NONINVASIVE METHODS IN CARDIOLOGY 2021

Edited by: **Cornélissen G., Siegelová J., Dobšák P.**

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Jarmila Siegelova

Noninvasive Methods in Cardiology in the Last 30 Years

Jarmila Siegelova

Department of Physiotherapy and Rehabilitation, Department of Sports Medicine and Rehabilitation, Faculty of Medicine, Masaryk University, St. Anne´s University Hospital in Brno, CZ

Noninvasive Methods in Cardiology in the last 30 years included a lot of scientific meeting at the Masaryk University, Faculty of Medicine with the international participation of University of Minnesota, namely Professor Franz Halberg (1919-2013), Professor Germaine Cornelissen, Dr. Othild Schwartzkopff (1922-2017), University of Graz, Professor Thomas Kenner (1932-2018), nowadays Professor Nandu Goswami, University of Paris, Professor Jean-Paul Martineaud (1931-2010), University of Bourgone, Jean-Eric Wolf, Dr. Jean-Christoph Eicher, Tohoku University of Sendai, Professor Masahiro Kohzuki. Very important scientific findings in chronobiology of blood pressure, blood pressure measurement beat by beat, ambulatory blood pressure monitoring and heart rate variability are presented and discussed in Masaryk University with the organized Professor Jarmila Siegelova, Professor Bohumil Fiser (1943-2011), Dr. Jiri Dusek, Professor Petr Dobsak and participations with Professor Jan Penaz (1926-2015), Professor Zdenek Placheta (1931-2014), Professor Pavel Braveny (1931-2018), Professor Marie Novakova and others from Masaryk University.

The personalities who leaved us and worked with us for many years, are remembered in our publications in Noninvasive Methods in Cardiology on https://www.med.muni.cz/noninvasive-methods-in-cardiology/cs.

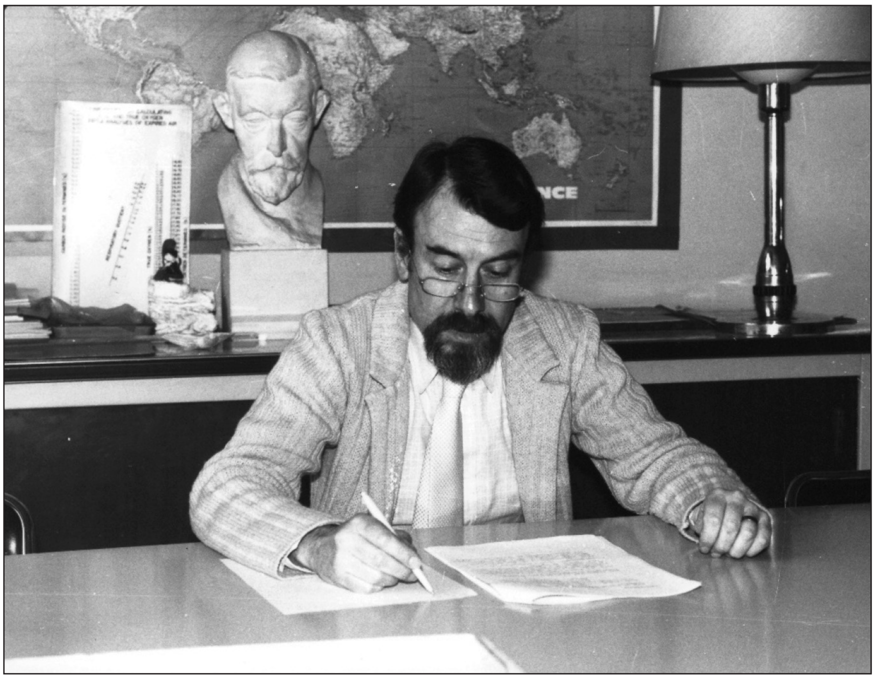
Professor Halberg is named as a father of chronobiology. The findings in chronobiology of blood pressure was proclaimed by Franz Halberg in Brno in cooperation with participants of Noninvasive Methods in Cardiology as Vascular Variability Disorders (VVDs) - risk factors of abnormal blood pressure and heart rate variability, which greatly increases the risk of adverse cardiovascular events. These results led to guidelines agreed upon at a Consensus meeting held at St. Anna Hospital, Masaryk University, Brno, Czech Republic, on October 6, 2008.

Other important topics are aimed to treatment of ischemic heart diseases due to cardiovascular rehabilitation, in patients with hypertension and therapy, with stroke, with heart failure, with renal failure and aging.

In the thirty years of the duration of Noninvasive Methods in Cardiology every year Congresses and proceedings of Noninvasive Methods in Cardiology in Masaryk University, Brno, the number of participants of abroad increased in our Masaryk University and Professor Petr Dobsak, who organized cooperation with Japan Universities, Assoc. Professor Michal Pohanka, Assoc. Professor Jiri Jancik, Dr. Jitka Svobodova, Dr. Hana Svacinova, Dr. Pavel Vank, Dr. Michaela Sosikova, Dr. Alena Havelkova, Dr. Petra Palanova, Dr. Veronika Mrkvicova, Mgr. Leona Dunklerova, Professor Marie Novakova, Dr. Zuzana Novakova, Dr. Jana Svacinova. The congresses and symposia in Masaryk University were visited every time from abroad by famous scientific personalities - Prof. Franz Halberg and Prof. Germaine Cornelissen from University of Minnesota, USA, Prof. Thomas Kenner, Rector of University and Dean of Medical Faculty, University of Graz, Austria and Prof. Jean-Paul Martineaud, Medical Faculty, Hopital Lariboisiere, Paris, France, Prof. Dr. Etienne Savin, Hopital Lariboisiere, University Paris, France, Prof. Jean-Eric Wolf, C.H.U. du Bocage, Dr. Jean-Christophe Eicher, C.H.U. du Bocage, University Dijon, France, Professor Kou Imachi, M.D., Ph.D., T.U.B.E.R.O., Tohoku University, Sendai, Japan, Professor Masahiro Kohzuki, M.D. Ph.D., Tohoku University, Sendai, Japan, Prof. Yambe Tomoyuki, M.D. Ph.D., Tohoku University, Sendai, Japan. In the last year there were in our meeting also new co-workers of Prof. T. Kenner, namely Prof. Dieter Platzer, University Graz, Prof. Nandu Goswami, Prof. Maxmilian Moser, University Graz, Prof. Daniel Schneditz, University Graz, Dr. Bianca Brix, University Graz.

5.6.1919 – 9.6.2013
*Professor **Franz Halberg,** M.D., Dr. h.c. (Montpellier), Dr. h.c. (Ferrara), Dr. h.c.(Tyumen), Dr. h.c. (Brno), Dr. h.c. (L'Aquila), Dr. h.c. (People's Friendship University of Russia, Moscow), Professor of Laboratory Medicine and Pathology, Physiology, Biology, Bioengineering and Oral medicine, University of Minnesota USA*

**29.9.1932 - †22. 12.2018*
*Prof. Dr. **Thomas Kenner**, M.D., Dr. h.c. mult. Dr. h. c., Universität Jena, 1990 Dr. h. c., Semmelweis University Budapest, 1998 Dr. h. c., Masaryk University Brno, 2000 Rector (president) Karl-Frances-Universitat, Austria 1989-1991 Dean of Medical School, Karl-Fraces Universitat, Austria, 1991-1997 Head, Department of Physiology, Karl-Frances-Universitat, Austria *27.3.1931-†29.11.2010*



Prof. ***Jean Paul Martineaud,*** *M.D.R*
Professor of Physiology, University Paris VII-Denis Diderot, France (1968-1995)
Head, Service d´explorations fonctionnelles de l´hôpital Lariboisiere, Paris, France (1968-1995)

**22.10.1943-†21.3.2011*
Prof. Bohumil Fiser, CSc. *Professor of Physiology, Masaryk University, Faculty of Medicine, Brno*
Head, Department of Physiology (1995-2008)
Minister of Health of Czech Republic (2000-2002)

Prof. MUDr. Pavel Braveny, CSc., prof. Franz Halberg, Masaryk University, Brno, 1994

Prof. Thomas Kenner and prof. Jan Penaz, CSc., Masaryk University, Brno, 1994

Professor Bohumil Fiser, As. Professor Michal Pohanka, Professor Thomas Kenner, Brigitte Kenner, Dr. Othild Schwartzkopff , Professor Franz Halberg, Dr. Jiří Dusek, Professor Jarmila Siegelova, Brno Congress Noninvasive Methods in Cardiology 2008

Professor ***Germaine Cornelissen,*** *PhD*
Director of Halberg Chronobiology Center
Professor of Integrative Biology and Physiology
University of Minnesota, USA

Professor ***Masairo Kohzuki,*** *M.D.*
Chairman, Department of Internal Medicine and Rehabilitation Science, Tohoku University Graduate School of Medicine, Sendai, Japan

Assoc. Prof. PD Dr. med. ***Nandu Goswami***
Chairman of Dept. of Physiology
Medical University of Graz, Austria

Prof. MUDr. Jarmila Siegelova, DrSc., Dr. Biaca Brix, Professor Masairo Kohzuki M.D:, Prof. PD Dr. med. Nandu Goswami. Dr. Jana Svacinova, Masaryk University, Brno 2019

We have a great luck that we could cooperate with internationally known excellent experts and scientist int the field of medicine physiology, pathophysiology and chronobiology and we appreciate it very much that we can continue in the cooperation with famous Universities all over the word.

10th Anniversary of Prof. MUDr. Bohumil Fiser, CSc. Death (22. 10. 1943 - 21. 3. 2011)

Jarmila Siegelova

Department of Physiotherapy and Rehabilitation, Department of Sports Medicine and Rehabilitation, Faculty of Medicine, Masaryk University, St. Anne´s University Hospital in Brno, CZ

Prof. Bohumil Fiser was Head of the Department of Physiology, Faculty of Medicine, Masaryk University, Brno in the years 1995-2008, Minister of Health of the Czech Republic in 2000-2002, Member of Executive Committee of WHO in 2003-2008. He was a highly regarded scientist of worldwide renown in the field of normal and pathological physiology and a successful organizer in health service, as it was described in the publications by Professor Franz Halberg et all. in World Heart Journal in 2011.

Professor Thomas Kenner wrote in 2013: In connection with discussions about medical education and medical and physiological activities, Franz Halberg coined the title "Every-day-physiologist" for the three of us: Prof. Bohumil Fiser, he himself and me (Fig. 1). The title includes a special consideration of the relation between physicians and patients.

Figure 1: *Professor B. Fiser and Professor T. Kenner in Masaryk University Brno in 2009*

The scientific and publication activities of Professor Fiser started in 1966 in the Department of Physiology, Faculty of Medicine Masaryk University and were described in Noninvasive Methods in Cardiology 2011 and 2013.

In this publication we want to remember his presence in the experiments done on himself first in the Department of Physiology where Professor Jan Penaz discovered volume clump method of noninvasive measurement of blood pressure beat to beat. To compare the noninvasive measurement of blood pressure with the invasive measurement of blood pressure in arteria brachialis, it was important to measure blood pressure continuously invasively and noninvasively by beat by beat measurement simultaneously in the person of Professor Fiser; the experiment is shown on the Figure 2. The experiment was done by Prof. Semrad and Prof. Penaz on the person of Professor Fiser under the assistance of Professor Siegelova.

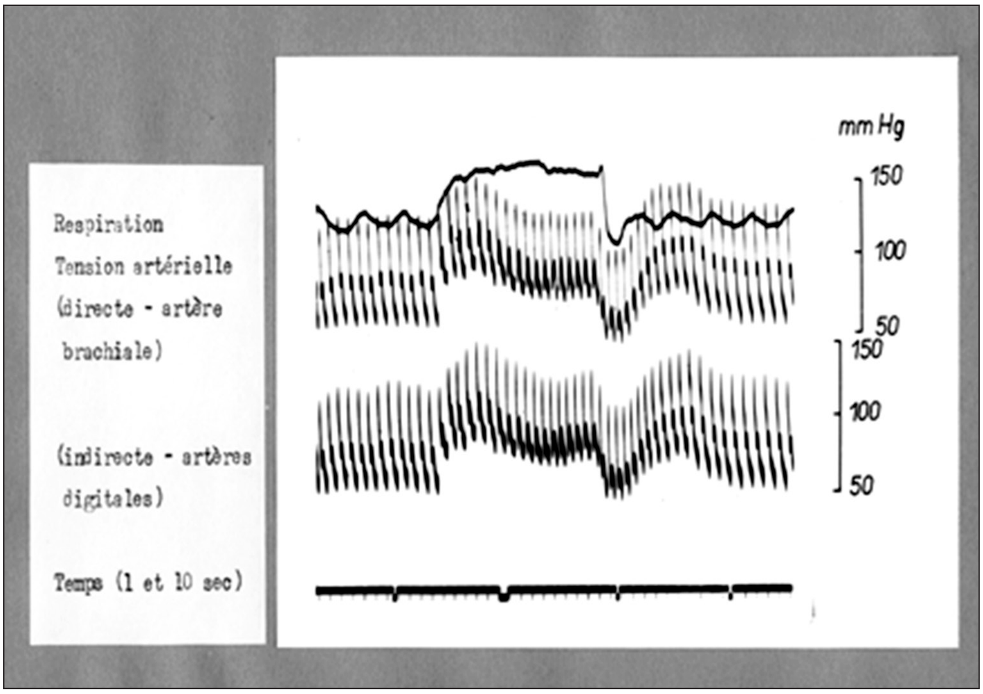


Figure 2: *Invasive and noninvasive measurement of blood pressure on the person of Professor Fiser*

Many years later, in 1995 we followed the opinion of Professor Franz Halberg to provide own measurement of blood pressure and heart rate in the time of some days and together with Professor Germaine Cornelissen, Halberg Chronobiology Center of the University of Minnesota (USA).

To compare circadian rhythm characteristics of systolic and diastolic blood pressure and heart rate, Professor Germaine Cornelissen, Professor Bohumil Fiser, Dr. Jiri Dusek and Professor Jarmila Siegelova measured them from January 13 to 20, 1995 by oscillometry by two different ambulatory monitors concomitantly at 30-min intervals blood pressure and heart rate. The results were described by Professor Cornelissen et al. in 1996 in Proceedings of Symposium Cardiovascular Coordination in Health and Blood Pressure Disorders.

Figure 3: *Chronobiological study of blood pressure in University of Minnesota, USA, 1995, from the right MUDr. Jiri Dusek, CSc., Professor MUDr. Jarmila Siegelova, DrSc., Professor Dr. Franz Halberg, USA, Professor Dr. Germaine Cornelissen, USA, Dr. Anna Portela, Spain and Professor MUDr. Bohumil Fiser, CSc.*

Figure 4 shows another example of 7-days / 24-hours ambulatory monitoring of blood pressure of Professor Fiser.

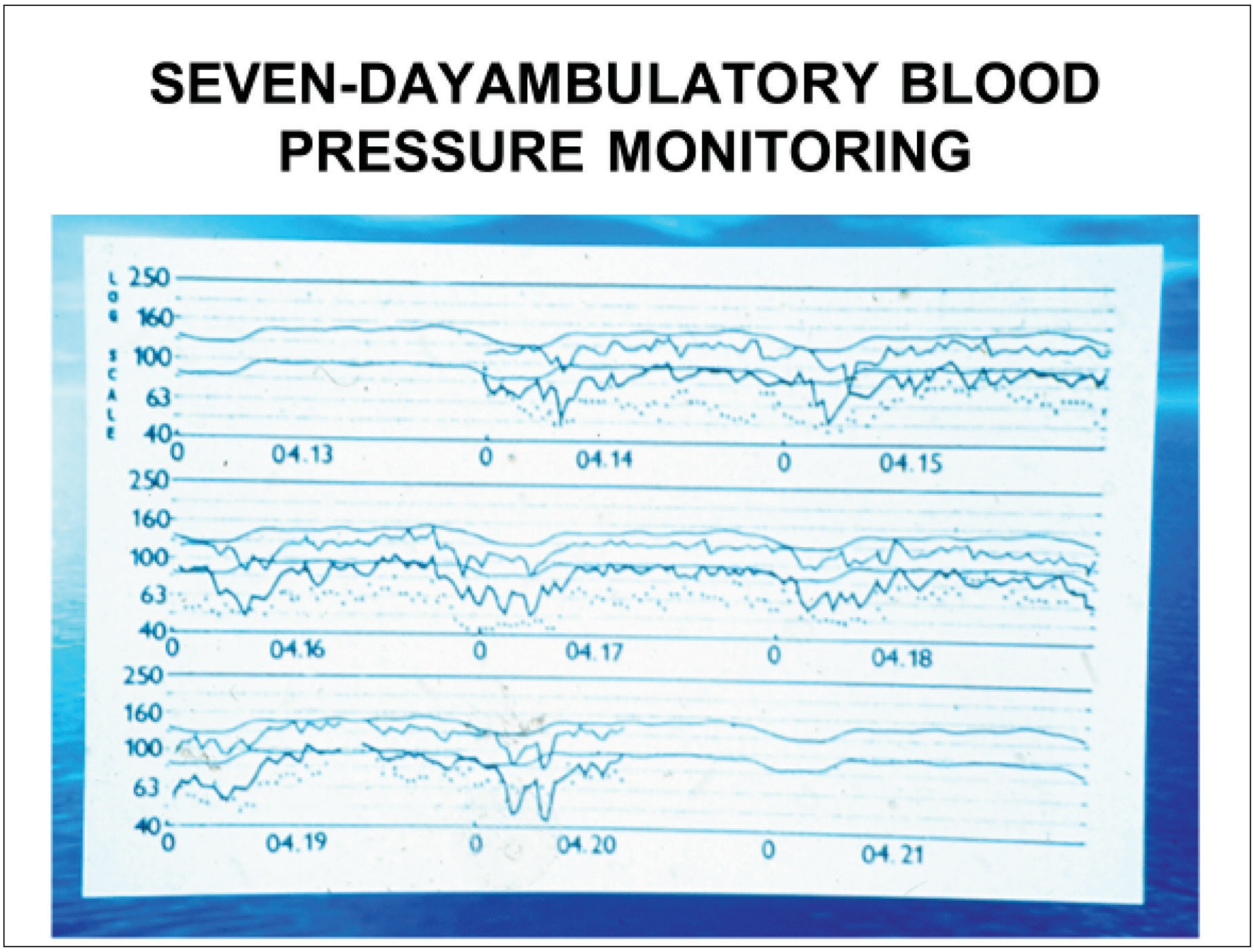


Figure 4: *Seven-day 24-hours ambulatory blood pressure monitoring on the person of Professor Fiser from April 14 to 20, 1998*

Ten years have passed since Professor Bohumil Fiser untimely death. Yet, his achievements are still fresh in our memory and continue to inspire all who were fortunate to know him. His extensive bibliography illustrates the active scientific career of Professor Fiser. The innovations he made in the field brought him to the Head the Department of Physiology at what used to be Purkinje – now Masaryk University. The Czech Republic could not have chosen a better person to serve as Minister of Health. The responsibilities Professor Fiser has been expanded even further when he served on the Executive Board of the World Health Organization.

We will continue to work in the footsteps of Professor Bohumil Fiser in medicine together with Professor Germaine Cornelissen, PhD, Director of Halberg Chronobiology Center, Professor of Integrative Biology and Physiology, University of Minnesota, USA and her scientific international team, with Professor Masairo Kohzuki, Chairman, Department of Internal Medicine and Rehabilitation Science, Tohoku University Graduate School of Medicine, Sendai, Japan, Assoc. Prof. PD Dr. med. Nandu Goswami, Chairman of Dept. of Physiology, Medical University of Graz, Austria and his scientific team and Professor Marie Novakova, Professor Petr Babula, Dr. Zuzana Novakova, Mgr. Jana

Svacinova from Department of Physiology MU and Department of Physiotherapy and Rehabilitation, Department of Sports Medicine and Rehabilitation, Professor Jarmila Siegelova, Professor Petr Dobsak and his team, Assoc. Professor Michal Pohanka, Dr. Jiri Dusek and others.

Prof. MUDr. B. Fišer, CSc., Minister of Health of the Czech Republic 2000 – 2002

Michal Pohanka
Department of Physiotherapy, Masaryk University Brno

It is for me a great pleasure to remember Professor Bohumil Fiser Minister of Health CZ under whom I worked in the function of Deputy Minister.

Professor Bohumil Fiser fulfilled this function very seriously with the strength of his whole personality.

After 19 years, Professor Fiser as Minister of Health is still highly valued and honored, as is proved by the following documents.

Prof. MUDr. B. Fiser, CSc. worked as a Minister in the Government under the leadership of Ing. Milos Zeman, CSc., the Prime Minister of the Czech Republic, nowedays President of the Czech Republic, who accepted the patronage on the „Noninvasive Methods in Cardiology 2021“.

Prezident České republiky

Miloš Zeman

uděluje

ZÁŠTITU

mezinárodní konferenci

„Noninvasive Methods in Cardiology 2021“

13. října 2021

V Praze dne 17. září 2021

The Congress "Noninvasive Methods in Cardiology 2021" dedicated to the memory of Prof. MUDr. Bohumil Fiser, CSc. takes places under the auspices of Ing. Milos Zeman, CSc., President of the Czech Republic and Prof. MUDr. Martin Repko, Ph.D., Dean of Faculty of Medicine, Masaryk University Brno.

The Government of the Czech Republic in 2001

Prof. MUDr. Bohumil Fišer, CSc. (22. 10. 1943 – 21. 3. 2011)

Zuzana Nováková, Marie Nováková
Department of Physiology, Faculty of Medicine, Masaryk University Brno, Czech Republic

Ten years has passed from premature decease of our colleague, highly respected scientist and university teacher, Professor Bohumil Fišer.

All his personal life was connected with Brno and almost all his professional life with Masaryk University, Faculty of Medicine. He left his Alma Mater only between the years 1998 – 2002, when he served as the Minister of Health.

Prof. Fišer was active in various academic and public functions. He was very active member of the Czech Physiological Society, being elected as a member of its executive board repeatedly. He attended its meetings regularly and discussed with profound knowledge of physiology on various topics presented there. Next to his almost 4-years engagement at the Ministry of Health, he was considerably active also in local politics.

It was not a single research topic what interested prof. Fišer. He worked both with animal models and human subjects. He was a very inventive person, with great background from mathematics and biophysics. At the beginning of his research carrier, he spent a remarkable period working on a model of isolated heart perfused according to Langendorff. He was always willing to help younger colleagues, share his experience, and give them valuable tips for laboratory work. In cooperation with prof. Peňáz, prof. Sieglová, prof. Semrád and prof. Honzíková, he studied blood pressure regulation and variability of cardiovascular functions in human subjects. He established numerous international collaborations.

Prof. Fišer loved to teach and the students perceived it and highly appreciated his approach. He belonged to those teachers that managed to fill up every lecture hall. He knew how to comment entertainingly on every sort of information and relate it to his life experience. The students knew that they would be instructed and amused at the same time. And this was the main reason of his pedagogical success: information based on a story is only exceptionally forgotten. For sure, there are thousands of doctors who feel to be positively affected by him both in their professional and personal lives.

We both spent with prof. Fišer more than two decades at the Department of Physiology. It was nice, stimulating journey at his side, enriching us both professionally and personally.

Circadian Rhythm Alterations of Leptin and Blood Pressure in Obesity

Germaine Cornelissen[1], Jarmila Siegelova[2], and Members of the Project on the BIOsphere and the COSmos (BIOCOS)

[1] *Halberg Chronobiology Center, University of Minnesota, Minneapolis, MN, USA;*
[2] *Masaryk University, St. Anna Teaching Hospital, Brno, Czech Republic*

Introduction

A weakened circadian system is associated with an elevated risk of disease, notably in relation to metabolism [1, 2]. Herein, we review some of the results on leptin and blood pressure in obesity obtained with many colleagues worldwide.

Leptin in normal-weight and obese women – studies by the late Brunetto Tarquini et al.

Leptin, a hormone predominantly made by adipose cells and enterocytes in the small intestine, helps regulate energy balance by inhibiting hunger, which in turn diminishes fat storage in adipocytes [3, 4]. In healthy normal-weight women (N=14), it is characterized by a circadian rhythm peaking around midnight [5]. In clinically healthy obese women (N=43), the circadian rhythm of serum leptin is characterized by an elevated rhythm-adjusted mean (MESOR) ($P<0.001$) and a reduced circadian amplitude ($P<0.05$) of leptin [5], Figure 1. There is a further 3-hour difference in the circadian phase of leptin between women with gynoid (lower-body fat, N=17) and women with android (upper-body fat, N=26) obesity ($P<0.001$) [5], Figure 2. The circadian rhythm of leptin correlates with that of insulin [5].

Figure 1: *As compared to normal-weight women, the circadian rhythm of serum leptin of clinically healthy obese women has an elevated MESOR and a reduced circadian amplitude. BMI: Body Mass Index (kg/m^2; WHR: waist-to-hip ratio (dimensionless); MESOR and 24-hour Amplitude of serum leptin expressed in ng/ml.*

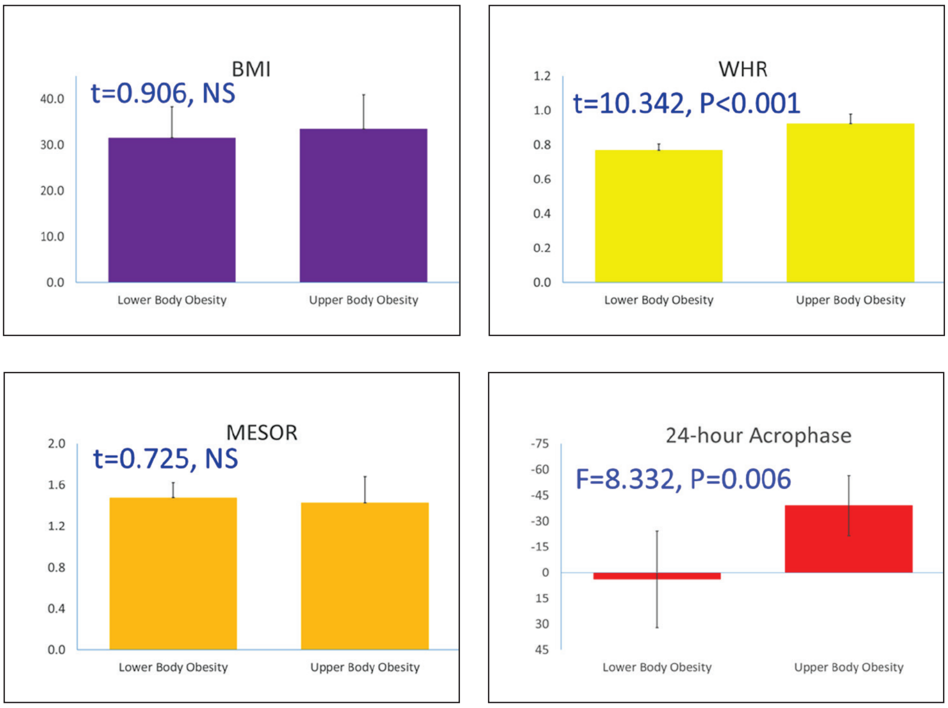


Figure 2: *As compared to women with gynoid obesity, women with android obesity have a similar BMI but a larger WHR. Their circadian rhythm of serum leptin has a similar MESOR but a later acrophase. BMI: Body Mass Index (kg/m^2; WHR: waist-to-hip ratio (dimensionless); MESOR of serum leptin expressed in ng/ml; 24-hour Acrophase expressed in (negative) degrees, with 360°≡24 hours, 0°=00:00.*

The study showed that human obesity is associated not only with higher mean concentrations of circulating leptin and with a blunted circadian amplitude that could contribute to leptin resistance, there is also a difference in the timing of the circadian rhythm as a function of body fat distribution. A different timing in a hormonal network of rhythms can mean too little or too much of one agent (leptin) in relation to others (insulin, cortisol, and others). The misaligned circadian rhythm of serum leptin observed in android obesity but not in gynoid obesity corroborates the notion that the regional distribution of adipose tissue may be more relevant to obesity-linked disorders than total fat mass itself [6]. Indeed, upper-body (android) obesity is reportedly associated with a higher risk of cardiovascular disease or metabolic disorders than lower-body (gynoid) obesity [6-8]. Accordingly, it has been proposed that, beyond weight loss, which remains a legitimate therapeutic target, aiming at reduction of waist circumference and circulating triglyceride concentrations, and improvement in cardiorespiratory fitness have been recommended [9].

Leptin in cord blood – studies by the late Brunetto Tarquini et al.

Already in cord blood, leptin concentrations are higher from infants born between midnight and noon (N=22) than from infants born between noon and midnight (N=21) ($t=2.976$, $P=0.005$) [10]. Cord blood leptin also correlates positively with birth weight [10]. These results are similar to those found in adult women, as summarized above.

Cord blood leptin concentration is elevated in the presence of a family history of obesity on the paternal side ($t=3.552$, $P<0.001$), but not on the maternal side ($t=0.882$, $P=0.382$). These results attest to the influence of intrauterine factors on birth weight and the subsequent risk of impaired glucose tolerance, diabetes, and obesity, as suggested by several longitudinal studies [11]. Early growth may be associated with long-term effects on metabolic and physiologic functions that, in turn, may increase the risk of disease later in life. Apart from size itself, risk later in life may also be determined by disproportion in growth, which may result from differences in the partition of nutrients between the mother and the fetus, the placenta and the fetus, or among different tissues of the fetus, such as precedence given to the growth of the brain, if necessary, at the expense of the growth of visceral or somatic tissues [12, 13].

Endothelial leptin receptor signaling – studies by Weihong Pan et al.

The importance of leptin signaling in the central nervous system is shown by diabesity in neuronal leptin receptor knockout mice. These neuronal-specific mutant mice are obese and develop diabetes early [14]. Endothelial leptin receptors are also important, particularly in receptor-mediated transport of leptin across the blood-brain barrier [15]. During the course of transport, leptin activates endothelial signaling through its receptors [16]. When fed regular rodent chow, endothelial-specific leptin receptor mutant (ELKO) mice show normal body weight and apparent influx of leptin across the blood-brain barrier, although brain parenchymal uptake of leptin is increased in studies by in situ brain perfusion [17].

A mutant mouse strain lacking endothelial leptin receptor signaling was shown to be partially resistant to diet-induced obesity [18]. On a regular chow diet, ELKO and wild-type (WT, control) mice showed a similar rate of weight gain. On a high-fat diet, however, ELKO mice gained less weight than

WT mice. The amount of fat was the same among groups at the start of study when mice were 6 weeks old, but at ages of 15 and 28 weeks, the percent fat was lower in the ELKO group than the WT group, when fed a high-fat diet ($P<0.01$). Food intake was circadian periodic in all groups, with more food consumed during the dark span when animals are active. The circadian rhythm in food intake was depressed in both strains on a high-fat diet compared to the control diet. ELKO mice did not increase food intake but reduced it in the light span when animals are resting ($P<0.05$) [18].

VO_2, VCO_2 and the respiratory exchange ratio (RER), recorded over 3 consecutive days, followed a circadian rhythm peaking during the active span [18]. On the high-fat diet, the circadian amplitude of VO_2 was reduced in the WT mice ($P<0.05$) but not in the ELKO mice. The ELKO mutation thus appeared to help mice preserve circadian features of oxygen consumption, both under the control and high-fat diets. The circadian amplitude of VCO_2 was reduced in both WT ($P<0.05$) and ELKO ($P=0.052$) mice, but to a lesser extent in ELKO than in WT mice. Although the obese mice showed a reduction in metabolic activity reflected by decreased VCO_2, the ELKO mutation helped preserve the circadian rhythm of VCO_2. There was no difference in the circadian parameters of RER between WT and ELKO mice, either on the control or high-fat diet. Compared with the control diet, the high-fat diet was associated with a lower RER in both WT ($P<0.001$) and ELKO ($P<0.05$) mice, as well as with a reduced circadian amplitude of similar extent in both strains. Heat dissipation was higher during the active dark span than during the resting light span. ELKO mice dissipated more heat than WT mice ($P<0.05$). A high-fat diet blunted the circadian rhythm of heat dissipation, particularly in ELKO mice. These results indicate that protection against obesity in this ELKO mouse model is mediated by a higher metabolic activity [18].

Abnormal endothelial function and circadian blood pressure variability in asymptomatic obese adults – studies by Alok Gupta et al.

The risk for cardiovascular disease was assessed by 7-day/24-hour ambulatory blood pressure monitoring (ABPM) and flow-mediated brachial artery dilatation in 10 normal-weight, 10 overweight and 15 obese individuals, all asymptomatic and apparently clinically healthy [19]. There were no differences in age or gender among the three groups.

Apart from too high (MESOR-hypertension) or too low (MESOR-hypotension) an average blood pressure, abnormal variations in blood pressure include an excessive pulse pressure (above 60 mmHg) and too large a circadian amplitude of blood pressure (CHAT, brief for Circadian-Hyper-Amplitude-Tension), illustrated in Figure 3. Other abnormal patterns of blood pressure and/or heart rate (known as Vascular Variability Disorders, VVDs) include a circadian phase of blood pressure diverging from that of heart rate, and a decreased heart rate variability, gauged by a standard deviation of heart rate below 7.5 beats/min [20, 21].

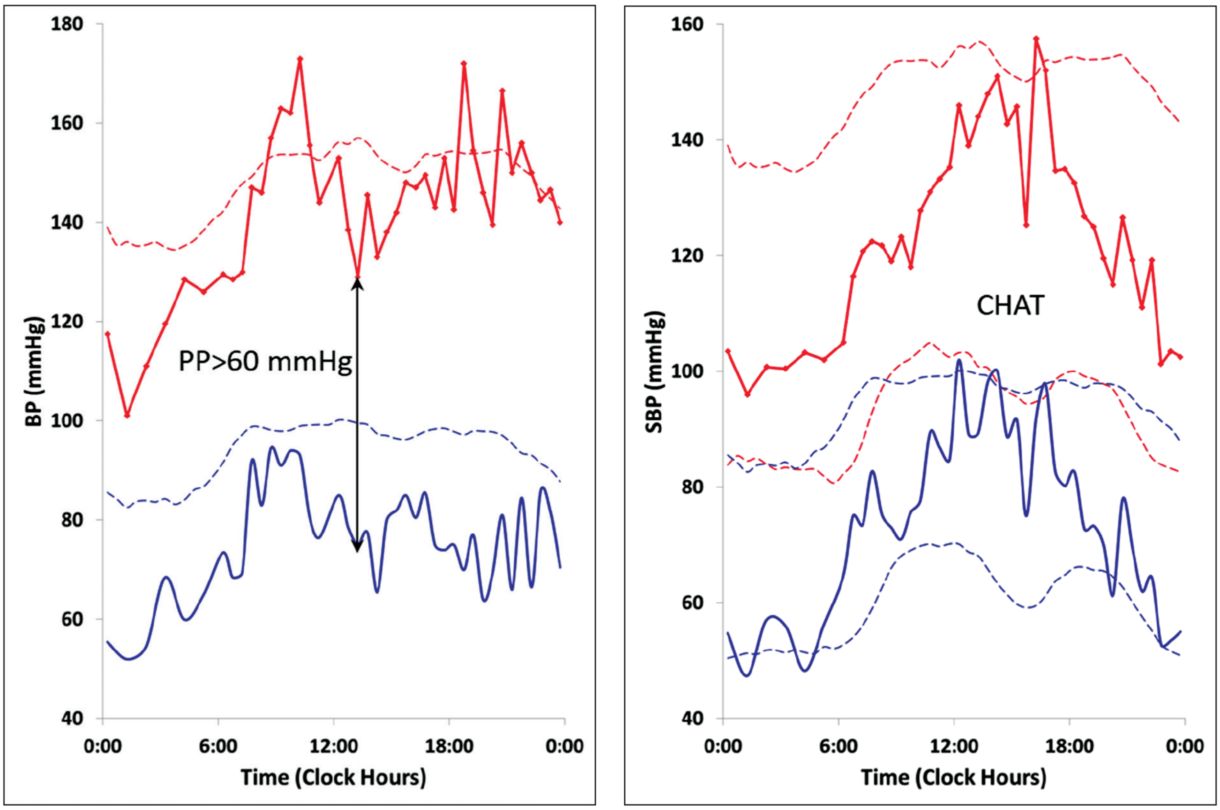


Figure 3: *Average circadian profiles of systolic (red) and diastolic (blue) blood pressure of patient with excessive pulse pressure (left) or excessive circadian variation in blood pressure (CHAT, right). Data collected around the clock at 30-minute intervals for 7 days by ABPM, stacked over single 24-hour span. Light dashed curves are upper 95% (left) or upper 95% and lower 5% (right) prediction limits of clinically healthy peers matched by gender and age.*

As compared to normal-weight and overweight adults, respectively, obese adults had a larger waist circumference (117±13 vs. 79±9 and 93±10, P<0.05). They were more likely to be MESOR-hypotensive (5/15 vs. 0/10 and 0/10, P<0.05), and to have abnormal circadian variation in blood pressure (8/15 vs. 0/10 and 0/10, P<0.05). In particular, they were more likely to have a pulse pressure above 60 mmHg (4/15 vs. 0/10 and 0/10, P<0.05). They were also more likely to have any kind of VVD (12/15 vs. 0/10 and 0/10, P<0.05).

In addition, endothelial dysfunction was present in 3 of 4 obese adults but not in the normal-weight or overweight adult examined (P<0.05) [19]. Brachial artery dilatation upon release of occlusion above the resting (reference) measure shows an increase in brachial artery diameter when endothelial function is normal. This was the case of the obese adult with no abnormality in circadian blood pressure variability. It showed a flatter brachial artery diameter after release of brachial artery occlusion (indicative of the presence of endothelial dysfunction) in obese adults with abnormalities in circadian blood pressure variability.

Comparing those obese adults who presented with abnormal circadian variability in blood pressure to the normal-weight and overweight adults, respectively, they have a larger waist circumference (P<0.05), an elevated fasting serum glucose (102±16 vs. 89±5 and 89±8, P<0.05), higher total cholesterol (223±38 vs. 181±23 and 180±20, P<0.05), higher low-density lipoprotein cholesterol (133±34 vs. 109±25 and 96±13, P<0.05)), and higher triglycerides (220±111 vs. 49±12 and 112±60, P<0.05) [19].

As compared to obese adults who have acceptable circadian variability in blood pressure and heart rate, obese adults presenting with one or more VVDs have a higher BMI (36±3 vs. 32±5). They have elevated systolic blood pressure (129±12 vs. 121±12), fasting serum glucose (102±16 vs. 94±6), high-specificity C-reactive protein (15±9 vs. 1.9±1.7), fibrinogen (593±97 vs. 411±13), and triglycerides (133±35 vs. 117±47). They also have a lower high-density lipoprotein cholesterol (46±13 vs. 52±12). High-sensitivity C-reactive protein and fibrinogen are elevated in the presence of different kinds of abnormal blood pressure behavior: MESOR-hypotension, MESOR-hypertension, CHAT, or excessive pulse pressure. Fasting serum glucose and glycosylated hemoglobin are also elevated in the presence of MESOR-hypertension and an excessive pulse pressure. These results indicate that asymptomatic obese adults with VVDs and abnormal endothelial function exhibit unfavorable cardio-metabolic profiles [19].

Blood pressure relation to body mass index and markers of inflammation – studies by Jerome L. Abramson et al.

Abramson et al. [22] reported a positive association of markers of inflammation and blood pressure variability. In a slightly extended subject population of 158 clinically healthy adults, the MESOR of heart rate and the pulse pressure were positively associated with C-reactive protein [23]. Pulse pressure correlated with body mass index (r=0.418, P <0.001), which correlated with C-reactive protein (r=0.431, P <0.001) and tumor necrosis factor (r=0.164, P<0.042).

In 30 young healthy individuals, mostly south-east Asian-Indian immigrants, monitored around the clock for 7 days, an increased body mass index is associated with a dampened circadian rhythm of systolic (P=0.01) and diastolic (P=0.053) blood pressure [24]. A positive association between pulse pressure and body mass index was also observed in other studies in the USA and the Czech Republic [25].

Discussion and Conclusion

Obesity is associated with a dampened circadian variation of circulating leptin [5] and blood pressure [24]. A disrupted circadian variation of blood pressure and/or heart rate and abnormal flow-mediated brachial artery dilatation only occurred in the presence of obesity [19]. Circadian blood pressure variability and endothelial function, along with subtle abnormalities of pro-inflammatory and glycemic milieu, can thus be novel measures for recognizing latent cardiovascular disease risk in otherwise asymptomatic obese adults [19]. Further work is needed to determine whether it can also guide the timely institution of countermeasures.

Dedication

This paper is dedicated to the memory of Bohumil Fiser (1943-2011) and Franz Halberg (1919-2013).

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Circadian Rhythm of Cortisol in Different Menstrual Cycle Stages of Clinically Healthy Women

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Introduction

The synthesis and secretion of cortisol are coordinated by the hypothalamic–pituitary–adrenal network. Cortisol exhibits a circadian rhythm that affects the brain, the autonomic nervous system, the heart, and the vasculature in preparation for the cardiovascular system to optimally function during these anticipated behavioral cycles [1]. Cortisol is one of the most potent hormones in human physiology. Nearly all cells of the body are potential cortisol targets. It provides one of the ways of transmitting the circadian message from the SCN to the peripheral tissues [1].

Mapping of the circadian adrenal cycle dates as far back as 1959 when Franz Halberg addressed the question as to when and what sequence body processes occur along the 24-hour scale [2]. Halberg recognized that organic regulations had survival advantage if they possessed a periodicity adaptable to that of the environment. Periodic changes in physiologic state may critically determine our chances for survival from exposure to noise, bacterial toxins, or other aggressors. The circadian cycle of the mammalian adrenal cortex, an endocrine entity intimately related to overall motor and mental activity, is not a direct or immediate response to the activities of everyday life. The rhythm persists in men active more or less continuously for two consecutive days in the absence of overt sleep. The onset of the rise in the corticosterone content of mouse serum, which is preparatory to activity, usually leads in phase the major daily bursts in gross motor behavior. Apart from the direct and well-known adrenal cortical reactions to environmental stimuli eliciting activity, the spontaneous physiologic activation of this gland occurs during sleep or rest [3]. The circadian rhythm in circulating cortisol has been extensively studied. Its stability for three decades on three continents has been highlighted [4]. As many other hormones, cortisol is also characterized by a pulsatile behavior [5, 6].

The aim of this study was to determine whether the circadian rhythm of cortisol depends on the menstrual cycle stage in clinically healthy women.

Subjects and Methods

Data collection

As part of a large epidemiological study conducted at the University of Minnesota [7], 85 records of plasma cortisol measured every 20 minutes for 24 hours were obtained from 26 clinically healthy women in three age groups at low or high risk of developing breast cancer. The age groups included adolescents, young adults, and postmenopausal women. The protocol aimed at examining each woman once in each season and in a different menstrual cycle stage. Not all intended recordings were obtained, however.

Data analysis

Each record was analyzed for circadian rhythm by fitting a 24-hour cosine curve to the data, which yielded estimates of the MESOR (Midline Estimating Statistic Of Rhythm, a rhythm-adjusted mean), the 24-hour amplitude and acrophase (measures of the extent of predictable change within a day and timing of overall high values recurring each day, respectively) [8].

Because season and menstrual cycle stage are confounded, in order to examine any effect of menstrual cycle stage, data need to be pooled across seasons. It is thus necessary to first determine whether there are seasonal differences in the circadian characteristics of cortisol. This can best be done based on data from the post-menopausal women who are no longer cycling. In order to secure as large a sample size as possible, any difference in terms of breast cancer risk was also determined in this group to see whether data could be pooled from women at low and high breast cancer risk. The effect of breast cancer risk was examined by Student's t-test applied to individual estimates of the MESOR, 24-hour amplitude and 24-hour acrophase. The effect of season on all three circadian parameters was assessed by one-way analysis of variance (ANOVA). It was possible to use these test statistics on the acrophase because they varied in a relatively narrow range away from 0˚.

Results

Means and standard errors (SEs) were computed for each group. No differences were found between post-menopausal women at low or high risk of developing breast cancer, Figure 1. After pooling data from both risk groups, no differences were found across seasons either for post-menopausal women, Figure 2.

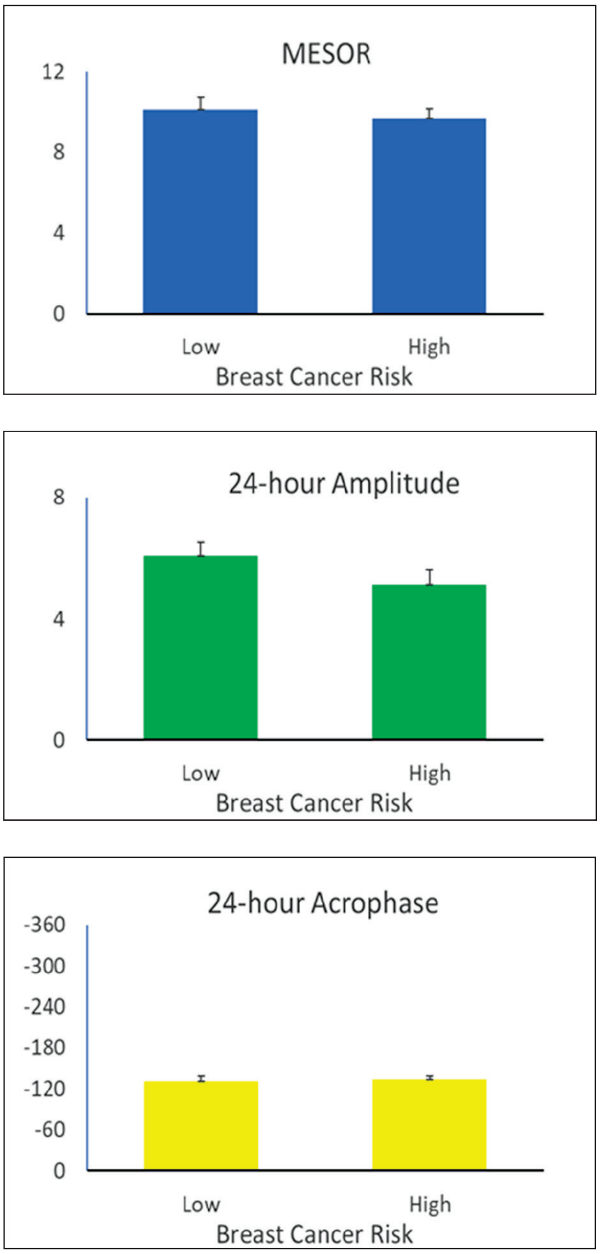

Figure 1: *Lack of difference in circadian rhythm characteristics between post-menopausal women at high vs. low breast cancer risk.*

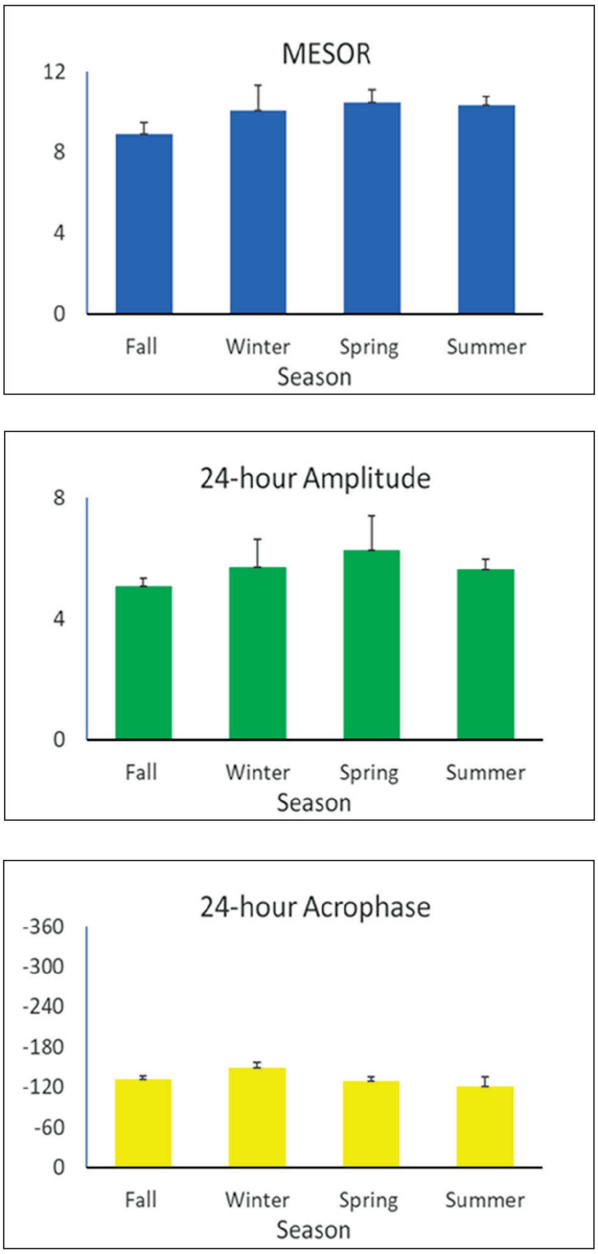

Figure 2: *Lack of difference in circadian characteristics among post-menopausal women examined during different seasons.*

Cortisol expressed in µg/dl (MESOR and 24-hour amplitude); 24-hour acrophase expressed in (negative) degrees, with 360°≡24 hours; 0°=00:00.

Since breast cancer risk and season were not found to affect circadian rhythm parameters of cortisol in post-menopausal women, data from adolescents or young adults were pooled across breast cancer risk before testing for an effect of menstrual cycle stage. A comparison of circadian rhythm characteristics between these two age groups found a small difference of about 1 hour in the 24-hour acrophase, but no difference in MESOR or 24 hours amplitude. An effect of menstrual cycle stage was thus assessed in each age group separately. As shown in Figure 3, no difference was found by menstrual cycle stage in either group.

Adolescents Young Adults

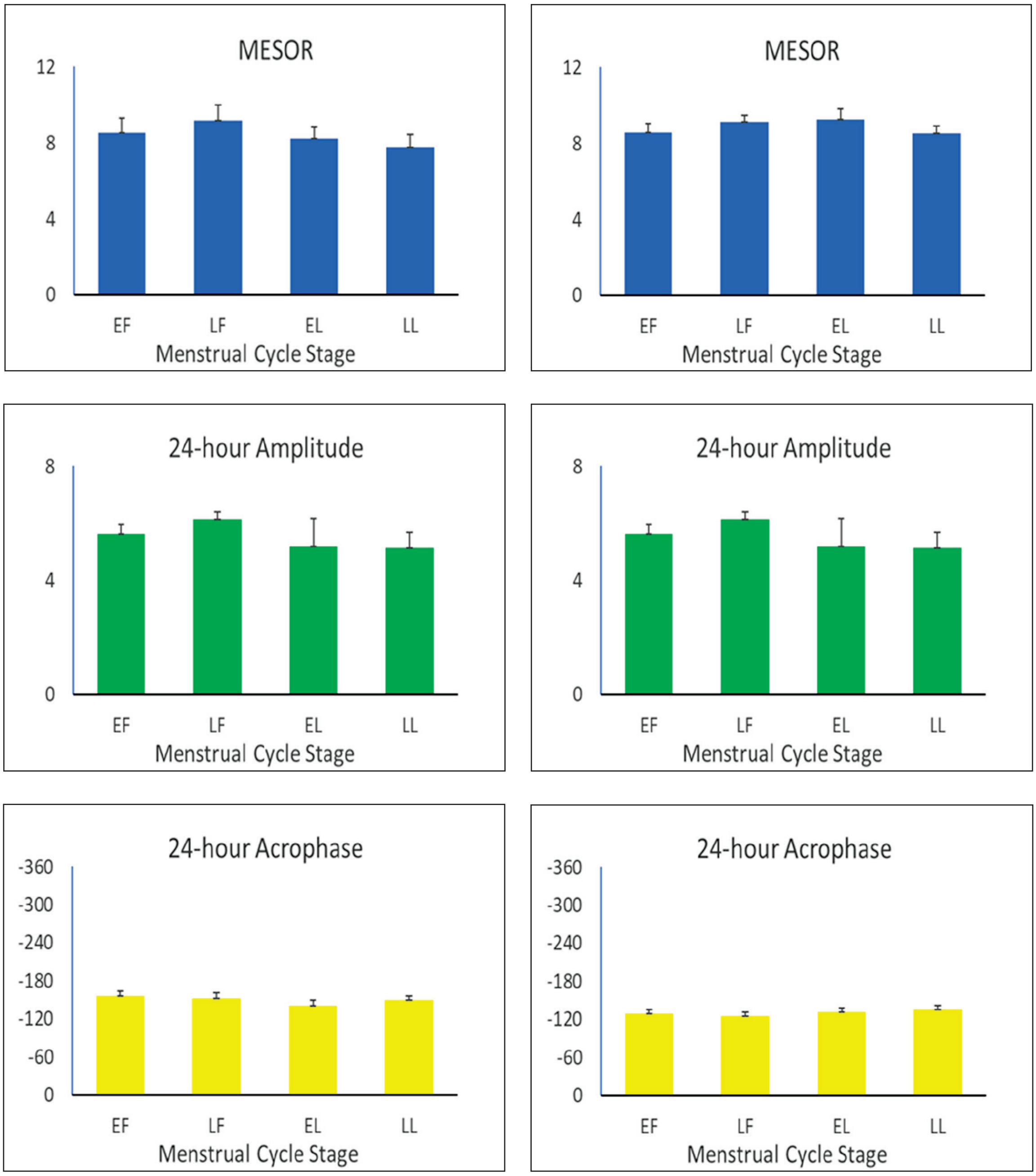

Figure 3: *Lack of difference in circadian rhythm characteristics among adolescents (left) or young adult women (right) examined during different menstrual cycle stages. EF: Early Follicular; LF: Late Follicular; EL: Early Luteal; LL: Late Luteal Cortisol expressed in µg/dl (MESOR and 24-hour amplitude); 24-hour acrophase expressed in (negative) degrees, with 360°≡24 hours; 0°=00:00.*

In addition to a strong circadian rhythm, cortisol also follows a pulsatile behavior, as shown in an individual record of a clinically healthy woman, Figure 4. Large pulses of cortisol are visible across the 24-hour period in this individual record.

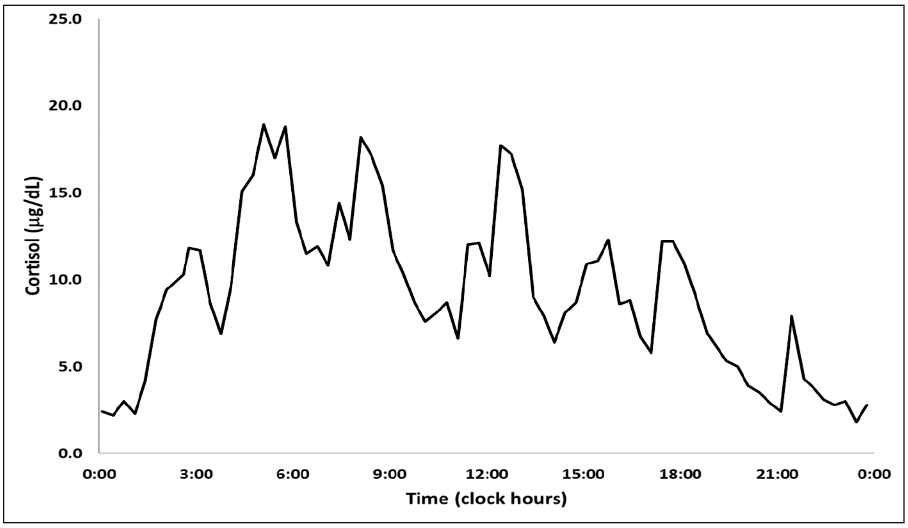

Figure 4: *Individual record of circulating cortisol of a clinically healthy woman (CM109).*

Figure 5 illustrates the circadian profiles of circulating cortisol in the two age groups of cycling women during each menstrual cycle stage. A prominent circadian rhythm invariably characterizes each record. Cortisol reaches a maximum around the time of awakening. It also exhibits a strong pulsatile behavior, which does not have the same pattern across women or menstrual cycle stages. Each individual record differs in terms of the height, width and number of pulses, which occur at different times throughout the 24-hour period.

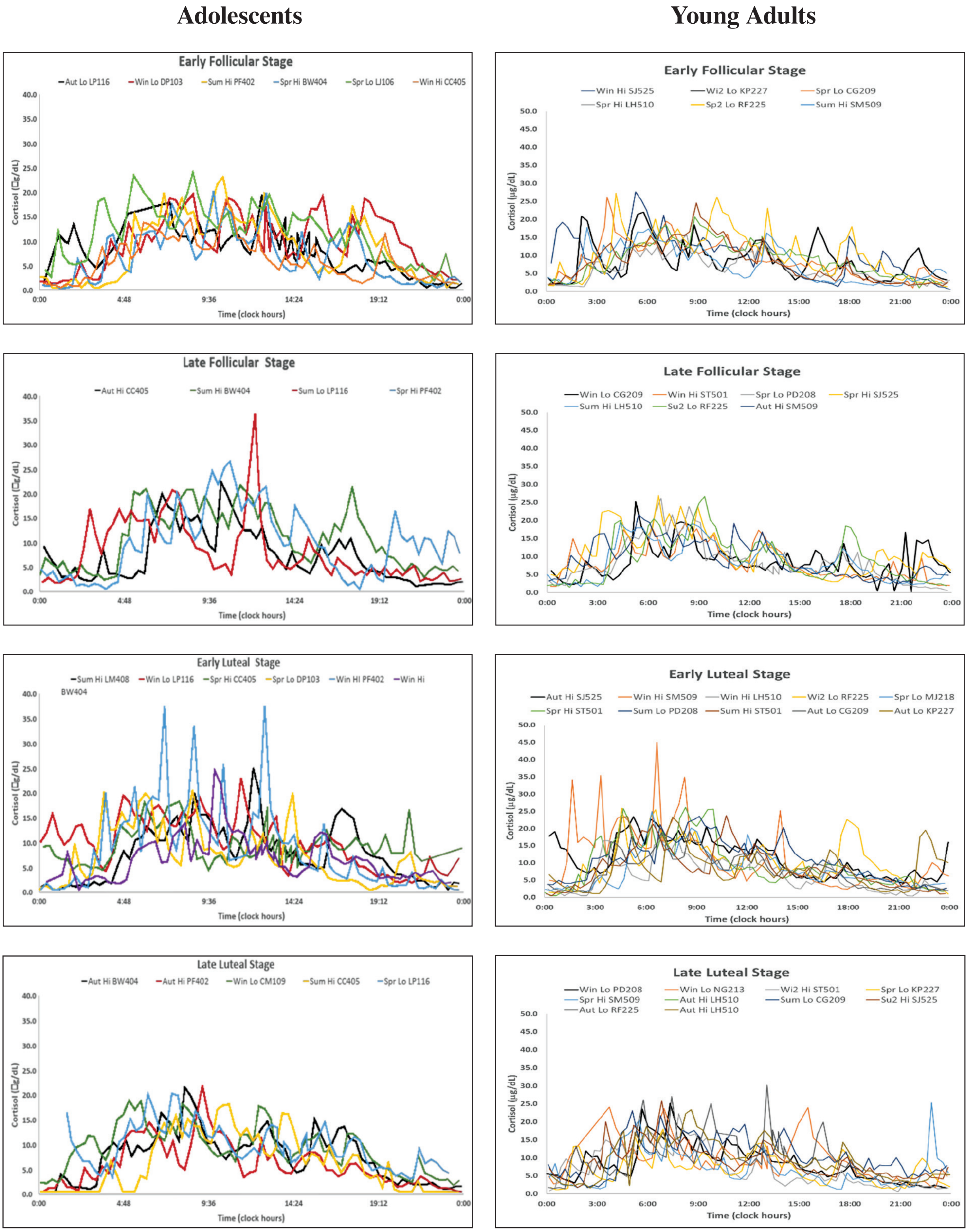

Figure 5: *Lack of difference in circadian rhythm characteristics among adolescents (left) or young adult women (right) examined during different menstrual cycle stages.*
EF: Early Follicular; LF: Late Follicular; EL: Early Luteal; LL: Late Luteal

Discussion and Conclusion

Cortisol is characterized by a prominent circadian rhythm and a pulsatile behavior. Lower values are reached at the beginning of sleep and highest values around the time of awakening. Whereas the circadian component is robust with no differences in MESOR, 24-hour amplitude or acrophase found in relation to breast cancer risk, season, age, or menstrual cycle stage, the pulsatile behavior of cortisol varies from one individual to another, and from one 24-hour profile to another in the same woman. Whether there are differences in pulsatile behavior as a function of menstrual cycle stage remains to be determined.

Some investigators reported higher circulating cortisol concentrations in the follicular than in the luteal phase of the menstrual cycle [9]. Other investigators, however, reported higher salivary cortisol concentrations in response to the Virtual Reality Version of the Trier Social Stress Test during the luteal compared to the follicular stage of the menstrual cycle [10]. The difficulty in assessing an effect of menstrual cycle stage on cortisol stems in part from the large irregular pulses superimposed on the circadian variation. Their determination requires dense sampling not invariably used in human studies. Longitudinal sampling is also important if changes in cortisol behavior occur near the time of ovulation when other hormones also undergo important changes. Sampling in the late follicular or early luteal stage, as done in this study, may not have been sufficiently close to the time of ovulation to capture peri-ovulatory changes in cortisol. A strong positive coupling has indeed been documented between the adrenocortical axis and the gonadal axis at the time of the initiation of the pre-ovulatory LH surge of the menstrual cycle in women [11]. Determination of plasma 17beta-estradiol, LH, ACTH and cortisol at the time of the pre-ovulatory LH surge suggested that the positive ACTH-cortisol-estrogen dependency, well documented in the female rat, also operates at mid-cycle during the menstrual cycle in women [11]. Cortisol and prolactin were also found to be elevated and to correlate with E2 secretion during and after ovulation, contributing to the attenuation of the ovulatory LH surge in infertile women [12].

Cortisol is an important stress hormone involved in several disease conditions [13-15]. In the general population, the cortisol concentrations measured in blood, urine, or hair are positively associated with elevated risk factors for cardiovascular disease [16], death from cardiovascular disease, and all-cause mortality [17]. A recent meta-analysis identified 11β-hydroxysteroid dehydrogenase (11β-HSD1) as a novel molecular target of interest for treating metabolic syndrome and type-2 diabetes mellitus. It is the major determinant of cortisol excess, and its inhibition alleviates metabolic abnormalities [1]. The assessment of the circadian and pulsatile behavior of cortisol are thus important both in terms of diagnosis and as a guide to treatment.

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Falls Risk in Older Persons, Circadian Rhythms and Melatonin: Current Perspectives

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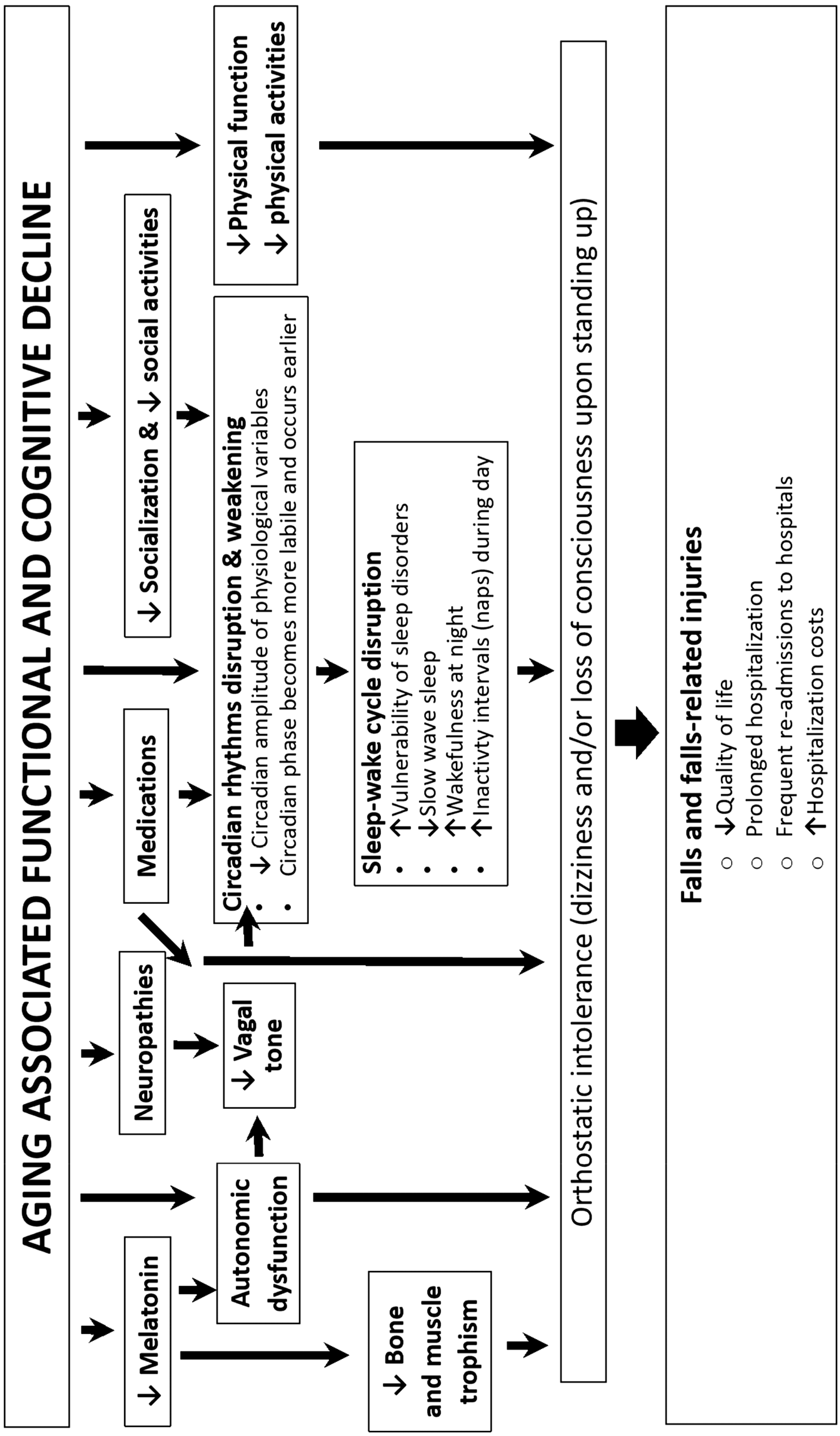
Aging associated weakening of the circadian system, including in aspects related to circadian phase and circadian amplitude, are very well known. As falls in older persons may be influenced by circadian rhythms, it important to assess if an actual association exists between the two. This is important because a better understanding of conditions in which falls occur (e.g. time of the day, week or year) can lead to the development and implementation of innovative countermeasures.

Similarly, aging processes are also known to be associated with an increased risk of autonomic dysfunction. For instance, a relation between heart rate variability and how it changes as persons age has been shown. What roles do the circadian rhythms of autonomous nervous system activity play in the maintenance of orthostatic tolerance? This needs to be investigated, especially in the context of aging.

Finally, a prominent circadian rhythm characterizes melatonin, which shows different peaks at different times of the day. It has also been reported that the amplitude of melatonin decreases as a function of age. Does this imply that a decrease in the circadian amplitude of melatonin leads to a higher risk of falls in older persons? Conversely, could melatonin supplementation be an effective countermeasure for preventing falls in older persons?

This overarching talk assesses the relationships between fall risk and the potential role circadian rhythms and melatonin play in mitigating this risk. This information is important for raising the awareness of healthcare workers, especially in aspects such as falls risk vulnerability in older persons and/or for the development of countermeasures.



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Prof. MUDr. Zdeněk Placheta, DrSc. (4. 4. 1931 - 1. 11. 2014)

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Prof. MUDr. Zdenek Placheta, DrSc., 4.4.1931 - 1.11.2014 will be remembered at the occasion of 90th years of birth as an exceptional expert in sport medicine, professor emeritus of Masaryk University and also an active sportsman in football. The personality of Prof. Placheta was earlier described Noninvasive methods of Cardiology 2015 and 2017.

Prof. Placheta completed his studies of medicine in Brno in 1956 and started his medical career in the Dept. of Anatomy, Masaryk University, under the leadership of excellent professor MUDr. K. Zlabek. Later he worked in the IInd Clinic of Internal Medicine, Masaryk University, under the leadership of Prof. MUDr. Polcak and he qualified in internal medicine. He moved to work in the Dept. of Sport Medicine, Masaryk University, Faculty of Medicine, St. Anna Hospital in Brno; in this time Doc. MUDr. Vladimír Drazil, CSc., was the head of the Dept. of Sports Medicine in the years 1963 – 1988. Prof. Zdenek Placheta be came a head of same department from 1988 to 1996.

His research was aimed to the physical fitness in young adults aged from 12 to 18 years. He published the results of his findings in the field of sports medicine and he published English written monographs Youth and Physical Fitness (1980) and Submaximal Exercise Testing (1988).

In 1996 he retired and gave the head position to Prof. MUDr. Jarmila Siegelova, DrSc., but following his retirement he continued to be active in the department and in 2000 he published another important monography „Zátěžová diagnostika v ambulantní a klinické praxi" (Stress diagnostics in outpatient and clinical practice), together with Prof. J. Siegelova and Prof. M. Stejfa, and also contributed to the teaching program of the department until his death.

Figure 1: *Prof. MUDr. Z. Placheta DrSc. and Prof. MUDr. Jarmila Siegelova DrSc. Brno, St. Anne´s University Hospital in Brno, 2006*

Figure 2: *International Congress "Noninvasive Methods in Cardiolology in 2007", held in Faculty of Medicine, Masaryk University, Brno, Komenskeho nam. 2. From the right we can see Prof. Thomas Kenner d.h.c.mult., Graz, Austria, standing in the discussion with Prof. MUDr. Zdenek Placheta DrSc. sitting Prof. MUDr. Petr Dobsak CSc., Prof. MUDr. Bohumil Fiser CSc., Prof. MUDr. Jarmila Siegelova, DrSc., and from behind Brigitte Kenner*

Prof. MUDr. Zdenek Placheta Dr.Sc., spoke English, French and German fluently and took part in international symposia, congresses and workshops in 1996 – 2014, being organized in Masaryk University every year by our department. Some of his participations are documented in the photographs together with the speakers from abroad - Europe, USA and Japan. He was also coauthor of some publications from our Congresses of Noninvasive Methods in Cardiology.

We thank Prof. Placheta very much for his friendship, collaboration, endeavour, and for pushing ahead the frontiers of knowledge in medicine and we will continue his work in the Department of Sports Medicine and Rehabilitation in St. Anna Hospital in Faculty of Medicine, Masaryk University, Brno.

Brno, October 2021 Prof. MUDr. Jarmila Siegelová, DrSc.
Prof. MUDr. Petr Dobšák, CSc.

Group Physiotherapy for Outpatients after COVID-19 in Department of Sport Medicine and Rehabilitation, St. Anne's University Hospital

[1,2,3]**Adam Vajčner,** [1,2]**Libor Dobšák,** [1,2]**Michaela Sosíková**

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[3]*First Department of Neurology, Faculty of Medicine, Masaryk University and St. Anne's University Hospital, Brno, Czech Republic*

Abstract

Present paper introduces novel protocol of group outpatient physiotherapy after COVID-19.

Long-lasting symptoms are developed after COVID-19 in many patients. These symptoms does not affect only physical health but also mental state. These symptoms include persistent respiratory distress, fatigue, impaired adaptation to movement and aktivity of daily living, physical and mental deconditioning, headache and joint pain etc. Recent literature highlights early rehabilitation in these patients as necessary. The paper aims to present a specific rehabilitation program of group physiotherapy for outpatients after COVID-19 disease at the rehabilitation clinic of the Department of Sports Medicine and Rehabilitation of the University Hospital at St. Anny in Brno.

The program is based on recommended rehabilitations´ standards for pulmonary rehabilitation in COVID-19 based on recent literature. It consists of 8 outpatients´ therapies twice a week. The therapy is conducted as a group, for 2-4 patients. We currently included 34 patients to participate in this program (age: mean 57 ± 13 SD, median 59 (min 29; max 82)). Group is heterogeneous, including patients with symptomatic, hospitalized and non-hospitalized diseases. Therefore, there are two physiotherapists in each group. Program focuses on persistent symptoms after disease of COVID-19. It aims on pulmonary rehabilitation, postural control in developmental position, proper sitting, endurance training. An integral part is the motivation of patients to physical activity and support self-confidence. Patients undergo initial and final clinical examinations by medical doctor, spirometry examination, questionnaire survey of fatigue and subjective perception of health in lung diseases. During therapy, finger pulse oximetry, heart rate, subjective Borg scale of dyspnea, and subjective perception of fatigue are monitored regularly, always at the beginning, during, and in the end of the therapeutic unit. Patients are actively guided and motivated to self-therapy and continue their learned physical behavior even after the end of the program. Program is still ongoing, thus data are not statistically evaluated. But patients report improving our quality of life.

Introduction

Present paper introduces novel protocol of group outpatient physiotherapy after COVID-19 with post-acute COVID syndrom or post-COVID syndrom. Persistent symptoms are occurred after COVID-

19 very frequently [5, 19, 20, 23]. Present study is based on actual pandemic situation of COVID-19 and its persistant health deconditions. Recent literature highlights early pulmonary rehabilitation as necessary part of interdisciplinary cooperation [2, 3, 6]. The presented novel program aims to a group physiotherapy.

These symptoms affect physical and mental health. These polymorfic symptoms typical for post-COVID syndrom are respiratory distress, fatigue, impaired adaptation to movement and activity of daily living, physical and mental deconditioning, headache, joint pain etc. Symptoms and syndroms are ilustrated on the figure no. 1. 5–10 % of patients over 12 w. after COVID-19 reported rezidual symptoms after COVID-19 are developer over 5 – 10 % of patients after COVID_19 even more then 12 weeks after disease [19, 20]. 1 704 003 infected patients were infected to October 2021 and 1 662 207 of them were recovered [1]. Theoretically it means approximately 83 000-166 000 post-COVID patients with persistent symptoms and indicated to pulmonary rehabilitation. Therefore, rehabilitation must also be effective for a larger number of these patients, and we assume that presented our novel therapeutic protocol, will be very effective.

Aim of our specific program is to achieved significant improvement of the subjective evaluation of the health, decreased of fatigue, improved functional physical parameters of spirometry, oximetry and heart rate during physical aktivity. We would like to motivate patient to physical aktivity, return them to work and improve their quality of life and decrease of severity for these symptoms. Finally, we try to find out specific effectivity of program´s pre setup to future maximize the effectivity of group physiotherapy for high number of patients.

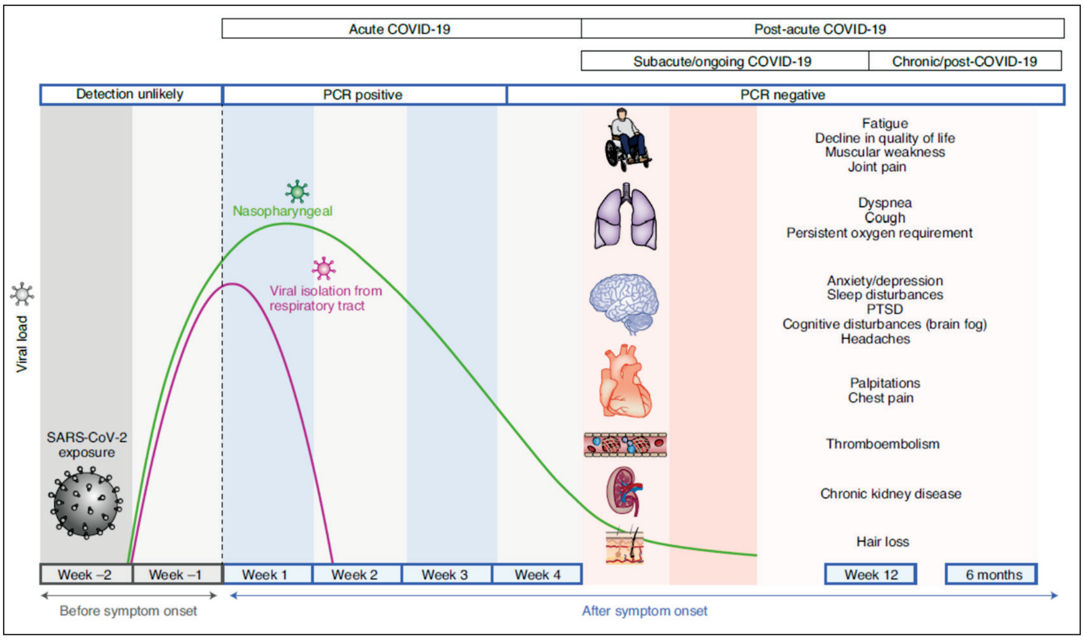

Figure 1: *Post-COVID syndrom [5].*

Materials and methods

Group of patients

Present descriptive data are ongoing, not final. Our group of patients consists from 34 subjects, with averege age of 57 years (SD 13; median 59, min 29, max 82). 17 men and 17 women are involved. Average BMI is 29.98, between pre-obesity grade and first obesity grade. More then 60 % of patients had 3 or more dominant symptoms (dyspnoea, fatigue, joint pain). Only 2 % were smokers. 61,8 % of patients during active infection had to be on oxygen therapy and hospitilized. 5 patients (14,7 %) were on mechanical ventilation during active infection. Patients started our program in average after 19 week after infection. But some of them started very early – 4 weeks after infection on the other hand, one patient started group therapy after 44 weeks after infection and still had dyspnoe and fatigue. 29 patients finished more then 50 % of sessions during this program. For more information see Table 1.

Table 1. *Group of patients (ongoing data)*

N = 34	average (SD); median (min; max)
Age (years)	**57** (SD 13); 59 (min 29; max 82)
Gender	**17** M/ **17** F
Weight	**90.5** (SD 22.3); 90 (min 52; max 140)
BMI	**29.98** (SD 5.75); 30.25 (min 19.13; max 43.21)
1-2 symptom (n; %)	**12**; 35.3 %
≥ 3 symptom (n; %)	**22**; 64.7 %
Smoking (n; %)	**2**; 5.9 % (1; el. cig.)
Oxygen Therapy (n; %)	**21**; 61.8 %
Hospitalized – Ox. Th. (n; %)	**16**; 47.1 %
Sympt. non-hospitalized (n; %)	**13**; 38.2 %
Hosp. – mechanical ventilation (n; %)	**5**; 14.7 %
RHB start after COVID 19 (weeks)	**19** (SD 13); 15 (min 4; max 44)

Protocol of Rehabilitation program

The program strongly based on standardized recommendations for pulmonary rehabilitation in COVID-19 [2, 3, 4, 12, 13]. It is conduct as outpatient group physiotherapy for 2 to 4 patients with persistent COVID-19 symptoms. Rehabilitation takes place at Department of Sport Medicine and Rehabilitation, St. Anne's University Hospital, Brno, Czech Republic. It started on April 2021, and it is still ongoing. Patients are indicated by medical doctor after examination.

All patients are also examined by spirometry, questionnaires assessment of fatigue (Multidimensional Assessment of Fatigue Scale – MAFS) and subjective assessment of pulmonary functions (COPD Assessment Test – CAT). Evaluation is setup as initial and final medical examination. Each patient is monitored continuously during each therapy by blood oxigenation, heart rate and subjective perceving of dyspnoe and perceiving of exertion using standardized Borg scales.

Spirometry (MedGraphics, PFS 1070) is exemined by well-experienced medical doctors in Department of Sport Medicine and Rehabilitation, St. Anne's University Hospital, Brno. Standard SVC, FEVC, FEV1, Tiffaneau index, FEFmax, FEF25, FEF75, FEF25-75 are measured in the bigining and in the end of the program [2, 3, 17, 18]. MAFS and CAT questionnaires are standardized for Czech language and both are established to evaluate symptoms during or after COVID-19 [3, 7, 14, 15]. Before first phase, in the middle and in the end of the session, we measure heart rate, oximetry by Digital finger pulse oximtery and heart rate measurement (OXY 300 Microlife [24]. Also patients are asked about dyspnoea and perceived exertion (standardized Borg scales). The Figure 2 ilustrates the course of therapy program

Each therapy session takes 60 minutes. The program lasts for 4 weeks, it means 8 sessions, twice a week. 2 well-experienced physiotherapists are present in each group. Also students of physiotherapy of Medical faculty Masaryk university are included. The therapy group is heterogeneous, including patients who were symptomatic, hospitalized and non-hospitalized during COVID-19 positivity. Program is based on specific therapeutic schedule of increasing intensity and consist of 5 therapeutic parts. These specific parts of program are: Warm-up phase, stretching and mobilization phase, postural-breathing phase, endurance phase – nordic walking, relaxation and stretching phase.

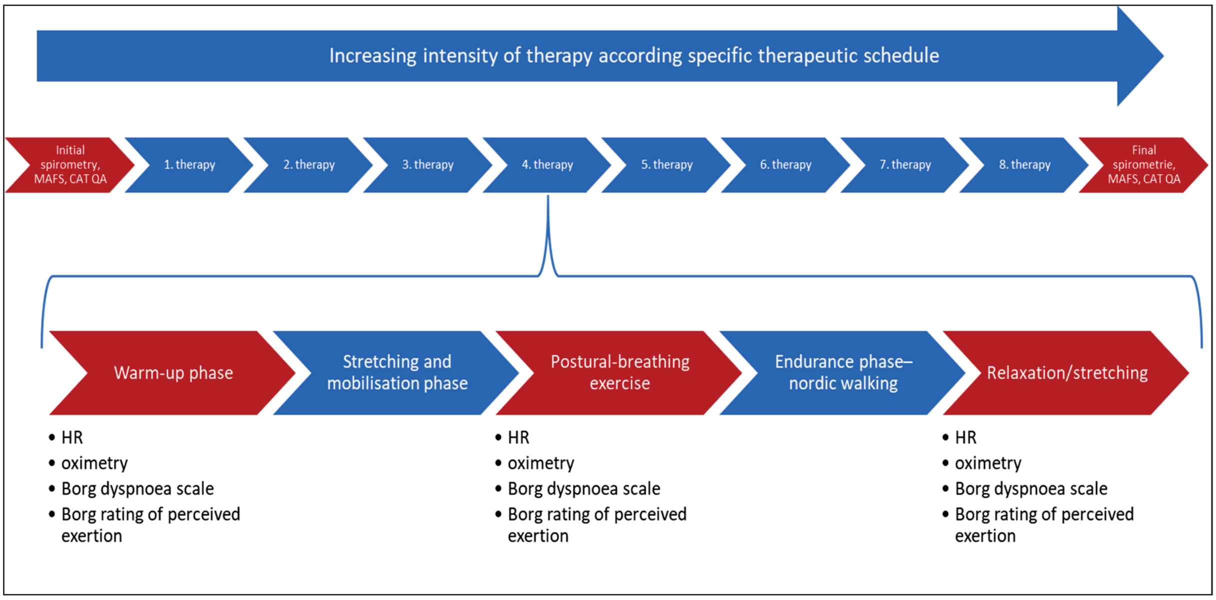

Figure 2: *Protocol of group physiotherapy program for outpatients after COVID-19*

Warm-up phase

Patients are educated about program, breathing cycles technics, measurements. It starts by training of breathing pattern, exspiration, inspiration, expectoration technic, autogenic drainage, active cycle of breathing techniques, breathing control, postural control in standing. Patients ecercise with nordic walking poles in standing and train clasic analytical excercises. [10, 16].

Figure 3: *Warm-up phase*

Stretching and mobilisation phase

Excersice in this phase is based on individual post-izometric relaxation and stretching of primary and secondary respiratory muscles – trapezius muscle, levator scapulae muscle, paravertebral muscles, scalenii muscles, deep neck extensors, pectorales muscles. Automobilization of sternocostal joints and Thoracic spine is also performed to autotherapy and ADL.

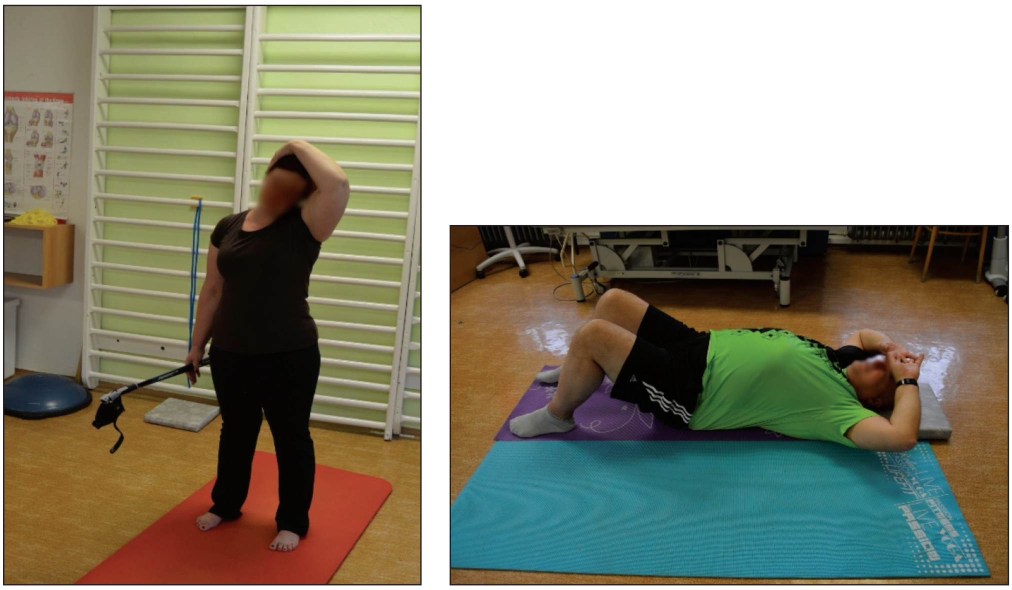

Figure 4: *Stretching and mobilisation phase*

Postural-breathing phase

The most important part of whole program. Aim is to reeducate the breathing pattern exercised in ontogenetic position. All position are based on developmental kinesiology used by physiotherapy concept called Dynamic Neuromuscular Stabilization according profesor Kolář. Ontogenetic global patterns improve activation of postural and respiratory muscle control. aplly Supine a prone position of 3rd to 6th month are used. Also postural vertical position as squat or standing from development are practiced. Strength exercise is performed in these position with using special equipment. Technics of Mindfulness increase efficiancy of movement [8, 9, 10, 16].

Figure 5: *Postural-breathing phase (according Kolář, DNS poster)*

Endurance phase – nordic walking training

This part of program can be performed inside and also outside. Patients train walking by special technic based on Nordig Walking locomotion stereotype/pattern. Our patient also walk on the stairs up and down, in first time with pauses between floors, and in the end of the program to the 4th floor in one time. Nordic walking is high demanding and effective form of walking. Through the support of the poles patients improve rotability of the thoracic spine and thus increase ability of proper activation by respiratory muscles [11, 21, 22].

Figure 6: *Nordic walking technic of locomotion*

Relaxation and final stretching phase

The last part of the one therapy session is relaxation and final stretching. We use stretching with NW poles, autogenous training according Schultz, partielly mindfulness (body image, body scan technics). Aim of this phase is to calm down and relax patient after performance and stretch activated muscles.

Figure 7: *Stretching*

Recommendations for hometherapy

We recommend to write down the locomotion diary to record steps achievements at least 3 times a week for 30 minutes. We motivate patient to regular exercises of their choice like yoga, sports and return to their work. Patients are encouraged to exercise daily according program´s therapy (postural actiavation, strength exercise, breathing excercise, Nordic walking, cycling) [2, 4].

Conclusion

This artical describes novel protocol of group rehabilitation program for outpatients after COVID-19. Program is still ongoing, thus these text is preliminary inform about benefits.

Results and statistical processing will be next year after increasing of number of patients to 50 in minimum. Patients are already reporting positive feedback as increasing assessed physical functions, decreased fatigue and improving of their well-being, motivation and increasing adaptation to stress and gaining self-confidence.

Pilot data about efficiency of therapy will be processed and evaluated according to the monitored parameters -by diploma theses and bachelor‘s thesis (Faculty of Medicine, Masaryk University, Brno, Czech Republic)

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Blood Pressure Variability at Rest and during Aerobic Exercises in Women with Ischemic Cardiac Diseses

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Introduction

Franz Halberg and Germaine Cornelissen with us using ambulatory blood pressure monitoring showed the need to account day-to-day changes of blood pressure and heart rate and the necessity to circadian assessment of the hour-to- hour variability in cardiovascular parameters, as was presented in Brno Consensus meeting in 2008 (1,2,3,4,7,8,). The Chronobiology center of Minnesota started with the international project BIOCOS with seven day/24 hours blood pressure monitoring (6). In patients with ischemic heart diseases using seven day/24 hours blood pressure monitoring we have shoved the BP variability in the days with exercise as well as without exercise (5).

Several studies shave reported that the benefit of antihypertensive treatment on hypertension-relate cardiovascular outcomes is associated not only with the average blood pressure but also with blood pressure variability. In some earlier studies there was the hypothesis that exact same doses of exercise evokes the same response of blood pressure and heart rate (9).

The purpose of the study

The aim of the study was to compare auscultatory measurements of systolic and diastolic blood pressure during cardiac aerobic exercise training lasting three weeks in women.

Methods

We examined 12 patients (women) with ischemic heart diseases, the age 60 ±8.9 years, height 166 ±6.7 cm, weight 78 ±11.7 kg. The cardiac patients - women were under therapy of betablockers. ACE inhibitors and statins. The intensity of aerobic training was determined individually according spiroergometry evaluation of the first ventilatory anaerobic threshold. Blood pressure measurements were provided using auscultatory measurement of BP at resting values, after warm-up period (10 minutes), at the peak of aerobic training period (40 minutes), at the cool-down period (10 minutes) twice a week, the training lasted tree weeks.

Results

Cardiovascular parameters at rest

Before starting second phase of cardiac rehabilitation systolic blood pressure variability of resting values in cardiac women is shoved Fig. 1.

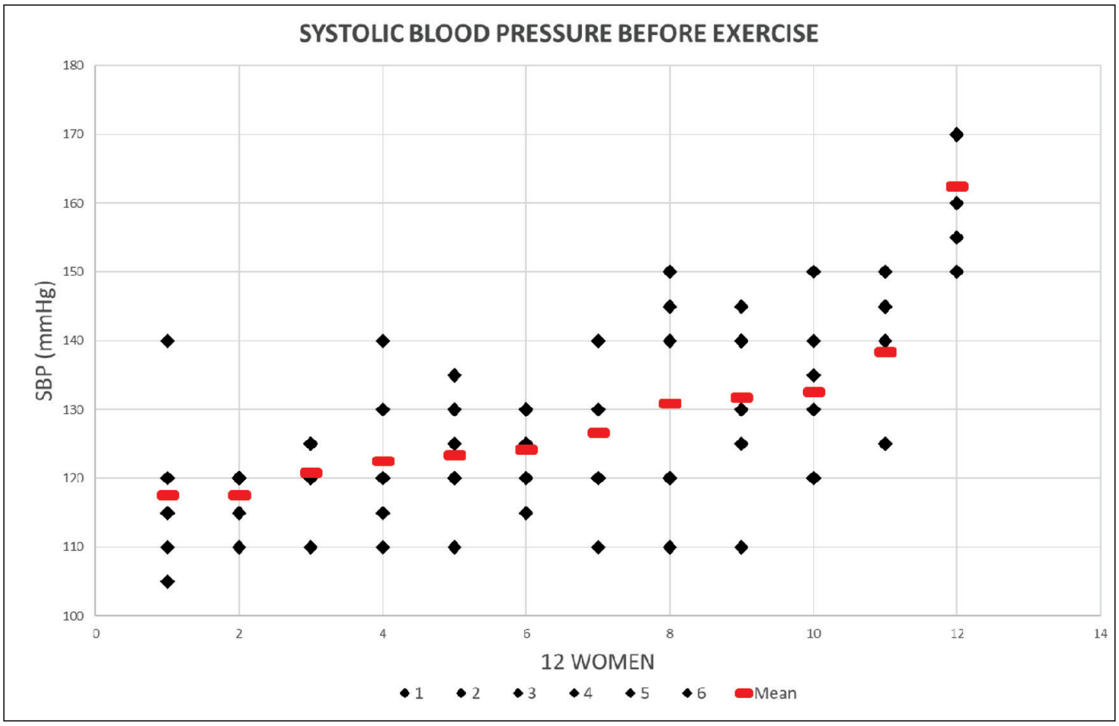

Figure 1: *Systolic blood pressure variability in individual resting values is given in black points is in every subjects, red lines shove the mean value*

Diastolic blood pressure variability of resting values in cardiac women is shoved Fig. 2.

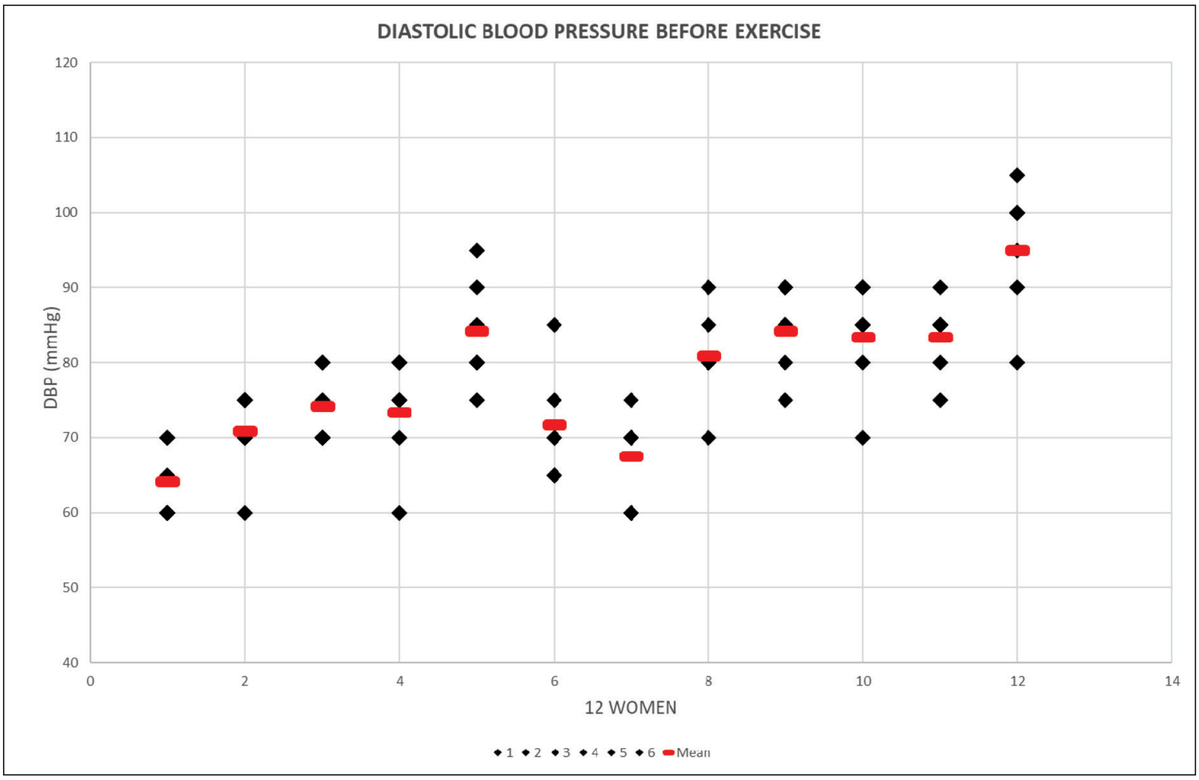

Figure 2: *Diastolic blood pressure variability in individual resting values is given in black points is in every subjects, red lines shove the mean value*

Heart rate variability of resting values in cardiac women is shoved Fig. 3.

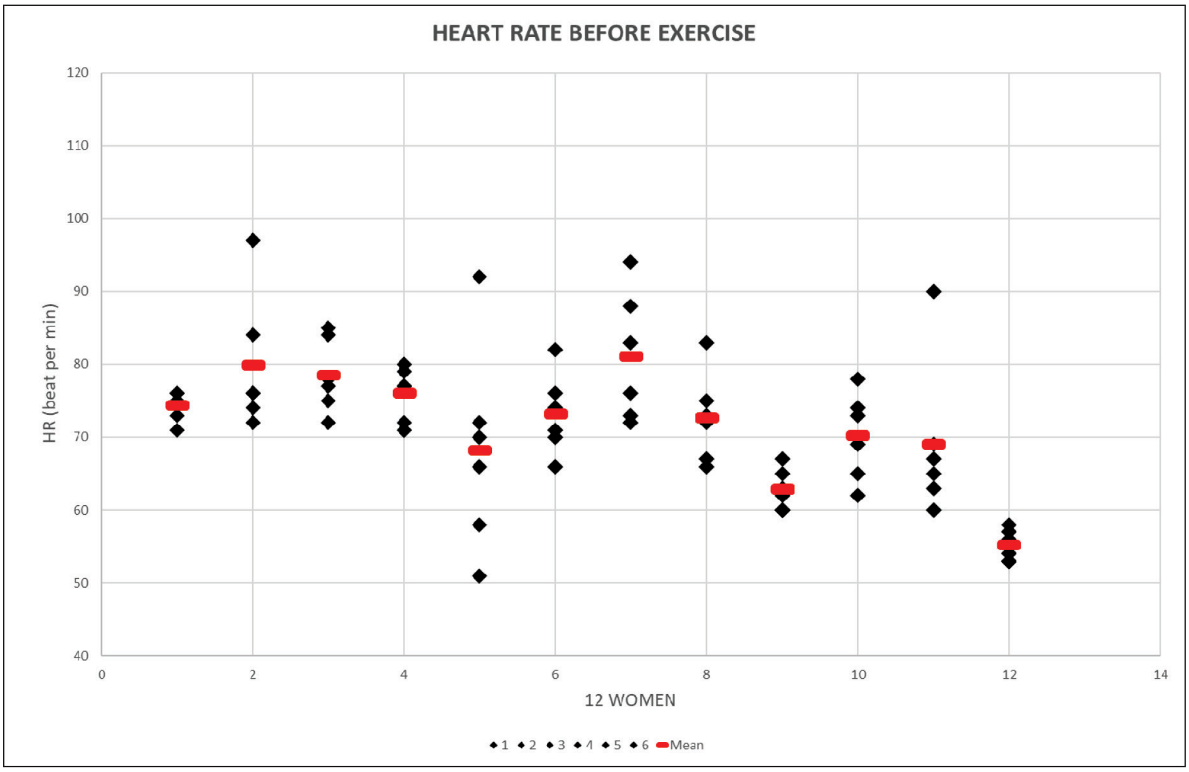

Figure 3: *Heart rate variability in individual resting values is given in black points is in every subjects, red lines shove the mean value*

Resting average values in the whole group of systolic blood pressure were 129.0 ±11.7 mmHg, of diastolic blood pressure 77.7 ±8.5 mmHg, heart rate 71.7 ±7.1 beat per minute.

Cardiovascular parameters after warm-up period

According to the exercise protocol there was fallowed the 10 min. warm-up period.

Systolic blood pressure variability after warm-up in cardiac women is shoved Fig. 4.

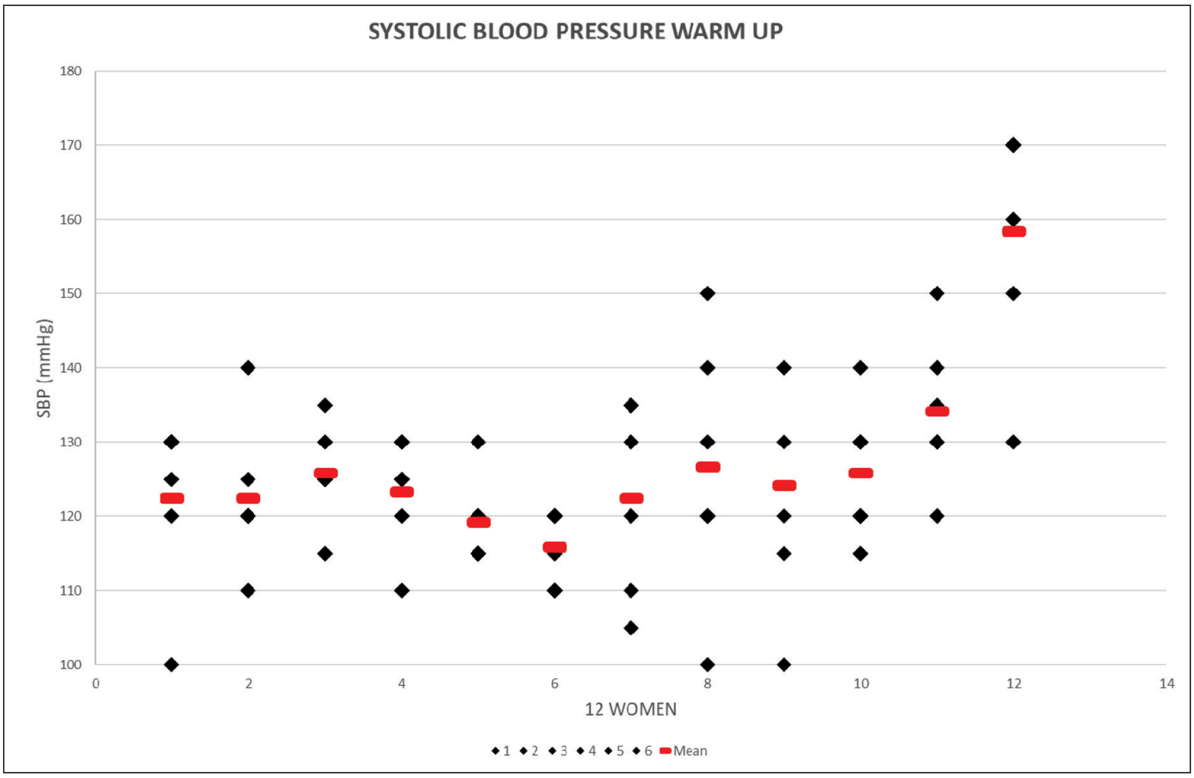

Figure 4: *Systolic blood pressure variability in individual measurement after warm-up period is given in black points is in every subjects, red lines shove the mean value*

Diastolic blood pressure variability measurement after warm-up period in cardiac women is shoved Fig. 5.

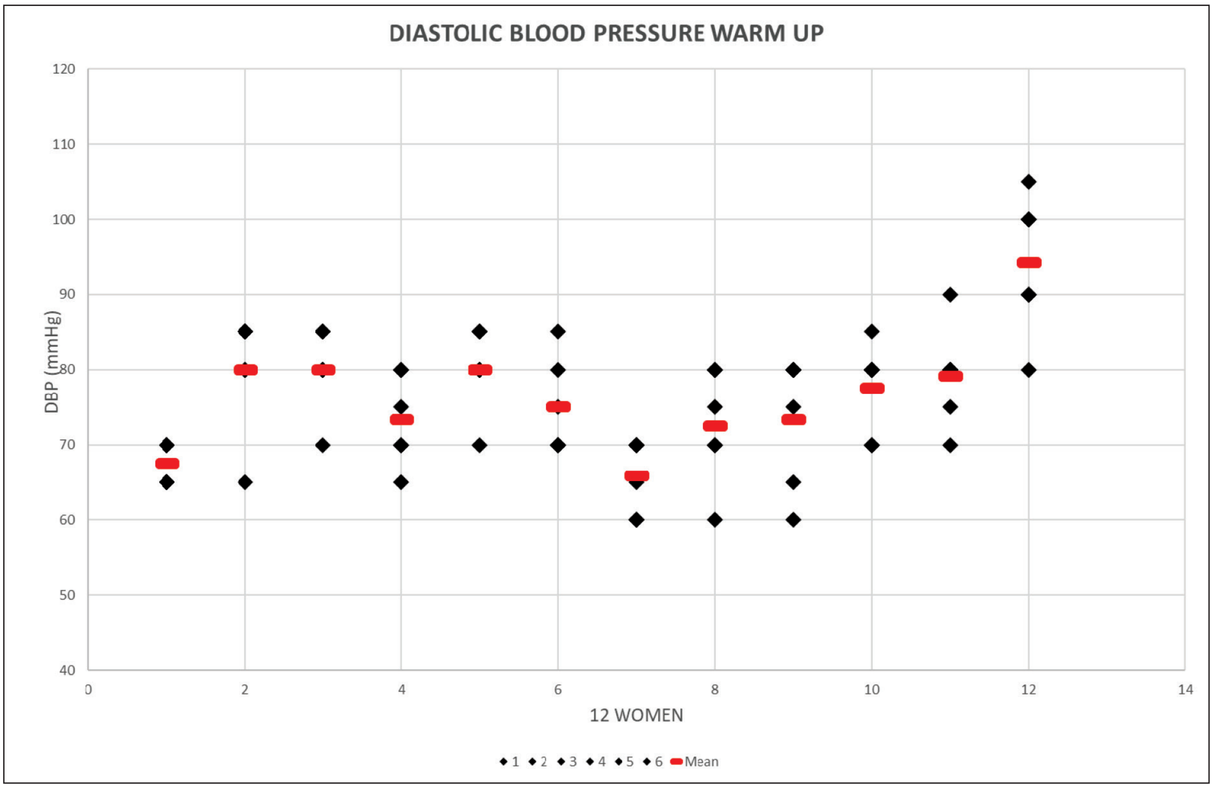

Figure 5: *Diastolic blood pressure variability measurement after warm-up period values is given in black points is in every subjects, red lines shove the mean value*

Heart rate variability measurement after warm-up period in cardiac women is shoved Fig. 6.

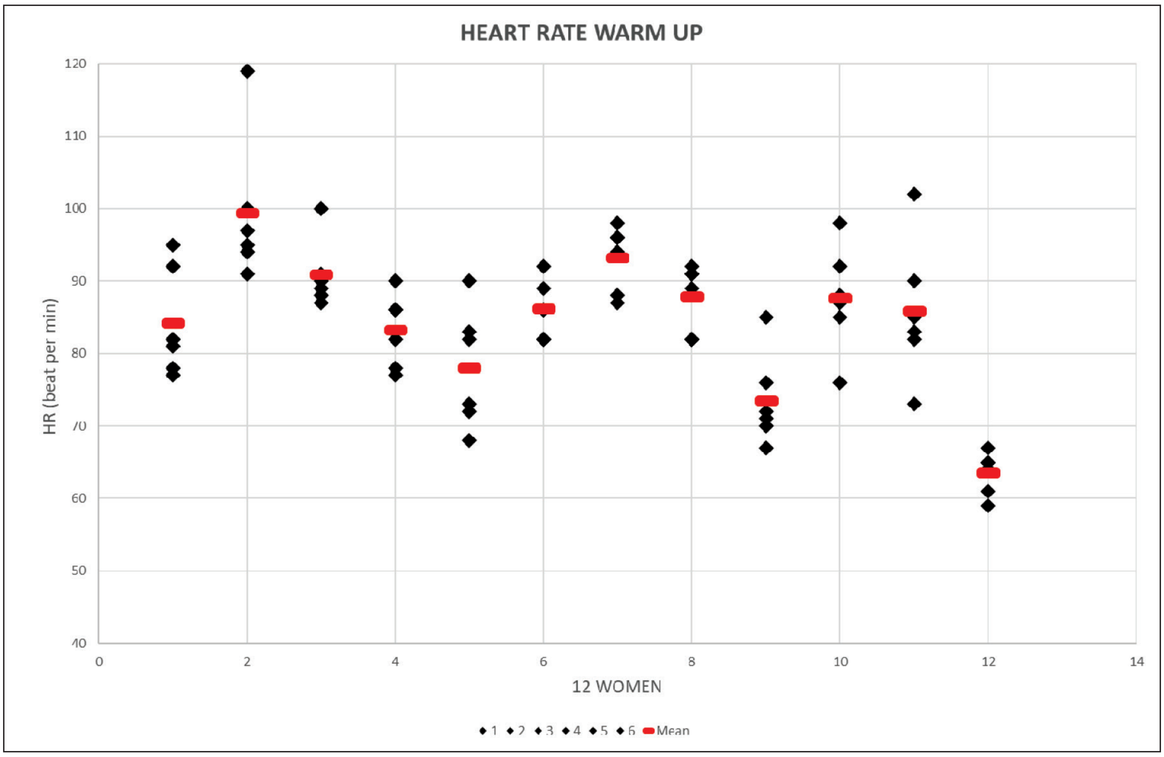

Figure 6: *Heart rate variability measurement after warm-up period is given in black points is in every subjects, red lines shove the mean value*

After warm-up period average values in the whole group of systolic blood pressure were 126.7 ±10.4 mmHg, of diastolic blood pressure 76.5 ±7.0 mmHg, heart rate 84.4 ±9.0 beat per minute.

Cardiovascular parameters at aerobic peak

The following aerobic exercise at the intensity of individual aerobic threshold of lasted 40 minutes. Systolic blood pressure variability at aerobic peak in cardiac women is shoved Fig. 7.

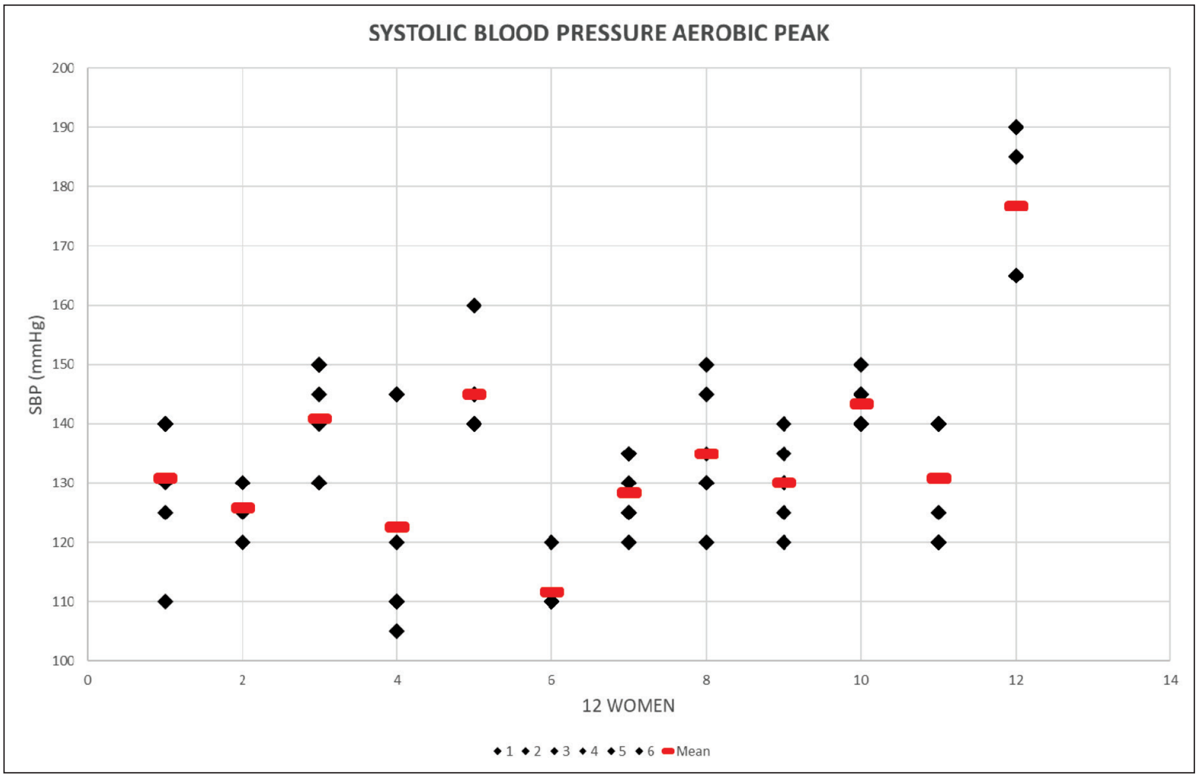

Figure 7: *Systolic blood pressure variability at aerobic peak in cardiac women is shoved is given in black points is in every subject, red lines shove the mean value*

Diastolic blood pressure variability at aerobic peak in cardiac women is shoved Fig. 8.

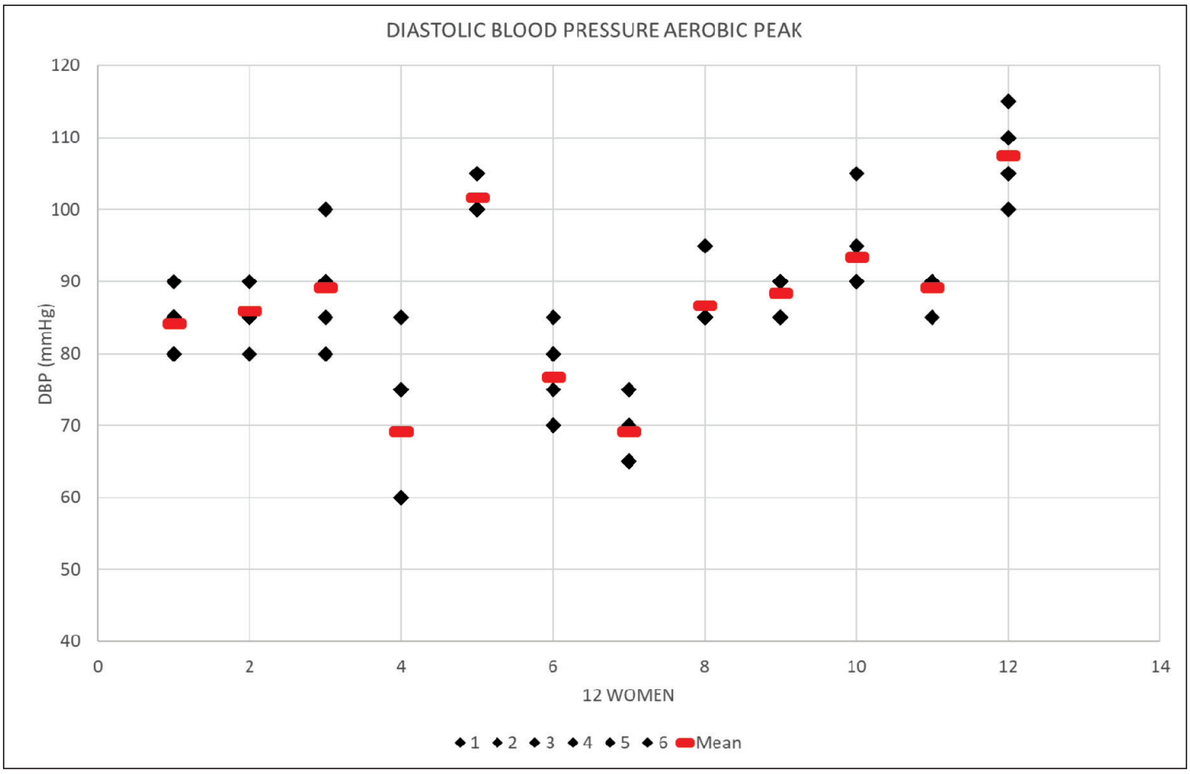

Figure 8: *Diastolic blood pressure variability at aerobic peak is given in black points is in every subjects, red lines shove the mean value*

Heart rate variability at aerobic peak in cardiac women is shoved Fig. 9.

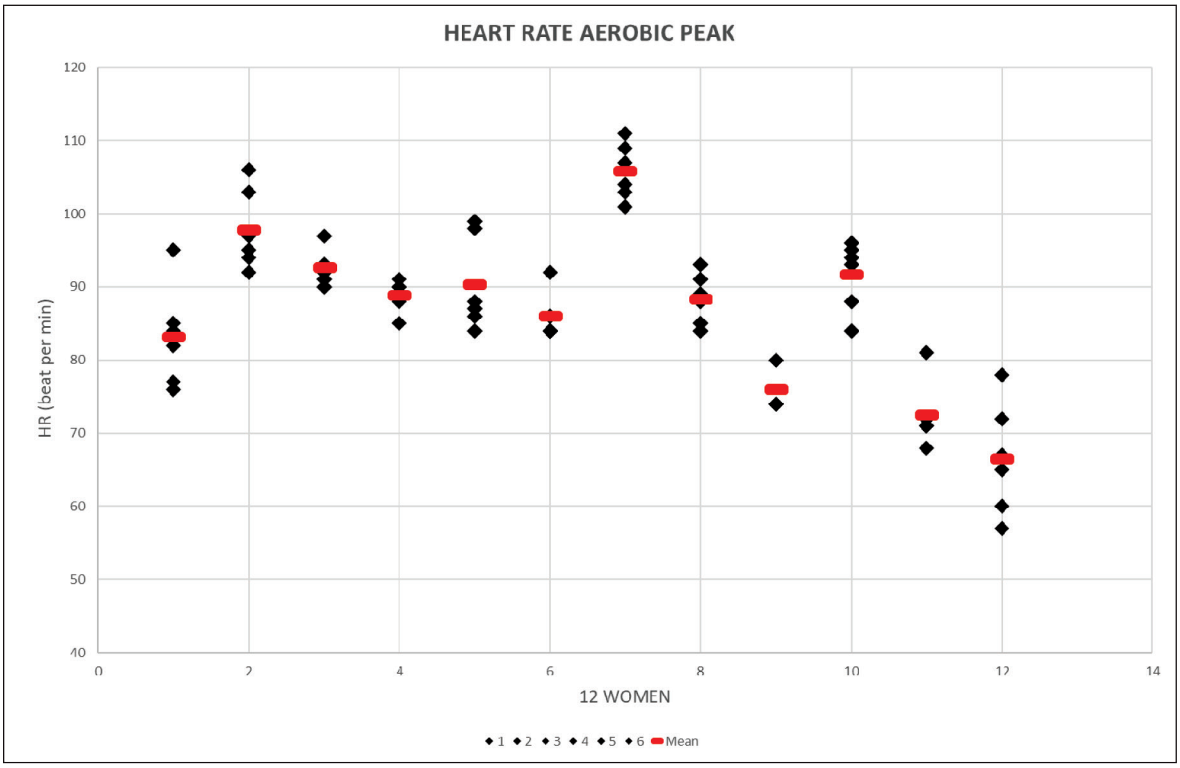

Figure 9: *Heart rate variability at aerobic peak is given in black points is in every subjects, red lines shove the mean value*

At aerobic peak - average values in the whole group of systolic blood pressure were 135.1 ±15.4 mmHg, of diastolic blood pressure 86.7 ±10.9 mmHg, heart rate 86.6 ±10.0 beat per minute.

Cardiovascular parameters after cool-down period

At the end of exercise fallowed cool-down period of 10 minutes. Systolic blood pressure variability after cool down period in cardiac women is shoved Fig. 10.

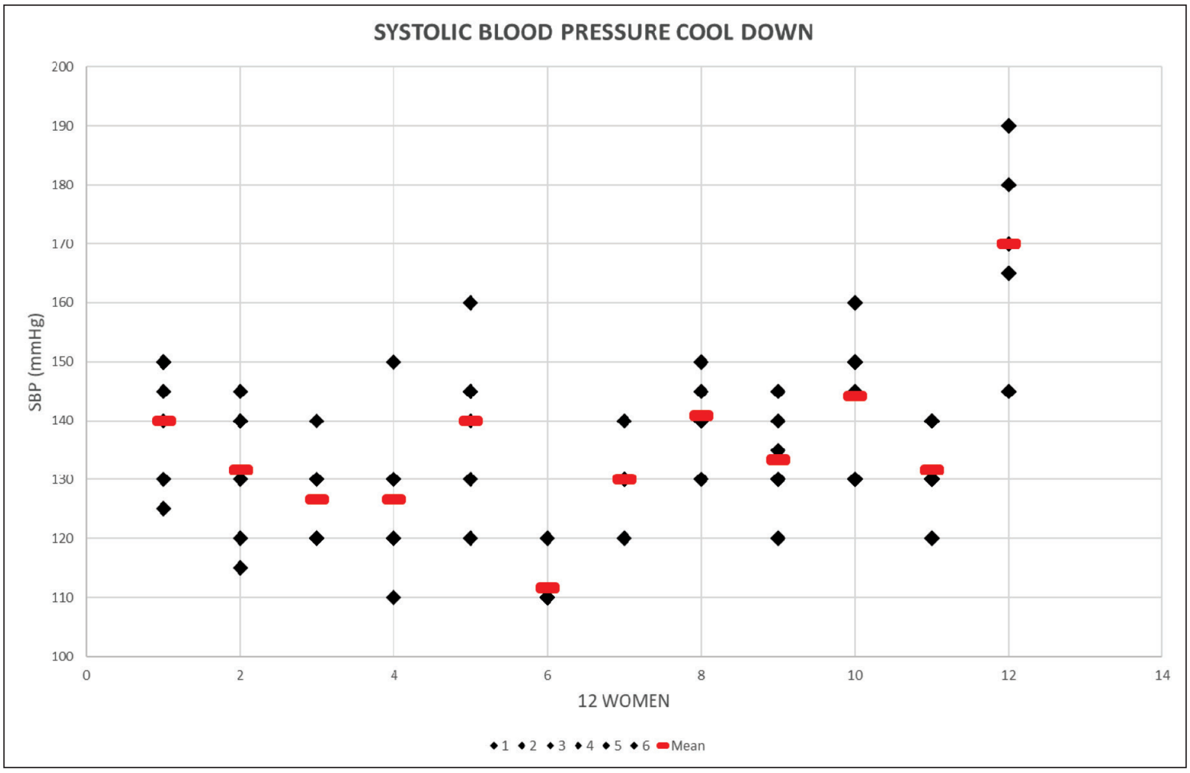

Figure 10: *Systolic blood pressure variability in after cool-down period is given in black points is in every subjects, red lines shove the mean value*

Diastolic blood pressure variability after cool-down period in cardiac women is shoved Fig. 11.

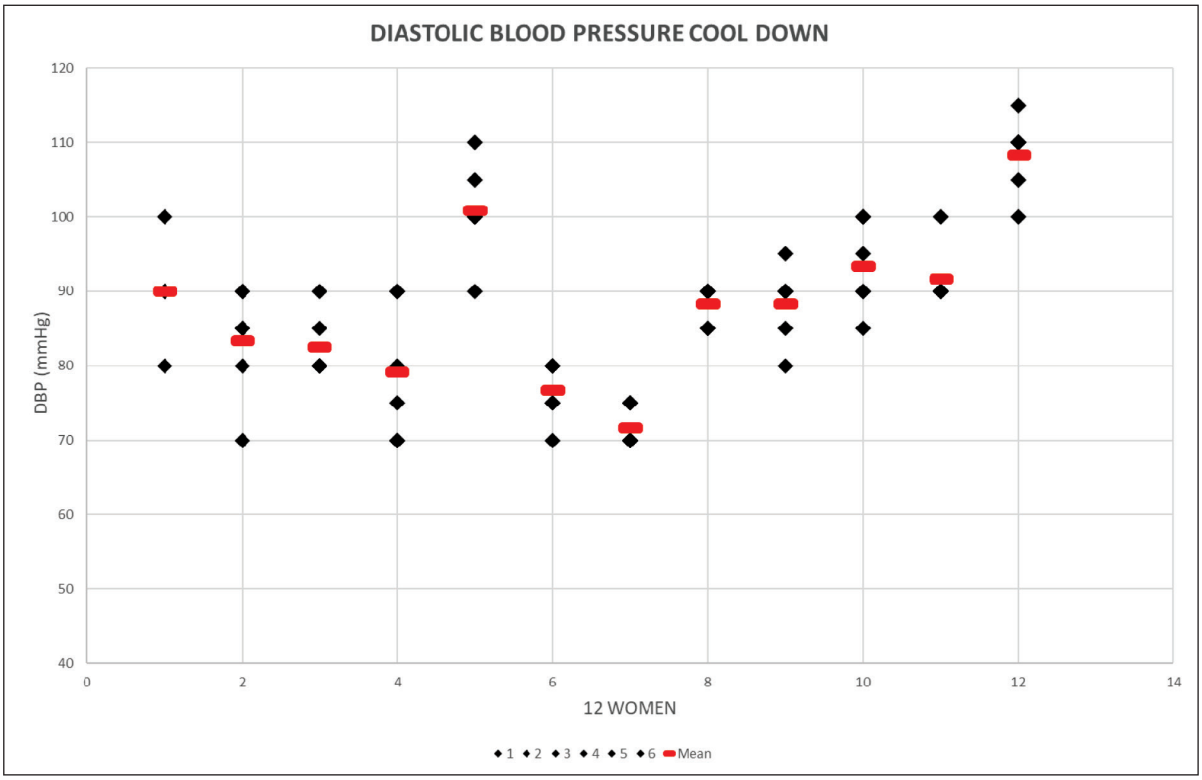

Figure 11: *Diastolic blood pressure variability after cool-down period is given in black points is in every subjects, red lines shove the mean value*

Heart rate variability after cool-down period in cardiac women is shoved Fig. 12.

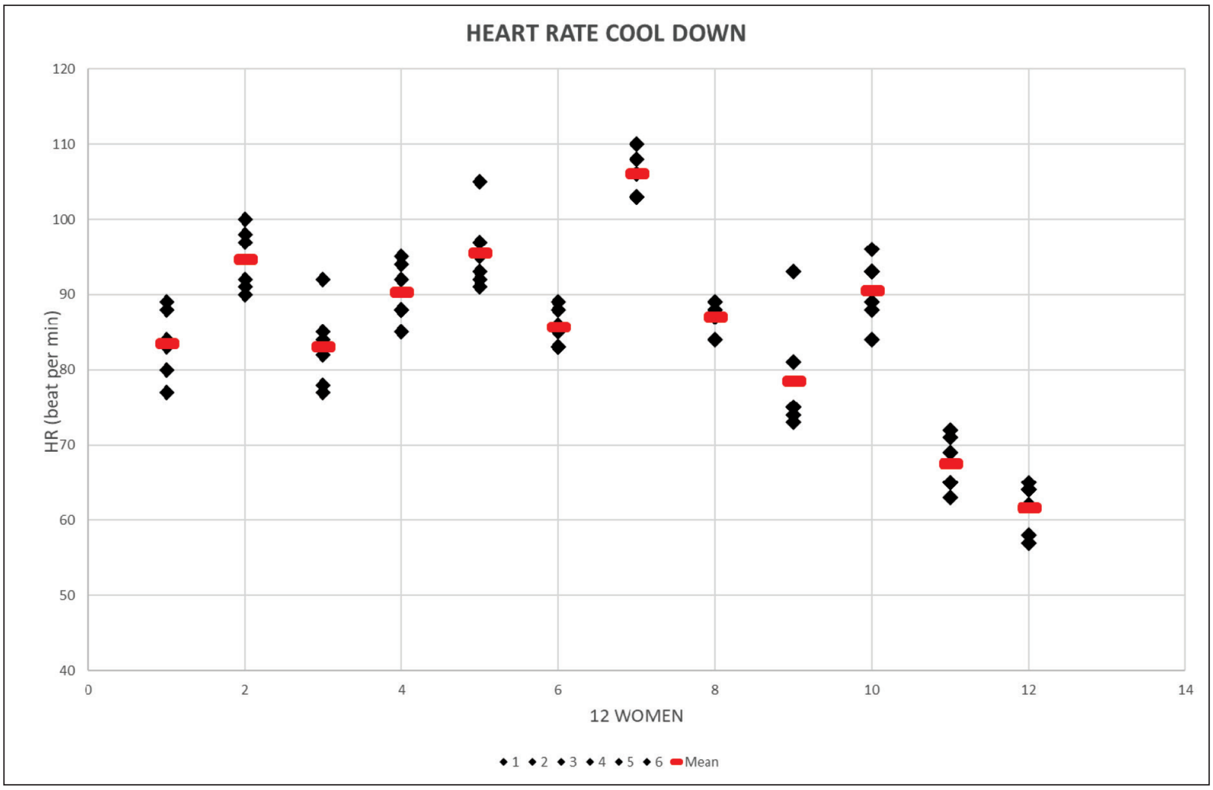

Figure 12: *Heart rate variability after cool-down period is given in black points is in every subjects, red lines shove the mean value*

After cool-down period - average values in the whole group of systolic blood pressure were 135.6 ±13.3 mmHg, of diastolic blood pressure 87.8 ±9.8 mmHg, heart rate 85.3 ±11.6 beat per minute.

Our results showed that systolic and diastolic blood pressure varies in resting values before exercise, after warm-up period, at the peak of aerobic exercise on the individual aerobic threshold value of load and after cool-down period from twenty mmHg to less mmHg.

Aerobic exercise did not influence the values of this variability. Variability of the heart rate is also present at period of aerobic exercise training.

Discussion and conclusion

In healthy individual blood pressure variability is regarded as a dynamic phenomenon including short-term, mid-term and long-term fluctuation resulting from an interaction of physical and psychic stimuli i. e. physical activity, mental stress, duration and quality of sleep, smoking, alcohol consumption, seasonal variation in temperature, modulated by variable individual reflex responses (10). According Cuspidi et all. variability and instability of blood pressure has emerged as an important predictor of cardiovascular morbidity and mortality.

For over half a century arterial blood pressure has been known for its high variability over time this key aspect har long been neglected in assessing cardiovascular risk in hypertensive patients

(11,12,). These data suggest that high visit-to-visit blood pressure variability may be a marker of high cardiovascular risk.

In this pilots study our results showed that systolic and diastolic blood pressure varies at the peak of aerobic exercise on the individual aerobic threshold value varies by repeated measurement contrary to the previous opinions.

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Exercise Therapy in Patients with Left-Ventricular Assist Device (LVAD)

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Abstract

Background. Thanks to technological progress, left-sided mechanical cardiac supports (LVADs) are nowadays a frequent alternative to heart transplantation. Thanks to LVAD, patients in the end-stage of chronic heart failure (CHF) have a significant improvement in their health. However, the degree of improvement is limited, and therefore, increased attention is paid to the possibilities of increasing functional fitness through regular physical activity.

Patients and methods. Twenty six patients (all M; mean age 58 ± 5.7 yrs) with terminal stage of CHF, were enrolled in the project. Two types of LVADs were implanted: HeartWare® (n = 14) and HeartMate3® (n = 12). At discharge, all patients were asked to perform physical activity at home for at least 60 min / day (recommended was low-to-moderate intensity aerobic training, such as walking and stationary or light cycling). The 6-minutes corridor walk-test (6CWT) was done for the assessment of the functional capacity and the European Quality of Life Questionnaire - Version 5D (EQ-5D) was used for the evaluation of the quality of life (QoL). The testing was realized before LVAD implantation, at discharge, after 3, 6 and 12 months.

Results. Only 12 patients were able to complete the 6CWT before implantation (the mean distance walked was 283 ± 94.5m). At discharge, all the 26 patients underwent the 6CWT test (distance walked was 299 ± 67.1m; P <0.05). After 3 months, 16 patients achieved the 6CWT (distance walked was 396 ± 80.7m; P <0.001); after 6 months, 14 patients attended the 6CWT (distance walked was 391 ± 111.8m; P <0.001); and after 12 months only 8 patients were tested (distance walked was 366 ± 132.2m; P <0.001). Similar results were obtained from the evaluation of the EQ-5D questionnaire, which showed a significant improvement in mean values from 54.9 ± 19.7% at baseline to 71.1 ± 16.1% at discharge (P <0.01); 75.7 ± 19.7% after 3 months (P <0.01); 78.6 ± 14.9% after 6 months (P <0.01); and at 62.8 ± 24.3% (P <0.04) after 1 year from the LVAD implantation.

Conclusion. Despite a number of limitations, especially the declining number of patients during long-term follow-up, the results obtained clearly confirm a significant improvement in submaximal physical activities and the quality of life of patients with implanted LVAD.

Key words

left-ventricular assist device – heart failure – exercise training – rehabilitation – functional fitness

Introduction

Regardless of the possibilities of modern state-of-the-art treatment methods, progression to the terminal state affects up to 25% of patients with end-stage chronic heart failure (1). In such cases, it is possible to choose 3 intervention options: heart transplantation (HT), mechanical cardiac support or palliative care (2). In the current situation of a rising trend in the number of new patients with CHF and a permanent shortage of suitable donors, VAD implantation appears to be the optimal strategy of "bridging" (until transplantation) or "destination therapy" for patients unsuitable for transplantation. Only in a smaller number of patients with CHF is it possible to use VAD as a "bridge to recovery", ie to achieve such a degree of restoration of cardiac function that it is possible to explant the device (2). Physical activity in the form of ambulatory (in hospital) or home training (ET) is a highly effective therapeutic strategy in patients with CHF due to the positive effects on increasing physical fitness and also in terms of prognosis (3, 4). However, with a few exceptions, in the past decades this intervention has not been sufficiently studied in patients with implanted VAD (5). The main reasons were the lack of experience, great variability of recommendations or even concerns about the risk of damage to the health of these patients (especially old age and the number of comorbidities). However, despite these limitations, consistent official recommendations were issued in 2018 to support the implementation of exercise in patients with VAD in clinical practice (6). The document evaluates current knowledge about the causes of limited fitness, presents available evidence on the benefits of exercise in patients with VAD, shows a series of recommendations regarding the choice of optimal ways of exercise in clinical practice, and finally discusses in detail the existing gaps in knowledge (6). Exercise acts as an activator of the sympathoadrenergic system, which mediates the cardiovascular response, allowing an increase in blood supply and higher oxygen consumption in peripheral tissues. The standard (‚normal') physiological response to exercise is a rise of heart rate (HR), increased myocardial contractility, and a consequent increase in cardiac output (CO). The body's ability to increase CO in response to higher metabolic transformation is a crucial factor in cardiovascular adaptation to exercise. This ability may be partially limited by the age of the organism, general fitness and event. and genetically (7). However, people with cardiac pathology are not able to respond adequately to physical and mental stress. Especially in patients with more severe heart failure, it is not possible to sufficiently increase CO due to irreversibly impaired functional and metabolic abilities. This has far-reaching pathophysiological consequences, manifested by global hypoperfusion, hypoxia and multiorgan insufficiency, including skeletal muscle mass (8). The characteristic end result is poor condition, hypo- or inactivity and chronic progression and worsening of the disease. Only a very limited number of publications examined the physical capacity of heart failure patients before and after LVAD implantation. Leibner et al. (2013) found a mean VO2peak of 11.2 ml/kg/min in 25 patients prior to LVAD implantation (9); after 1 year the VO2peak remained at the same level (11.2 mL/kg/min; NS). Similarly, Dunlay et al. (2014) observed a VO2peak of 11.5 ml/kg/min before LVAD implantation; nearly all patients showed a VO2peak below 14 mL/kg/min after LVAD implantation as well (10). In both studies, however, everyday activities (ADL) and the quality of life improved considerably (9, 10). Although functional capacity usually improves compared to the pre-implantation status, VAD recipients still experience an impaired exercise capacity (11), and usually their VO2peak is about <50% of the predicted value. Exercise training (ET) is highly recommended in HF because of its beneficial effects on functional capacity and prognosis. Only recently, it has been proposed also in VAD recipients. This pilot study aimed to evaluate submaximal physical fitness and quality of life in a group of patients with LVAD at discharge, and after 3, 6 and 12 months from the implantation.

Patients and methods

From 2018, we designed and started the project of regular fitness monitoring and exercise training in patients with implanted LVAD. In total, 26 patients (all M; mean age 58 ± 5.7 years) with end-stage of CHF, were included in the project. Two types of LVADs were implanted: HeartWare® (n = 14) and HeartMate3® (n = 12); (Fig. 1). Pump speed was set at 7.000 rpm.

Figure 1: *Two types of LVAD were implanted* (Sources: https://europe.medtronic.com/xd-en/healthcare-professionals/products/cardiac-rhythm/ventricular-assist-devices/heartware-hvad-system.html; https://www.omnimedics.cz/produkty/abbott-heartmate-3-lvas)

LVAD was implanted from the left minithoracotomy of the 5th intercostal space and ministernotomy (2 x 7 cm incision) instead of the middle sternotomy. At discharge, all patients were instructed about the importance of performing physical activity at home for at least 60 minutes per day (depending on the individual conditions). Recommended activities included low-to-moderate intensity dynamic large muscle group exertion (e.g. walking, stationary or light cycling). During the entire course of exercise training at home, the patients were asked to pay a great attention to the prevention of falls and sudden changes in body position. Any activities that could cause undesirable overload or damage to the body (e.g. competitive or contact sports) should be avoided. Everyone was advised to stop physical activity immediately if any of the warning signs of exercise intolerance appeared, such as light headedness, severe dyspnea, chest pain or discomfort, tachycardia, fainting, dizziness, extreme fatigue or claudication. The 6-minutes corridor walk-test (6CWT) was selected for the assessment of the functional capacity. 6CWT is a standardized examination tool both for the objective assessment of submaximal fitness and for the detection of reduced exercise tolerance due to cardiopulmonary restriction (12). The test is very simple and can be used very well to objectify the overall physical fitness of patients after LVAD implantation. To assess the subjective perception of exertion (ratio of perceived exertion or RPE) during and after the test, two Borg scales (scales 1-10 or 6 to 20) can be used (13). 6CWT measures the distance walked in meters and the result is then compared with the predicted values (14). The European Quality of Life Questionnaire - Version 5D (EQ-5D) was used for the evaluation of the quality of life (QoL). EQ-5D is a questionnaire assessing the health of the patient in 5 items, which focus on mobility, self-care, routine activities, difficulties (including pain) and depression. A three-point scale is used to objectively evaluate individual items, which determines the degree of disability. Subjective evaluation of health status is performed using the Visual Analog Scale in the range 0-100 (0 is the worst possible health status, 100 is the best health status perceived by the patient). The EQ-5D questionnaire has a wide range of use in clinical trials, in which each patient can assess the current state of his health at any time. Depending on the functional status all the above mentioned tests were done before implantation, at discharge, after 3 and 6 months, and after 1 year after LVAD implantation.

Statistical analysis. Standard descriptive statistics were applied in the analysis. Continuous variables at study entry, study course and study end and their difference were described using mean supplemented by standard deviation; due to available sample size both parametric and non-parametric descriptive statistics were adopted. Value p=0.05 was adopted as a level of statistical significance in all analyses. Statistical analysis was computed using SPSS 22.0.0.1; IBM Corporation, 2014 (15).

Ethics. The study was approved by local Ethic committee and all included patients signed informed consent based on the „WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI: Ethical Principles for Medical Research Involving Human Subjects“ (updated in Fortaleza, Brazil 2013) and orders of GCP European community.

Results

Standard part of the early rehabilitation in all the patients after LVAD implantation was daily exercise in bed, initially in supine position (in this phase, bed-side ergometers with a programmable workload were used, enabling passive movement as well). Then verticalization followed and gradually full mobilization (approx. within 2 weeks). During the next phase of rehabilitation, the patients individually started the training with aerobic endurance elements up to 2-3 times a day. At discharge, the patiens were instructed about a suitable type of aerobic exercise, mainly walking, bicycling or ergometer cycling. Initially, a recommended maximum training duration was 10 min 2-3 times/day, then, taking into account the individual workload tolerance, the training duration was gradually extended to 30-60 min/day. Out of 26 patients included, only 12 (46%) were able to complete the 6CWT before implantation and walked the mean distance of 283 ± 94.5m. However, at discharge, all the 26 patients underwent the 6CWT test and walked a distance of 299 ± 67.1 m; this improvement reached only weak statistical significance compared to the pre-implantation period ($P < 0.05$). After 3 months, only 16 patients achieved the 6CWT and scored the value of 396 ± 80.7m ($P < 0.001$); 6 patients died, 1 had orthotopic heart transplantation (OTS), 3 had arrhythmias and 1 covid-19 infection). After 6 months, 14 patients attended the testing, and achieved the result of 391 ± 111.8 m ($P < 0.001$); 0 died, 2 had OTS, 8 did not attend the test and 2 failed to finish the test due to dyspnea). Finally, 12 months after implantation, only 8 patients were tested and achieved the distance walked of 366 ± 132.2 m ($P < 0.001$); 0 died, 3 had OTS, 4 had lower limb pain, and 11 did not attend the test (Fig. 3). The main reason of the quite important absence of patients for 6CWT and for QoL assessment was the problem with transport, because a major part of the patients came from different areas of the state and remote residence (even hundreds of km). Nevertheless, these results clearly confirm a significant improvement in submaximal activities after LVAD implantation. Similar results were obtained from the evaluation of the EQ-5D questionnaires, which showed a significant improvement in mean values from 54.9 ± 19.7% at baseline to 71.1 ± 16.1% at discharge ($P < 0.01$), to 75.7 ± 19.7% after 3 months ($P < 0.01$), to

78.6 ± 14.9% after 6 months ($P < 0.01$), and to 62.8 ± 24.3% ($P < 0.04$) after 1 year from the LVAD implantation (Fig. 3).

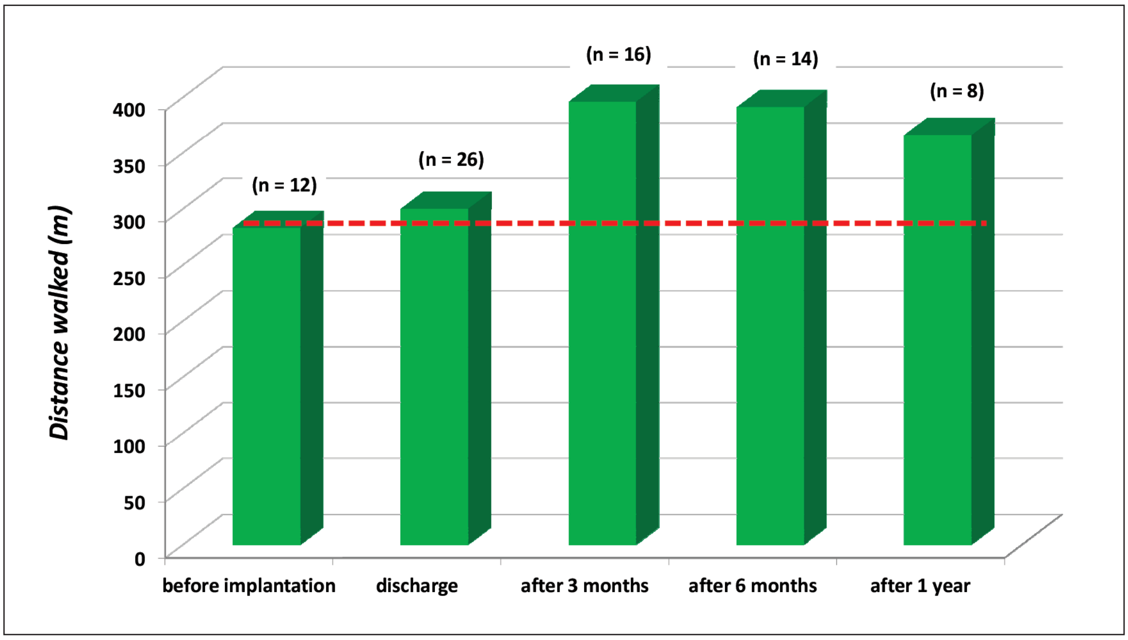

Figure 2: *Graph showing the results of 6CWT.*

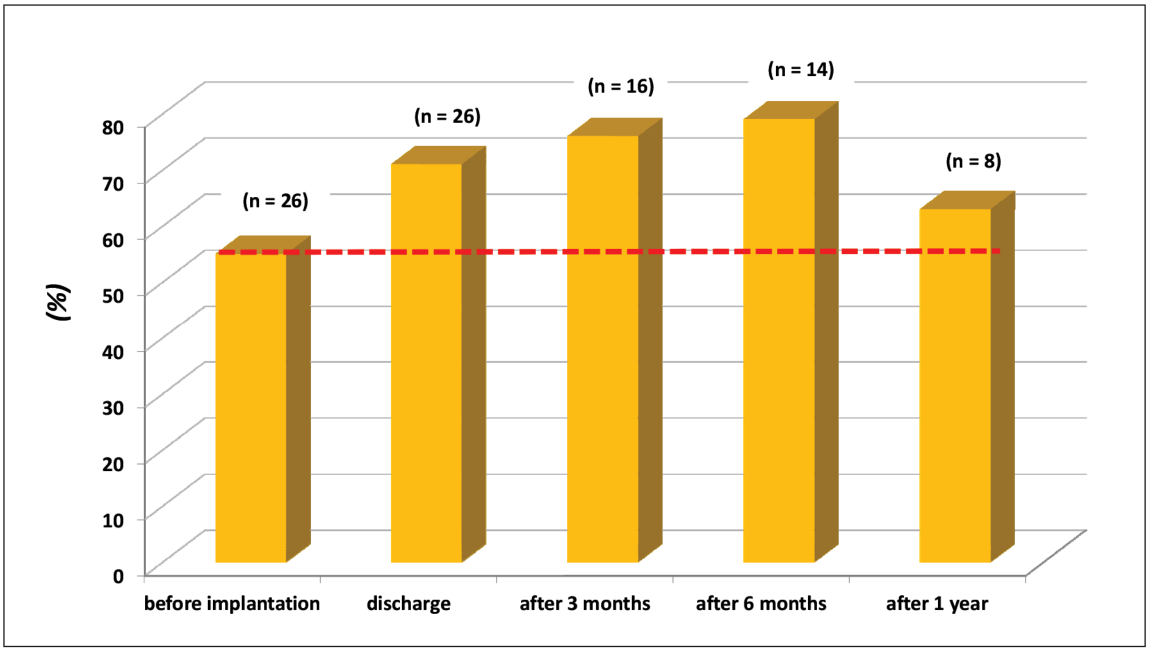

Figure 3: *Graph showing the results of EQ-5D.*

Discussion

This small pilot study showed that mild intensity aerobic endurance training can significantly improve functional capacity and QoL in patients after LVAD implantation. This effect is long-term and can rightly be assumed to be an important stabilizing element of health. The effectiveness and safety of endurance training in patients with CHF has been repeatedly demonstrated in a number of clinical studies over the past 3 decades (16, 17, 18). It is confirmed that a number of chronic pathological conditions incl. CHF, is accompanied by general deconditioning and especially the loss of muscle mass of the lower limbs (19). Therefore, one of the main goals of rehabilitation is training the muscles of the lower limbs, which plays a key role in maintaining self-care, independence and activities of daily living (ADL). As with other chronic conditions, in patients with LVAD, training should initially be of low intensity, which can then be gradually increased over time. The intensity of the load should be chosen individually so that it is not too demanding (or even exhausting) for the patient and without an increased frequency of breathing and risk of dyspnea onset. Regular endurance-type activity (such as walking or bicycling) initiates of significant adaptive changes in the leg muscles and an important factor in preventing both muscle deconditioning and reducing cardiovascular risk in patients with end-stage CHF (20). Experience with the recommendation of optimal physical activity in patients with LVAD is still exceptional, but even from the few existing information there is a significant positive effect on physical fitness (21, 22, 23). The available up to the present published data suggest that overall fitness remains severely limited even after LVAD implantation. Physical capacity essentially depends on the CO generated and/or on the arteriovenous O_2 difference, which together contributes to the oxygen supply to the skeletal muscles. The only adjustable element in the VAD is the number of revolutions per minute (rpm). A lower rpm means reduced CO, increased risk of thrombosis or heart failure. Conversely, increased speed may increase the risk of suction effect and LV cavity collapse. The optimal rpm setting can be determined using echocardiography. The vast majority of currently used LVADs are rotary pumps of the axial or centrifugal type operating at a constant speed and generating a continuous flow (CF). These pumps are sensitive to changes in preload and afterload, and the main mechanism that leads to an increase in LVAD output at constant speed, is a decrease in the pump's head pressure (24). LVAD implantation creates a special condition in which two pumps work in parallel - artificial (LVAD) and biological (residual activity of the left ventricle). Both systems are able to contribute to the overall perfusion stability of the organism (Fig. 4). As already mentioned, most currently used pumps generate a continuous flow, and the stable number of rpm ensures a constant output. As a result, the flow through the LVAD can be increased during exercise with both exercise-dependent tachycardia and an increase in left ventricular end-diastolic pressure associated with increased preload (22, 26).

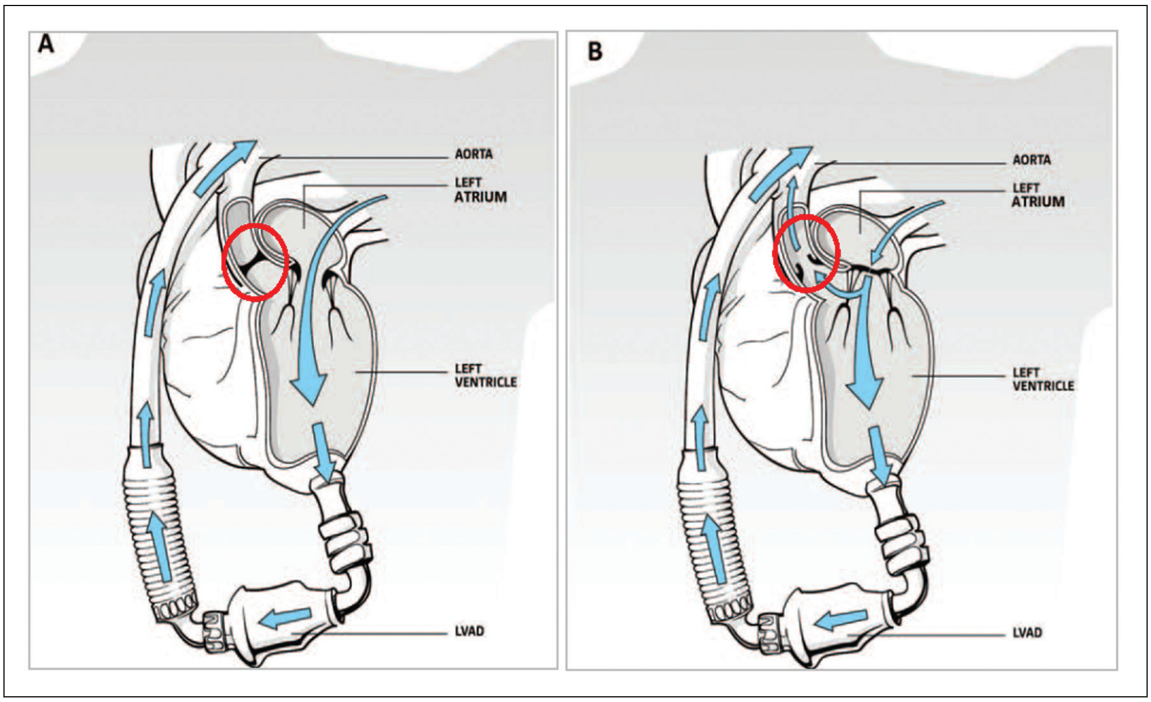

Figure 4: *Hemodynamic conditions at rest (A): cardiac output usually is generated exclusively by the pump flow whereas the aortic valve is closed. Hemodynamic conditions during exercise (B): cardiac output usually is generated by pump flow and native heart output whereas the aortic valve is opened (From: Reiss N. et al., 2016; cit. No. 22).*

At rest, LVADs of CF type provide most of the CO, while during exercise the contribution of residual biological myocardial activity to increased CO is quite variable. After LVAD implantation, most patients experience so-called reverse LV remodeling and improvement of its ejection fraction (LVEF). This is extremely important because patients with higher EF can be expected to have higher CO (21) during exercise. This assumption was confirmed by a study in 30 patients with LVAD; there was a significant decrease in VO2peak in patients with EF <40% when the pump output was reduced to 6000 rpm. No significant changes were found in patients with EF >40% (27). Reduction of mechanical overload of the left ventricle (LV) is the main purpose of VAD implantation, and therefore, it is necessary to carefully set the pumping parameters of the device (28, 29). Pump flow is determined by engine power, speed and specific VAD properties. However, due to the inaccurately determined volume of blood flow through the aortic valve, only a rough estimate of CO is possible, which is additionally affected by the residual contractile function of the left ventricle. During exercise, the effect of residual cardiac function on the resulting CO depends on the interaction of right and left ventricular contractile reserves (21, 22). Another important factor limiting the maximum CO during exercise is the grade of right ventricular dysfunction (RV) in a situation of increased venous return (30). Impairment of right ventricular hemodynamics has been shown to be a major reason for the increase in fatal complications in the post-VAD implantation period (31). Therefore, maintaining a good functional state of the right heart is vital for adequate left ventricular filling and cardiac output. I sum, adaptation to exercise in patients with VAD is still a complex and not fully identified problem. Most of the available information comes from studies, which have mostly focused on one limiting factor that reflects the integrated stress response. For this reason, precise recommendations for the regulation of physical activity have not yet been developed. Positive experiences have recently been published about the effects of exercise in patients with VAD on the improvement of central (CO) and peripheral hemodynamics (muscle perfusion and oxygenation). At the same time, however, there is also information about the negative consequences of physical activity on lung function, especially the worsening of lung diffusion, very likely due to congestion of fluid in the pulmonary system (32).

Conclusion

The effect of increased LVAD flow in response to various types of submaximal exercise remains unclear. Due to the complex interaction of residual biological left ventricular function, LVAD and blood circulation, it is not known exactly whether and to what extent the LVAD itself contributes to the tolerance of maximal and submaximal exercise (33). However, although the available experience and evidence about the rehabilitation of patients with LVAD is still limited, it is clear that patients with LVAD can easily undergo rehabilitation based on exercise training and provided with respect to specific conditions. Maintaining sufficient blood flow through the pump is needed to prevent suction, maintain optimal blood pressure and perfusion stability of the periphery. The length and intensity of rehabilitation should lead to a level of physical fitness appropriate to the individual needs of the patient, mainly gaining independence in daily activities and improving the quality of life. There is no doubt that prolonging survival in patients with LVAD is closely linked to achieving and maintaining optimal physical fitness. Although physical training is a basic rehabilitation intervention, a comprehensive approach must be chosen for these patients, including the issue of mental health and the limitation of risk factors. In the near future, it will be necessary to create a sufficiently number of qualified professional rehabilitation facilities that would organize, provide and manage the provision of specific care to patients with LVAD (34).

Disclosure

The authors declare no conflict of interest.

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The Effects of Physical Activity on Cognitive Function, Self-sufficiency and Somatic Parameters in Patients with Vascular Dementia

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Abstract

Cognitive dysfunction is one of the abnormalities that occur frequently in the population. There are many possibilities to influence these dysfunctions - for example: physical activity, cognitive rehabilitation, pharmacotherapy. The aim of our pilot study was to determine whether targeted physical activity (bipedal walking) has an effect on cognitive function in patients with vascular cognitive impairment. The partial aim of the study was to evaluate the effect of walking on the change in self-sufficiency during daily activities and the change in Body Mass Index (BMI) values. Twenty nine probands with a diagnosed stroke and cerebral arteriosclerosis were followed for one month. A Garmin Vívofit 3 watch was used to record the monthly movement intervention, which monitored the number of steps taken throughout the research. The effect of the movement intervention was evaluated using the MoCA test (Montreal cognitive test) and the BI test (Barthel index), and the weight and height of the probands were measured for the BMI evaluation. These values were measured at the beginning and end (after 1 month) of the intervention. Statistical and clinical analysis showed significant changes in the relationship between the number of steps and the improvement in cognitive function, self-sufficiency and BMI. Exercise therapy (walking) has a positive effect on improving monitored functions and therefore it should be included in the daily exercise regime.

Key words:

Dementia – walking - physical aktivity – rehabilitation - cognitive function - self-sufficiency - Body Mass Index

Introduction

Cognitive disorders are among the diseases with a relatively high incidence. According to the dependence on the other person during daily activities, we divide cognitive disorders into two main types, namely mild cognitive impairment and dementia (1). Our study focuses on dementia with a vascular etiology occurring mainly in patients after stroke or in patients with cerebral atherosclerosis. Evidence of a positive effect of movement on the cardiovascular and metabolic system, affecting pain or improving mobility is described in the literature (2). The proper function of the human cognitive component is equally important for a full life (3). Therefore, the influence of physical activities on human cognitive functions is investigated (4). Dementia is diagnosed using neuropsychological tests such as the Mini Mental State Examination (MMSE), the Addenbrood Seven-Minute Test (5) and The Montreal Cognitive Assessment (MoCA) (6). Cognitive disorders are treated with pharmacological and non-pharmacological therapies (7). In non-pharmacological treatment through behavioral therapy, we strive to motivate the patient and its activation, to train the cognitive and physical components together with ADL in order to improve the mental and physical side and reactivate the individual (8). Aerobic exercise supports optimal brain function (9). One of the leisure physical activities as a means of health promotion and disease prevention is walking (10).

Aim

The aim of our study was to evaluate the effect of movement therapy (walking) on cognitive functions, self-sufficiency and somatic parameters in patients after stroke, transient ischemic attack or with confirmed incidence of atherosclerosis treated in outpatient and neurological outpatient clinics in Ostrava, Olomouc and Prostejov. In connection with the aim of the work, scientific questions were defined and hypotheses were assigned to them:

Question number (No) 1: How does cognitive function change after physical activity within complex monthly therapy? (Hypothesis H01: There is no statistically significant change in cognition (MoCA) after complex therapy with physical activity).

Question No. 2: How does self-sufficiency change after physical activity within complex monthly therapy? (Hypothesis H02: There is no statistically significant change in self-sufficiency (BI) after complex therapy with physical activity).

Question No. 3: How do somatic Body Mass Index (BMI) values change after physical activity during complex monthly therapy? (Hypothesis H03: There is no statistically significant change in BMI after complex therapy with physical activity).

Subjects and Methods

Characteristics of the research group

For evaluation, 29 patients (11 men and 18 women), mean age 69 years, with a stroke and proven atherosclerosis of the cerebral vessels were included (Table 1). Inclusion criteria: Diagnosed stroke or atherosclerosis, ability to walk, ability to use a Garmin Vivofit3 watch, stabilized condition, research collaboration, signed informed consent.

Table 1: *Descriptive statistics of the measured values of the research group of individual validation tests MoCA, BI and BMI before the beginning of physical activity and subsequently after its end together with their differences and the average number of steps during the day.*

Variable	Number	Average	Mean	Minimum	Maximum	Standard Deviation
Age	29	67,82	69,00	44,00	83,00	9,41
MoCA 1	29	22,56	23,00	15,00	29,00	2,89
MoCA 2	29	24,48	25,00	15,00	30,00	3,72
MoCA R	29	1,93	1,00	−4,00	7,00	2,65
BI 1	29	95,56	95,00	75,00	100	5,77
BI 2	29	97,78	100	85,00	100	3,76
BI R	29	2,22	0,00	−5,00	15,00	4,00
BMI 1	29	28,78	27,53	19,7	37,18	4,42
BMI 2	29	28,42	27,62	19,4	36,7	4,48
BMI R	29	−0,36	−0,3	−1,66	0,09	0,37
Steps	29	5935,56	6100,00	1600,00	11000,00	2224,55

Legend of table 1: MoCA 1 and MoCA 2 - Montreal Cognitive Test before and after intense physical activity; MoCA R - difference of measured values of MoCA 1 and MoCA 2; BI 1 and BI 2 - Barthel index before and after intense physical activity; BI R - measured difference of BI 1 and BI 2 values, Steps - average of steps taken over a period of one month.

Methodology

The enrolled patients underwent two measurements - the beginning and the final measurement (after one month). Patient measurements included body measurements using a Tanita altimeter and scale to determine BMI and to adjust watch parameters individually). At the same time, patients had two validation tests - the Barthel index-based test (BI) for self-sufficiency and the Montreal MoCA cognitive test to assess cognition. Upon completion of the tests, each participant was explained the proper use of the watch, which was individually calibrated and worn on the left wrist. The Garmin Vivofit 3 watch recorded physical activity 24 hours a day for four weeks. Thus, the probands did not remove the device in order to avoid an inaccurate record of the number of steps. During this time, the measured data were gradually stored in the watch‘s memory. After one month, the subjects had control measurements of body values and test sets (MoCA and BI), then handed in a Garmin Vivofit 3 Watch to evaluate the average number of steps taken. The STATISTICA 13 program was used to process the measured data and test the hypotheses using the Wilcoxon paired test.

Results

Results for research question No. 1

It was found that physical activity in complex therapy affects the cognitive component in test subjects. According to the resulting p-value ($p = 0.002$) obtained from the Wilcoxon paired test (Table 2), it was confirmed that there was a significant change, and therefore we can reject H01 and thus confirm

HA1 as amended: „There is a statistically significant change in cognition after complex therapy with physical activity.“

Table 2: *Wilcoxon paired test of two variable values. MoCA 1 before the start of exercise therapy and MoCA 2 after the end of exercise therapy*

A pair of variables	Wilcoxon paired test (Patient_Data_V3) The labeled assays are significant at the p <.05 level		
	number of valid	Z	p-value
MoCA 1 a MoCA 2	29	3,11	0,002

Legend of Table 2: MoCA 1, MoCA 2 - Montreal Cognitive Test (before and after intervention); Z - test parameter; p-value - significance level.

Results for research question No. 2

It was evaluated and confirmed that physical activity can change self-sufficiency in normal daily activities. According to the resulting p-value (p = 0.013) obtained from the Wilcoxon paired test (Table 3), it was found that there was a significant change and therefore we can reject H02 and thus: There is a statistically significant change in self-sufficiency after intensive therapy in complex monthly therapy.

Table 3: *Wilcoxon paired test for the pair of variable values BI 1 before the start of exercise therapy and BI 2 after its end*

A pair of variables	Wilcoxon paired test (Patient_Data_V3) The labeled assays are significant at the p <.05 level		
	number of valid	Z	p-value
BI 1 a BI 2	29	2,49	0,013

Legend to Table 3: BI 1, BI 2 - Barthel index before and after exercise intervention; Z - test parameter; p-value - significance level.

Results for research question No. 3

It was found that physical activity in complex therapy affects the BMI value. According to the resulting p-value (p = 0.001) obtained from the Wilcoxon paired test (Table 4), it was confirmed that there was a significant change, and therefore we can reject H03 in favor of HA3, which reads as follows: There is a statistically significant change in BMI after physical activity as part of a comprehensive monthly therapy.

Table 4: *Wilcoxon paired test for a pair of BMI 1 variables before the start of exercise therapy and BMI 2 after the end of exercise therapy*

A pair of variables	Wilcoxon paired test (Patient_Data_V3) The labeled assays are significant at the p <.05 level		
	number of valid	Z	p-value
BMI 1 a BMI 2	29	4,18	0,001

Legend of Table 4. BMI 1, BMI 2 - Body mass index (before and after the intervention); Z - test parameter; p-value - significance level.

Discussion

The main aim of the study was to determine the possible connection between the movement regime and cognitive functions, self-sufficiency and somatic parameters in patients with a stroke or atherosclerosis.

Discussion on Research Question No. 1

In accordance with the evaluated statistical results, it is clear that there is a significant difference in the measured values after daily walking training within one month. Similarly, several studies have shown that physically active people are more resistant to the risk of developing dementia in later life (11, 12, 13, 14). This was also confirmed by a recent study by Young et al. (2), who evaluated the results of a total of eleven studies in which healthy individuals over the age of 55 performed regular aerobic training to improve cardiorespiratory capacity in relation to possible effects on cognitive function. The effects of training have been shown to have a positive effect, specifically on thinking speed, memory and auditory attention. Groot et al. (15) published a meta-analytical randomized control study with a larger sample and a different approach within the heterogeneity of the studies. This study looked at a total of eighteen studies involving a total of 802 patients with a mean age of 79.7 ± 4.2 years with diagnosed dementia without significant motor features divided into intervention and control groups. The mean duration of interventions was 15 ± 10 weeks with a mean frequency of 183 ± 185 minutes per week. Cognitive function testing was performed via MMSE and ADL capability according to BI. The studies focused on aerobic, anaerobic or combined exercise units. The overall effect of physical activity interventions with respect to cognitive functions in patients with dementia was found. Interventions were mainly caused by aerobic but also combined types of exercise. Among other things, aerobic exercise has been shown to contribute to the improvement of ADL.

Discussion on Research Question No. 2

A statistically significant result showed that there is an improvement in self-sufficiency in daily activities in the tested persons. The results of our study correspond to the results of similar studies. A published systematic review (16) examined the effect of physical activity on mobility, physical ability and functional activities in people with dementia. There were a total of 20 studies with a total of 1378 probands, of which nine studies demonstrated medium to high quality methodology. Of these studies, eight report that intense physical activity improves the mobility and physical abilities of people diagnosed with dementia. In individual studies, physical activity was mostly supplemented by other interventions, in addition to a very small part of the sample with pure movement therapy. The main requirement was that each intervention included a component of physical activity such as walking, endurance and balance training or functional exercises.

Discussion on Research Question No. 3

In our study, a significant correlation between aerobic walking physical activity and BMI was demonstrated. The result shows that movement affects the BMI value. The mean BMI of the total group of 29 patients before the start of aerobic training was 28.7 ± 4.41 kg / m^2 and decreased to 28.42 ± 4.48 kg / m^2 after the end of the monthly intervention. According to the BMI evaluation table, we can find out that the values of patients fall into the area of overweight. The issue of overweight and the associated risk of physical health problems was addressed by the author Yuenyongchaiwat (17). He states that the increasing value of BMI today due to low physical fitness together with poor lifestyle poses a threat in terms of mental health, musculoskeletal stress and the incidence of cardiovascular disease. Therefore, he focused on the possible influence of overweight through the effects of a 12-week walking program in 35 overweight probands (BMI ≥ 25 kg / m^2). The results of the study found that there were significant reductions in body weight, waist circumference, BMI and body fat percentage in the 30 subjects who completed the 10,000 daily steps.

Conclusion

The results of our study show that there is a statistical significance of the effect of physical activity on the cognitive component, self-sufficiency and weight, respectively BMI. The effects of physical activity are still being explored in relation to the issue.

Acknowledgment

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Declaration

No conflict of interest.

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International Congress Chronobiology in Medicine and Sports

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«CHRONOBIOLOGY IN MEDICINE AND SPORTS»
dedicated to the 100th anniversary of the birth of Prof Franz Halberg

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Conference program

DAY 1 - 07/ 12/ 2020

TIME	PRESENTATION	SPEAKER
10.00	Greetings from the Director of the Medical Institute (RUDN University)	**A.Y. Abramov** Doctor of Medical Sciences, Professor, Director of the Medical Institute of the RUDN University (Moscow, Russia)
10.20	Centenary Celebration of Franz Halberg, a maverick ahead of his time	**Germaine Cornelissen Guillaume** Professor, Integrative Biology and Physiology Director, Halberg Chronobiology Center, University of Minnesota (Minneapolis, USA)
10.40	Echocardiography implication on myocardial rhythmicity dysfunction	**Brian Mendel** MD, PhD, Department of Cardiology and Vascular Medicine, National Cardiovascular Center Harapan Kita, (Jakarta, Indonesia)
11.00	Long-term cooperation of the Medical Institute of the RUDN University (Russia) and Halberg Chronobiology Center, University of Minnesota	**Sergey Chibisov** MD, PhD, FICN, V.A. Frolov Department of General Pathology and Pathological Physiology, Medical Institute of the RUDN University (Moscow, Russia)
11.20	Seven day/24-h ambulatory blood pressure monitoring in night shift workers in health service	**J. Siegelova** Department of Physiotherapy, Department of Sport Medicine and Rehabilitation, Faculty of Medicine, Masaryk University (Brno, Czech Republic)
11.40	«When to Exercise; to reduce sympathetic activity and its adverse effects, for health promotion»	**Jan Fedacko** MD, PhD, FICN, Faculty of Medicine, PJ Safaric University (Kosice, Slovakia)
12.00	«Chronoptimizing recovery in sports»	**Yulia Koriagina** Doctor of Biological Sciences, Professor, Head of the Center for Biomedical Technologies, Federal State Budgetary Institution «North-Caucasian Federal Scientific and Clinical Center of the Federal Medical and Biological Agency» (Yessentuki, Russia)

RUDN university

CERTIFICATE OF PARTICIPATION

presented to

Jarmila Siegelová

for presenting oral paper

"Seven day/24-h ambulatory blood pressure monitoring in night shift workers in health service"

in International Scientific and Practical Conference «Chronobiology in Medicine and Sports»

dedicated to the 100th anniversary of the birth of Prof Franz Halberg

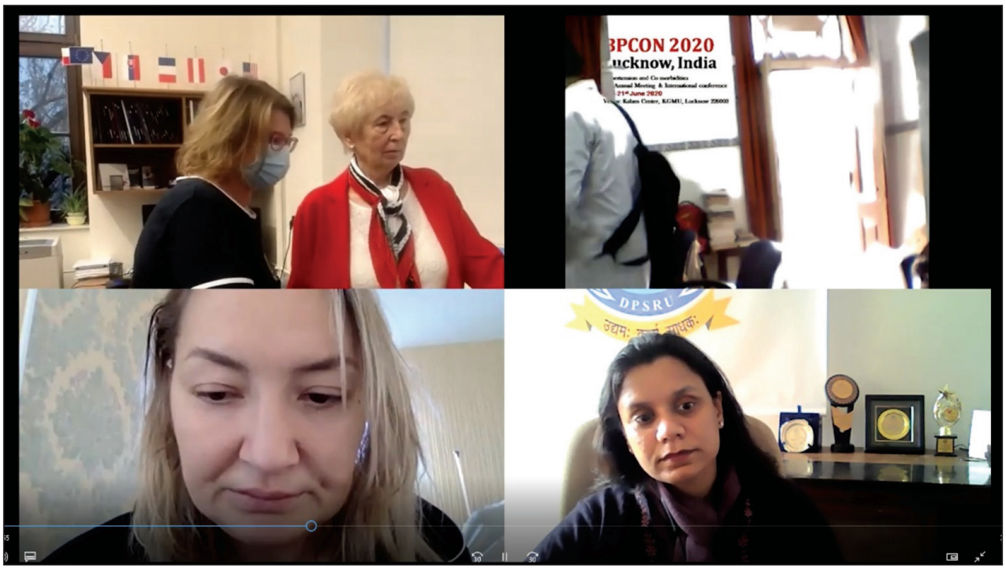
held on December, 7th – 9th 2020

Chairman of the Conference organizing committee,

Prof. ALEXEY ABRAMOV

Presentation Prof. Cornelissen on-line

Presentation Prof. Cornelissen on-line



Discussion on-line

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Dedicated to Franz Halberg, MD, PhD, at his 100th Anniversary (1919-2013)

Edited by

Sergey Chibisov, Gushchina S Yulia, Omar A Bawareed,
Ram B Singh, and Germaine Cornelissen

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