International Journal of Computer Vision and Signal Processing, 1(1), 32-37(2021)

Comparison of Prognostic Determinants after Myocardial Infarction using Holter ECG Data at 72-h

Emi Yuda*, Itaru Kaneko

Center for Data-driven Science and Artificial Intelligence
Tohoku University,Japan

Yutaka Yoshida

School of Design Architecture
Nagoya City University, Japan

Junichoro Hayano

Heartbeat Science Lab Co., Ltd., Japan

Abstract

Development of in medical sensor technology, it is possible to measure human bio-signals over long periods of time. In particular, electrocardiogram (ECG) data obtained by long-term measurement in hospitals can contribute to the construction of bioindicators for human diseases, which have high prognostic power for cardiac diseases. In previous studies, it has predicted the presence of myocardial necrosis, vascular occlusion, and myocardial ischemia mainly by detecting characteristic ECG findings such as abnormal Q waves, ST interval elevation, and coronary T waves from ECG waveform. In this study, we compared heart rate variability (HRV) indices predictive of myocardial infarction calculated from 72-hour Holter ECG RR interval data with indices calculated from 24-hour data. The HRV indices of 5 subjects in the young group (mean 22 y) and 5 subjects in the middle-aged group (mean 46 y) were compared, and we revealed the usefulness of the 72-hour data for some indices, such as standard deviation NN interval (SDNN).

Contribution of the Paper: We have shown that it is desirable to analyze data obtained from long-term measurements in order to calculate prognostic indices for cardiac diseases using heart HRV indices.

Keywords: Holter ECG, Long-time data analysis, Monitoring, Heart rate variability (HRV), Bio-signal processing

IJCVSP

ISSN: 2186-1390 (Online)
http://cennser.org/IJCVSP

Article History:
Received: 29 April 2021
Revised: 20 July 2021
Accepted: 15 September 2021
Published Online: 16 September 2021

1. INTRODUCTION

The circadian clock controls human rhythms and the oscillation of intracellular proteins on 24-h cycle. The mechanism of this biological clock is common to all life, from molds to humans. The rhythms (cycles) of living organisms include ultradian rhythm; a few tens of minutes to a few hours, circadian rhythm; about 24 hours, circabidian rhythm; about 2 days, circalunar rhythm; about 1 month, and circannual rhythm; about a year. Of these, circadian rhythms have been the main subject of research in temporal biology, and there are few studies on biological rhythms in human longer than 24-h. Due to these characteristics of circadian rhythm, it is well-known that human rhythms are 24 hours. Therefore, the human condition was estimated from 24-hour data. In addition, due to the technical problems of sensors, especially of the sensor batteries, it has been considered difficult to measure more than 24 hours bio-signals, such as ambulatory ECG, pulse wave, and acceleration.

*Corresponding author

Email addresses: emi.a.yuda@tohoku.ac.jp (Emi Yuda), itaru-k@acm.org (Itaru Kaneko), yyoshida@sda.nagoya-cu.ac.jp (Yutaka Yoshida), hayano@acm.org (Junichoro Hayano)

Circadian rhythm is formed intrinsically, but have mechanisms to be modified by external stimuli such as light, temperature, and food. Human rhythms also follow a 25-h light-dark cycle, and when we are placed in complete darkness, the cycle becomes non-synchronized with the 25-h cycle (free-run). The non-synchronized cycle is then reset by a stimulus such as light or dark. It is thought that the suprachiasmatic nucleus of the brain influences the cycles in human body. When the body is placed in a non-periodic cycle, circadian rhythms are disrupted, which can lead to discomfort and circadian rhythm sleep disorder [1, 2]. It has also been found to affect work performance [3]. In short, humans have biorhythms, and behavioral patterns and activity levels vary from day to day. Therefore, it is important to consider activity levels and posture when interpreting biological signal data such as ECG, pulse wave, and respiratory curve under daily activities.
However, in recent years, in the field of human bio-signal research, advances in sensor technology have made it possible to measure data under daily activities for long periods of time. For example, in the field of Holter ECG research, research on 24-hour data measurement has been the main focus [4-10]. In the field of Holter ECG research, for example, research on 24-hour data measurement has been mainly [4-10], and these data have been stored, and Holter ECG recordings have been utilized to advance research on 24-hour ECG big data [11-13]. The 24-hour data analysis of bio-signals is also useful for the study of human biorhythms. For example, rhythmic disorders such as sleep time (bed in time) discrepancy can be screened at an early stage from bio-signal analysis of acceleration and ECG. However, the study of biorhythms longer than 24 hours has not progressed due to the difficulty of data measurement, and thus no useful index has been established. In order to quantitatively extract patterns of change and variables that predict patterns of abnormality, it is desirable to analyze data measured over long periods of time.
In this study, we compared the HRV indices obtained by analyzing the 72-hour Holter ECG RR intervals data with the data from a normal 24-hour Holter ECG data, focusing on the indices of prognostic determinants after myocardial infarction. After myocardial infarction, sudden death due to fatal arrhythmia and worsening of heart failure are often observed. Therefore, it is necessary to establish a reliable index as a prognostic factor after myocardial infarction, but there is no such useful index. In recent years, indices obtained by analyzing ECG waveform are thought to be useful in predicting the prognosis of myocardial infarction, and several studies have been conducted. However, no consistent results have been obtained [14-16]. In this study, long-term ambulatory ECG were recorded under daily activities for 72 consecutive hours and HRV indices were compared with the conventional 24-hour method. The authors have no conflict of interest related to this research.

2. METHODS

2.1. Protocol

10 healthy male and female subjects (age 20 - 65y), including 5 young (4 males and 1 female, mean 22y) and 5 middle-aged (4 males and 1 female, mean 46y) were recruited. Subjects wore a Holter ECG (Cardy Pico+03, Suzuken Co., Ltd., Japan) for 72-hour, and RR interval (RRI) were recorded for 3 consecutive days. To avoid the effect of seasonal variations, the experiment was conducted on 3 consecutive days in July. All subjects were healthy individuals with no underlying medical conditions.The Holter ECG sensor were of the 24-hour measurement type, so the subjects wore a new sensor every 24 hours. RRI data and triaxial body acceleration data were stored in memory of those device. After 72-hour measurement, we extracted the CSV data of the RRI and body acceleration data from the Holter ECG sensor using the Holter ECG data analyzer (Cardy Analyzer 05, Suzuken Co., Ltd., Japan) and analyzed the data with mean $\pm$ 95 percent confidence interval (CI).

2.2. Holter ECG sensor

The Holter ECG sensor is a medical sensor that is routinely used for continuous monitoring of ECG in an outpatient setting for the diagnosis of arrhythmia and myocardial ischemia (MI). This sensor incorporates a triaxial accelerometer, which allows simultaneous visualization of body acceleration and body position. Since many heart rate variability indices are affected by posture, it is necessary to evaluate posture simultaneously. A single of Holter ECG sensor can measure for 24-hours, record 100,000 heartbeats of ECG waveforms and RR interval time series, and store the data in the device (digital memory system). The data is stored in the device and analyzed offline after recording. In this experiment, the ECG was measured for 72 hours by changing the sensors, 300,000 heartbeats were measured in one experiment. The external dimensions of the sensor are W28 x D42 x H9 mm, and its weight is 13 g. Therefore, it is not felt to be worn. The recordingchannels are three ECG channels, one pacemaker pulse channel, and three acceleration channels. The memory capacity is 256 Mbytes, the A/D conversion is 10 bit (20 V/dig, 8 ms sampling), and the frequency response is 0.05 - 40 Hz.

2.3. Analysis of RR interval

The RR interval (RRI), which is the interval from one heartbeat to the next. It is actually not constant, normal for the RRI to fluctuate. HRV analysis is a non-invasive bio-assessment technique and an indicator of the cardiac autonomic nervous system [17]. HRV power decreases with age, furthermore, autonomic disturbances bias the autonomic balance toward sympathetic dominance and promote cardiovascular degeneration, especially in the elderly [17-19]. Decreased HRV power is due to an increased sympathetic nervous system and decreased parasympathetic

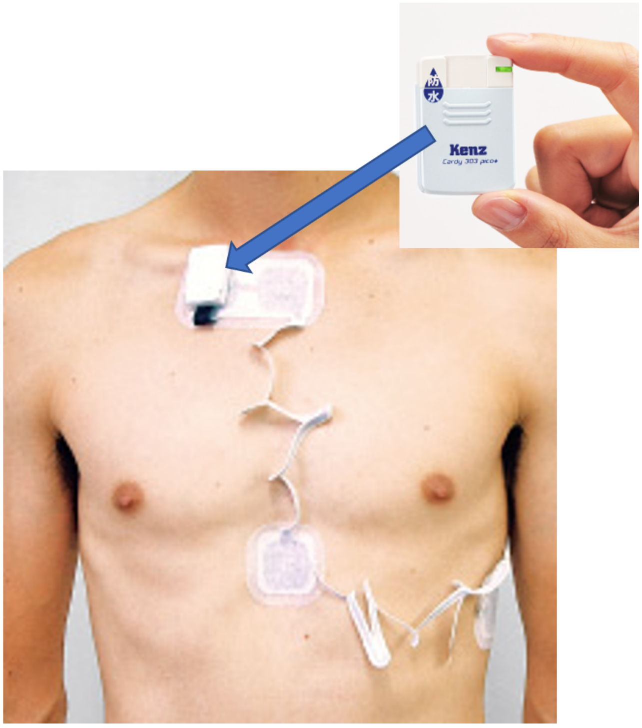

Figure 1: Holter ECG sensor.
This Holter ECG sensor can store data of human ECG RR interval, acceleration and posture for 24 hours and more. In this experiment, we changed this sensor every 24-hours and measured the data for 72-hours. In Holter ECG monitoring, where measurements are taken over a long period of time under daily life, there are many factors that can introduce noise into the ECG waveform, such as body movement and sweating, and proper electrode attachment is essential to reduce these effects as much as possible and obtain a clean ECG waveform. In this experiment, the electrodes of the Holter ECG were attached to the appropriate 3 points as shown in this figure. Before starting the recording, the amplitude of the waveform and noise contamination were checked on the monitor.

nervous system and has been associated with mortality from heart failure, especially in the elderly [18, 19].
Indices of heart rate variability include time domain and frequency domain. The following time-domain indices are commonly evaluated.

- HR: Mean of all heart rates
- Mean (ms): Mean of RR interval
- SDNN (ms): Standard deviation of RR intervals
- RMSSD (ms): The square root of the mean of the squares of the differences between successive adjacent RR intervals (index of vagal tone strength)
- NN50: the total number of differences between consecutive adjacent RR intervals greater than 50 ms (index of vagal tone strength)
- pNN50 (percent): Percentage of heartbeats in which the difference between consecutive adjacent RR intervals exceeds 50 ms (index of vagal tone strength)

The frequency domain is a HRV index calculated by computing the power spectrum from the RRI time series data and integrating the power in a given frequency domain. Power spectrum density (PSD) is one of the most commonly used methods to analyze the periodic structure of data in time series data analysis. The power spectrum of HRV is calculated by the nonparametric estimation method. The nonparametric method calculates the heart rate variability power spectrum directly from the time series data without using a model described by a few parameters. The formula for calculating the power spectrum is as follows.

$$\lim_{T\to\infty}\int_{-\frac{T}{2}}^{\frac{T}{2}}|x(t)|^2 = \int_{-\infty}^{\infty} S(\omega)d\omega \qquad (1)$$

The power of the HRV is a quantity defined as the square of the signal x(t), and the left side of the above equation represents the time average of the power of the signal x(t) when the time width is extended to infinity. The left side of the above equation represents the time average of the power of the signal x(t) as the time width is extended to infinity, which is the power of the signal x(t) per unit time. The right side is a frequency analysis of the power per unit time defined on the left side. By breaking down the total power into waves with regular periods, it expresses how much each frequency wave contributes to and constitutes the total power. $S(\omega)$, the power spectral density (PSD), is the quantity that indicates the fraction of the total power contributed by each frequency wave. In this equation, is the angular velocity, a variable that is proportional to the frequency $f(= 1/T)$ $(\omega = 2/T)$. The following indices of heart rate variability in the frequency domain are commonly evaluated.

- ULF: Ultra low frequency component ($<$ 0.003 Hz)
- VLF: Very low frequency component (0 - 0.05Hz) (reflects vasomotor activity, renin-angiotensin system, and thermoregulation)
- LF: The mid-frequency component (0.05 - 0.20 Hz) (reflects the baroreceptor system)
- HF: High-frequency component (0.20 - 0.35Hz) (reflects the respiratory system fluctuations)

The HF component is affected by parasympathetic activity induced by respiration, the LF component is affected by sympathetic and parasympathetic activity, and the LF component is affected by sympathetic and parasympathetic activity, and the VLF component is affected by sympathetic and parasympathetic activity. LF/HF is then used as an index of sympathetic nerve function. To obtain the frequency components, HRV analysis is used; the LF component has a peak around 0.1 Hz, and the HF component has a peak around 0.25 Hz. The power of the HF component is an indicator of parasympathetic nerve function, and the power of the LF/HF component is an indicator of sympathetic nerve function. In this study, indices of HRV in the time series domain and frequency domain obtained from RRI were calculated from 72-hour and 24-hour data for comparison.

2.4. Calculation of HRV parameters

We calculated and compared the time series domain parameters and frequency domain parameters for 72-hours and 24-hours. The time domain parameters calculated in this study are Mean and SDNN, and the frequency domain parameters are ULF, VLF, LF, and HF indices. This study was conducted with the approval of the Ethical Review Committee of the Graduate School of Medicine, Nagoya City University, Japan (Approval No. 60-18-0211, approved March 22, 2019).

3. RESULTS

Mean and SDNN were reproducible for 72-hours unchanged in both young and middle-aged. Mean NN showed no significant difference between young and middle-aged but SDNN was larger in young. 0-24h and 24-48h showed a greater difference in young, but not between young and middle-aged subjects. There was no significant of body acceleration difference between young and middle-aged. Overall, there was little change in the middle-aged, and the rate of change was greater in the young. Mean NN showed no significant difference between 24-48 hours, but changed at 48-72 hours in the young. SDNN showed significant changes in 3 days in both young middle-aged. ULF showed no significant changes in either middle-aged or young adults. The 72-hour change was significant in both young and middle-aged. The changes were greater in the young, especially for 3 days. In the 72-hour comparison, there were no significant changes in any of the frequency domain parameters. However, when comparing the rate of change from 24-hours and 72-hours data, the change in ULF was smaller than the change in HF.

4. DISCUSSION

By the treatment of myocardial infarction, its mortality rate is decreasing, but in order to improve the prognosis after hospital discharge, it is necessary to identify prognostic determinants after myocardial infarction. Long-term monitoring is indispensable for discovering indicators that reveal the relationship between various lifestyle habits and diseases such as cancer, stroke, and myocardial infarction. The study of indicators that predict biological conditions is useful for extending healthy life expectancy. It is also important to clarify the incidence of myocardial infarction

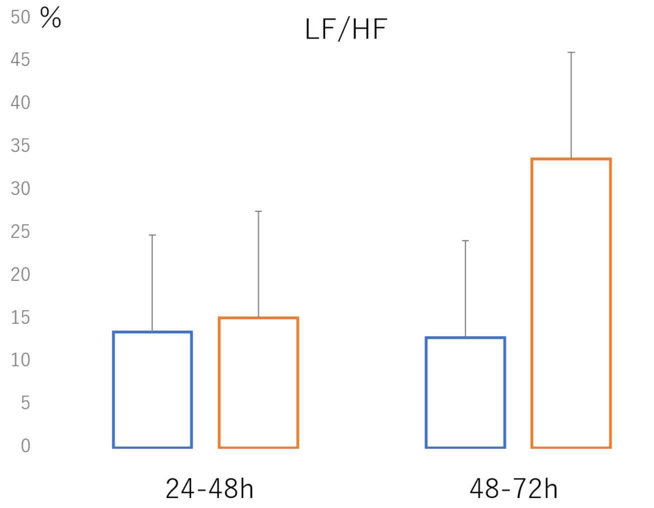

Figure 2: Figure 2. Example of comparison of one of HRV indices (LF/HF)
This figure shows the LF / HF power ratio (comparison between the day 2 and day 3). Blue bar is the average of the young group and orange bar is the average of the middle-aged (percent). This value represents the overall balance of sympathetic and parasympathetic nerves. A high indicates sympathetic dominance, and a low indicates parasympathetic dominance. However, it should be considered that it reflects the increased parasympathetic activity due to the high RSA (breathing) effect during regular deep breathing. The LF / HF ratio is calculated with the corrected value.

by long-term follow-up, and sensors that can be used under daily activities, such as Holter ECG, are suitable for "long-term follow-up.

In previous studies, it has predicted diseases from ECG waveforms measured mainly in hospitals. However, there are no studies using heart rate variability indices, which are based on the ECG waveform itself. As for prediction from ECG waveforms, it has been shown that the longer the data, the better, but these are ECG waveform research, not HRV index studies. Therefore, this study is the first challenge and a new attempt. And the evaluation from time domain and frequency domain indices is insufficient, and it will be essential to analyze nonlinear dynamics indices such as DFA1 in the future.

In Japan, there is no nationwide registration system for the incidence of cardiovascular diseases such as stroke and acute myocardial infarction, and the approximate number of incidents of cardiovascular diseases in medical institutions is determined using DPC (diagnosis procedure combination) data. DPC is a system introduced in 2003 to classify patients based on their diagnosis and the medical procedures (treatments and procedures) performed. The purpose of this system is to optimize medical costs. The prognosis of an individual's disease is important for the optimization of medical costs. And it is necessary to calculate the index from the long-term data of individuals. This study is the first to compare the 72-hours HRV index with the 24-hours HRV index for a new index in the era of continuous monitoring, but it has several limitations.

First, the subjects were healthy individuals, and in order to examine the clinical significance of heart rate variability index as a prognostic factor from the 72-hour ECG, it was originally desirable to analyze data from the acute and chronic phases after myocardial infarction. After that, the data should be retrieved retrospectively, and survival analysis by Cox proportional hazards regression is generally performed according to each index of HRV [20, 21]. Prognosis should be retrospectively analyzed by Cox proportional hazards regression according to each index of HRV and the relative risk rate should be calculated.

Secondly, the 72-hour continuous measurement in this study does not take into account individual biological rhythms such as sleep time and lifestyle, and only compares the 72-hour and 24-hour HRV indices based on prognostic factors after myocardial infarction. In the future, it is desirable to combine the analysis with lifelog and other characteristics of the subject. Until now, most long-term ECG studies have been conducted on hospitalized patients, and few studies have analyzed 72-hour long-term ECG during daily activities. The present study is a valuable attempt to understand the long-term data of healthy people under daily activities.

In this study, SDNN was found to fluctuate greatly over 72 hours in both young and middle-aged subjects. Since it is known that sympathetic activity is increased during exercise [17]. In short, when was the data measured; the value of the index is affected by when the data was measured. This is an important point because in the case of ECG data obtained from hospitalized patients, there is no change in activity or body position because most patients are bedridden. In this study, however, we showed that the values of the indices under daily activities differed depending on the measurement day. The heart rate variability index differs with different activity patterns. Of course, there have been many studies on body acceleration and HRV indices, but most of them have been conducted after one week [22].

The significance of this study lies in the fact that it clarified that the point of time at which the data is measured is an important point. By comparing the heart rate variability indices of 72-hours and 24-hours in young and middle-aged subjects, we confirmed that the daily activity and heart rate variability indices differed even in 3 consecutive days. The development of information and communication technologies has given rise to new sensing technologies for measuring various information in real field. The number of days during which the human body can be monitored by wristwatch-type wearable devices is prolonging, and pulse waves and ECG are becoming easier to measure during daily activities. As the technology of bio-metric measurement advances, research on bio-signal processing is necessary to extract useful information from the data to estimate the human biological state, and the identification of rhythms and prediction of diseases are among the useful indicators. This data analysis results is expected to be applied not only to medicine but also to sports and welfare fields because it captures the dynamic movements of the body. In addition to medical care, the technology is expected to be applied to sports and welfare fields.

5. CONCLUSIONS

The results of this study showed that the HRV index from the 72-hours measurement was reproducible; the change in HRV was greater in the young than in the middle-aged. The variance in ULF; one of HRV indicators, ultra-low frequency component (< 0.003 Hz) was smaller than that in other indices, with little difference by age. Therefore, when estimating prognosis by analyzing 24-hour data, ULF was found to be one of the indicators with less variation in 72-hours, and it was found to be one of the robust indicators. Identifying individual biorhythms from 72-hour data is a future challenge; especially length that exceeds more 24-hour rhythm (circadian rhythm). For future research, what is the index that improves the prediction accuracy in long-term measurement is an issue. However, in this study, we showed one of the indexes that can estimate the biological condition even by 24-hour measurement. The results of this study suggest a direction for one of the utilization of 72-hours data.

ACKNOWLEDGMENT

This publication was supported by Suzuken Memorial Foundation research grant (Emi Yuda). And this research was partially supported by the Ministry of Education, Science, Sports and Culture, Grant-in-Aid for Scientific Research (B) 2020-202320H04270, Makoto Yoshizawa, and Tohoku University Center for Gender Equality Promotion Research grant (TUGUM Project, Emi Yuda).

References

1. Silva PM, Nobre FL. Biological rhythms in man. Particular aspects in medicine. Acta Med Port. 1993 Feb;6(2):95-9.

2. Sirota Jh, Baldwin Ds, Villarreal H. Diurnal variations of renal function in man. J Clin Invest.29(2):187-92, 1950.

3. Bjerner B, Holm A, Swensson A.Diurnal variation in mental performance; a study of three-shift workers.Br J Ind Med.Apr;12(2):103-10, 1955.

4. Lobodzinski SS, Laks MM. New devices for very long-term ECG monitoring. Cardiol J. 2012;19(2):210-4.

5. Verberk WJ, Omboni S, Kollias A, Stergiou GS. Screening for atrial fibrillation with automated blood pressure measurement: Research evidence and practice recommendations. Int J Cardiol. 2016 Jan 15;203:465-73.

6. Palladino A, D'Ambrosio P, Papa AA, Petillo R, Orsini C, Scutifero M, Nigro G, Politano L. Management of cardiac involvement in muscular dystrophies: paediatric versus adult forms. Acta Myol. 2016 Dec;35(3):128-134.

7. Koester C, Ibrahim AM, Cancel M, Labedi MR. The Ubiquitous Premature Ventricular Complex. Cureus. 2020 Jan 7;12(1):e6585.

8. Ryan M, Lown B, Horn H. Comparison of ventricular ectopic activity during 24-hour monitoring and exercise testing in patients with coronary heart disease. N Engl J Med. 1975 Jan 30;292(5):224-229.

9. Lown B, Calvert AF, Armington R, Ryan M. onitoring for serious arrhythmias and high risk of sudden death. Circulation. 1975 Dec;52(6 Suppl):III189-98.

10. Krieger R, Engel UR, Burckhardt D, Boschung P. Frequency and type of arrhythmias in patients with chronic coronary disease. Z Kardiol. 1976 Feb;65(2):157-65.

11. Yuda E, Ueda N, Kisohara M, Hayano J. Redundancy among risk predictors derived from heart rate variability and dynamics: ALLSTAR big data analysis. Electrocardiol 2021 Jan;26(1):e12790.

12. Yuda E, Kisohara M, Yoshida Y, Hayano J. Constituent factors of heart rate variability ALLSTAR big data analysis. Wireless Networks. 2020; 26: 4819-4823.

13. Hayano J, Kisohara M, Yoshida Y, Sakano H, Yuda E. Association of heart rate variability with regional difference in senility death ratio: ALLSTAR big data analysis. SAGE Open Medicine 2019;7:1-7.

14. Hosseini K, Vasheghani-Farahani A, Hosseinsabet A. Decreased longitudinal systolic strain rate of the left atrial myocardium as one of the earliest markers of atrial cardiomyopathy in subjects with brief paroxysmal atrial fibrillation. J Clin Ultrasound. 2020 Oct;48(8):476-485.

15. Korodi S, Toganel R, Benedek T, Hodas R, Chitu M, Ratiu M, Kovacs I, Mester A, Benedek I. Impact of inflammation-mediated myocardial fibrosis on the risk of recurrence after successful ablation of atrial fibrillation - the FIBRO-RISK study: Protocol for a non-randomized clinical trial. Medicine (Baltimore). 2019 Mar;98(9):e14504.

16. Alqarawi WA, Ramirez FD, Nery PB, Redpath CJ, Sadek MM, Green MS, Birnie DH, Nair GM. Identifying and Managing Premature Ventricular Contraction-Induced Cardiomyopathy: What, Why, and How? Can J Cardiol. 2017 Feb;33(2):287-290.

17. Hayano J, Iwase S, Orimo S.Clinical Assessment of the Autonomic Nervous System, Springer; 1st ed. 2017, p.325.

18. Hottenrott K, Hoos O, Esperer HD. Heart rate variability and physical exercise. Current status. Herz. 2006 Sep;31(6):544-52.

19. Parvaneh S, Howe CL, Toosizadeh N, Honarvar B, Slepian MJ, Fain M, Mohler J, Najafi B. Regulation of Cardiac Autonomic Nervous System Control across Frailty Statuses: A Systematic Review. Gerontology. 2015;62(1):3-15.

20. Podd S, Hunt J, Sulke N. Home Orthostatic Training in Elderly Patients with Vasovagal Syncope - A Prospective Randomised Controlled Trial. Eur Cardiol. 2015 Dec;10(2):123-127.

21. Takeda H, Owada K, Kurosawa K, Katohno E, Techigawara M, Awano N, Maruyama Y. Heart Rate Variabilities as Prognostic Factor of Acute and Old Myocardial Infarction. J. Electrocardiology 16:3 1996, 252-262.

22. Yuda E, Moriyama Y, Mori T, Yoshida Y, Kawahara M, Hayano J. Acute effects of endurance exercise on nocturnal autonomic functions in sedentary subjects: A pilot study. Journal of Exercise Rehabilitation. 2018, 14:113-117.