ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 11, Issue, 04, pp. 46526-46530, April, 2021
https://doi.org/10.37118/ijdr.21707.04.2021

RESEARCH ARTICLE OPEN ACCESS

ASSESSMENT OF DRUG USE AND QUALITY OF LIFE IN PATIENTS WITH TYPE 2 DIABETES USING VILDAGLIPTIN AND SPECKLE TRACKING CHANGED

Raldner Borges Réges[1] and Maíla Martins Oliveira[*2]

[1]São João de Deus Health Complex. Divinópolis, Minas Gerais, Brazil
[2]State University of Minas Gerais. Divinópolis, Minas Gerais, Brazil

ARTICLE INFO

Article History:
Received 13th January, 2021
Received in revised form
14th February, 2021
Accepted 06th March, 2021
Published online 30th April, 2021

Key Words:

Diabetes mellitus, Quality of life, Medication use, Chronic disease, Health education.

Corresponding author:
Raldner Borges Réges

ABSTRACT

Introduction: It is of key importance to assess medication use in type 2 diabetes mellitus patients. Quality of life should also be investigated, as it may be affected by the required therapeutic strategies. **Objective:** Assessing medication use and quality of life in type 2 diabetes mellitus patients using vildagliptin. **Materials and methods:** It is a longitudinal, prospective and intervention study. Sociodemographic, clinical, and other three tools were collected. Two for quality-of-life assessment and one for medication use assessment. The 32 patients were followed for seven months and received vildagliptin. Speckle tracking echocardiography, laboratory tests, follow-up with cardiologist, endocrinologist and weekly empowerment workshops with a multidisciplinary team were performed, as well as telephone contact. **Results:** When comparing B-PAID and WHOQOL-bref scores before and after the intervention, p-value was <0.001 in all domains. Regarding speckle tracking, there was improvement, and the mean speckle tracking of patients was -15.4% and -17.6%. Patients' mean glycated hemoglobin was 9.5% and at the end of the intervention was 6.9%. Regarding medication use, at the end of the intervention, patients were engaged. It was also observed improvement of hemodynamic parameters and physical fitness, with proportional increase of the metabolic equivalent value. **Conclusions:** The empowerment program associated with treatment optimization and medication use improved the metabolic control of type 2 diabetes mellitus in users of this study.

Citation: ***Raldner Borges Réges and Maíla Martins Oliveira.*** **2021.** "Assessment of drug use and quality of life in patients with type 2 diabetes using vildagliptin and speckle tracking changed", *International Journal of Development Research*, 11, (04), 46526-46530.

INTRODUÇÃO

Type 2 diabetes mellitus is the most frequent type and corresponds to approximately 90% of cases of diabetes mellitus, affecting mainly the adult, although its diagnosis has been increasing in children and adolescents. It is a disease of multifactorial etiology, presenting as risk factors obesity, advanced age, family history and sedentary lifestyle, but the genetic factor is dominant (CDC, 2016). Currently there are accurate methods and subclinical diagnosis of micro and macrovascular lesions, among these, speckle tracking, which is an echocardiographic technique that, unlike the previous ones, has better accuracy and is easy to use at the bedside (Omoto et al., 1984). In addition to the early diagnosis of complications, the evaluation of drug treatment, as well as the quality of life of patients with diabetes mellitus, is essential to achieve metabolic control and prevention of chronic complications.

MATERIALS AND METHODS

This is a larger longitudinal intervention study conducted from April 2017 to November 2017.

The study was carried out at the outpatient clinic of metabolic endocrine diseases of the São João de Deus Health Complex, in the city of Divinópolis, MG, in the Unified Health System sector. Patients with type 2 diabetes mellitus were approached during the routine of their outpatient consultations, having as inclusion criteria:patients of both sexes, between 18 and 60 years old, with decompensated type 2 diabetes mellitus, with HbA1c greater than 7.0%, non-adherent to drug treatment, evaluated by the measure of treatment measure (MAT) and with speckle tracking greater than -20% and exclusion: pregnant women and patients with end-stage failure on hemodialysis,patients who discontinue treatment and/or do not attend any of the workshops, illiterate patients and non-consent to participate in the research. Data collection occurred in three moments. At the first moment, called moment 1 (M1), which occurred in April 2017, patients were selected. Patients who were not engaged to treatment were approached by applying the MAT questionnaire. The MAT questionnaire is an instrument used to evaluate the patient's behavior in relation to the daily use of prescribed drugs, composed of seven items, on a Likert scale of six points, from 1 (always) to 6 (never) (Delgado and Lima, 2001). Patients whose MAT result was below 3.0 were considered non-engaged to treatment. As the altered speckle tracking and the HbA1C > 7.0%, were also inclusion criteria, these were the first tests to be

performed after the questionnaire was applied. The sample consisted of 32 patients (NO=32). After the sample was defined, a few more complementary laboratory tests were performed. After laboratory tests, the following questionnaires were applied: B-PAID and WHOQOL-bref. Data collection was chosen in the form of an interview, considering the possibility of the subjects presenting visual difficulty and low instructional level. During the interview, there was no intervention of the researcher in the patients' answers. Each interview lasted, on average, 10 to 15 minutes. Transthoracic echocardiography was performed using a device (iE 33, Philips) by a trained and registered cardiac echographer, according to a standardized protocol and the recommendations of the Brazilian Society of Echocardiography and Cardiovascular Imaging. The left ventricular ejection fraction was calculated using the Simpson rule (Lang et al., 2005). Screening with speckle tracking was performed with continuous monitoring of the electrocardiogram. The speckels tracking analysis was performed offline using commercially available Philips Advanced Quantification Software (QLAB version 8.1) (Russo et al., 2013). As the longitudinal global speckle tracking (GLS) is represented by negative values, with more negative numbers, it expresses greater systolic shortening and therefore better function. We adopted the terminology "GLS lower" referring to fewer negative values, therefore expressing less systolic shortening. The patients were supplied after the interviews with the drug of the Class of DPP-4 inhibitors, vildagliptin, which was provided free of charge by the São João de Deus Health Complex, where it is standardized, associated with metformin.

The drug was prescribed after consultation with a cardiologist and endocrinologist. At that time, the patients' drug therapy was also optimized, such as the suspension of sulfas in some patients who used this drug, the adjustment of insulin therapy (15 patients in the sample already used insulin), in addition to the optimization of the medications for continuous use of the patient. Patients used individualized treatment throughout the study period. In the second stage of the research, called moment 2 (M2), performed after 3 months of drug treatment maintained and occurred in July 2017, another series of laboratory test were performed and at that moment, the Bruce Protocol was applied, on the treadmill or exercise bike and medical consultations were performed with endocrinologist and cardiologist.The estimated time for the return of this patient was 3 months, because the recommendation of the Brazilian Diabetes Society advises reassessments, every 3 months, after the start of a medication (SBD, 2017). The physical exercise protocol was conducted by a medical professional qualified by the Brazilian Society of Ergometrics and physical educator. The educator was involved in aerobic exercises, localized muscle endurance and flexibility with 2 formats of biweekly sessions lasting 60 min/session. Also, in July 2017, a multiprofessional intervention was initiated, with weekly periodicity and lasting 4 weeks, including nutrition workshops, psychology, nursing and with physical educator. The workshops lasted 50 minutes. In the workshops, actions were carried out with the respective professionals: Nutritionist, Psychologist, Nursing and Physical Educator.At the beginning of November 2017, about 3 months after the end of the workshops, corresponding to the third and final stage of the research (M3), the patients were reevaluated by means of laboratory tests. The speckle tracking and the Bruce Protocol were also performed, in addition to the reapplication of the B-PAID and WHOQOL-bref questionnaires. At that time, the patients received individual care with a cardiologist, endocrinologist and nutritionist.

RESULTS

Thirty-two patients were selected and completed the study, mostly female, aged 37 to 59 years old, with a mean time of diagnosis of the disease of 11.3 ± 8 years. The majority had hypertension (93.8%) and the same percentage was not a smoker (93.8%). About 31% were etilist. Regarding food, most did not diet (96.9%) and only 18.8% of the sample performed physical activity. In relation to functional class, a significant improvement is observed between moment 1 (M1), before the intervention, and moment 3 (M3), after the intervention. Of the 14 patients classified as Functional Class II in M1, all began to be classified as Functional Class I in M3.Of the 14 patients classified as Functional Class III in M1, 13 (92.9%) started to be classified as Functional Class I in M3. Patients who belonged to Functional Class I remained unchanged (Table 1).

Table 1. Functional class, before and after the intervention (NO=32)

M1	M3		Total*
	Functional Class I	Functional Class II	
	n (%)	n (%)	
Functional Class I	4 (100,0%)	0 (0,0%)	4 (100,0%)
Functional Class II	14 (100,0%)	0 (0,0%)	14 (100,0%)
Functional Class III	1 (7,1%)	13 (92,9%)	14 (100,0%)
Total	19 (59,4%)	13 (40,6%)	32 (100,0%)

*McNemar paired test; Value p < 0.001; M1 = moment 1 of the research; M3= moment 3 of the search

There was an improvement in laboratory parameters after the intervention, with the GGT, mean in (M2), was 48.3 U/L and, at the end of the intervention (M3), it was 35.3 U/L. Creatinine (CR) mean, in (M2), was 1.0 mg/dl and, at the end of the intervention (M3), it was 0.9 mg/dl. Regarding the CrCl, in (M2), the average was 79.0 mL/min and at the end of the intervention (M3), it was 90.9 mL/min (p<0.001). Regarding speckle tracking, there was a great improvement, and the average speckle tracking of patients in M1 was approximately -15.4% and in M3, it was -17.6%. The same can be observed in relation to ET, because the mean of patients in (M2) was 4.2 MET and in M3, it was 7.2 MET. There was an increase from M2 to M3 with an average difference of -3.0 MET (Table 2). Drug treatment was evaluated at the first moment of the study, as an inclusion criterion and evaluated in M3 after the intervention. The initial mean was 2.5 points in the MAT questionnaire at the beginning of the study and, at the end of the intervention, the patients obtained an average of 5.7 points, i.e., previously non-adherent patients, now they were classified as adherent, p<0.001. In the evaluation of quality of life through the B-PAID and WHOQOL-bref scales, there was an improvement in all domains, in the comparison between M1 and M3 (Table 3). It was observed that the B-PAID presented a higher mean score before the intervention (M1), indicating impairment of quality of life in all domains and in the total score compared to the scores after the intervention (M3), (p<0.001). The final score presents an average difference of 43 points from the pre-intervention moment to the post-intervention, evidencing a significant effect of the intervention, that is, better quality of life of patients in view of the items evaluated by B-PAID (Table 3). The WHOQOL-bref presented, in general, in all domains before the intervention (M1), lower mean scores (below 35 points) and at the end of the study (M3), presented higher scores (above 80 points), with an average difference of 50.8 points in the total score, indicating a significant effect of the intervention (p<0.001). Specifically, in all its domains there was improvement, and the physical domain was the one with the highest average difference (51.5 points) from the pre-post moment (p<0.001) (Table 3).

DISCUSSION

In the present study, the mean time of diagnosis of the disease was 11.3 ± 8 years. Ferreira et al. confirm the positive correlation observed between the time of diagnosis of diabetes mellitus and the B-PAID score, which indicates suffering (Ferreira et al., 2013). In another study, it was found that most patients had a diagnosis time between 10 and 20 years (Bernini et al., 2017).The longer the time of diagnosis, the more complications worsen, and treatment intensifies, leaving individuals with more distress and vulnerable. The context that involves the diagnosis of diabetes mellitus, the burden of information about the disease, its complications, health care, lifestyle changes, among others, are often generators of emotional stress.

adhering to diabetes mellitus control is the main cause for the

Table 2. Laboratory exams, image and exercise test, before and after the intervention (NO=32)

Comparisons	Average	Standard deviation	Averagedifference	CI 95% foraveragedifference		*p**
SpeckleTracking M1	-15,4	3	2,2	1,1	3,3	<0,001
SpeckleTracking M3	-17,6	3,4				
CT M2	172,1	50,7	13,5	-0,3	27,3	0,056
CT M3	158,6	42,1				
LDL M2	97,8	39,4	13,9	3,3	24,6	0,012
LDL M3	83,8	31,3				
HDL M2	43,9	8,3	-1,3	-4,5	1,9	0,416
HDL M3	45,2	11,4				
TRGL M2	174,4	93	26,8	0	53,7	0,05
TRGL M3	147,6	47,8				
TGO M2	25,3	9,1	2,6	0,3	4,9	0,026
TGO M3	22,6	7,1				
TGP M2	26,9	12,7	3,8	0,8	6,8	0,014
TGP M3	23,1	10				
GGT M2	48,3	29,2	13	5,6	20,4	<0,001
GGT M3	35,3	15,5				
Ur M2	41,8	14,3	4	0,9	7,1	0,014
Ur M3	37,8	9,3				
Cr M2	1	0,3	0,1	0,1	0,2	<0,001
Cr M3	0,9	0,2				
ClCr M2	79	24,7	-11,9	-17	-6,8	<0,001
ClCr M3	90,9	26,6				
MET M2	4,2	1,9	-3	-3,7	-2,3	<0,001
MET M3	7,2	2,7				

*Paired T-test; 95% CI = confidence interval; M1 = moment 1 of the research; M2 = moment 2 of the research; M3 = moment 3 of the research; CT = total cholesterol; LDL = low density lipoprotein; HDL = high density lipoprotein; TRGL = triglycerides; TGO = glutamic-oxalacetic transaminase; TGP = glutamic-pyruvic transaminase; GGT = GT range; Ur = urea; Cr = creatinine; ClCr = creatinine clearance; MET = metabolic equivalent.

Table 3. Comparison of the scores of the B-PAID and WHOQOL-bref scales, before and after the intervention (NO=32)

Variables	NO	Average	Standard deviation	Averagedifference	CI 95% for averagedifference		*p**
B-PAID							
Emotional Domain							
M1	32	38,9	11	25,6	19,7	31,5	<0,001
M3	32	13,3	14				
Domain Treatment							
M1	32	7,7	2,9	6,5	5	7,9	<0,001
M3	32	1,2	2,9				
Domain Feeding							
M1	32	10,1	2,9	6,6	5	8,2	<0,001
M3	32	3,6	3,5				
Social Domain							
M1	32	5,8	2,2	4,5	3,6	5,4	<0,001
M3	32	1,3	1,9				
Total Score							
M1	32	62,4	17,5	43	33,9	52,1	<0,001
M3	32	19,4	21				
WHOQOL - BREF							
Physical Domain							
M1	32	31,8	21	-51,5	-60,9	-42	<0,001
M3	32	83,3	11,1				
Psychological Domain							
M1	32	33,9	24	-50,7	-60	-41,3	<0,001
M3	32	84,5	10				
Social Domain							
M1	32	33,9	26,9	-51	-62	-40,1	<0,001
M3	32	84,9	14,3				
Environmental Domain							
M1	32	34	18	-49,9	-57,6	-42,2	<0,001
M3	32	83,9	9				
Final Score							
QV M1	32	33,4	20,9	-50,8	-59,5	-42	<0,001
QV M3	32	84,1	8,4				

*Paired T-test; M1 = moment 1 of the research; M3 = moment 3 of the research; 95% CI = confidence interval; QOL = quality of life.

Drastic changes in lifestyle have repercussions on psychic and social aspects, directly reflecting on their quality of life (Silva-e-Oliveira et al., 2017). In the investigation of drug treatment at both moments, a positive evaluation was obtained. Compliance with the dosing schedule is directly conditional on therapeutic efficacy, and adherence to therapy is essential, which occurs in compliance with verbal and written instructions by a health professional in relation to pharmacological treatment (Dossa et al., 2015). Lack of treatment life. They represent individual, social, economic costs for the patient, the family, health institutions and society (Oliveira et al., 2013). One of the factors related to low drug use is financial. Although some medications are provided by the Unified Health System, they are not always available. According to a study conducted with 216 patients with type 2 diabetes mellitus in Tanzania, the reasons for low use are more frequently related to the high cost of medications (Rwegerera, 2014). Another study shows that those who had to pay part of the

treatment had about 80.0% lower treatment and the polytherapy used in therapeutic regimens for type 2 diabetes mellitus favored 2.4 times lower treatment support compared to those who used only one drug (Tavares et al., 2016). The combination of therapy, in a rational way, can maximize the control of target parameters, together with glycemic control, to minimize risks, reduce the chances of the emergence and development of comorbidities and enable lower spending of health services with these patients (Penaforte et al., 2017). Most complications of type 2 diabetes mellitus patients can be prevented through good disease control, which should be pursued by the entire team of professionals who assist diabetic patients. The therapeutic approach to this disease goes beyond the prescription of hypoglycemic drugs, but related to constant education, behavior changes associated with healthy eating and physical activity (Boscariol et al., 2018).The overall evaluation scale does not specify WHOQOL-bref showed improvement in quality of life. The domain of the WHOQOL-bref where the highest satisfaction occurred after the intervention was the physical domain. Further studies evaluating the various types of physical exercise, volume and intensity are necessary (Ely et al., 2017). The practice of physical exercise is one of the main ways to reduce the risk of type 2 diabetes mellitus and several other chronic diseases, such as heart diseases. Its role in the control of diabetes mellitus is related to glucose metabolism, reduction of body fat and efficacy against insulin resistance, since it induces skeletal muscles to make use of insulin for energy metabolism (Carvalho et al., 2015). It is observed in the results of the research, that patients are currently with glycemic control within the goal recommended by the Brazilian Diabetes Society. Although the quality of life in diabetic patients depends on numerous variables, the presence of complications seems to be the most important determinant for this satisfaction and well-being of patients, and adequate glycemic control is associated with a better quality of life (Depablos-Velasco et al., 2014).

The results found in the B-PAID scale corroborate our findings on the life satisfaction scale, this has an inverse relationship between the score and quality of life, and we can observe that the patients presented a great improvement in satisfaction with quality of life. Corroborating our findings, another study shows the decrease in means on the B-PAID scale (Brito et al., 2016). In relation to echocardiography with speckle tracking, this is an emerging echocardiographic technique that allows characterizing myocardial deformation, producing advanced measures of systolic and diastolic function (Mátyás et al., 2018; Bauer et al., 2011). In this study, during speckle tracking, it was observed that even patients who had the left ventricle ejection fraction preserved or with subclinical findings had altered longitudinal tracking speckle and were metabolically decompensated.Corroborating our findings, another study mentions that the measurements derived from the 3D-STE of GLS were impaired, and the ejection fraction of the left ventricle was preserved in patients with type 2 diabetes mellitus. According to this author, GLS was related both to the presence and accumulation of diabetic microvascular complications and especially to cardiac autonomic neuropathy (Enomoto et al., 2016). A meta-analysis of 16 studies showed that GLS has a higher prognostic value than the left ventricular ejection fraction to predict major cardiac events and the entire cause of mortality (Kalam et al., 2014). Two recent studies: NOMAS and CABL deserve to be highlighted because they have identified that GLS is an independent predictor of incident cases of atrial fibrillation, subclinical brain disease, HF and the combined outcome of myocardial infarction, ischemic stroke and cardiovascular death (Russo et al., 2013a; 2013b; 2014).

One study shows that altered HbA1c showed correlation with early change in longitudinal tracking speckle (Pickham et al., 2014). Another study shows these findings, where GLS were found to have decreased slightly in patients with diabetes mellitus with HbA $_{1c}$ <7%, but significantly deteriorated if the blood glucose level was not tightly controlled (HbA $_{1c}$ $\geq$ 7%).The results show that the longitudinal systolic contraction of the VE seems more vulnerable to alterations in myocardial dysfunction, corroborating the findings of some previous studies (Ceyhan et al., 2012; Ernande et al., 2010; Li et al., 2014). This implies that GLS may be a sensitive indicator of preclinical VE dysfunction in patients with diabetes mellitus, particularly in those with uncontrolled blood glucose levels (Zhang et al., 2013). After the intervention, we observed that with the improvement of the patient's speckle tracking, there was concomitantly clinical, laboratory and functional class improvement. Diabetic cardiomyopathy is often associated with the development of heart failure. In this sense, the early identification of left ventricular dysfunction will allow early and effective therapeutic intervention.Cardiac speckle tracking is a useful, noninvasive instrument that assesses structural cardiac changes, such as left ventricular hypertrophy, the severity of systolic and diastolic dysfunction, assuming prognostic value in this group of individuals.

CONCLUSIONS

In respect to the objectives of the study, it was considered that it was possible to evaluate medication adeb and quality of life in patients with type 2 diabetes mellitus, in addition to evaluating treatment adhering by validated questionnaires and analysis of general scores of instruments that assess quality of life. One of the proposals of this research was also to evaluate whether at the end of the program there was an improvement in the speckle tracking and metabolic equivalent, which was evidenced in the results and discussion. At the same time, the patients had improved quality of life and laboratory test results. The limitations found in this study were time because the research took seven months, and the duration of empowerment workshops, which took place for one month.The strength of this study is reflected in the results presented both in the improvement of quality of life and medication adhering, attested by the validated questionnaires, as well as by the clinical, laboratory, imaging and metabolic equivalent improvement.The satisfaction of contributing to the patient's empowerment is unmatched and realizing that he has an intrinsic ability to manage care with his disease, becoming evident how much the support of the multidisciplinary team is necessary. It is expected that this study will contribute to direct health interventions and bring information about patients, aiming to improve the quality of life and self-care of type 2 diabetes mellitus.

ACKNOWLEDGEMENTS

To the Health Complex of São João de Deus, our gratitude and our thank you.

REFERENCES

Bauer M, Cheng S, Jain M, Ngoy S, Theodoropoulos C, Trujillo A, … &Lio R (2011). Echocardiographic speckle-tracking based strain imaging for rapid cardiovascular phenotyping in mice. Circ Res. 108(8):908–16.

Bernini LS, Barrile SR, Mangili AF, Arca EA, Correr R, Ximenes MA, ... & Gimenes C (2017). O impacto do diabetes mellitus na qualidade de vida de pacientes da Unidade Básica de Saúde. CadBras Ter Ocup. 25(3):533-41.

Boscariol R, Ouchi JD, Gonzaga MFN, Maragna RG (2018). Diabetes mellitus tipo 2: educação, prática de exercícios e dieta no controle glicêmico. Rev Saúde em Foco.10:138-50.

Brito GMG, Gois CFL, Zanetti ML, Resende GGS, Silva JRS (2016). Quality of life, knowledge and attitude after educational program for Diabetes. Acta Paul Enferm. 29(3):298-306.

Carvalho SS, Silva TMA, Coelho JMF (2015). Contribuições do tratamento não farmacológico para Diabetes Mellitus Tipo 2. Rev Epidemiol Control Infect. 5(2):1-13.

Centers for Disease Control and Prevention (2016). Basics about diabetes. Atlanta: CDC.

Ceyhan K, Kadi H, Koç F, Çelik A, Öztürk A, Önalan O (2012). Longitudinal Left Ventricular Function in Normotensive Prediabetics: A Tissue Doppler and Strain/Strain Rate Echocardiography Study. JASE. 25(3):359-56.

Delgado AB, Lima ML (2001). Contributo para a validação concorrente de uma medida de adesão aos tratamentos. Psic Saúde & Doenças. 2(2):81-100.

Depablos-Velasco P, Salguero-Chaves E, Mata-Poyo J, Derivas-Otero B, García-Sánchez R, Viguera-Ester P (2014). Quality of life and satisfaction with treatment in subjects with type 2 diabetes: results in Spain of the PANORAMA study. Endocrinol Nutr. 61(1):18-26.

Dossa AR, Grégoire JP, Lauzier S, Guénette L, Siroius C, Moisan J (2015). Association between loyalty to community pharmacy and medication persistence and compliance, and the use of guidelines recommended drugs in type 2 diabetes: a cohort study. Medicine (Baltimore). 94(27):e1082.

Ely KZ, Spode F, Barcella RC, Schonhofen IV, Paiva D, Pohl HH, Possuelo LG (2017). Exercício físico na diabetes mellitus, uma revisão narrativa. Cinergis. 18(Supl1):381-5.

Enomoto M, Ishizu T, Seo Y, Kameda Y, Suzuki H, Shimano H, ... &Aonuma K (2016). Myocardial dysfunction identified by three-dimensional speckle tracking echocardiography in type 2 diabetes patients relates to complications of microangiopathy. J Cardiol. 68(4):282-7.

Ernande L, Rietzschel ER, Bergerot C, De Buyzere ML, Schnell F, Groisne L, … &Derumeaux G (2010). Impaired myocardial radial function in asymptomatic patients with type 2 diabetes mellitus: a speckle-tracking imaging study. J Am SocEchocardiogr. 23(12):1266-72.

Ferreira DSP, Daher DV, Teixeira ER, Rocha IJ (2013). Repercussão emocional diante do diagnóstico de diabetes mellitus tipo 2. Rev Enferm UERJ. 21(1):41-6.

Kalam K, Otahal P, Marwick TH (2014). Prognostic implications of global LV dysfunction: a systematic review and meta-analysis of global longitudinal strain and ejection fraction. Heart. 100(21):1673-80.

Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, … & Stewart WJ (2005). Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr. 18(2):1440–63.

Li R, Yang J, Yang Y, Ma N, Jiang B, Sun Q, Li Y (2014). Speckle tracking echocardiography in the diagnosis of early left ventricular systolic dysfunction in type II diabetic mice. BMC Cardiovasc Disord. 14(141):1-8.

Mátyás C, Kovács A, Németh BT, Oláh A, Braun S, Tokodi M, … &Radovits T (2018). Comparison of speckle-tracking echocardiography with invasive hemodynamics for the detection of characteristic cardiac dysfunction in type-1 and type-2 diabetic rat models. CardiovascDiabetol. 17:1-13.

Oliveira NL, Ribeiro F, Alves AJ, Teixeira M, Miranda F, Oliveira J (2013). Heart rate variability in myocardial infarction patients: effects of exercise training. RevPortCardiol. 32(9):687-700.

Omoto R, Yokote Y, Takamoto S, Kyo S, Ueda K, Asano H, ... &Koyano A (1984). The developmente of real-time two-dimensional Dopller echocardiography and its clinical significance in acquired valvular diseases. With special reference to the evaluation of valvular regurgitation. Jpn Heart J. 25(3):325-40.

Penaforte KL, Araújo ST, Fernandes VO, Barbosa IV,Cestari VRF, Montenegro Jr RN (2017).Association between polypharmacy and the adherence to pharmacological treatment in patients with diabetes. Rev Rene. 18(5):631-8.

Pickham D, Flowres E, Drew BJ (2014). Hyperglycemia is associated with corrected QT prolongation and mortality in acutely ill patients. J Cardiovasc Nurs. 29(3):264-70.

Russo C, Jin Z, Elkind MS, Rundek T, Homma S, Sacco RL, Tullio MRD (2014). Prevalence and Prognostic Value of Subclinical Left Ventricular Systolic Dysfunction by Global Longitudinal Strain in a Community-Based Cohort. Eur J Heart Fail. 16(12):1301-9.

Russo C, Jin Z, Homma S, Elkind MS, Rundek T, Yoshita M, … & Tullio MRD (2013a). Subclinical left ventricular dysfunction and silent cerebrovascular disease: the Cardiovascular Abnormalities and Brain Lesions (CABL) study. Circulation. 128(10):1105–11.

Russo C, Jin Z, Liu R, Iwata S, Tugcu A, Yoshita M, ... &Tullio MRD (2013b). LA Volumes and Reservoir Function Are Associated With Subclinical Cerebrovascular Disease. JACC. 6(3):313-23.

Rwegerera GM (2014). Adherence to anti-diabetic drugs among patients with Type 2 diabetes mellitus at Muhimbili National Hospital, Dar es Salaam, Tanzania- A cross-sectional study. Pan African Medical J. 17(252).

Silva-e-Oliveira J, Amélio PM, Abranches ILL, Damasceno DD, Furtado F (2017). Variabilidade da frequência cardíaca com base na estratificação de risco para diabetes mellitus tipo 2. Einstein (São Paulo). 15(2):141-7.

Sociedade Brasileira de Diabetes (2017). Conduta terapêutica no diabetes tipo 2: algoritmo SBD 2017. São Paulo: SBD.

Tavares NUL, Bertoldi AD, Mengue SS, Arrais PSD, Luiza VL, Oliveira MA, ... &Pizzol TSD (2016). Fatores associados à baixa adesão ao tratamento farmacológico de doenças crônicas no Brasil. RevSaude Publica. 50(supl2).

Zhang X, Wei X, Liang Y, Liu M, Li C, Tang H (2013). Differential Changes of Left Ventricular Myocardial Deformation in Diabetic Patients with Controlled and Uncontrolled Blood Glucose: A Three-Dimensional Speckle-Tracking Echocardiography–Based Study. JASE. 26(5):499-506.

****