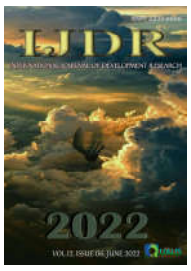
ISSN: 2230-9926

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

IJDR

International Journal of Development Research
Vol. 12, Issue, 06, pp. 56647-56651, June, 2022



RESEARCH ARTICLE OPEN ACCESS

AUTONOMIC FUNCTION EVALUATED BY EWING METHOD IN POST-COVID INDIVIDUALS IN THE MUNICIPALITY OF GURUP-TO

Wellington Carlos Da Silva[1], Bruno Victor Mendes Silva[2], Irla Dos Santos Oliveira[2], Anna JúliaGuedes De Miranda[2], GuilhermeFavaroBoracini[2] ,João Victor Moreira Barbosa Ribeiro[2], Rafaela Chaves Campos[2], Sávia Denise Herreira[3], Kenianogueiraayresargeo[3] and Waghner Frank Ribeiro Pereira[4]

[1]Academic of the Physiotherapy course at Gurupi University - Unirg; [2]Academic of the medical course of gurupi university – Unirg; [3]Professor of the Physiotherapy course – Unirg; [4]Graduated in Physiotherapy

ARTICLE INFO

Article History:
Received 10th March, 2022
Received in revised form
27th April, 2022
Accepted 19th May, 2022
Published online 22nd June, 2022

Key Words:
Heart Rate Variation,
Autonomic Nervous System,
Ewing Tests.

Corresponding author:
Kilma Manso R. da Rocha

ABSTRACT

Introduction: heart because it is an organ possessing its own ritmicity, needs to be regulated moment-to-moment to respond adequately to stimuli both endogenous and exogenous to the organism and such modulation is exerted by action of the Autonomous Nervous System (ANS) by two antagonistic pathways, the sympathetic trunk and the vagal parasympathetic, which together dictate the ritmicity and the natural variability of the frequency (HRV). From several clinical trials and varied methodologies proposed to study and understand the control of THE exercised over the heart, the five Ewing tests have been increasingly validated in the scientific environment and accepted for showing good results under epidemiological focus, making it possible to evaluate the degree of integrity of the connection between neural systems and the cardiac motor. Although still limited, evidence obtained from patients with covid-19 suggests that the virus has disproportionately affected preexisting cardiovascular diseases, as well as other comorbidity conditions, including diabetes and chronic respiratory diseases. Objective: to evaluate, through clinical trials of Ewing, the integrity of the ANS of 19 post-covid patients registered and seen at the Clinical School of Physiotherapy of the University of Gurupi (CEF-UnirG). The benefit will be extended to non-patients of CEF-UnirG, but recovered from covid-19. The project will run only when it receives final cep-unirg approval. Material and Method: 150 participants will be recruited composing the sample of post-covid 19 individuals, all with signatures in the TCLE. The basic instrumentation will be an electrocardiograph (ECG) and a blood pressure meter (BP) and protocols for the application of the five clinical trials of Ewing of a noninvasive nature, three related to the parasympathetic through measurements of the magnitudes of HRV and two of the sympathetic function involving blood pressure variation (APV). For this, ECG and BP data will be quantified, defined and expressed as intervals and/or indicators, which are compared with the normality standards proposed by Ewing et al. will determine the level of sensitivity and specificity, in addition to the degree of reproducibility, providing the methodological viability of Ewing tests in the evaluation of the integrity of THE in post-covid individuals 19.

Citation: ***Marclineide Nóbrega de Andrade Ramalho, Larissa Layne Soares Bezerra Silva, Paula Daniella de Abreu et al.*** "Autonomic function evaluated by ewing method in post-covid individuals in the municipality of gurup-to*", International Journal of Development Research*, 12, (06), 56647-56651.

INTRODUCTION

The heart is an organ consisting of syticial tissues, whose cells or cardiomyocytes have their own ritmycity. This property is under the command of pacemaker cells, capable of spontaneously generating action potentials that propagates radiating to the walls of the four cardiac chambers, responsible for generating mechanical work, blood ejection (systole) and blood filling (diastole).

Heart rate (HR) is the rhythmic rate in beats per minute (BPM), and its neural regulation is performed by the Autonomic Nervous System (ANS). The ANS originates in the Central Nervous System (CNS) in the bulbar part of the brainstem and has two branches, the sympathetic, which acts on the entire myocardium and the parasympathetic via vagus nerve, which acts on the sinoatrial node (SA, pacemaker region), atrial myocardium and atrioventricular node (AV). The electrical impulses, under joint action of the ANS, from

the SA node, propagate throughout the atrial mass before being transmitted to the ventricular myocardial mass via av node and perform rhythmic contractions, boosting and returning instant-to-instant, the blood mass as cardiac output (DC) to the whole organism. These two autonomic pathways operate tonically, moment-by-moment, in an antagonistic way, where the sympathetic increases HR, while the parasympathetic decreases HR, and at any time may have predominance of one over the other. It is for this reason that the changes in HR, sometimes increased (shorthand), sometimes decreased (bradycardia), imposed by the two routes of THE, are normal homeostatic responses to endogenous physiological stimuli or exogenous environmental, such as breathing, physical activities, stress, hemodynamic changes, intermediate metabolism, sleep/wake states, fight/flight reaction, anxiety, stress, etc. reflecting the functional integrity of the SNA. For normotensive individuals, blood pressure (BP) is relatively stable in different parts of the vascular bed, as it is determined almost exclusively by two hemodynamic variables: CD and peripheral vascular resistance (PVR). Roughly, it is defined by: BP= DC x RVP, being CD, in turn, defined by: DC = VS x FC, where VS is systolic volume of ventricular ejection dependent on venous return and both, Vs and HR regulated by the SNA.

The baroreflex system works as follows: in the vascular walls of the aortic arch and carotid sinus, there are glossopharyngeal and vague nerve terminations (baroreceptors) sensitive to pressure increases (increased CD and/or PVR), therefore, when stimulated by stretching, they send electrical impulses to the CNS that inhibits sympathetic discharge in the heart and, via vagus nerve (acetylcholine) decreases in HR and PVR and decrease in BP, a clinical condition known as "vagal brake", that is, a bradycardia. Situations of removal of the vagal brake, are those where the volume of systolic ejection (SV) is below normal decreasing the CD, which promotes bp drop and baroreceptors are not stimulated, removing sympathetic inhibition and prevailing the action of sympathetic terminations (norepinephrine) in the heart with increases in HR and contraction force (aquicardia). From the above, it is clear that cardiac functionality depends on the complexity, especially on the integrity of the baroreflex system interposed between the heart and the CNS mediated via ANS. There are several clinical trials and varied methodologies to study and evaluate this reflex circuit, among them the Ewing tests, which show operational practicality and easy assimilation in understanding their constructs and theoretical foundations compared to other methods. There are five trials proposed by Ewing, three of them measure the frequency variations (HRV) associated with the performance of the parasympathetic autonomic system and two measuring the variations in blood pressure associated with the actions of the sympathetic system. In the current pandemic, evidence obtained from patients with covid-19, although restricted to notifications and still limited to extensive studies, suggests that the virus has disproportionately affected preexisting cardiovascular diseases, as well as other comorbidity conditions, including diabetes and chronic respiratory diseases. These were the starting point for the elaboration of this project, which aims to evaluate, through clinical trials of Ewing, the integrity of the ANS of post-covid patients registered and seen at the Physiotherapy School Clinic of the University of Gurupi (CEF-UnirG), extending the benefit to non-patients of CEF-UnirG, but recovered from covid 19 in the municipality of Gurupi-TO.

METHODOLY

Indivíduos que serão recrutados para compor o tamanho amostral, são pacientes pós-covid 19, cadastrados e atendidos na Clínica Escola de Fisioterapia da Universidade de Gurupi (CEFUNIRG) e participantes voluntários do município de Gurupi que foram infectados por Covid 19 e recuperados. O local de atendimento, recrutamento e cadastro será na recepção da CEFUNIRG, onde panfletos serão entregues para os possíveis participantes, tanto para os já cadastrados pós-covid, quanto para os não cadastrados, porém para estes, com a condição de apresentar documentos referentes a alta e/ou recuperados de covid 19 (apêndice 1), explicando o teor da pesquisa e o seu objetivo junto com nomes dos pesquisadores e formas de contato (telefone, Whatzapp ou redes sociais). Uma vez o indivíduo e/ou o paciente desejar se voluntariar para este projeto, será fornecido um questionário (apêndice 3), junto com o Termo de Consentimento Livre e Esclarecido (TCLE, anexo) que deverá ser preenchido com dados pessoais e contato para agendar data e horário declarado pelo participante. O local onde serão realizados os ensaios é uma sala no interior da CEFUNIRG destinada para atendimento de pacientes pós-covid 19 de Reabilitação Cardiopulmonar, contendo no seu interior os seguintes equipamentos: ciclo ergométrico (bicicleta e esteira), esfigmomanômetro, estetoscópio, oxímetro de pulso, dinamômetro manual, cronômetro, concentração de O2, maca cirúrgica e cadeira para repouso, exceto o Eletrocardiógrafo que será emprestado do laboratório de Fisiologia e Biofísica para finalidades deste projeto de pesquisa.

Inclusion Criteria: It will be included post-covid patients 19 seen at the Cliníca School of Physiotherapy - UnirG, those who were hospitalized and have 4 weeks of diagnosis or those who were not hospitalized and have 14 days of diagnosis, both with negative PCR, according to criteria of the Brazilian Association of Physiotherapy and Intensive Care (ASSOBRAFIR), in addition to being with heart and respiratory rates, blood pressure and oxygen saturation within normal limits, since four of the tests will require minimum to moderate physical exertion and one of them maximal effort. At the time of registration, participants should read the TCLE (annex) referring to the content of the project and procedures to which they will be submitted and, if they consent, they must sign as a testimony as registered as a voluntary participant of this research. They will then be numbered on a first-come, first-served basis and whenever they reach 10 entries thereafter, they will be notified to appear at CEF-UNIRG on the day and time of the week and, thus, successively, week by week, the process will be repeated until they reach the pre-established sample size.

Exclusion Criteria: Post-covid patients who do not have minimum conditions to undergo the trials proposed by Ewing, such as heart rate, respiratory rate, blood pressure and oxygen saturation outside normal limits or those who do not have the recommendations of the rehabilitation criteria proposed by ASSOBRAFIR.

METHODOLOGICAL PROCEDURES AND DATA COLLECTION INSTRUMENTS

There will be five tests to be applied to have a greater range of the results, as they will be analyzed for the degree of sensitivity, specificity and reproducibility. Clinical trials will always be applied by the same properly trained operators of the research group (see schedule), estimating attendance of 10 participants per week. The actual time spent to apply the tests for each participant of the research will be 30 minutes, but will be extended to 60 minutes, taking into account the preparation of the environment (hygiene) and instrumentation, in addition to the time for accommodation and rest of the participants, especially with regard to blood pressure measurements. 1) HR variation to deep breathing: Individual will be kept seated, calm and comfortable connected to the ECG and marking the beginning of each inspiration of 5 seconds and each expiration of 5 seconds, totaling six breaths in 1 minute. Regarding data processing, the following criterion will be adopted: The lowest RR interval of inspiration and the longest RR interval of expiration, in each cycle, will be converted into BPM units (beat per minute) and expressed as the mean of the maximum and minimum HR difference of the six cycles recorded in the ECG. 4) BP variation when standing up: The individual will be lying down and being relaxed for 4 minutes, during which BP will be measured. It is requested to get up quickly standing upright and during the first minute it is again moved PA. As for data processing, the following criterion will be adopted: The difference between lying systolic pressure and standing systolic pressure is calculated. Note: If the result of this specific test is abnormal, there is a serious risk of having severe sympathetic impairment. Table 1 presented below shows the five tests named

above and their respective ranges of values related to normality, borderline and abnormality conditions.

Table 1. The tests were appointed and standardized values, according to the classifications of states of normality, borderline and abnormality by Ewing et al

	Deep Breathing	PA Variation
Normal	≥ 15 BPM	≤ 10 mmHg
Borderline	11 to 14 BPM	11 to 29mmHg
Abnormal	≤ 10 BPM	≥ 30 mmHg

RESULTS AND DISCUSSION

The unbalance in the functioning of the ANS may result from disorders induced by various diseases (VANDERLEI et al. 2009). In this line of reasoning, they made it necessary to conduct epidemiological studies separately between the activities of the sympathetic and the parasympathetic, because the unbalance was almost always evidenced in the different pathophysiology of the cardiovascular system and associated with high mortality rates. Thus, from the methodological advent of the various quantitative markers to evaluate THE, the Heart Rate Variability (HRV) parameter became, in relation to the others, conducive to researching the association of ANS *versus* Cardiac Activity. HRV are oscillations measured in the ECG between RR intervals of repetitive QRS waves of the heartbeat, which may reflect changes resulting from the performance of the ANS on HR (TASK, 1996; RAJENDRA AU, et al., 2006). The experimental hrV method, however, although disseminated because it is a noninvasive and easy-to-use instrument, showed some difficulty in its interpretation due to its complexity because it presents several indexes in its use. The large number of publications and the complexity presented in the analysis of the mathematical modeling of their indexes, caused the European Society of Cardiology and the American Society of Cardiac Stimulation and Electrophysiology to join forces in a consortium of task forces in order to standardize the nomenclature used, as well as its indexes and measurement methods (PORTELLA, 2006).

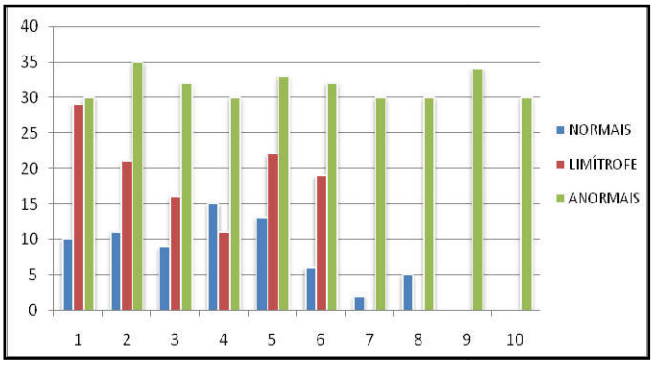
After its standardization, it has become a tool that has been shown to be relatively efficient in the analysis of cardiac autonomic function in healthy individuals, athletes and also in patients with various diseases (VANDERLEI, et al. 2009; MARK, et al., 2011). HRV analyses, based on linear methods, can be performed according to two variables, one of them operated in the time domain and the other in the frequency domain (ROCHA, ALBUQUERQUE, ALBANESI FILHO, 2005). In the time domain, mathematical indicators are expressed in milliseconds and are obtained in records with times longer than 10 minutes, where the variation in the duration of the intervals between QRS complexes, resulting from the depolarizations that occurred in the sinoatrial node and, from which the various indices are mathematically defined, each with its interpretations referring to sympathetic or parasympathetic or associated control (MARK et al., 2011; ROCHA, ALBUQUERQUE, ALBANESI FILHO, 2005; BARBOSA and BELASCO, 2011). In the frequency domain, in turn, the indicators are expressed in Hertz and are obtained from records of wave intensities observed at smaller time intervals and their harmonic wave components called Fourier trigonometric series, the mathematical indicators are defined, each interpreted according to performances of the vagus, respiratory modulation and sympathetic/parasympathetic joint action (VANDERLEI et al. 2009; POIRIER et al., 2003). The viability and applicability of the HRV method and the obtaining of respective indices, therefore, has become an important tool in the clinical understanding of pathophysiological variables, since increases in HRV, may indicate good response to various stimuli in the physiological adaptation of the organism and its maintenance moment-to-moment, presupposing a condition of stability of the biological system, while reductions in HRV are pointed out as predictors of diseases or appearance of events patients with known diseases (VANDERLEI et al. 2009; PAIVA et al., 2011; BÄR et al., 2005; CHANG et al., 2010).

With this, the study of HRV became a good candidate to evaluate the degree of control of THE individuals, both under normal and pathological conditions, using the indicators measured as predictors of diseases and possible injuries in existing pathological conditions, and also, because it is noninvasive, also suitable for evaluating, epidemiological approach, adult populations and children. The studies addressing autonomic dysfunction in a wide variety of clinical conditions and in primary neural degenerations involving the NAS pathways with the HRV method (PORTELLA, 2006), however, produced some controversial results, such as in the correlation with the prognosis of acute myocardial infarction (BARRON and LesH, 1996) and other diseases (BACH, ILIANA, ELIAHOU, 1979; CAMPESE, et al., 1981; EWING and WINNEY, 1975; HEIDBREDER, SHAFFERHANS, HEILAND, 1985; MAILIK, WINNEY, EWING, 1986; NAIK et al., 1981), partly due to complex mathematical indicators that are difficult to interpret and the other, the lack of better standardization of clinical trials. This required research and development of new clinical trials that could inform with discernment and ease both the presence and degree of dysfunction of THE. In the 1980s, Ewing and collaborators proposed such standardization (EWING and CLARK, 1982; EWING et al., 1985; EWING, 1992), using protocols that assess cardiovascular reflexes, but which can also report damage at any other point of THE, both sympathetic ly and parasympatheticly, proposing mathematical indicators with moderate complexity. After being recommended at a conference on diabetic neuropathy (*San Antonio Conference on Diabetic Neuropathy*, 1988), they gained projection and use in several epidemiological clinical trials. In Brazil, the Ewing protocol was successfully validated by Boer et al. (1998) *comparing healthy individuals versus patients* with high probability of presenting an ANS dysfunction.

Of the five tests proposed by Ewing, three evaluate the parasympathetic function and two the sympathetic function, and the data obtained from HRV and blood pressure transformed into indices and, by means of statistical techniques, the degree of sensitivity and specificity can be determined, in addition to the degree of reproducibility and methodological viability, with the advantage that clinical trials are performed with simple procedures with minimal material and equipment accessible in laboratories of research, clinics and outpatient environments for the use of health professionals with relatively low costs. O boletim da *American College of Cardiology* vem notificando os profissionais de saúde que, dentre os pacientes que foram hospitalizados pelo novo coronavírus, 50% possuíam doenças crônicas e, destes, 40% possuíam doença cardiovascular ou cerebrovascular. Entre os casos fatais, 86% tinham acometimento respiratório e, destes, 33% acometimentos cardíacos associados e 7% acometimentos cardíacos isolados. Os estudos envolvendo associação do coronavírus e doenças cardiovasculares, mostra que a infecção viral leva a uma série de reações responsáveis por desequilibrar doenças cardiovasculares que antes estavam compensadas. Os pacientes com doenças cardiovasculares prévias têm alterações em seu sistema imunológico, além de um estado inflamatório crônico latente, o que pode agravar a evolução da doença. Em geral, pessoas acima de 60 anos ou que tenham doenças respiratórias, de origem cardiovascular ou diabetes, estão mais propensas a contrair a doença, tanto que a OMS aconselha para esta população, maior cuidado em evitar aglomerações ou locais com pessoas doentes.

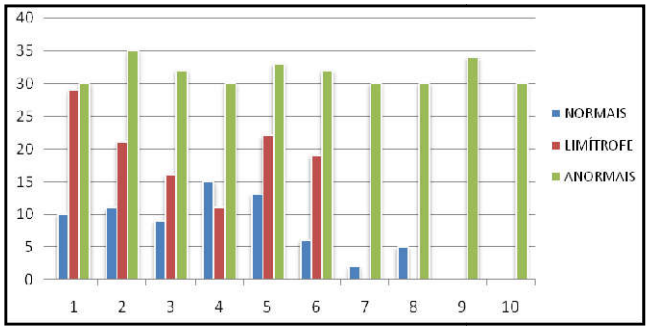
Em pandemias passadas por vírus respiratórios, a mortalidade por doenças cardiovasculares chegou a ultrapassar todas as outras causas, ficando à frente da pneumonia em outras situações. Os pacientes com doenças crônicas, hipertensão, diabetes e que já tiveram alguma doença cardíaca como infarto ou passaram por alguma cirurgia cardiovascular ou que tem insuficiência cardíaca, são grupos de maior risco, aparentando existir neste grupo predisposição para desenvolver a forma grave da doença, não especificamente para ser contaminado pelo covid-19. Initially, covid-19 was understood as a lung disease, but it soon became clear that it is a systemic disease, which attacks virtually all organs and functions of the body. Recent data show that more severe damage of the new coronavirus may be to the heart, and myocarditis is a problem that begins to be noticed more frequently,

even in patients who did not present severe and even asymptomatic conditions. Myocarditis is not necessarily a serious condition, but in some cases it can lead to heart failure, so cardiovascular complications need to be seen carefully. The new coronavirus can affect any structure of the heart, causing inflammation and thrombosis in the vessels and tissues, warns the Brazilian Society of Cardiology, and the virus can affect the cardiovascular system with various manifestations, such as myocardial injury, heart failure, arrhythmia, myocarditis and shock as shown in a small sampling study conducted in Germany and published in the journal JAMA Cardiology, where the researchers studied 100 people, with an average age of 49 years who recovered from covid, most of which were asymptomatic or had mild symptoms. About two months after diagnosis, scientists submitted patients already fully cured for MRI scans and made alarming findings: about 80% of them had cardiac abnormalities and 60% had myocarditis. Another study also published in JAMA Cardiology showed a worrying number with autopsies performed on 39 patients who died of covid-19 who revealed the presence of the virus in the myocardium in 60% of cases. Although these studies are considered to be small ly sampled and their conclusions are not yet fully understood, it is already clear to experts that it is common for a patient who is young and apparently overcame covid-19 to present some heart problem, and scientists in various parts of the world are still trying to understand how the new coronavirus causes myocarditis and other cardiovascular anomalies. It is not known whether it is caused directly by the virus to the heart or if it stems from the violent immune response of the organism causing sequelae in the heart and its connections. After the data collected foolishly a number of 24 volunteers, being men and women was obsevardo who hears a change in some patients in their autonomic system sympathetic and parasympathetic thus causing some alternation in their daily lives after they have contracted the virus of the covid-19.



Graph 1. Correlation of volunteers who entered the normality levels, borderline and abnormalities in relation to the deep breathing test

Deestre the 24 volunteers 10 entered the level of abnormality and may have alterations in the autonomic system sympathetic and parasympathetic and were instructed to proucura medica help and physiotherapy, the other 14 volunteers entered the levels of normality and borderiform where they were also informed of the importance of having a redized care to have a better quality of life.



Graph 2. Correlation of volunteers who entered the normality levels, borderline and abnormalities in relation to the arterial pression test (P.A)

In this Second grafico was evaluated the arterial pretion of the 24 registered volunteers, the same 10 patients who presented alteration in the deep breathing test also presented alteration in the arterial pression test with numerous signifiable and alarming, after the data analysis was notified esa patients to better investigate these changes in their cardiovascular system .

CONCLUSION

Therefore, according to the data collections performed by the team of this trabralho, of noting that through the EWING tests in a patient who contracted the virus of the covid-19 there was a very great meaning in relation to the abnormality of the sitema outoma impatico and parasimpatico where 10 vonluntarios entered the level of abnormality, all the way that also in this research observed that 6 volunteers were in the borderline level and 8 volutary at the level of normality through from tests, the volunteers who presented abnormality received guidance to go to the doctor and also physiotherapy to make a treatment to improve these distubios caused by the covid-19. However, it was observed that it mentions more studies involving these thematics, with larger numbers of volunteers and even mesme with other EWING tests to better clarify these changes in the sympathetic and parasympathetic autonomic system aiming that these changes can be treated for better quality of life of the people who were left with the sequelae of covid-19.

REFERENCES

Angelis K, MSB Saints, MC Irigoyen. Autonomic Nervous System and Cardiovascular Disease. *Journal of the Society of Cardiology of Rio Grande do Sul* 2004, p.1-7.

Bach C, Iliana A, Eliahou HE. Autonomic nervous system disturbance in patients on chronic hemodialysis. *Isr J Med Sci* 1979; 15: 761-764.

Bär K, Letzsch A, Jochum T, Wagner G, Greiner W, Sauer H. Loss of efferent vagal activity in acute schizophrenia. J Psychiatr Res 2005;39(5):519. http://dx.doi.org/10.1016/j.jpsychires.2004.12.00

Barbosa JLR, Belasco DJ. Avaliação da Variabilidade da Frequência Cardíaca em Pacientes com Lesão Medular. *Rev Neurocienc* 2011;19(2):294-9.

Barron HV, Lesh MD. Autonomic nervous system and sudden cardiac death. *J Am Coll Cardiol* 1996; 27: 1053-1060.

Boer CAA, Mocelin AJ, Matsuo T. Validação dos testes de Ewing para avaliação de disfunção autonômica. *Arq Neuro Psiquiatr* 1998; 56 (2): 250-254.

Cambri LT; Oliveira FR; GevaerdMS. Modulação autonômica cardíaca em repouso e controle metabólico em diabéticos tipo 2. HU Revista 2008; 34(2):115-21.

Campese YM, Romaff MS, Levitan D et al. Mechanisms of autonomic nervous system dysfunction in uremia. *Kidney Int* 1981; 20: 246-253.

Chang J, Yoo C, Yi S, Hong K, Lee Y, Oh H, et al. Changes in heart rate dynamics of patients with schizophrenia treated with risperidone. Prog Neuropsychopharmacol Biol Psychiatry 2010; 34 (6): 924. http://dx.doi.org/10.1016/j.pnpbp.2010.04.017 Consensus reached for autonomic definitions. World Neurol 1996; 11 (3): 1-15. Ed.

Ewing DJ. Analysis of heart rate variability and other non-invasive tests with special reference to diabetes mellitus. In Bannister R; Mathias CJ (eds). Autonomic failure. 3 New York: Oxford, 1992: 312-333.

Ewing DJ, Clark BF. Diagnosis and management of diabetic autonomic neuropaty. Br Med J 1982; 285: 916-918.

Ewing DJ, Martin CN, Yong RJ et al. The value of cardiovascular autonomic function tests: 10 years' experience in diabetes. Diabetes Care 1985; 8: 491-498.

Ewing DJ, Winney R. Autonomic function in patients with chronic renal failure on intermittent hemodialysis. Nephron 1975; 15: 424-429.

Heidbreder R, Shafferhans K, Heiland A. Autonomic neuropathy in chronic renal insufficiency: comparative analysis of diabetic and nondiabetic patients. Nephron 1985; 41: 50-56.

Mailik S, Winney RJ, Ewing DJ. Chronic renal failure and cardiovascular autonomic function. Nephron 1986; 43: 191-195.

Mark L R, Chad M T, Christian A O, Thai V, Kenneth GP. Clinical Applications of Heart Rate Variability in the Triage and Assessment of Traumatically Injured Patients. Anesthesiol Res Pract 2011;2011:1-8.

Naik RB, Mathias CJ, Wilson CA et al. Cardiovascular and autonomic reflexes in hemodialysis patients. Clin Sci 1981; 60: 165-170.

Ozkaya E, Gursoy E, Demir A, Erenberk U, Sogut A, Dundaroz M R. Autonomic nervous system dysfunction and their relationship with disease severity in children with atopic asthma. Respir Physiol Neurobiol 2012;183: 206-10. http://dx.doi.org/10.1016/ j.resp.2012.07.002

Paiva VC, Santana KR, Silva BM, Ramos PS, Lovisi JC, Araújo CG, et al. Comparação entre métodos de avaliação da modulação vagal cardíaca. Arq Bras Cardiol 2011;97(6):493-501. http://dx.doi.org/10.1590/S0066-782X2011005000109

Portella RB. Disfunção na regulação autonômica vagal cardíaca em pacientes com hipertireoidismo subclínico sem cardiopatia aparente [dissertação].Rio de Janeiro: Universidade Federal do Rio de Janeiro; 2006, 63p.

Rajendra AU, Paul JK, Kannathal N, Lim CM, Suri JS. Heart rate variability: a review. Med Bio Eng Comput 2006;44(12):1031-51. http://dx.doi.org/10.1007/s11517-0060119-0

Rocha RM, Albuquerque DC, Albanesi Filho FM. Variabilidade da frequência cardíaca e ritmo circadiano em pacientes com angina estável. *Rev Socerj* 2005;18(4):429-42.

San Antonio Conference on Diabetic Neuropathy. Report and recommendations of San Antonio conference on diabetic neurophaty. Diabetes 1988; 37:1000-1004.

Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation 1996;93(5):1043-65. http://dx.doi.org/10.1161/01.CIR.93.5.1043

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(2):205-17. http://dx.doi.org/10.1590/S0102-76382009000200018

****