Article **Journal of Physiotherapy and Medical Technology**
June, 2022 Vol.6 No.15 14-21

Heart rate behavior on the menopause stages

Comportamiento del ritmo cardíaco en las etapas de la menopausia

MADAGLENO-ARROYO, Dulce[1]*†, SANCHEZ-BARAJAS, Mauricio[2], GARCIA-PEREZ, Marysol[1] and CORDOVA-FRAGA, Teodoro[1]

[1]*Division de Ciencias e Ingeniería, Universidad de Guanajuato campus León, Loma del Bosque N. 103, Lomas del Campestre, 37150 León, GTO, Mex.*
[2]*IMSS, HGZC/MF N. 21, Departamento de Medicina Interna, Coral N. 103, San Rafael, 37380 León, GTO, Mex.*

ID 1st Author: *Dulce, Madagleno-Arroyo* / **ORC ID**:

ID 1st Co-author: *Mauricio, Sanchez-Barajas* / **ORC ID**: 0000-0002-0906-2991

ID 2nd Co-author: *Marysol, Garcia-Perez* / **ORC ID**: 0000-0002-0201-5914, **CVU CONACYT ID**: 775396

ID 3rd Co-author: *Teodoro, Cordova-Fraga* / **ORC ID**: 0000-0002-6486-7530, **CVU CONACYT ID**: 122005

DOI: 10.35429/JP.2022.15.6.14.21 Received March 12, 2022; Accepted June 15, 2022

Abstract

Introduction: The behavior of the heart rate in the different menopause stages is a parameter that should be considered in the high incidence of cardiovascular disease. Objective: A comparative study of 200 women aged 25 to 57 is presented. Methodology: The women were divided into four groups: pre-menopausal, peri-menopausal, early post-menopausal and late post-menopausal, registers were obtained by using the heart rate a polar clock for four hours, then a questionnaire was applied to measure anxiety, sexual interest, and perception of stress and serum levels of FSH and cortisol. Results: During perimenopause, the heart rate shows a greater number of decreases and/or elevations ($p < 0.001$) showing that at this stage the heart rate is unstable. Discussion In the early post-menopause, the heart rate was higher compared to the rest of the stages. The heart rate at perimenopause is unstable, presenting greater variation than the previous stages and in the early pre-menopause, heart rate is higher than the other stages. Conclusion The heart rate during the perimenopause is unstable presents greater variation than the other stages and in the early pre-menopause the heart rate is higher than the rest of the stages studied

Heart rate, Menopause, Polar watch, Women

Resumen

Introducción: El comportamiento de la frecuencia cardiaca en las diferentes etapas de la menopausia es un parámetro que debe considerarse en la alta incidencia de enfermedad cardiovascular. Objetivo: Se presenta un estudio comparativo de 200 mujeres de 25 a 57 años. Metodología Las mujeres fueron divididas en cuatro grupos: premenopáusicas, perimenopáusicas, postmenopáusicas tempranas y postmenopáusicas tardías, los registros se obtuvieron utilizando la frecuencia cardiaca un reloj polar durante cuatro horas, posteriormente se aplicó un cuestionario para medir ansiedad, interés sexual y percepción de estrés y niveles séricos de FSH y cortisol. Resultados: Durante la perimenopausia, la frecuencia cardiaca muestra un mayor número de descensos y/o elevaciones (p <0,001) lo que demuestra que en esta etapa la frecuencia cardiaca es inestable. Discusión En la postmenopausia precoz, la frecuencia cardiaca fue mayor en comparación con el resto de etapas. La frecuencia cardiaca en la perimenopausia es inestable, presentando mayor variación que las etapas anteriores y en la premenopausia precoz, la frecuencia cardiaca es mayor que las demás etapas. Conclusión: La frecuencia cardiaca en la perimenopausia es inestable presenta mayor variación que las demás etapas y en la premenopausia precoz la frecuencia cardiaca es mayor que el resto de etapas estudiadas

Frecuencia cardiaca, Menopausia, Reloj polar, Mujeres

Citation: MADAGLENO-ARROYO, Dulce, SANCHEZ-BARAJAS, Mauricio, GARCIA-PEREZ, Marysol and CORDOVA-FRAGA, Teodoro. Heart rate behavior on the menopause stages. Journal of Physiotherapy and Medical Technology. 2022. 6-15: 14-21

* Correspondence to Author (e-mail: dm.magdalenoarroyo@gmail.com)
† Researcher contributing first author

Introduction

Menopause is the cessation of menstruation for 12 continuous months without any pathology. The average age of menopause has been reported in 51.4 years (Potter, Schrager, Dalby, Torell, & Hampton, 2018). The ovaries no longer secrete enough progesterone and 17β estradiol and estrogens are only produced in small amounts, due to these changes the secretion of the follicle-stimulating hormone (FSH) and luteinizing hormone (LH) rise (Garrido-Latorre, Lazcano-Ponce, López-Carrillo, & Hernández-Avila, 1996).

Four stages of menopause are identified: 1) pre-menopause, 2) peri-menopause, 3) early post-menopause and 4) late post-menopause (Harlow *et al*., 2012). Peri-menopause begins with events such as changes in the usual period of menstruations greater than 7 days or the intermittency of some menstrual periods, while early post-menopause includes the defined period of time as the first 5 years after the final menstrual period, this period includes the first year of absence of menstruation (which is the point defined as the postmenopausal pass) plus the next 4 years of it, and the late post-menopause that begins 5 years after the final menstrual period until death (Butler & Santoro, 2011).

It is known that during post-menopause, women have a greater risk of cardiovascular disease (Sánchez-Barajas, Figueroa-Vega, Ibarra-Reynoso, Moreno-Frías, & Malacara, 2015). The incidence of cardiovascular disease in Mexico is very high and represents the leading cause of death in the country (Garcia-Garcia *et al*., 2006). However, cardiovascular diseases, particularly coronary heart disease, have a low incidence in premenopausal women (Stevenson, Tsiligiannis & Panay, 2018). Other authors have investigated the relationship between early menopause and coronary heart disease as well as heart attacks where it was concluded that early menopause was associated with these conditions in an important way (Wellons, Ouyang, Schreiner, Herrington, & Vaidya, 2012). Previous studies have revealed a relationship between postmenopausal symptoms with disturbances in heart rate variability (Lee, Kang, Kim, Park, & Song, 2011). During menopause, there is a decrease between the R-R intervals of the QRS complex implying that there is an increase in heart rate (HR) (Brockbank, Chatterjee, Bruce, & Woledge, 2000).

Estrogens influence the improvement of the arterial wall response to lesions, promote re-endothelization and prevent coronary artery spasm through vasodilation mediated by increases in nitric acid production, among other functions. Therefore, the absence of estrogens in women after menopause suggests a loss of cardioprotective effects, involving cardiovascular risk.

A cross-sectional study conducted in Mexico (Iñigo-Riesgo, Torres-Gómez, Lofte-Navarro, Cortés Sanabria & Godoy-Muzquiz, 2009) reported that levels of total cholesterol and LDL cholesterol are higher in the group of postmenopausal women; Miguel-Soca *et al*. (2014), in their study, they observed that menopausal women presented blood pressure levels higher than the control group, that is, with a higher risk of hypertension, these results have been consistent obtaining the same results with other studies (Vongpatanasin, 2009).

In this paper is presented the analysis of the heart rate performed based on the measurements in 200 women during the pre-, peri- and postmenopause for comparative purposes and its association with symptoms such as sleep disorder, loss of sexual interest, perception of stress, and levels of FSH and cortisol. In addition, an automated learning model based on linear discriminant analysis is presented as the first proposal for the classification of women in the different stages studied.

Methodology

Patients

Two hundred women aged from 25 to 57 years participated in this study, they were divided into four groups: 50 volunteers for each stage of menopause. All they belong to the General Hospital of Zone with Family Medicine No. 21, in the City of León Guanajuato, accomplish the inclusion criteria: no history of heart disease, intake of antiarrhythmic drugs, thyroid diseases, without hormone replacement therapy, without evidence of neoplastic diseases and not having any infectious process. Prior to the study information and voluntarily, they signed the informed consent letter that the present investigation did not imply any type of risk for their physical, psychological and/or social health, in addition, the project was approved by the Research Ethics Committee in Health.

ISSN 2523-6849

Data collection

For study information, all volunteers were cited the study day at 8 am. The clinical studies were taken, as well as the anthropometric data questionnaires and psychological symptoms. After 15 minutes of rest (in order that the parameters of the heart rate were normalized between 70 and 80 beats per minute), the RS400 CX polar clock (Polar, Finland) was used and registered their respective heart rate for 4 hours (Sánchez-Barajas *et al*., 2015). The women carried out their ordinary activities (without having control of these with the intention of being able to record the activity of the heart rate in the most daily possible environment and with the routine activities of each of the participants) and returned to deliver the watch. The measurements were downloaded in a database.

Heart rate

For the heart rate measurement, a Polar RS400 CX Polar Running Computer Wireless Watch type monitor was used (developed in Kempele, Finland); following the measurements, physiological interpretation and clinical use of research Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (Malik *et al*., 1996). The validation of the use of this device for the acquisition has been validated by Gamelin *et al*., (2006).

Questionnaires

For the evaluation of physical and psychological symptoms, the measurement of depression and sleep disturbance were performed by using a modification to the scale of depression measurement developed (Licht, Qvitzau, Allerup, & Bech, 2005). The score included 8 points: sadness, problems with work and occupation, fatigue, unsystematic pain, guilt, decreased verbal activity, suicidal tendencies, slow thinking and sleep disturbance. Sadness was classified into five categories in terms of frequency, from no = 0 to always = 5; work and occupation in four categories, from no problems = 0 until you cannot work for more than 3 h = 4; fatigue in four categories, from no = 0, even feels very weak = 4; non-systematized pains in three categories, from no = 0, to often = 3; feeling guilty in five categories.

From doesn't have = 0 until he has allusions of guilt = 5; decrease in verbal activity in five categories, from no = 0, to always = 5; suicidal thoughts in five categories, from never = 0, to have attempted suicide = 5 and slow thinking in three categories, from normal = 0, to frequent = 3. Sleep disturbance was measured with two questions: Do you have trouble falling asleep? and do you have sleep disturbances in the morning? with three response categories (from no = 0, to constants = 3.

Anxiety was assessed through a questionnaire based on aspects related to the following symptoms: dyspnoea, palpitations, tremor, agitation, and fear of madness, each item was scored as Yes (value of 1) or No (value of 0). Total scores ranged from 0 to 14 points (Licht *et al*., 2005).

The measurement of the perception of stress was measured using a Cohen adapted instrument (Cohen, Kamarck, & Mermelstein, 1983) that contains 14 questions related to the frequency of inability to control life, feeling nervous or stress, safety for handling personal problems among others aspects.

Loss of sexual interest was assessed with a single question about the frequency of this symptom (from no, to severely).

Analysis of data

The analysis was performed for each group: menopause, premenopause, perimenopause, early post-menopause, and late post-menopause. The registration of each participant was made for four hours, which was characterized by the number of peaks it had, that is, the number of times the signal presented values outside the normal range of each patient's heart rate; to obtain this number, it was used a signal detection algorithm based on the z-score. These peaks represent instability of the signal, the greater the number of peaks detected, the greater the instability of the register.

Differences in heart rate between groups were tested using analysis of variance (ANOVA) and a posterior Tukey test. The principal component analysis was used to know the variables with the greatest weight in the description of the four groups studied.

ISSN 2523-6849

It was interesting to know if there were any correlations among these resulting variables, so Pearson's correlation coefficients were subsequently calculated for each combination of variables.

Results

In Table 1, the average heart rate (HR) is shown per group with their respective confidence intervals.

Group	N	Mean HR	CI al 95 %	σ
Pre-menopause	50	87.90	81.49 – 85.95	9.37
Peri-menopause	50	87.36	79.33 – 85.02	10.98
Early post-menopause	50	97.16	87.63 – 93.54	13.26
Late post-menopause	50	90.10	83.05 – 87.16	7.90

N: Sample size
HR: Heart Rate
CI: Confidence intervals

Table 1 Confidence intervals of HR for the climacteric stages

The ANOVA test of a factor for the four groups shows that there are significant differences between the means of the groups with a significance of $p = 7.5 \times 10^{-5}$ at an $F = 7.625$. Tukey's post hoc test shows that early postmenopause has significant differences with the rest of the groups; when compared with premenopause $p = 0.001$, with perimenopause $p = 8 \times 10^{-5}$ and with late post-menopause $p = 0.021$ (see figure 1).

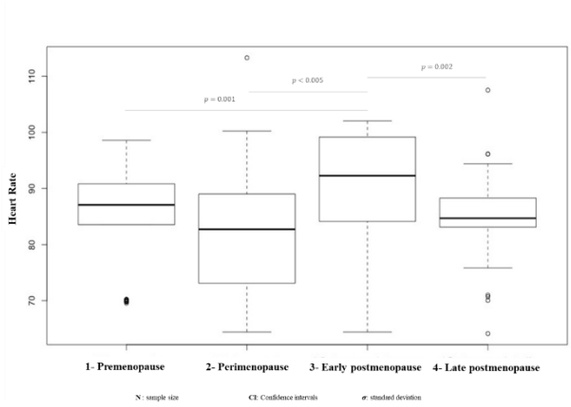

Figure 1 Graphs of average HR boxes among study groups. It is observed that the average HR of the early postmenopausal group is above the rest significantly

This group has an average HR higher than the rest of the groups and based on the ANOVA it can be said that therefore the early post-menopause group is characterized by a higher HR than the other stages and that they are not due to chance.

The one-way ANOVA test for the four groups showed that there are significant differences between the means of the groups with $p = 7.5 \times 10^{-5}$ at an $F = 7.625$. Tukey's post hoc test shows that early post-menopause has significant differences when compared to the other groups; when compared with pre-menopause $p = 0.001$, with perimenopause $p < 0.005$ and with late postmenopause $p = 0.021$.

Therefore, early post-menopause had a higher average of HR than the other statistically significant groups.

Heart Rate Instability

In figure 2 is shown the result of applying the peak detection algorithm in a heart rate signal. Each participant is characterized by having a certain number of peaks in their registry. As long as, in table 2 is shown the average number of peaks detected in the signal for each stage of the study.

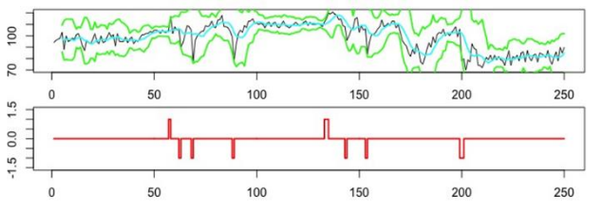

Figure 2 Graph of the z-score algorithm implemented in a signal. The algorithm can detect sudden changes in the signals of the HR thus presenting in the second graph the time in which there are changes greater than 3.5 standard deviations from the average recorded up to that moment

Group	N	Average peaks of the signal	CI al 95 %
Pre-menopause	50	17.60	16.16 – 19.12
Peri-menopause	50	26.82	25.24 – 28.34
Early post-menopause	50	22.04	20.20 – 23.78
Late post-menopause	50	23.34	21.60 – 24.86

N: Sample size
HR: Heart Rate
CI: Confidence intervals

Table 2 Confidence intervals of the number of peaks in the HR signal

ISSN 2523-6849

The ANOVA after the application of the algorithm shows a $p = 2.87 \times 10^{-11}$ and $F = 19.83$. Tukey's post hoc test resulted in a significance of $p < 0.005$ between perimenopause and premenopause; $p = 0.001$ between perimenopause and early postmenopause and $p < 0.005$ between perimenopause and late post-menopause, therefore, perimenopause showed greater instability in HR during the four hours of registration.

Analysis of psychological and somatic symptoms, HR, FSH and cortisol

The PCA of the 4 study groups showed that 84.69 % of the information is found in the first two components (see figure 3). The first component contains 70.02 %, this first component showed that FSH is the variable that has the greatest influence when separating the pre and perimenopausal stages with the postmenopausal stages, while component 2, showed the following important variables in the description of the groups, which were: HR, BMI, cortisol, perception of stress, loss of sexual interest and sleep disorder; of these, cortisol and stress perception seems to have a greater influence on the description of perimenopause, while the heart rate inclines its influence towards early and late post-menopause, this is summarized in table 3.

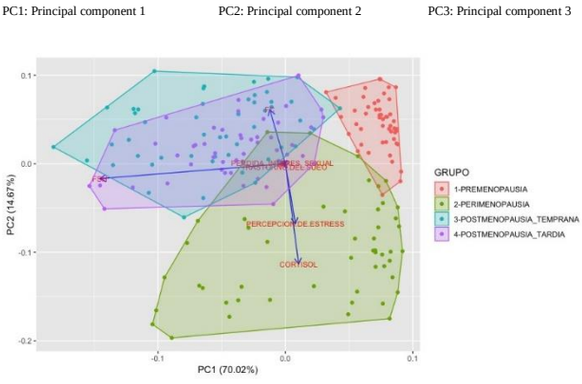

Figure 3 PCA Results

It is observed that FSH is the variable with more weight in the first main component, while cortisol, HR, the perception of stress is more significant in the second component.

	PC1 (70.02 %)	PC2 (14.67 %)	PC3 (10.08 %)
HR (Heart rate in beats per minute)	-0.08	0.42	-0.90
BMI (Body mass index kg / m^2)	-0.02	-0.00	-0.08
FSH (Follicle stimulating hormone mUI / ml)	-0.99	-0.12	0.04
Cortisol (ng / ml)	0.07	-0.77	-0.42
Perception of stress	0.05	-0.46	-0.12
Loss of sexual interest	-0.02	0.01	0.01
Sleep disorder	-0.01	-0.03	0.01

Principal Component 1
PC2: Principal Component 2
PC3: Principal Component 3

Table 3 Weights of the variables in the main components

The rest of the variables such as HDL and LDL cholesterol levels measured, as well as glucose and triglycerides, are variables with less importance in the characterization of climacteric stages.

From the significant correlation (with a 95 % confidence level) among the variables with the greatest weight, it was found that between perimenopause and early post-menopause, HR has a negative correlation ($\rho = -0.29$ and $\rho = -0.28$ respectively) with loss of sexual interest; in pre-menopause, there is a positive correlation ($\rho = 0.28$) between HR and FSH levels [mIU / ml]; in perimenopause, a positive correlation ($\rho = 0.28$) between the perception of stress with sleep disorder and in the early postmenopausal group there is a negative correlation between HR and sleep disorder ($\rho = -0.28$).

Discussion

The study of the heart rate signals using the z-score algorithm showed that the stage of perimenopause presents greater instability in the HR register. Neves *et al*. (2007), have reported that during menopause there is an imbalance in the control of the ANS over the cardiovascular system, so the instability found in this study may be related to changes in the ANS over the cardiovascular system.

In the analysis of the average HR in the different stages of the climacteric, it was found that the average HR of early post-menopause is significantly higher compared to the other groups (Mercuro *et al*., 2000).

ISSN 2523-6849

A higher than average HR implies that there is a significant percentage of women who manage a higher HR than normal HR, and therefore could indicate cardiovascular risk alert (Mercuro *et al*., 2000), this does not happen with the late postmenopausal group, although it should be mentioned that if it has an average HR higher than the premenopausal group (which can be considered as a control group), however, these differences are not significant.

These results show congruence with the studies carried out by Brockbank *et al*. (2000), where they show that during menopause there is a decrease between the R-R intervals of the QRST complex implying that there is an increase in heart rate.

It is known that estrogens affect the cardiovascular system (Kaunitz & Manson, 2015), for example, it has been studied on arterial hypertension that estrogen deficit after menopause induces insulin resistance by inducing proinflammatory cytokines and increased oxidative stress while accompanying hyperinsulinism favors sympathetic stimulus that causes vasoconstriction and sodium retention in the kidney which favors arterial hypertension (Navarro Despaigne, 2015).

Although the relationship between estrogens and heart rate has not been specifically found as such, it is intuited that estrogens may be the cause of these differences in the different stages studied (Kaunitz & Manson, 2015; Navarro Despaigne, 2015; Newson L, 2018).

In the PCA analysis, it was found that of all the variables recorded for each participant, the most important variables to describe the different stages were the FSH, which stands out for having a greater weight in the first main component, cortisol, perception of stress, HR, loss of sexual interest and sleep disorder, the latter variables are mostly found in the second main component. This set of variables can describe 84.9 % of the information regarding the stages of the climacteric.

The result of having the FSH variable in the first main component is consistent with the current fact of using FSH levels to determine if a woman has entered menopause, FSH is, therefore, an effective indicator in the differentiation of the stages of climacteric, which coincides with other authors (Gao *et al*., 2018).

On the other hand, in this work, the second main component shows the following most important variables: cortisol, perception of stress, sleep disorder and HR, being that HR was not expected to be one of the important variables at the time of describing these stages.

The correlation between variables shows that in women in the early perimenopausal and postmenopausal state, the average HR had a negative correlation with the loss of sexual interest, as the stages of menopause progress, accentuating in postmenopausal women observing a decrease in sexual desire (Yangin, Kukulu, & Sözer, 2010), the HR is going up, while the sexual interest is decreasing every time.

A positive correlation between HR and FSH levels was found in the group of premenopausal women and for the perimenopause group, a positive correlation between HR with sleep disorder and finally in the early postmenopausal group a negative correlation between HR and sleep disorder, the latter is explained by the fact that sleep disorders generate a state of chronic stress that is related to an increase in cortisol production, in addition to a greater activity of the sympathetic system and as a result a state of chronic inflation (Javaheri & Redline, 2017).

Regarding the HR correlation with FSH during the premenopausal period, nothing similar is reported in the literature and is also discussed between future works. Studies of the stages of menopause that start from premenopausal to postmenopausal are important if it wants to know the characteristics of heart rate.

Conclusions

The heart rate during the perimenopause is unstable, presents greater variation than the other stages and in the early pre-menopause, the heart rate is higher than the rest of the stages studied.

Cardiovascular diseases are the leading cause of death in women reaching 50 years of age, with heart rate being an important parameter in this stage.

ISSN 2523-6849

The higher the heart rate, the greater the risk of cardiovascular disease, that is, the lower the life expectancy.

Acknowledgements

Authors thank the Dirección de Apoyo a la Investigacion y al Posgrado – UGTO for the partial support under grant DAIP-2021/59023 and all the Hospital-IMSS patients enrolled in this study

References

Brockbank C L, Chatterjee F, Bruce S A, and Woledge R C (2000). *Heart rate and its variability change after the menopause*. Exp Physiol 85(3): 327-330. DOI.org/10.1111/j.1469-445X.2000.01902.x

Butler L, and Santoro N (2011). *The reproductive endocrinology of the menopausal transition*. Steroids 76(7): 627-635. DOI.org/10.1016/j.steroids.2011.02.026

Cohen S, Kamarck T, and Mermelstein R (1983). *A global measure of perceived stress*. Journal of Health and Social Behavior 24(4): 385-396. DOI.org/10.2307/2136404

Gamelin FX, Berthoin S and Baquet G (2006). *The validity of the Polar S810 heart rate monitor to measure R-R intervals at rest*. Med Sci Sports Exerc 38(5):887-893. DOI:10.1249/01.mss.0000218135.79476.9c.

Gao L, Wu X, Zhu X, Jin Q, Ma Q, and Sun A, (2018). *Follicle-stimulating hormone associates with metabolic factors in postmenopausal women*. Gynecological Endocrinology 34(12):1035-1038. DOI: 10.1080/09513590.2018.1482868

Garcia-Garcia, G., Aviles-Gomez, R., Luquin-Arellano, V. H., Padilla-Ochoa, R., Lepe-Murillo, L., Ibarra-Hernandez, M., & Briseño-Renteria, G. (2006). *Cardiovascular risk factors in the Mexican population*. Renal Failure 28(8): 677-687. DOI.org/10.1080/08860220600936096.

Garrido-Latorre F, Lazcano-Ponce E C, López-Carrillo L, and Hernández-Avila M (1996). *Age of natural menopause among women in Mexico City*. International Journal of Gynecology and Obstetrics 53(2): 159-66. DOI.org/10.1016/0020-7292(96)02655-0.

Harlow, S. D., Gass, M., Hall, J. E., Lobo, R., Maki, P., Rebar, R. W… De Villiers, T. J. (2012). *Executive summary of the stages of reproductive aging workshop* + 10: *Addressing the unfinished agenda of staging reproductive aging*. In the Journal of Clinical Endocrinology and Metabolism 97(4):1159-68. DOI.org/10.1210/jc.2011-3362

Iñigo-Riesgo C, Torres-Gómez LG, Lofte-Navarro CA, Cortés-Sanabria L, Godoy-Muzquiz RJ (2009). *Cardiovascular risk factors in the climacteric*. Ginecol Obstet Mex. 77(12): 535-543

Javaheri S, and Redline S, (2017). *Insomnia and Risk of Cardiovascular Disease*. Chest. 152(2): 435-444. DOI: 10.1016/j.chest.2017.01.026.

Kaunitz, A. M., & Manson, J. E. (2015). *Management of menopausal symptoms*. Obstetrics and Gynecology 126(4): 859-876. DOI.org/10.1097/AOG.0000000000001058

Lee, J. O., Kang, S. G., Kim, S. H., Park, S. J., & Song, S. W. (2011). *The relationship between menopausal symptoms and heart rate variability in middle-aged women*. Korean Journal of Family Medicine 32(5): 299-305. DOI.org/10.4082/kjfm.2011.32.5.299

Licht, R. W., Qvitzau, S., Allerup, P., & Bech, P. (2005). *Validation of the Bech-Rafaelsen Melancholia Scale and the Hamilton Depression Scale in patients with major depression; is the total score a valid measure of illness severity*? Acta Psychiatrica Scandinavica 111(2):144-149. DOI.org/10.1111/j.1600-0447.2004.00440.x

Marek Malik, J. Thomas Bigger, A. John Camm, Robert E. Kleiger, Alberto Malliani, Arthur J. Moss, Peter J. Schwartz, (1996). *Heart rate variability. Standards of measurement, physiological interpretation, and clinical use*. European Heart Journal 17(3): 354-381. DOI.org/10.1093/oxfordjournals.eurheartj.a014868

Mercuro, G., Podda, A., Pitzalis, L., Zoncu, S., Mascia, M., Melis, G. B., & Rosano, G. M. C. (2000). *Evidence of the role of endogenous estrogen in the modulation of the autonomic nervous system*. American Journal of Cardiology 85(6):787-789, A9. DOI.org/10.1016/S0002-9149(99)00865-6

ISSN 2523-6849

Miguel-Soca P, Rivas-Estévez M, Sarmiento-Teruel Y, Mariño-Soler A, Marrero-Hidalgo M, Mosqueda-Batista L (2014). *Risk Factors of Cardiovascular Disease in Menopausal Women*. Rev Fed Arg Cardiol. 43(2): 90-99. http://www.fac.org.ar/2/revista/14v43n2/art_orig/art_orig04/soca.php.

Navarro Despaigne, C. D. A. (2015). *Menopause and hypertension: From biology to clinical practice. Revista Cubana de Medicina* 54(3): 239-251.

Neves V, Silva de sá M, Gallo L, Catai A, Martins L, Crescencio JC, Perpétuo N, Silva E (2007). *Autonomic modulation of heart rate of young and postmenopausal women undergoing estrogen therapy*. Braz J Med Biol Res. 4(40): 491-499.
DOI: 10.1590/s0100-879x2007000400007

Newson L (2018). *Menopause and cardiovascular disease*. Post-Reprod Health 24(1):
44-49. DOI:10.1177/2053369117749675

Potter B, Schrager S, Dalby J, Torell E, and Hampton A, (2018). *Menopause*. Primary Care: Clinics in Office Practice 45(4): 625-641. DOI.org/10.1016/j.pop.2018.08.001.

Sánchez-Barajas M, Figueroa-Vega N, Ibarra-Reynoso L del R. Moreno-Frías C, and Malacara J M, (2015). *Influence of heart rate variability and psychosocial factors on carotid stiffness, elasticity, and impedance at menopause*. Archives of Medical Research 46(2): 118-126. DOI.org/10.1016/j.arcmed.2015.02.006

Stevenson J C, Tsiligiannis S, Panay N, (2018). *Cardiovascular risk in perimenopausal women*. Curr Vasc Pharmacol 17(6):591-594. DOI:10.2174/1570161116666181002145340.

Vongpatanasin, W. (2009). *Autonomic regulation of blood pressure in menopause*. Seminars in Reproductive Medicine 27(4): 338-345.
DOI.org/10.1055/s-0029-1225262

Wellons, M., Ouyang, P., Schreiner, P. J., Herrington, D. M., & Vaidya, D. (2012). *Early menopause predicts future coronary heart disease and stroke: The Multi-Ethnic Study of Atherosclerosis*. Menopause 19(10): 1081-1087. DOI.org/10.1097/gme.0b013e3182517bd0

Yangin, H. B., Kukulu, K., & Sözer, G. A. (2010). *The perception of menopause among Turkish women*. Journal of Women and Aging 22(4): 290-305. DOI.org/10.1080/08952841.2010.518880

ISSN 2523-6849