ (13 men aged 71.62 [SD, 7.27] years and 24 women aged 70.25 [SD, 6.66] years) and 168 DM− (71 men aged 72.25 [SD, 8.24] years and 97 women aged 71 [SD, 6.79] years (Table 1).

Table 1 – Characteristics of studied elders from Aiquara-BA, Brazil.

		n	%
Sex	Female	120	58.5
Race/color	Non White	170	82.9
Diabetes mellitus	Present	37	18.0
Hypertension	Present	141	68.8
Family income	≤1 Salary	166	81.0
Smoking habit	Absent	114	55.6

Table 2 – Frequency domain parameters (LF and HF bands, LF/HF ratio) from DM+ and DM− elders dwellers in Aiquara-BA.

	DM+	DM−	Total	P*
Low frequency (LF)	52.55 (42.86–57.31)	58.41 (50.90–58.11)	53.41 (50.49–56.91)	0.33
High frequency (HF)	47.12 (42.47–56.79)	41.53 (41.53– 48.66)	46.20 (42.74–49.09)	0.31
Ratio LF/HF	1.12 (1.06–2.19)	1.40 (1.79–2.53)	1.36 (1.75–2.39)	0.21

Values are median and interquartile range.
* Mann–Whitney test.

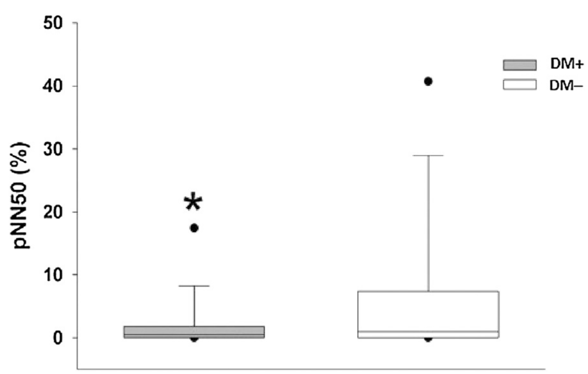

Fig. 1 – Parasympathetic tone, measure through pNN50, from DM+ (*n* = 37) and DM− (*n* = 168) elders from Aiquara-BA. *Significant difference between groups (P < 0.05).

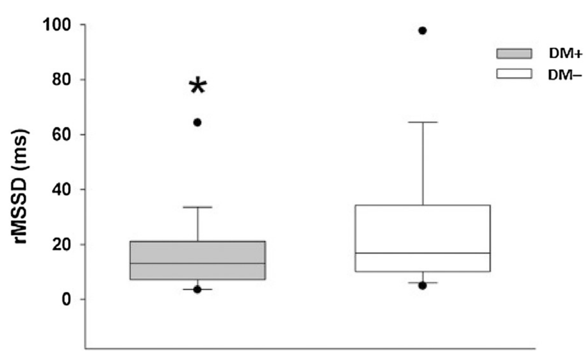

Fig. 2 – Parasympathetic tone, measure through rMSSD, from DM+ (*n* = 37) and DM− (*n* = 168) elders from Aiquara-BA. *Significant difference between groups (P < 0.05).

Comparisons between DM+ and DM− did not showed differences for LF and HF bands as well as the LF/HF ratio ($P > 0.05$). Table 2 presents the results from frequency domain analysis.

Differently, the studied time domain parameters, rMSSD and pNN50, showed a significant difference between DM+ and DM− elders ($P < 0.05$). The median of rMSSD was 14.21 (interquartile range, 9.69–23.63) and pNN50 0.55 (interquartile range, 0.00–3.63), Figs. 1 and 2 show the pNN50 and rMSSD results, respectively. It was observed that DM− elders exhibit greater rMSSD and pNN50, indicating a greater parasympathetic tone at rest.

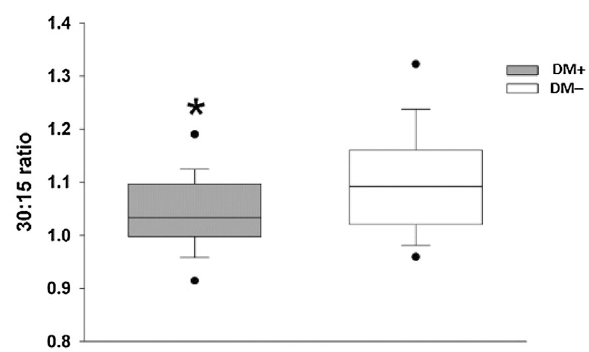

Fig. 3 – Parasympathetic modulation during the lying-to-standing test, measure through 30:15 ratio, from DM+ (*n* = 36) and DM− (*n* = 156) elders from Aiquara-BA. *Significant difference between groups (P < 0.05).

The results from 30:15 ratio, median of 1.08 (interquartile range, 1.02–1.15), obtained during the lying-to-standing test, are shown in Fig. 3 and showed a significant difference between DM+ and DM− elders ($P < 0.05$). It is important to note that the 30:15 ratio was obtained in 192 individuals, because 13 individuals were not able to perform the lying-to-standing test.

According to the adopted classification for the 30:15 ratio, 20.3% (*n* = 39) were classified as abnormal responses and 79.7% (*n* = 153) as normal. Stratifying subjects by groups, a significant trend ($P = 0.03$) was observed, with an abnormal parasympathetic response and posture change in DM+ elders, since 33.3% of them showed an abnormal 30:15 ratio, while only 17.5% of DM− showed an abnormal result. The distribution according the DM+ and DM− group is shown in Table 3.

4. Discussion

We examined some parameters of short-term HRV and its association with diabetes mellitus in an elderly sample from a small town in Brazil. A significant difference between DM+ and DM− elders was observed for some indexes of parasympathetic modulation of the heart (RMSSD and ratio 30:15). HRV parameters from frequency domain decreased in DM+ subjects, but did not achieve statistical significance. Autonomic control of the heart through HRV assessment is inexpensive, easy and non-invasive. For these reasons, it is a potential candidate to be a good predictor of cardiovascular diseases in healthy and unhealthy subjects. A low HRV is associated with a risk increase of 32–45% to a first cardiovascular event in a population with no cardiovascular disease [20,21].

Table 3 – Ratio 30:15 results from DM+ and DM− elders dwellers in Aiquara-BA.

	DM+ (*n* = 36)		DM− (*n* = 154)	
	n	%	*n*	%
Normal ratio 30:15	24	66.7	129	82.5
Abnormal ratio 30:15	12	33.3	27	17.5

An impaired autonomic control of the heart, characterized by a hyperactive sympathetic system and a hypoactive parasympathetic system, may be associated with various pathological conditions [21,22]. Specifically, a poor parasympathetic activity has been associated with a wide range of conditions including cardiovascular diseases [22]. Impairment of vagal modulation can be measured by values of pNN50 < 3% and rMSSD < 25 [9]. Our results of time domain parameters evidenced a significant difference between DM+ and DM− elders for rMSSD and pNN50. Based on the premise that values of pNN50 < 3% and rMSSD < 25 indicate impaired vagal modulation, we found that ~63.9% (61.9% for pNN50 and 66.0% for rMSSD) of DM− and ~82.4% (81.0% for pNN50 and 83.7% for rMSSD) of DM+ elders showed this deleterious condition. These findings corroborate previous studies that found an age-related change in all parameters of HRV due to aging, especially in parasympathetic cardiac activity indexes [23,24]. Additionally, the greater proportion of DM+ elders with suggested, impaired vagal modulation may suggest that diabetes mellitus hastens the age-related changes in the autonomic control of the heart.

It is proposed that elevated blood glucose levels have an adverse effect on cardiac autonomic function. The found abnormalities by this research in time domain (pNN50 and rMSSD) are consistent with previous studies that found reduced vagal activity in diabetic patients suggesting parasympathetic damage [25,26]. Interestingly, there is a hypothesis that ANS dysfunction precedes the onset of diabetes mellitus, once the pancreas is highly innervated with parasympathetic fibers [27]. Notwithstanding, the cardiac autonomic impairment seems to be present in early stages of diabetic metabolic impairment and progressively worsens. DM+ subjects who participated in a cohort study showed a faster temporal decrease in HRV than DM− ones, suggesting that they had lower time domain parameters of HRV (SDNN, rMSSD and RR interval) than DM− individuals [9,28,29].

Frequency domain analysis of HRV from DM+ and DM− elders showed a decreased LF and LF/HF ratio for DM−, and greater HF values for DM+. However, differently from time domain parameters of HRV, there was no significant difference between DM+ and DM− elders for frequency domain parameters. The reason for the absence of statistical significant difference between DM+ and DM− elders could be attributed to the fact that frequency domain measures of HRV require more sophisticated techniques and are subject to greater error than time domain measures [8]. Another widely used parameter to identify autonomic dysfunction is the 30:15 ratio and in this study we found a difference between the DM+ and DM− groups [30,31]. Long-term results show that the 30:15 ratio average gradually decreases with time in DM+ patients and have an independent predictive value with regard to all-cause mortality [31]. Even though we have not followed the subjects for any time period, a reduction in this index of parasympathetic modulation among DM+ patients was demonstrated by us. This may be due to a decreased vagal tone, possibly owing to vagal nerve injury by the long duration of diabetes mellitus [32,33].

As exposed previously, as well as the pNN50 and rMSSD, the 30:15 ratio reflects the parasympathetic modulation of the heart, but it is obtained during a dynamic condition, thus being indicative of vagal cardioprotection during many daily tasks where postural changes are necessary [34].

5. Conclusions

Our study showed difference between the studied groups, especially at time domain parameters related to parasympathetic activity, suggesting that elders with diabetes mellitus have a worse parasympathetic modulation. Since HRV assessment is inexpensive, easy and non-invasive, we suggest the use of this tool for identifying DM+ elders with impaired vagal cardioprotection, allowing immediate therapeutic interventions.

Conflict of interest

All authors declare no conflict of interest.

Ethical approval

This article does not contain any studies with human participants performed by any of the authors.

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REFERENCES

[1] Koehlmoos TP, Anwar S, Cravioto A. Global health: chronic diseases and other emergent issues in global health. Infect Dis Clin North Am 2011;25:623–38. ix.

[2] WHO. World health statistics 2012. Geneva: World Health Organization; 2012.

[3] Voss A, Heitmann A, Schroeder R, Peters A, Perz S. Short-term heart rate variability – age dependence in healthy subjects. Physiol Meas 2012;33:1289–311.

[4] Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, Paciorek CJ, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. Lancet 2011;378:31–40.

[5] Petrofsky J, Berk L, Al-Nakhli H. The influence of autonomic dysfunction associated with aging and type 2 diabetes on daily life activities. Exp Diabetes Res 2012;2012:657103.

[6] Makrantonaki E, Schönknecht P, Hossini AM, Kaiser E, Katsouli M-M, Adjaye J, et al. Skin and brain age together: the role of hormones in the ageing process. Exp Gerontol 2010;45:801–13.
[7] Makrantonaki E, Zouboulis CC. Dermatoendocrinology. Skin aging. Hautarzt 2010;61:505–10.
[8] De Meersman RE, Stein PK. Vagal modulation and aging. Biol Psychol 2007;74:165–73.
[9] Xhyheri B, Manfrini O, Mazzolini M, Pizzi C, Bugiardini R. Heart rate variability today. Prog Cardiovasc Dis 2012;55:321–31.
[10] Astrup AS, Tarnow L, Rossing P, Hansen BV, Hilsted J, Parving H-H. Cardiac autonomic neuropathy predicts cardiovascular morbidity and mortality in type 1 diabetic patients with diabetic nephropathy. Diabetes Care 2006;29:334–9.
[11] Taçoy G, Açikgöz K, Kocaman SA, Ozdemir M, Cengel A. Is there a relationship between obesity, heart rate variability and inflammatory parameters in heart failure? J Cardiovasc Med (Hagerstown) 2010;11:118–24.
[12] Brasil MdS. Estatudo do Idoso 1a. Brasília: Ministério da Saúde; 2003.
[13] IBGE IBdGeE. IBGE Cidades; 2012, Available from: http://www.ibge.gov.br/cidadesat/topwindow.htm?1.
[14] Gamelin FX, Berthoin S, Bosquet L. Validity of the polar S810 heart rate monitor to measure R-R intervals at rest. Med Sci Sports Exerc 2006;38:887–93.
[15] Task Force TF of TES of C and TNAS of P and E. Guidelines Heart rate variability. Eur Heart J 1996;17:354–81.
[16] Rolim LCdSP, Sá JRd, Chacra AR, Dib SA. Neuropatia autonômica cardiovascular diabética: fatores de risco, impacto clínico e diagnóstico precoce. Arq Bras Cardiol 2008;90:e24–32.
[17] Vanderlei LCM, Pastre CM, Hoshi RA, Carvalho TD, Godoy MF. Noções básicas de variabilidade da frequência cardíaca e sua aplicabilidade clínica. Rev Bras Cir Cardiovasc 2009;24:205–17.
[18] Ewing DJ, Martyn CN, Young RJ, Clarke BF. The value of cardiovascular autonomic function tests: 10 years experience in diabetes. Diabetes Care 1985;8:491–8.
[19] Boer CAdA, Mocelin AJ, Matsuo T. Validação dos testes de Ewing para avaliação de disfunção autonômica. Arq Neuropsiquiatr 1998;56:250–4.
[20] Hillebrand S, Gast KB, de Mutsert R, Swenne CA, Jukema JW, Middeldorp S, et al. Heart rate variability and first cardiovascular event in populations without known cardiovascular disease: meta-analysis and dose–response meta-regression. Eur Pac Arrhythmias Card Electrophysiol 2013;15:742–9.
[21] Pumprla J, Howorka K, Groves D, Chester M, Nolan J. Functional assessment of heart rate variability: physiological basis and practical applications. Int J Cardiol 2002;84:1–14.
[22] Thayer JF, Lane RD. The role of vagal function in the risk for cardiovascular disease and mortality. Biol Psychol 2007;74:224–42.
[23] Bonnemeier H, Richardt G, Potratz J, Wiegand UKH, Brandes A, Kluge N, et al. Circadian profile of cardiac autonomic nervous modulation in healthy subjects: differing effects of aging and gender on heart rate variability. J Cardiovasc Electrophysiol 2003;14:791–9.
[24] Reardon M, Malik M. Changes in heart rate variability with age. Pacing Clin Electrophysiol 1996;19:1863–6.
[25] Tarvainen MP, Lipponen JA, Al-Aubaidy H, Jelinek HF. Effect of hyperglycemia on cardiac autonomic function in type 2 diabetes. Comput Cardiol (2010) 2012;39:405–8.
[26] Alves RL, Freitas FM, Fernandes ASN, Ferraz SC, Silva Ed, Corrêa CL, et al. Modulação autonômica e capacidade funcional em indivíduos portadores de diabetes mellitus do tipo 1 e 2. J Hum Growth Dev 2012;22:321–7.
[27] Carnethon MR. The association among autonomic nervous system function, incident diabetes, and intervention arm in the diabetes prevention program. Diabetes Care 2006;29:914–9.
[28] Schroeder EB, Chambless LE, Liao D, Prineas RJ, Evans GW, Rosamond WD, et al. Diabetes, glucose, insulin, and heart rate variability: the Atherosclerosis Risk in Communities (ARIC) study. Diabetes Care 2005;28: 668–74.
[29] Singh JP, Larson MG, O'Donnell CJ, Wilson PF, Tsuji H, Lloyd-Jones DM, et al. Association of hyperglycemia with reduced heart rate variability (The Framingham Heart Study). Am J Cardiol 2000;86:309–12.
[30] Makwana K, Kalasava K, Mehta H. Prognosis of cardiac autonomic neuropathy in patients with diabetes mellitus. Int J Diabetes Res 2013;2:1–5.
[31] May O, Arildsen H. Long-term predictive power of simple function tests for cardiovascular autonomic neuropathy in diabetes: a population-based study. Acta Diabetol 2011;48:311–6.
[32] Vinik AI, Erbas T, Casellini CM. Diabetic cardiac autonomic neuropathy, inflammation and cardiovascular disease. J Diabetes Investig 2013;4:4–18.
[33] Spallone V, Ziegler D, Freeman R, Bernardi L, Frontoni S, Pop-Busui R, et al. Cardiovascular autonomic neuropathy in diabetes: clinical impact, assessment, diagnosis, and management. Diabetes Metab Res Rev 2011;27:639–53.
[34] Zhao M, Sun L, Liu J-J, Wang H, Miao Y, Zang W-J. Vagal nerve modulation: a promising new therapeutic approach for cardiovascular diseases. Clin Exp Pharmacol Physiol 2012;39:701–5.