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Review article

Physical activity as a measure of autonomic control in patients with metabolic syndrome. Narrative review

Actividad física como medida de control autonómico en pacientes con síndrome metabólico. Revisión narrativa

A atividade física como medida de controle autonômico em pacientes com síndrome metabólica. Revisão narrativa

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ABSTRACT

ABSTRACT

The metabolic syndrome considers a group of disorders that increase the risk of Chronic Noncommunicable Diseases. In this sense, prevention and treatment have focused on physical activity as an effective method to restore heart rate variability and decrease health risks. The objective of this review was to describe the behavior of heart rate variability in relation to the practice of physical activity in patients with

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metabolic syndrome. The metabolic syndrome has been associated with sympathetic predominance and parasympathetic withdrawal that presents a risk of Chronic Noncommunicable Diseases that can be restored with regular practice of physical activity. Physical activity can restore the heart rate variability related to the metabolic syndrome, however, other studies are required to try to explain all the conditions to which the autonomic balance responds.

Keywords: Exercise; Autonomic nervous system; Heart rate; Metabolic syndrome.

RESUMEN

El síndrome metabólico considera a un grupo de trastornos que aumentan el riesgo de padecer enfermedades crónicas no transmisibles. En este sentido, la prevención y tratamiento han centrado a la actividad física como un método eficaz para restaurar la variabilidad del ritmo cardíaco y disminuir los riesgos sobre la salud. Esta revisión se planteó como objetivo describir el comportamiento de la variabilidad del ritmo cardíaco frente a la práctica de actividad física en pacientes con síndrome metabólico. El síndrome metabólico se ha relacionado con un predominio simpático y una retirada parasimpática que presenta un riesgo de enfermedades crónicas no transmisibles que puede ser restaurada con la práctica regular de actividad física. La actividad física puede restaurar la variabilidad del ritmo cardíaco relacionada al síndrome metabólico, no obstante, se requieren de otros estudios que intenten explicar todas las condiciones a las que responde el balance autonómico.

Palabras clave: Ejercicio; Sistema nervioso autónomo; Frecuencia cardíaca; Síndrome metabólico.

RESUMO

A síndrome metabólica é um grupo de perturbações que aumentam o risco de padecer Doenças Crônicas Não Transmissíveis. Neste sentido, a prevenção e o tratamento concentraram-se na atividade física como um método eficaz para restaurar a variabilidade do ritmo cardíaco e diminuir os riscos para a saúde. Esta revisão visa descrever o comportamento da variabilidade do ritmo cardíaco em relação à prática da atividade física em pacientes com síndrome metabólica. A síndrome metabólica tem sido associada com predominância simpática e retirada parassimpática que apresenta um risco de doenças crônicas não transmissíveis que podem ser restauradas com atividade física regular. A atividade física pode restaurar a variabilidade do ritmo cardíaco, relacionada com a síndrome metabólica, no entanto, são necessários mais estudos para tentar explicar todas as condições às quais o equilíbrio autonómico responde.

Palavras-chave: Exercício; Sistema nervoso autónomo; Ritmo cardíaco; Síndrome metabólico.

INTRODUCTION

The metabolic syndrome (MS) is considered a major threat to health worldwide. It is not yet clearly, however, generally considers a group of disorders that occur simultaneously increasing the risk of developing Chronic Noncommunicable Diseases

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(CNTD) as, heart disease, obesity, and type II diabetes, among others (Robles, & Carlos., 2013; Saboya., et al., 2016). This syndrome reports a very diverse prevalence, reaching up to 27.3 % depending on the definition used in relation to the criteria and reference values in metabolic parameters as involved (Robles, & Carlos., 2013; Saboya., et al., 2016).

Currently, the literature has widely used the time variation that occurs between consecutive heartbeats (heart rate variability) as a measure that reflects the activity of the autochthonous nervous system on the cardiac function (Espinosa-Salinas, et al., 2015; Rosales-Soto, Corsini-Pino, Monsálves-Álvarez, & Yáñez-Sepúlveda, 2016; Altini, Van Hoof, & Amft, 2017; Perrotta, Jeklin, Hives, Meanwell, & Warburton, 2017; Veloza, et al., 2019). In this sense, the variability of heart rate has allowed to register and analyze the action of the autonomous nervous system and the nervous vagal system on the cardiac function in the called autonomous balance. The autonomous balance is characterized by a decrease in the heart rate marker and an increase in its variability, while a state of imbalance is characterized by increases in heart rate and decreases in its variability, as a result of the sympathetic predominance and the withdrawal of the vagal tone involved in the physiopathology of arrhythmogenesis, sudden cardiac death, arterial hypertension, obesity and insulin resistance (Espinoza-Salinas., et al., 2015; Espinoza-Salinas, Acuña-Vera, Sánchez-Aguilera, & Zafra-Santos., 2016; Yadav, Yadav, Agrawal, Sah, & Islam., 2017; Rodríguez Pena et al., 2019; Espinoza-Salinas., González-Jurado., Burdiles-Álvarez., Arenas-Sánchez, & Bobadilla-Olivares., 2020).

At present the prevention and/or treatment of the metabolic syndrome has been centered in the use of pharmacological and non-pharmacological therapies, suggesting among the latter, the practice of physical activity and/or physical exercise as an effective way to reduce body weight and restore the sympathetic-vagal balance (Miguel Soca., et al., 2012; Álvarez, et al., 2014; Yadav, et al., 2017; Kinoshita, et al., 2018). In this sense, physical activity programs have proven to be fundamental in the prevention of chronic noncommunicable diseases related to the metabolic syndrome. However, these are still being studied, due to the lack of consensus related to the interpretations of heart rate variability as a measure of autonomous control in health and disease (Billman, Huikuri, Sacha, & Trimmel., 2015; Laborde, Mosley, & Thayer., 2017; Shaffer, F., & Ginsberg., 2017).

For this reason, the objective of this review was to describe the behavior of heart rate variability in face of physical activity in patients with MS.

DEVELOPMENT

Metabolic syndrome and autonomic balance

The metabolic syndrome is considered a great threat to health worldwide, it is not yet clearly defined because of the heterogeneity between diagnostic criteria, however, in general he considers a group of disorders that occur simultaneously increasing the risk of developing CNTD, (Robles, & Carlos., 2013; Savoy et al., 2016).

This syndrome reports a very diverse prevalence, reaching up to 27.3 % depending on the definition used in relation to diagnostic criteria and reference values (Robles, & Carlos., 2013; Saboya et al., 2016), therefore, the literature has raised the linkage

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of diagnostic criteria related to metabolic syndrome with the variability of heart rate, (Sheema, & Malipatil., 2015; Yadal., et al., 2017; Goit, Pant, & Shrewastwa., 2018; Sessa., et al., 2018; Triggiani., 2019; Veloza., et al., 2019) (Table 1 and Table 2).

Table 1. - Diagnostic criteria for metabolic syndrome

Criterios diagnósticos	Panel de tratamiento para adultos III	Organización Mundial de la Salud	Asociación Americana de Endocrinología Clínica	Federación Internacional de Diabetes
Triglicéridos \geq 150 mg/dL.	X	X	X	X
Colesterol de baja densidad: $<$ 40 mg/dL para hombres. $<$ 50 mg/dL para mujeres.	X	X	X	X
Presión Arterial $>$ 130/85 mm Hg.	X	X	X	X
Insulina Resistencia o IR		X		
Glucosa en ayuna $>$ 100 mg/dL.	X		X	X
Glucosa en 2 horas $>$ 140 mg/dL.			X	
Obesidad abdominal: \geq 94 cm en hombres. \geq 88 cm en mujeres.	X			X
Índice masa corporal $>$ 24,9.		X	X	
Microalbuminuria anormal.		X		
Número de criterios diagnóstico	3 + Insulina Resistencia.	$>$ 2	Criterio Clínico	obesidad abdominal

Source: Adaptation of the work of Robles & Carlos (2013).

Table 2. - Measurements of cardiac variability according to temporal, spectral and non-linear domains

	Temporal	Espectral	No lineal
RR		ULF	- SD1
Mean heart frequency		VLF	- SD2
SDNN			
RMSSD		LF	SD2/SD1
PNN50		HF	
		LF/HF	
		Total Power	

RR: Measures of the intervals R-R; SDNN: Standard deviation of all intervals RR; RMSSD: Square of the mean root of the R-R adjacent intervals joint; PNN50: Number of the adjacent intervals that varies more than 50 ms; ULF: Ultra low frequency; VLF: Low frequency; LF: Low frequency; HF: High frequency; LF/HF: Low and high frequency relationship; SD1: Short-term variability of the heart rate; SD2: Long-term variability of the heart rate; SD2/SD1: Long-term and short term variability relationship.

Source: Adapted from the works of Tarvainen et al (2014). Triggiani et al (2016), Shaffer & Ginsberg (2017), Rahman, Habel & Contrada (2018).

The autonomous balance is directly governed by the autonomic nervous system through its sympathetic and parasympathetic branches (Koch-Villegas., et al., 2018), so that measures of heart rate variability have allowed monitoring of the sympathetic-vagal relationship associated with the unhealthy style of life states and pathologies like, high blood pressure, insulin resistance, proliferation of adipose tissue, cardiovascular risk factors and MS (Espinoza-Salinas, et al., 2015; Sánchez, Sánchez, & Suárez, 2015; Veloza et al., 2019). In this context, a predominance in



vagal activity may favor coronary irrigation, allowing a longer diastole and a shorter hypoxic period in the left ventricle, while, conversely, a sympathetic predominance is linked to increased cardiovascular morbidity and mortality regardless of the existence of other cardiovascular risk markers, such as metabolic, hemodynamic, trophic, and rheologic abnormalities (Sassi et al., 2015; León Regal et al., 2016; Wu D., et al., 2017; Rodríguez Pena, et al., 2019).

Physical activity as a measure of autonomous control

The practice of regular exercise is associated with positive adaptations in body composition, physical condition, levels of chronic inflammation and indices of heart rate variability, reflected in increases in parasympathetic tone and reductions in sympathetic activation, related to an inhibition of chronic inflammation and release of pro-inflammatory cytokines (Espinoza-Salinas., et al., 2020). In this sense, it is known that aerobic-type physical activity generates favorable changes related to autonomic restoration, mortality, inverse remodeling of the left ventricle, functional capacity and quality of life, while in physical exercise conditions around 50 % of VO₂max are related to a withdrawal in the vagal activity and progressive increases of sympathetic activity. On the contrary, high intensities have been associated with an influence of the sympathetic pathway, the mechanism of synorespiratory arrhythmia and baroreflex influence in exercise conditions (García Manso., 2013; Espinoza-Salinas et al., 2016, 2020; Hernández García, et al., 2018). On the other hand, physical activity against resistance or resistance to muscle strength has been associated with a synergistic effect in terms of improvements in aerobic capacity (Hernández García., et al., 2018). Concerning physical activity against endurance or with endurance to muscular force, it has been related with a synergetic effect in order to improve the aerobic capacity and the sensitivity of baroreceptors and chemoreceptors associated to decreases in sympathetic activity directly and indirectly in resting conditions, which contributes to improve the chronotropic response to subsequent physical efforts by increasing the variability of heart rate in resting conditions. However, it is important to consider that patients diagnosed with heart failure usually present decreases in their functional capacity and tolerance to physical activity and/or exercise, so their participation in cardiac rehabilitation programs should always be considered based on the cost-benefit assessment of these programs (Segovia, Manterola, González, & Rodríguez-Núñez, 2017; Hernández García et al., 2018).

Following this line of argument, patients who performed some type of physical activity increased the magnitude of the variables of the time domain as opposed to subjects who did not receive conventional medical treatment, what suggest that the physical activity is not only limited to sympathetic-inhibitory responses, but also to parasympathetic excitatory responses in the cardiovascular control mechanisms of these patients (Segovia et al., 2017).

On the other hand, both heart rate variability and body composition have been studied separately on numerous occasions, so that there is still not an abundant literature that can explain all the modular mechanisms of autonomic balance in patients with overweight and/or obesity in conditions of rest and exercise (Sánchez, Sánchez, & Suárez, 2015). For this reason, it is important to consider the relationship between these two variables and their influence on health, since it is extremely important when making interventions both at the preventive and diagnostic levels. In this regard, the aerobic physical activity generates physiological responses

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modulated by sympathetic and endocrine stimuli, directly associated to the intensity of work, which also trigger other responses at the level of multiple cell lines, such as the increase in insulin sensitivity, modulation of the immune response and stimulation of endogenous antioxidant systems, modulated by the activation of AMPK and TLR-4, so that physical activity constitutes one of the main therapeutic resources used to combat obesity (Espinoza-Salinas *et al.*, 2015; 2016; 2020).

In this context, moderate- and high-intensity physical activity is an effective way to reduce body weight and restore autonomic balance, counteracting the vagal decrease during the autonomic activation time from sensory afferences of muscle fibers type III and IV in subjects with high levels of adiposity, insulin resistance, type II diabetes and insufficiency (Miguel Soca, *et al.*, 2012; Álvarez, *et al.*, 2014; Yadav, *et al.*, 2017; Kinoshita *et al.*, 2018). As for the autonomic balance after exercise, this produces volume/pressure overload in the carotid body (main peripheral arterial chemical receptor) that stimulates the activation of baroreflex as a compensator of the blood pressure increases that induces, at first stage, of vagal decrease and a posterior decrease of the heart rate (Espinoza-Salinas., *et al.*, 2020). This phenomenon leads to the presumption that the first phase of post-exercise recovery is modulated by the central nervous system, while the slow phase is regulated by the autonomic signals. However, some exceptions should be considered, such as subjects with high blood pressure, since they would not always achieve significant adaptations related to the restoration of the vagal autonomic balance due to the hypertensive response that makes it difficult for the heart function to adapt to minimal physical or mental stress conditions (Almeida, *et al.*, 2017; Rodríguez Pena, *et al.*, 2019).

On the other hand, at present, literature has postulated multiple theories that try to explain how adiposity could modify the neuronal activity involved in the autonomic nervous system and the thermogenic adaptation enhanced in conditions of weight gain both at rest and in exercise (Sheema, & Malipatil., 2015; Yadav., *et al.*, 2017; Trigani *et al.*, 2019). However, unfortunately all the mechanisms of sympathetic-vagal balance related to obesity, insulin resistance, and heart failure have not yet been established (Espinoza-Salinas *et al.*, 2015; Rosales-Soto., *et al.*, 2016; Segovia., *et al.*, 2017; Goit, Pant, & Shrewastwa, 2018).

Autonomic balance in cardiovascular disease and obesity

Cardiovascular diseases have been related to hemodynamic changes and myocardial damage, since one of the first responses generated in these patients is the activation of afferent and efferent fibers of the autonomic nervous system, which contribute to the sympathetic-vagal imbalance, generating sympathetic activation and vagal withdrawal reflected in a decreased heart rate variability (Segovia, *et al.*, 2017).

In this regard, a sympathetic predominance and vagal withdrawal can influence the systolic volume through variations in the contractile force and the redirection of blood flow to areas of higher vascular demand due to the stimulation of adrenergic receptors β_1 , β_2 and β_3 sensitive to adrenaline, which, in turn, trigger a series of chemical reactions on the calcium pump and the action potential of non-contractile cells in the sinus node that generate increases in heart rate and decreases in the variability of it. In contrast, a vagal predominance inhibits the sympathetic pathway resulting from activation of calcium channels and acetylcholine M1, M2, M3, and M5 receptors in the sinus node, producing decreases in heart rate and increases in heart variability of this one (Sessa *et al.*, 2018; Veloza *et al.*, 2019).

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In this context, a predominance of sympathetic activity and vagal withdrawal could be related to a decrease in baroreflex sensitivity and metaboreceptors common to both cardiovascular disease and obesity, while the mechanisms of the autonomic balance related to the adipose tissue and the resistance to insulin have made us presume that the pro-inflammatory processes caused by the cytokines TNF- α and IL-6 and the release of hormones such as adiponectin, resistin, leptin and visfatin can cause modifications on the autonomic balance reducing the physical capacity (Espinoza-Salinas *et al.*, 2015).

The above findings emphasize the need for future research to establish all the factors that can influence the balance of autonomy, since this knowledge is not yet clear (Rahman, Habel, & Contrada, 2018).

The excess of adiposity seems to be related to the variability of heart rate, while women seem to have a lower variability of heart rate compared to men, suggesting a protective effect against arrhythmias and against the development of coronary diseases. However, these differences are reduced throughout life due to the loss of estrogen (Sánchez, Sánchez, & Suárez., 2015). On the other hand, the most favorable cardiac variability profiles are associated with moderate and vigorous physical activity in children and adolescents with lower adiposity and better physical condition, while heart rate variability in adults and older adults is related to body composition; however, this relationship is still among said, because there is no consensus regarding the level of influence of body mass on heart rate variability, despite the fact that some research has suggested a relationship between sympathetic-vagal balance and factors such as age, sex, adiposity, sedentary lifestyle, sleep quality, and stress (Sánchez, Sánchez, & Suárez., 2015).

Most of the studies reviewed propose that sympathetic-vagal imbalances are directly related to the pathogenesis of diseases such as obesity, insulin resistance, type II diabetes, heart failure, among others related to metabolic syndrome (Espinoza-Salinas *et al.*, 2015; Sánchez, Sánchez, & Suárez., 2015; León Regal *et al.*, 2016; Rosales-Soto., *et al.*, 2016; Altini, Van Hoof, & Amft., 2017; Perrotta *et al.*, 2017; Segovia *et al.*, 2017; Yadav *et al.*, 2017; Wu D *et al.*, 2017; Veloza *et al.*, 2019; Rodríguez Pena *et al.*, 2019; Espinoza-Salinas *et al.*, 2020).

Finally, the findings reviewed by this review allow to better understand the behavior of the cardiac variability in the metabolic syndrome.

CONCLUSION

Physical activity plays a fundamental role in the diagnosis, prevention and treatment of the MS, because it is capable of diminishing and even restoring the state of sympathetic-vagal imbalance. Therefore, other studies are still required to try to determine and explain all the mechanisms involved in the autonomic control in the diverse pathologies that compose the metabolic syndrome.



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The authors declare not to have any interest conflicts.

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The authors have participated in the writing of the work and analysis of the documents.



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