Faculty of Medicine • Masaryk University • Brno • Czech Republic

Department of Functional Diagnostics and Rehabilitation

PROCEEDINGS

SYMPOSIUM

NONINVASIVE METHODS IN CARDIOLOGY

Edited by: F. Halberg, T. Kenner, B. Fišer, J. Siegelová

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CONTENS

PERSONAL CONSIDERATIONS ON OBSERVATION AND EVIDENCE IN PRACTICAL MEDICINE

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Dedicated to Prof. MUDr. Zdenek Placheta, DrSc.

The task of physicians is either to support health of persons, to try to heal those who became sick or to reduce pain and discomfort, and to console.
Essential activities within the field of medicine have been, and still are based on observation and experience. Any patient is a unique person and not a statistical item. The modern assumption that medicine can only be based on statistical evidence, in my opinion is an arrogance.
And even, where evidence seems to be obvious it also seems obvious that quite often consequences of evidence and of observations are neglected.
In the following text I want to discuss some items to which I have some personal connection.
My relation to Ignaz Semmelweis results from the fact that in 1932 due to the obvious neglect of hundred years of evidence my mother died of puerperal a few days after my birth in the University clinic of Vienna.
The second topic - sudden infant death syndrome (SIDS) - shows, that on one hand a wrong hypothesis can lead to useful results and on the other hand, observation-based experience has helped to establish reasonable prophylactic effects.
The third topic – peptic ulcer – is again based on personal experience. It turns out that apparently no disease can be explained by just one single cause.

I. SEMMELWEIS

Against tremendous opposition and against malicious critical arguments by a majority of leading specialists Ignaz Semmelweis (1818 – 1865) introduced the correct prophylactic measures to prevent puerperal fever after delivery. He demanded from students and physicians to clean their hands with chlorinated water before they were touching the women in labour. The success proved that his observations and conclusions were correct. It is important to note that his proposition was made before any bacteria had been discovered. As seen from our current knowledge, at the time of Semmelweis the theories about the cause of puerperal fever were quite absurd.
Even in our days, when the etiology of infectious diseases like puerperal fever is well known, it is still necessary to demand hand-washing of physicians to prevent the transmission of diseases from patient to patient. Not only to avoid infection in connection with labour, but also in order to avoid any kind of hospital acquired infections (HAI) it is necessary to enforce cleaning of the hands of physicians. Weiss et al. (2006) point out that

several studies show that the rate of hand-washing in medical staff was between a third and a half of what was objectively required. They report, furthermore, that in the United States alone, there are two million cases of hospital acquired infections per year, 90000 of which end with the patient's death.
The correct measure against a disease was introduced without knowledge of the causing agent. Now, in spite of our knowledge the correct measures are in a surprisingly high percentage neglected.
It seems to be urgently necessary to teach medical students not only knowledge and skill but also behaviour, including cleanliness, proper dressing and washing of hands.

II. SIDS
When in 1976 a cooperation started between the department of physiology and the pediatric clinic in Graz, an incredible number of theories about the etiology of the so called sudden infant death syndrome (SIDS) could be found in textbooks. Some items on this list now are unequivocally obsolete. However, the existence of such a list indicates that the real cause of the terrible phenomenon is not yet found. One recent assumption about the etiology in the seventies was, that sleep apneas observed in infants indicate a particular high risk for sudden death.
A publication by A. Steinschneider (1972) about 2 cases of sudden infant death out of 5 children in a family had stimulated an incredible number of studies about apnea in infants and – consequently - also the invention of sleep monitors for infants at risk. The children described by Steinschneider showed episodes of apnea such that the author concluded that apnea is the essential risk factor, or even cause of sudden death in infants. Our group joined this international trend by recording the respiration of babies during sleep. We also performed retrospective studies about particular observations by the parents of deceased babies. The results enabled us to establish a list of possible risk indicators and, thereof a corresponding questionnaire for the mothers of newborn. More recently we have summarized our own results as well as literature in a book (Kurz et al. 2000).
20 years after Steinschneider's publication mentioned above, it was found through confession of the parents that they had murdered the two children by suffocation.
Nevertheless, it is interesting that even the misinterpreted observation by Steinschneider has led by the stimulation of research to a closer proof that problems of respiration play a role in SIDS. Furthermore, it was more clearly shown which type of respiratory problem may be dangerous, and which are the limits between normal and abnormal.
So far it seems clear that no single etiologic factor can be found which makes an explanation of SIDS possible. Therefore, the attempt for a more general model of interaction between three risk factors was proposed by Filiano and Kinney (1994), which is known as "triple-risk model". The three fatally interacting factors are: critical child, critical time and critical stress.
The "critical child" can be summarized as the effect of its genetic and epigenetic predisposition.
The "critical time" was already observed in the 19 th century by Paltauf (1889). Many further observations, including our own findings agree with the fact that the highest incidence of SIDS can be observed in the time of second and third month of life.
The "critical stress" summarizes in my opinion several possible risk factors or events: prone position during sleep, overheating, cigarette smoke, neglect or unrest in the environment of the baby. (See Kurz et al. 2000).
Furthermore, the influence of chronobiological factors which lead to circadian or circannual predilection of the time of SIDS is documented.

The possible influence of cosmic cycles was discussed in a study by Halberg's group (Kenner et al. 2003). Such an influence could possibly explain worldwide long time trends in the incidence of SIDS.
As far as the practical results of the campaign for the prevention of SIDS is concerned which was initiated by our group in Graz, the incidence of SIDS in the Austrian province Styria decreased significantly in the years since begin of our study. The campaign consists of information for the parents (mainly mothers), a "risk" questionnaire, pediatric counselling and, in cases of suspected risk, polygraphic sleep monitoring.

III. PEPTIC ULCER

During my years of chairmanship of the department of Physiology I taught besides the main lecture - among other topics - also lectures on "physiology of psychosomatic reactions". Physiology of the human person includes necessarily body and psyche. Students in general – and particularly, before they receive too much one sided indoctrination – have a high sensitivity for the recognition of the human personality of patients, a capability which includes a psychosomatic access to the patient.
In 1984 the work by Marshall and Warren (2) about their discovery of the presence of the helicobacter pylori (HP) in the stomach and its relation to peptic ulcer disease was published. One professor of internal medicine in Graz made – with respect to this discovery – the following remark to some students: "Now we know the real and unique cause of peptic ulcer. Therefore, we no more need mysterious psychosomatics for explanation." With such a statement he nearly triggered a political controversy with the students who regarded this remark as a provocation.
Because of my own experience and reports in the literature as described below, my position with respect to this problem is the following: In the case of peptic ulcer similar to the SIDS-example, the etiology follows a "triple risk". There is on one hand ample proof that HP plays an essential role. On the other hand not everybody who has HP in his stomach will necessarily get an ulcer. A general precondition and a trigger event certainly also play a role.
My own experience as a "patient" was the following:
In the diary notes from my time of deanship I find the note: "On Tuesday Dec. 15, 1992, I had to chair the most unpleasant conference ever".
On Dec 17 I had to be transported to a hospital because of massive gastric bleeding from an ulcer. Before this event I never had any gastric problems.
I received the necessary therapy. Since that never again had I further problems with my stomach. Only 6 years later, on recommendation of a friend, an eradication of HP (which had been found in the biopsy of the mucosa) was performed.

The following is a report about observations by an Austrian surgeon who was one of my teachers during my studies at the medical school in Vienna. I knew O. Bsteh very well because in his hospital in the city of Mistelbach (Lower Austria) I had performed my first steps as a student in practical surgery and internal medicine.
In 1952 O. Bsteh, published a book in which he summarized his experience on the development of peptic ulcer. The patients who were treated in this hospital came from a quite homogeneous population of farmers. Therefore his observations are important for the study of the chronopathology of occupational factors.
In the years from 1936 to 1947 the number of inhabitants in the area was about 70000. In this time 1026 persons with peptic ulcer have been treated in the hospital. From the 1026 persons, 821 were treated surgically; the others received internal medical treatment.
The most severe event of the peptic ulcer-disease is the perforation. Bsteh (1952) reports in his book 185 cases of perforation within 17 years. The numbers of perforations per years

show a minor variation between 9 and 20 cases per year. The age of the patients was between 30 and 50 years.
The main reason why it appears worthwhile to present this short report about Bsteh's results is the observation of a clear circannual distribution. As can be seen in the following table, there is a unique and marked peak in the summer months of June and July.

January	6
February	2
March	8
April	9
May	15
June	30
July	34
August	22
September	17
October	18
November	12
December	12

Total 185 ulcer perforations in the years 1936 to 1947 (Bsteh 1952)

Bsteh's interpretation of the peak incidence of ulcer perforation in June to July is derived from the fact that the highest physical and psychological stress in farmers is connected with the time before and during the harvest season. During this time, in addition to the daily heavy workload, the time of sleep is reduced. Furthermore, during this time climatic events as heat, rain and thunder-storms, variation of barometric pressure, may have influence on the autonomic nervous system.
Interestingly enough, other authors find other periods of increased incidpence of peptic ulcer.
Lauda (1949), an experienced Professor for internal medicine in Vienna mentions from his observations regarding a city population, spring and fall as typical times for the outbreak of ulcer disease.
More recently Savarino et al. (1996) find high incidence in October to December and in January to March. They observed that there was no parallel circannual fluctuation of duodenal ulcer, gastric acidity and Helicobacter Pylori infections in the studied patients. In addition it seems noteworthy that, according to Halberg (1986, 1987) the circadian time course of plasma gastrin is not in phase with the acidity in the gastric fluid. In other words, there appears no synchronization between the variables ulcer, acidity, plasma gastrin, and Helicobacter infection.
Svanes et al. (1998) find a circasemiannual periodicity with peaks in May to July and November to December. They assume that exogenous environmental and/or societal factors play a significant role although they add that the variations in ulcer perforation may also be related to endogenous biological rhythms.
It seems noteworthy, that in each of the four publications mentioned here, the timing is different, which may be due to the different occupational activities of the patients. The phase of the periodicity of the ulcer disease is influenced by societal and environmental stress factors. If there are broader peaks or even two distinct peaks in the circannual frequency distribution of certain symptoms of ulcer-disease, this may be due to the mixing of different populations, or of groups with different occupations.

The opinion that by the explanation of one of the causes of a disease the complete etiology has been found, certainly, is a mistake. Even before the discovery of the Helicobacter it was clear, that the ulcer-disease must have several cooperating causes. And even, if one of the necessary conditions now can be abolished, the other set of conditions still may be of importance.
The role of a vagotonic shift of the autonomic nervous system was already well known in older literature. There is no question that acidity of the gastric secret and the presence of Helicobacter belong to essential preconditions of gastric ulcer. However, it seems that there are still many open questions about the interaction of further etiologic components.
Based on my personal experience there is no question in my mind that psychosomatic factors and stress play an essential role as trigger for the generation of the disease.

CONCLUSION AND SUMMARY

For this report I have chosen out of my life and my development as person, teacher and scientist, three topics to which I have some specific relation. In the introduction I have shortly explained the kind of relation that make these examples especially interesting for me. Of course, there would be quite a number of other, equally ineresting examples. However, I feel that the three examples demonstrate on one hand some particular weakness of medical and on the other hand some strength of medical practice.
The weakness results from the possibility of obvious neglect of the consequences of simple and clear observations and of evidence. The strength comes from the fact that medicine is not only science but also an art. Performing medicine as an art means that simple and clear observations should never be neglected. From all three examples one can conclude that diagnostic as well as therapeutic conclusions can be drawn from observations and not only from statistical evidence.
As far as teaching is concerned there is currently a trend, which I consider as contra-productive. In order to reduce the teaching load, more and more so called "virtual teaching" is used. This means simply, that the students – far away from teacher and from patients - learn by sitting behind a computer screen where the instructions are presented. I see the danger that more and more also patients will be considered as virtual entities.
The kind of knowledge and behaviour that can be taught by such a technique is not what is essentially necessary to educate physicians.

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SEVEN DAY BLOOD PRESSURE MEASUREMENT: CONTRAVERSION IN SINGLE 24-H PROFILES OF BLOOD PRESSURE AND HEART RATE

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INTRODUCTION

Currently, 24 hour monitoring of BP by ambulatory functioning devices is a gold standard, reserved for special cases of high BP, left uninterpreted in terms of its time structure. General reliance upon a single measurement (or a single 24-hour profile) of BP, however, has been dubbed "flying blind" (1) and is at variance with the documented (2, 3) need to meet requirements, stated repeatedly for over a century by opinion leaders, i.e., that we must evaluate periodic BP variations before a patient is examined. This proposition, at the turn of the 20th century, suggested by a leader at NIH as well (5), is greatly facilitated by modern hardware and software in the new millennium (6, 7).

Aim. To examine the relative merits of long-term blood pressure (BP) monitoring, analyzed time-structurally (chronomically, from chronome = time structure). Two aspects of sphygmochrons -- summaries of the temporal dynamics of BP and heart rate (HR) monitoring -- are examined in 4 cases with focus on the diagnosis of an elevation of the midline-estimating statistic of rhythm, MESOR, M, and of the double circadian amplitude, 2A, of BP by the assessment of a 7-day record as a whole and separately for each day of 7 days -- as a minimum at the outset of monitoring in health.

METHODS

Subjects and methods. Four medical scientists, 3 on hypotensive medications, wore an automatic ambulatorily functioning device around the clock with gaps. Data were summarized in both daily and weekly analyses. The midline-estimating statistic of rhythm, or MESOR, is determined by the fit of a cosine curve; the same fit can provide estimates of the double amplitude, 2A, gauging the extent of predictable periodic change, and of the acrophase, gauging the timing of change at each period, characterizing the data. Disorders can occur at each, but tentative reference values in the form of prediction intervals are currently available only for the circadian, and even in this case remain to be improved by setting up lifetime follow-ups of subjects who were "clinically healthy" at the time of monitoring, a task that remains to be done. With such qualifications, we have used tentative reference limits to illustrate the tasks ahead in diagnosing, more rigorously than is now possible, circadian MESOR-hypertension and circadian hyper-amplitude-tension (CHAT) or circadian

overswing. We are fully aware that the attempt to have gender and age-specified reference limits will have to be greatly improved by already-found differences as a function of ethnicity and, above all, by gradually eliminating from the reference data base all those "clinically healthy" subjects who subsequently fell ill or whose lifespan could not be assessed because of an accident, eventually keeping only those who died in their sleep at a very advanced age, still to be determined. In our classification of BP disorders according to both a 24-hour vs. a 168-hour abnormality, again according to both the MESOR and double circadian amplitude, we emphasize that the extent of abnormality in each case can and should also readily be considered and should further qualify the percentage of MESOR-hypertension per day or per week, by the corresponding average hyperbaric indices per day and per week, and should again qualify the percentage of CHAT per day and per week by the average circadian double amplitude. These added measures provide the critical estimations of the severity of the condition. The examples illustrated thus far and to a limited extent only with the % days or weeks of an abnormal MESOR and/or circadian double amplitude, suffice to demonstrate that the current gold standard of a 24-hour profile is not sufficient to reliably describe the presence or absence and the time course of the two blood pressure disorders examined, of an excessive M or an excessive A.

RESULTS

Subject 1: YW, a cardiologist, currently in his 19th year of monitoring, used the Colin ABPM first and an A&D instrument thereafter. Figure 1a shows weekly summaries of MESORs, top, initially consisting mainly of acceptable values with few exceptions over the first 13 years and greater fluctuations and more values above the acceptable MESOR thereafter. Already during an entire week in 1989, however, a week-long data summary would have supported the diagnosis of MESOR-hypertension and, in current conventional (often hurried) practice, based on single measurements or at best upon 24-hour profiles, a week-long abnormality might indeed constitute a stimulus to treat. But the one-week span is followed by MESOR-normotension for weeks (and validates the clinical custom to ask the patient to return in a month, albeit we do not recommend only another spotcheck that could be done on a roller coaster in some cases). In the lower half of the figure the circadian double amplitude exceeds only on few occasions its limit of acceptability. By contrast, in Figure 1b the daily summary over the same time span, as in Figure 1a, shows wider swings of the MESOR as well as of the double amplitude and reveals the dangers of basing a diagnosis of CHAT in particular, but also of MESOR-hypertension, on a single 24-hour record. Many more acceptable 24-hour records can follow several abnormal consecutive records and whether either abnormality is transient or lasting must be observed before one starts possibly unwarranted treatment, perhaps for a lifetime, for a condition that persisted only for a short time.

Clinical trials that show benefit from treating "spotcheck" pressures above 120 mmHg come to mind (8) but may not be applicable to the individual, e.g., to YW. In this case, there was also a change in monitors coincidental with a change in MESOR toward the end of the record and a possibly slightly increasing trend with time is confounded by the change of instrumentation.

When incomplete records are discarded and the analysis is assessed only on a week documented by a minimum of 224 values (/week), the abnormality appears to be rarer, perhaps because of the sparser record. Thus, there is no CHAT, when occasional CHAT was seen certainly based on daily summaries and in weekly summaries when the decimation of incomplete data is less thorough since weekly records with as few as 116 values are analyzed. Thus, CHAT can come about more frequently than in the case, for which records with fewer

than 224 values per week were discarded. The comparison of results in Figure 1a serves to emphasize the role of the density of the record in diagnosing CHAT.

There is shows CHAT above the horizontal dotted line and MESOR-hypertension to the right of the second vertical dotted line. Thus, the coexistence of the two conditions is seen in the upper right section in 2.3% of the days investigated. Overall MESOR-hypertension is present in only 13% of the monitored days considered and CHAT overall is rarer yet, only seen in 7%. When weekly summaries are made, keeping all records with 116 or more values or only those with 224 values/week, in Figures 1e and 1f, respectively, the incidence of MESOR-hypertension decreases to 7.5 or 3.7% and that of CHAT to 0.6%. This result can be interpreted on an individualized basis as supporting the decision not to use hypotensive medication, even if a trial on many, almost certainly including many false positives at entry and false negatives at its end (8) could be taken to constitute an indication to treat in such a case.

Subject 2, OS, a pediatrician, after coronary artery bypass grafting (CABG), aortic valve replacement, and two hip replacement surgeries, taking atenolol for cardiac arrhythmia, had a history of acceptable blood pressures since she wrote her doctoral thesis in medicine on BP. Her BP M and 2A seem to be perfectly acceptable in the light of Figure 2a, which is a summary of analyses of week-long data intervals. The picture of a clean bill of BP health when 168-hour intervals are summarized does not appreciably change in Figure 2b when 24-hour data intervals are analyzed, for M on top. At the bottom of this figure, an occasional circadian blood pressure overswing is seen on a number of days as values crossing the horizontal upper limit of the 95% prediction interval during spans when no CHAT was apparent in the corresponding weekly summaries of Figure 2a. In daily records, Figure 2c, OS is never MESOR-hypertensive, but on quite a few occasions has circadian overswing. In Figure 2d, with weekly summaries, she has 0% abnormality of either M or 2A. CHAT has sometimes been shown to be present in clinical health, but usually only for a few days at a time, presumably under emotional loads (and the 24-h record in the 7-day perspective can actually serve as a load [stress] test) (9). Circadian overswing, however, must not be diagnosed based on records of 24 hours, dubbed transient CHAT suggested that a week be a bare minimum to rule in BP health, but not to rule out either CHAT or MESOR-hypertension, when they occur on occasion, as CHAT does in OS.

Figure 3 represents data from a treated MESOR-hypertensive physiologist (FH), who himself had had two sets of CABGs performed years earlier. The Figure 3a data were taken while his greatly loved daughter, herself a physician, visited for several days from out of town. The June 17 arrow shows his BP during what to him at the time appeared to be a friendly discussion of his legacy, bracketed by a prior and a succeeding day. If only the three days in row A are considered, we see an unusual BP elevation, above the time-varying upper limits shown as a wavy curve, above which a blackened area corresponds for several hours to consecutive values that exceed by far the upper limit of a chronodesm, a 95% prediction interval. Occasional values reach or exceed 200 mm Hg. This seemingly most unusual behavior loses somewhat in prominence in row B when more days bracketing the discussion are displayed. The blackened area in row A becomes just one event among others obtained in everyday life, not identified by any association, but shown by arrows. There is no question that emotions can raise the BP; equally clearly, the very high values when a monitor records them beat-to-beat can be single or very few high values, without the subject being aware of any emotion. The same subject's 24-hour BP summaries are shown in Figure 3b. Under a closely (weekly) self-supervised treatment, every so often FH has MESOR-hypertension, as shown on top of the figure, and, as seen on the bottom, there are also many days with circadian hyper-amplitude-tension. If we summarize his experience, again based on 24-h profiles, he has MESOR-hypertension for 12.1% of the time. With the relatively successful

treatment of his M, if not otherwise, he also exhibits circadian overswing 49.9% of the time, if 36 or more measurements/day are analyzed and records with greater gaps are discarded.
Figure 3c in turn shows weekly summaries, and now his percentage, MESOR-hypertension is less than half of what it was in daily summaries, and % CHAT has also been reduced from 45.9 to 26.9%. This case also shows that weekly summaries should be the routine diagnostic basis, but are best complemented by daily ones, so that daily CHAT is not altogether ignored, and if it persists, an attempt can be made to reduce it by whatever methods, notably relaxation procedures, are available, and helpful.
Figure 4 shows data of a physician-morphologist (GK), a man known to be hypertensive and treated for this condition since his 30s, monitored automatically from his 70s at half-hour intervals around the clock, with very few gaps. Figure 4a shows again, with a weekly supervision of his BP and changes in treatment made accordingly, that he can completely eliminate neither MESOR-hypertension, nor circadian overswing, but when it occurs the extent of excess pressure seems to be relatively small. When in turn, in Figure 4b, 24-hour intervals are summarized, some of the smoothing by weekly analyses is lost, and in particular a great variability in double amplitude becomes apparent, the 2A reaching high values. Each of this subject's data set is also summarized yearly, again to compare the presence in a given subject of the two conditions considered herein. Invariably, some dots lie on the right of the vertical line indicating MESOR-hypertension, and those above the horizontal dotted line indicate circadian overswing. It was not possible to eliminate abnormal Ms and 2As, weekly summaries of the data and an adjustment of treatment notwithstanding. In this subject, the fit of a polynomial to the data suggested, only after smoothing, that CHAT is more frequent at intermediate values, as found in a population (10). When daily values are summarized in this figure MESOR-hypertension is "controlled" two-thirds of the time and CHAT barely more than one-third of the time. Again, a weekly summary is the best overall interpretation, and we find, as in the case of FH, that GK has traded some CHAT, that is a higher 2A (and higher risk [2, 3]) for a lesser M (Figure 4c, 4d).

DISCUSSION

A 24-h profile corresponds to a single circadian cycle. Others have pointed out, as have we (12), that a 24-hour profile of blood pressure and heart rate is equivalent to taking the pulse for one second, i.e., for one cardiac cycle. The variability at hand from day to day has been emphasized earlier, is particularly great in so-called borderline hypertension, and overall as well, it is hardly negligible. The question now revolves around the practicality of chronomic analyses and the instrumentation for data collection, in this order of importance. Self-measurements are practical and cheap, and chronomic analyses are offered free of charge from corne001@umn.edu, until a Phoenix Project provides user-friendly software to all comers. Continuous self- or automatic monitoring gains in importance when our perspectives broaden, taking into account alterations not only of the circadian rhythm and all their characteristics at all is mapped thus far and of trends with age.
Blood pressure (BP) varies with age: we must not assume that once diagnosed as hypertensive, a given patient will continue to have high blood pressure for the rest of his/her life. A treated hypertensive with systolic values around 200 mm Hg can become an untreated MESOR-hypotensive with systolic values under 100 mm Hg. BP changes in many patients vary greatly along the scale of hours and days and further during weeks and months (2), so that during the same monitoring span there are both hyper- and hypotensive values. BP also varies along the scale of years and decades (3). We here show that blood pressure disorders also vary, whether they are treated or untreated. We must not fly blind (1). Disorders include

alterations of the BP M and 2A, and other aspects of BP and HR variability; the latter can represent a risk greater than a high BP.
For the current surveillance of BP, the chronomic analysis, carried out in the Halberg Chronobiology Center, is available for all comers. Data are obtained by monitoring during very different spans (from 1 day to many weeks and longer). These data are analyzed for differing total spans; if so, however, the results are not comparable. The problem of standardizing interval lengths for analyzing BP series for CHAT detection is to be considered and standardized at international meetings, and is here proposed for consensus discussions on such occasions.

CONCLUSION

7-day monitoring and both daily and overall analyzes are recommended, with the urgent task of collecting international reference standards in health starting with medical students and including high school students, each followed up for a lifetime to retain the records for reference values only of those who remain healthy for their lifespan. The relative merits of tolerance intervals (13, 14) vs. prediction intervals (15, 16) and the need to age-qualify reference intervals (17, 18), preferably based on clinically healthy "test pilots" monitored starting at birth (19), are also major issues, as is the task to convey the sample used to replace reference values for men and women above a certain age (20).

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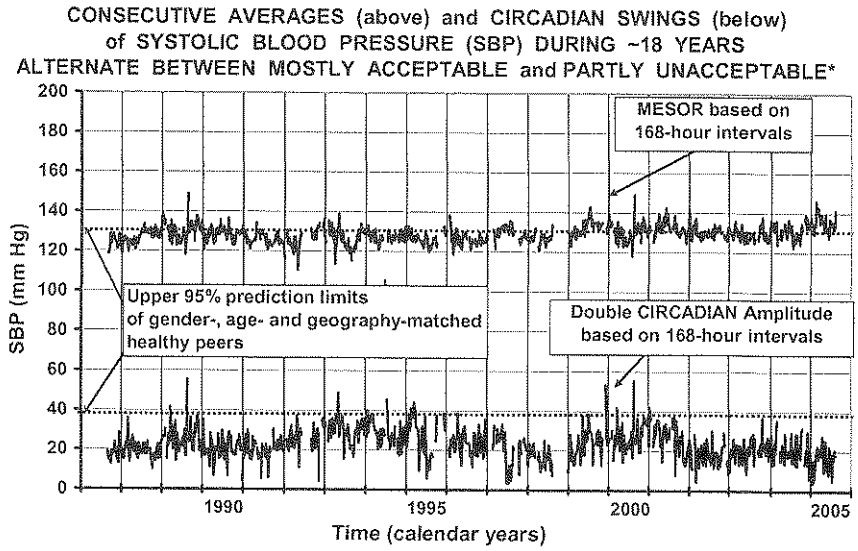
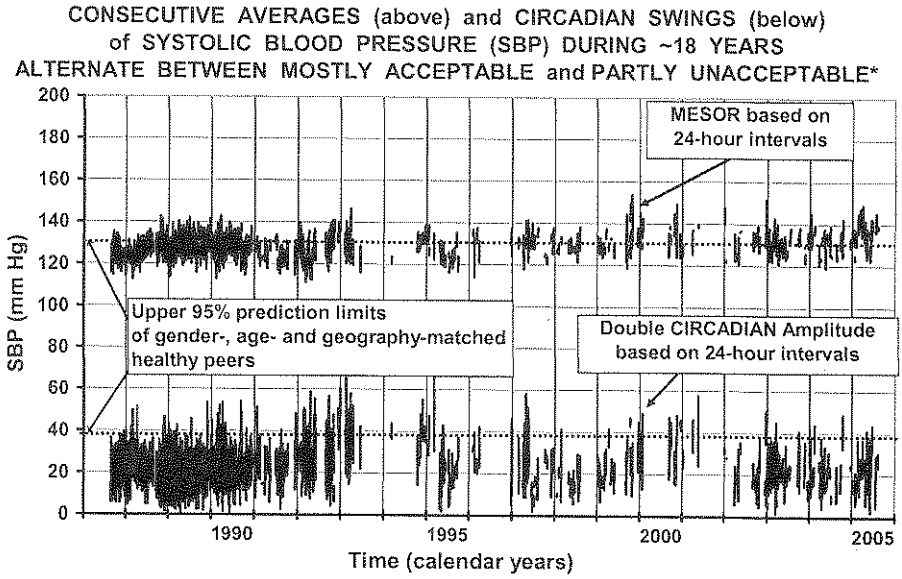
Fig. 1a



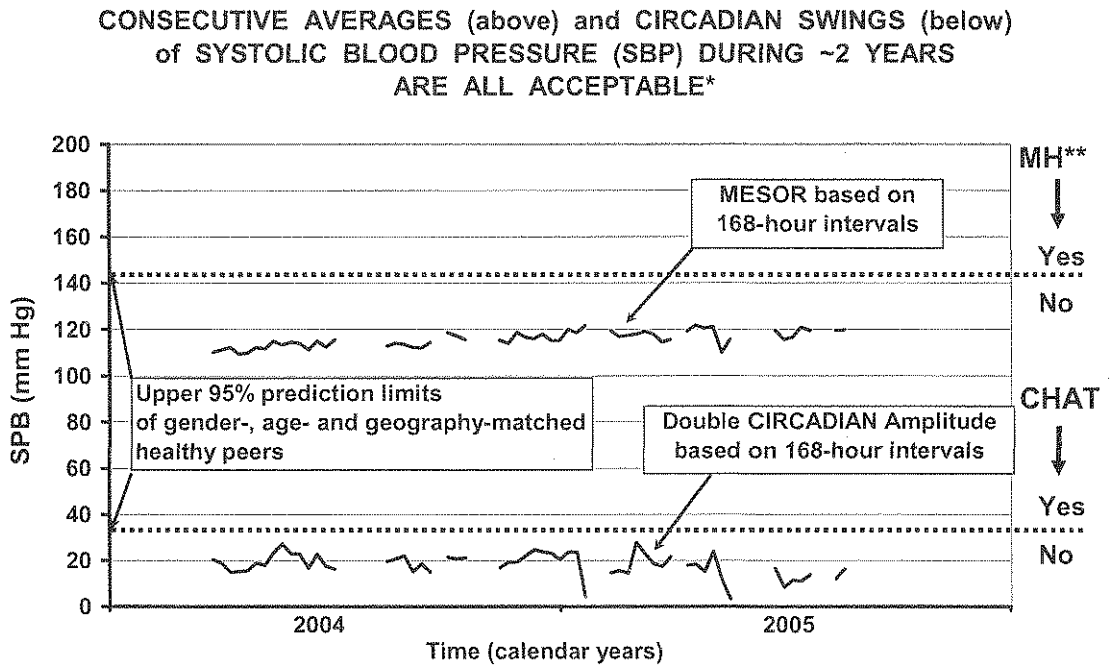
* Results from non-overlapping 168-hour intervals in serial sections on half-hourly around-the-clock data; YW (M, 35 - 53 y). Weekly records with fewer than 116 values discarded.

Fig. 1b



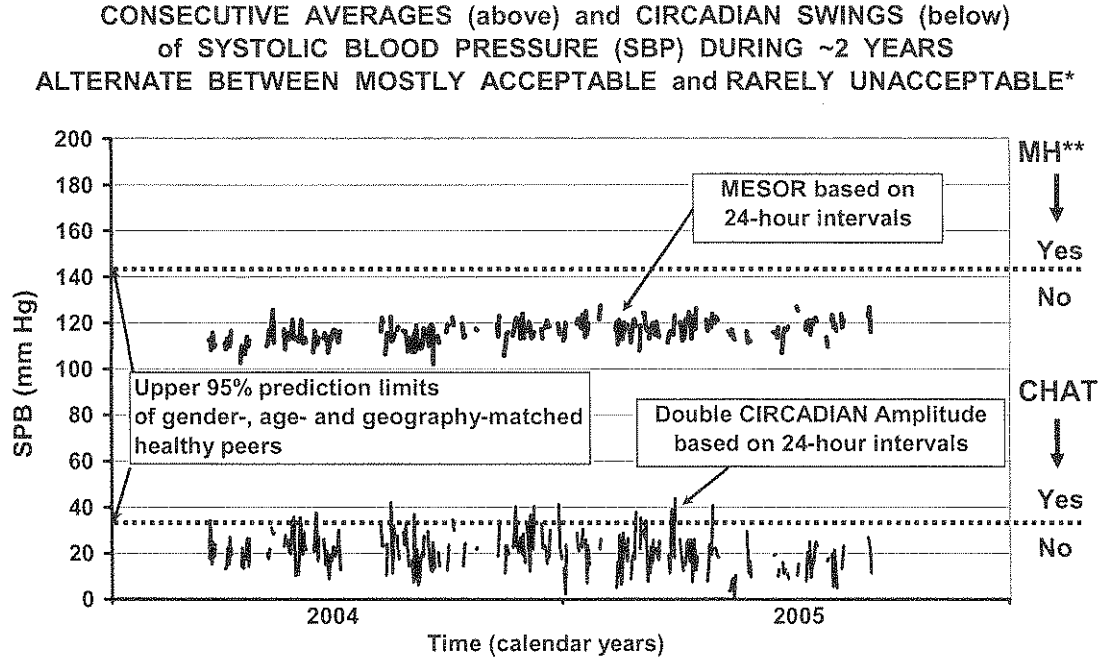
* Results from non-overlapping 24-hour intervals in serial sections on half-hourly around-the-clock data; YW (M, 35 - 53 y). Daily records with fewer than 36 values discarded.

Fig. 2a



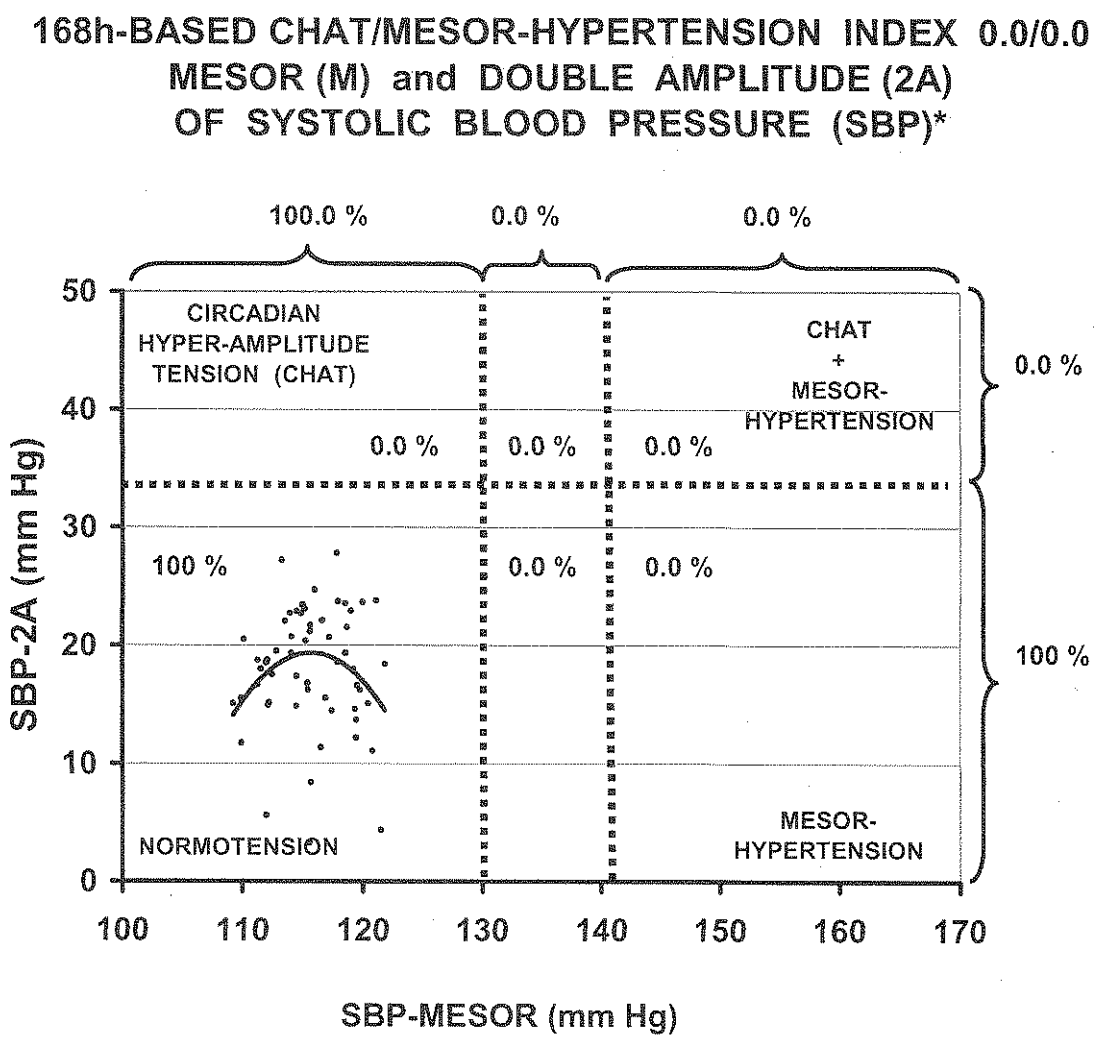
* Results from non-overlapping 7-day intervals in serial sections on half-hourly around the clock data; OS (F, 81-82 y) on atenolol treatment. ** MH = MESOR-Hypertension, CHAT = Circadian Hyper-Amplitude Tension. When 1-day intervals are used, occasional unacceptable results occur.

Fig. 2b



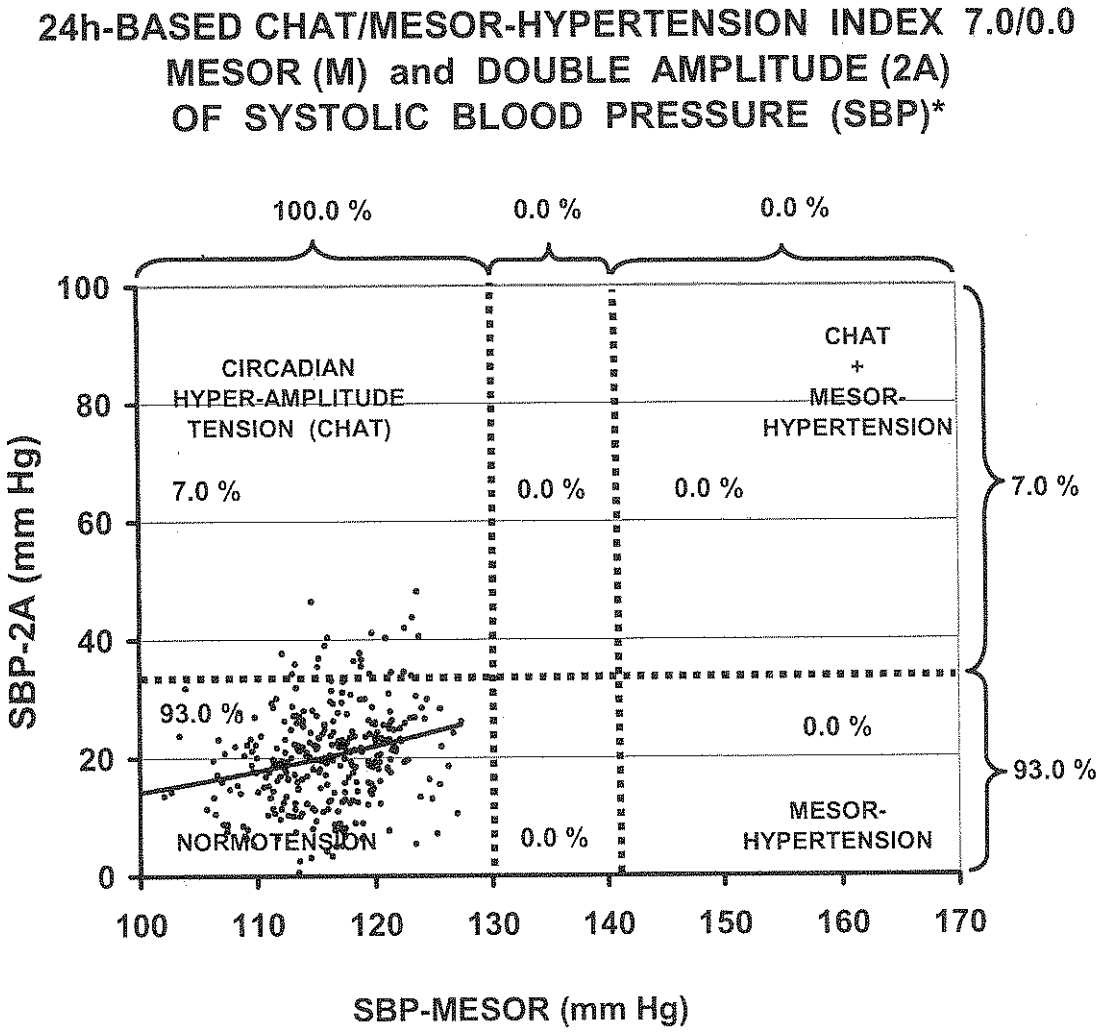
* Results from non-overlapping 7-day intervals in serial sections on half-hourly around the clock data; OS (F, 81-82 y) on atenolol treatment. ** MH = MESOR-Hypertension, CHAT = Circadian Hyper-Amplitude Tension.

Fig. 2c



* OS (F, 81-82 y in 2005-2006) on (25 mg/day, on awakening) atenolol treatment. Results from non-overlapping (fractionated) serial sections over weekly intervals on half-hourly around-the-clock measurements analyzed. Weekly records with fewer than 224 values discarded.

Fig. 2d

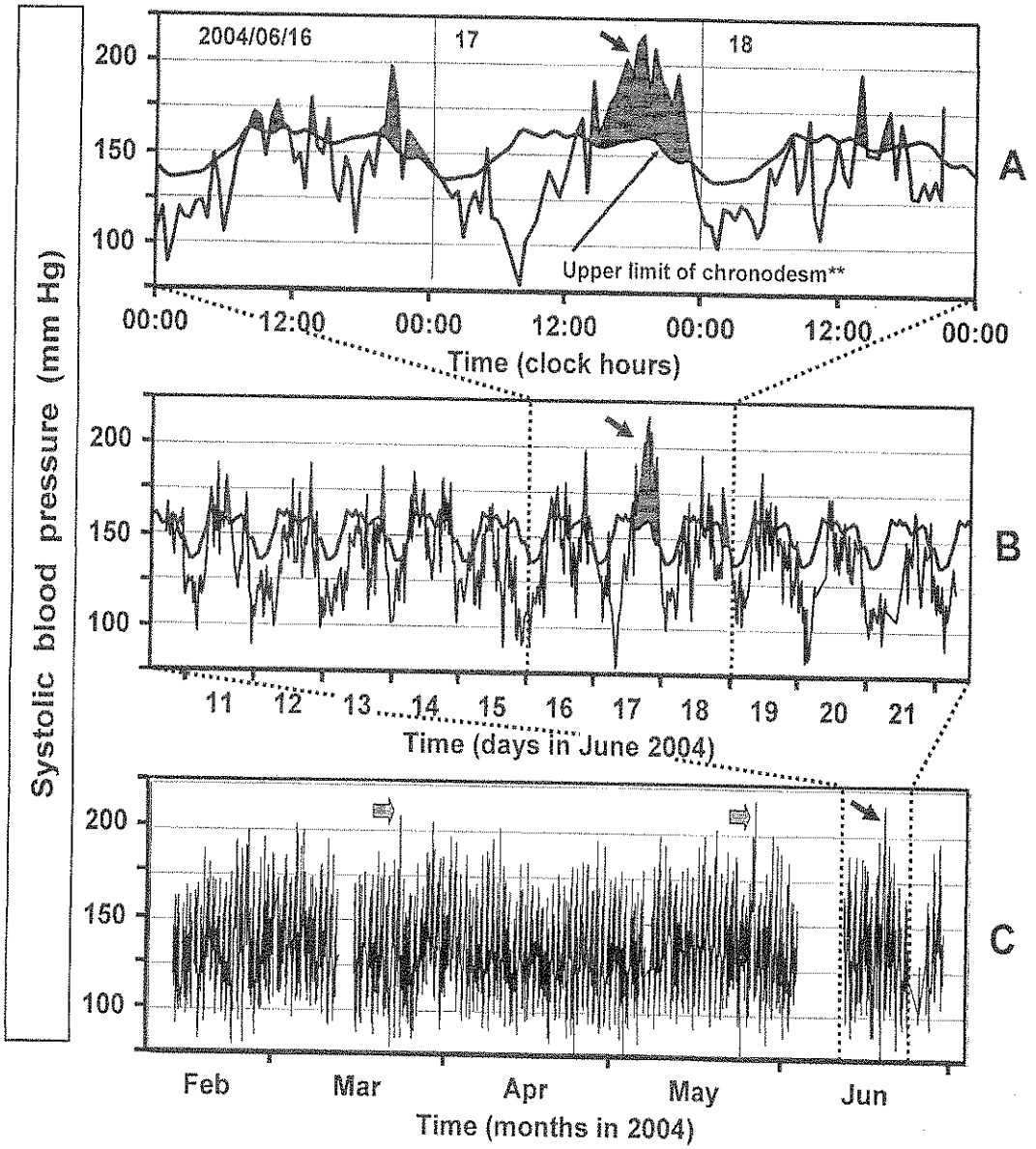


* OS (F, 81-82 y in 2005-2006) on (25 mg/day, on awakening) atenolol treatment. Results from non-overlapping (fractionated) serial sections over daily intervals on half-hourly around-the-clock measurements. Daily records with fewer than 36 values discarded.

Fig. 3a

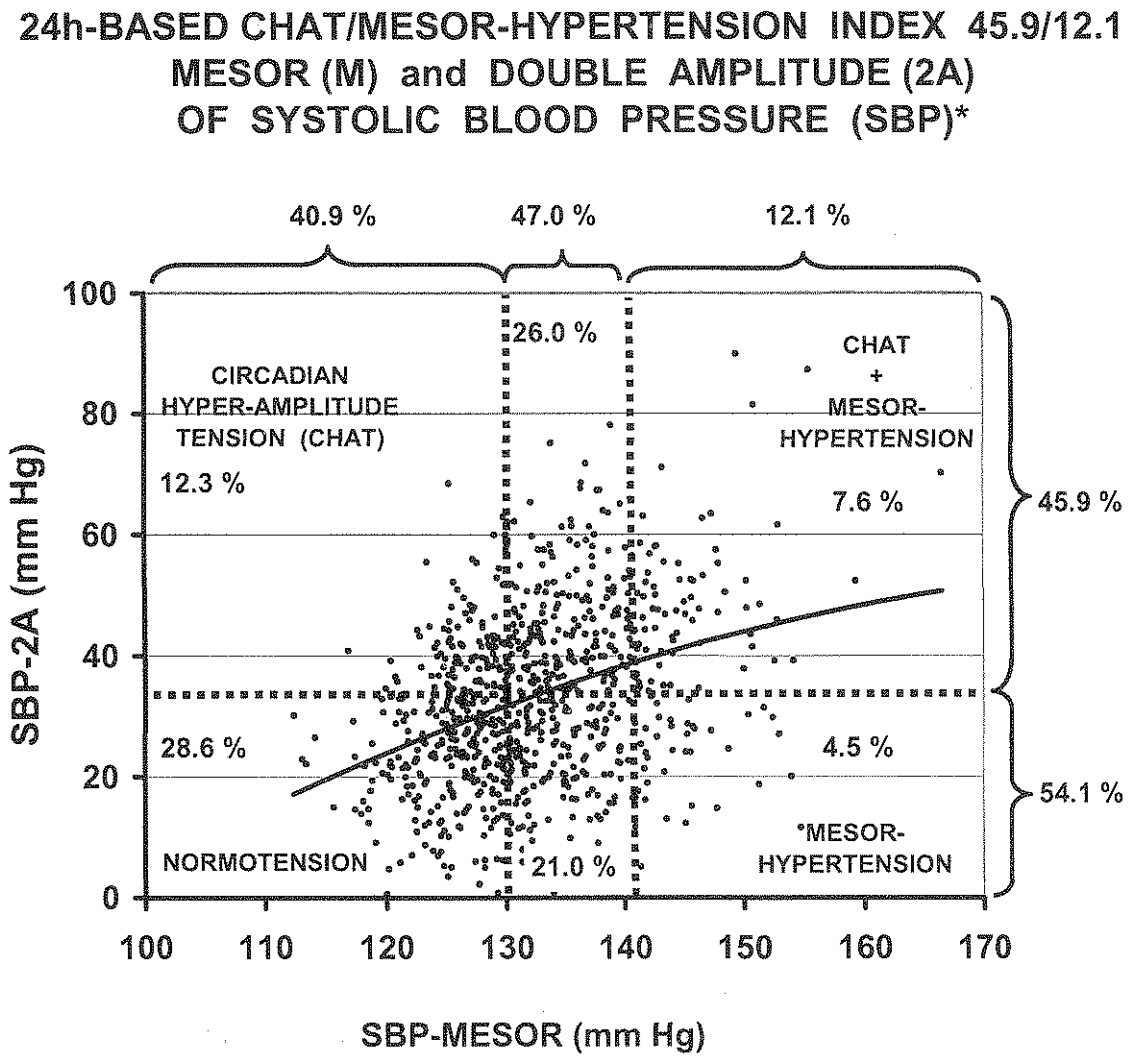
15-21-FH-OSCI

A FATHER's DISCUSSION WITH HIS DAUGHTER CONCERNING A PROFESSIONAL LEGACY (↘)*



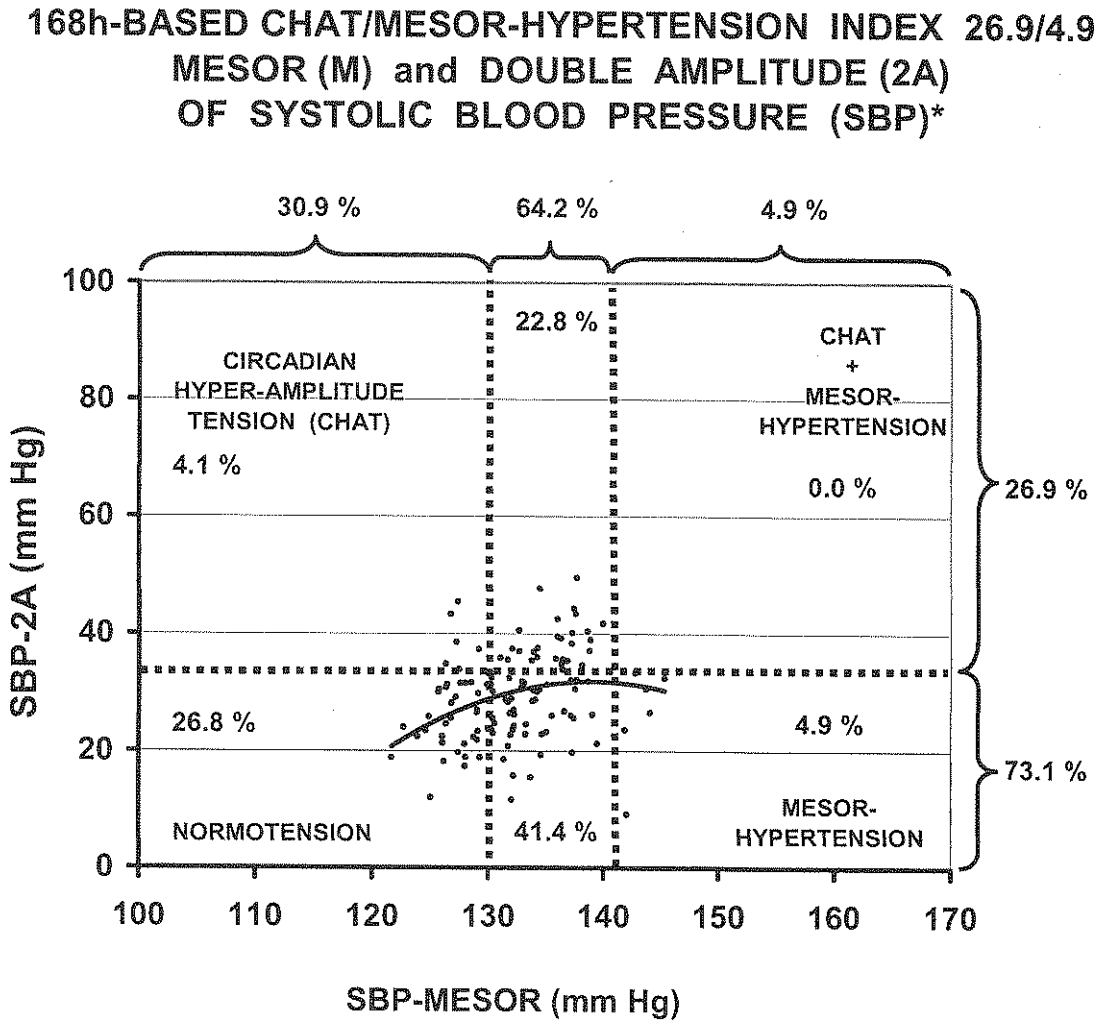
* Record of about 30-minute blood pressures of an 84-year old man (FH) shown in an increasingly broader perspective of 3 days (A), 12 days (B) and 5 months (C).
** Time-specified limit derived from clinically healthy peers of the same gender and similar age.
NOTE: "Unique" event (↘) is not unique when the perspective is broadened (⇨).
Diary recommended!

Fig. 3b



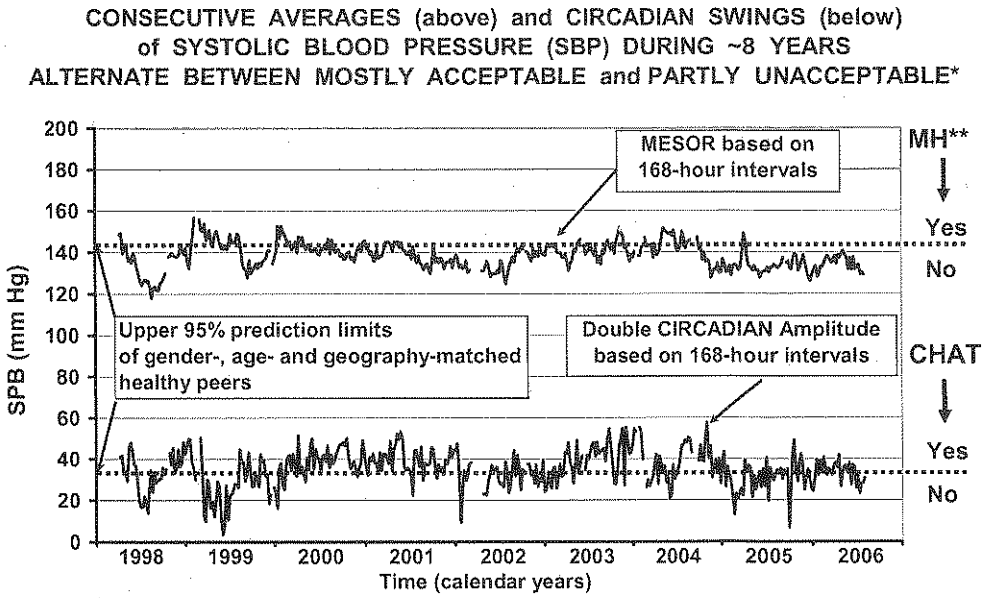
* FH (M, 82 - 87 y in 2001-2006) on different treatments varied in dosing and timing.
Results from non-overlapping (fractionated) serial sections over daily intervals on half-hourly around-the-clock measurements analyzed. Daily records with fewer than 36 values discarded.

Fig. 3c



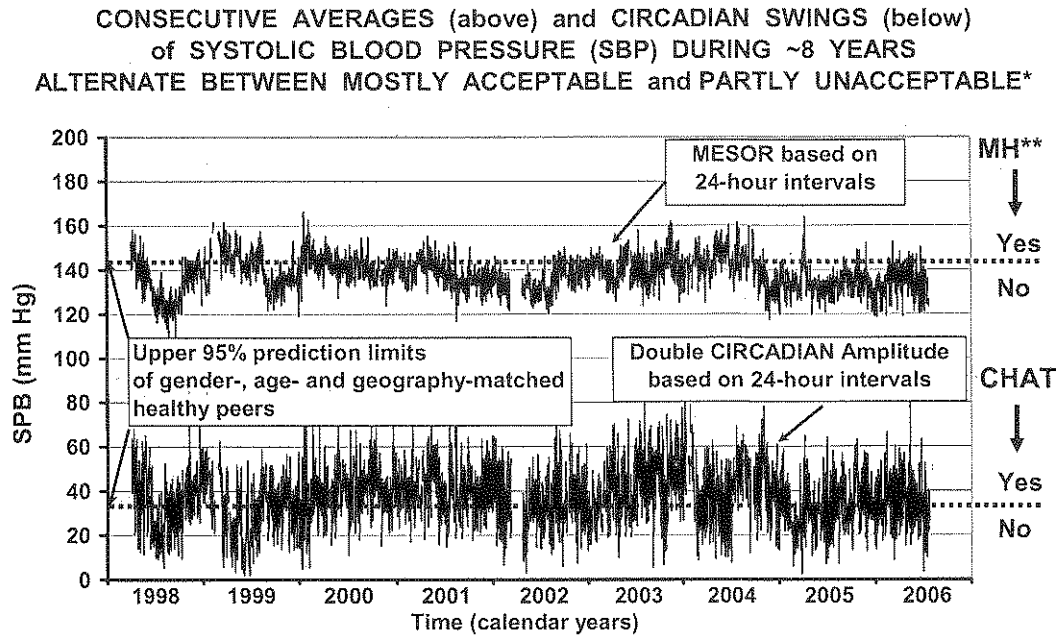
* FH (M, 82 - 87 y in 2001-2006) on different treatments varied in dosing and timing.
Results from non-overlapping (fractionated) serial sections over weekly intervals on half-hourly around-the-clock measurements analyzed. Weekly records with fewer than 224 values discarded.

Fig. 4a



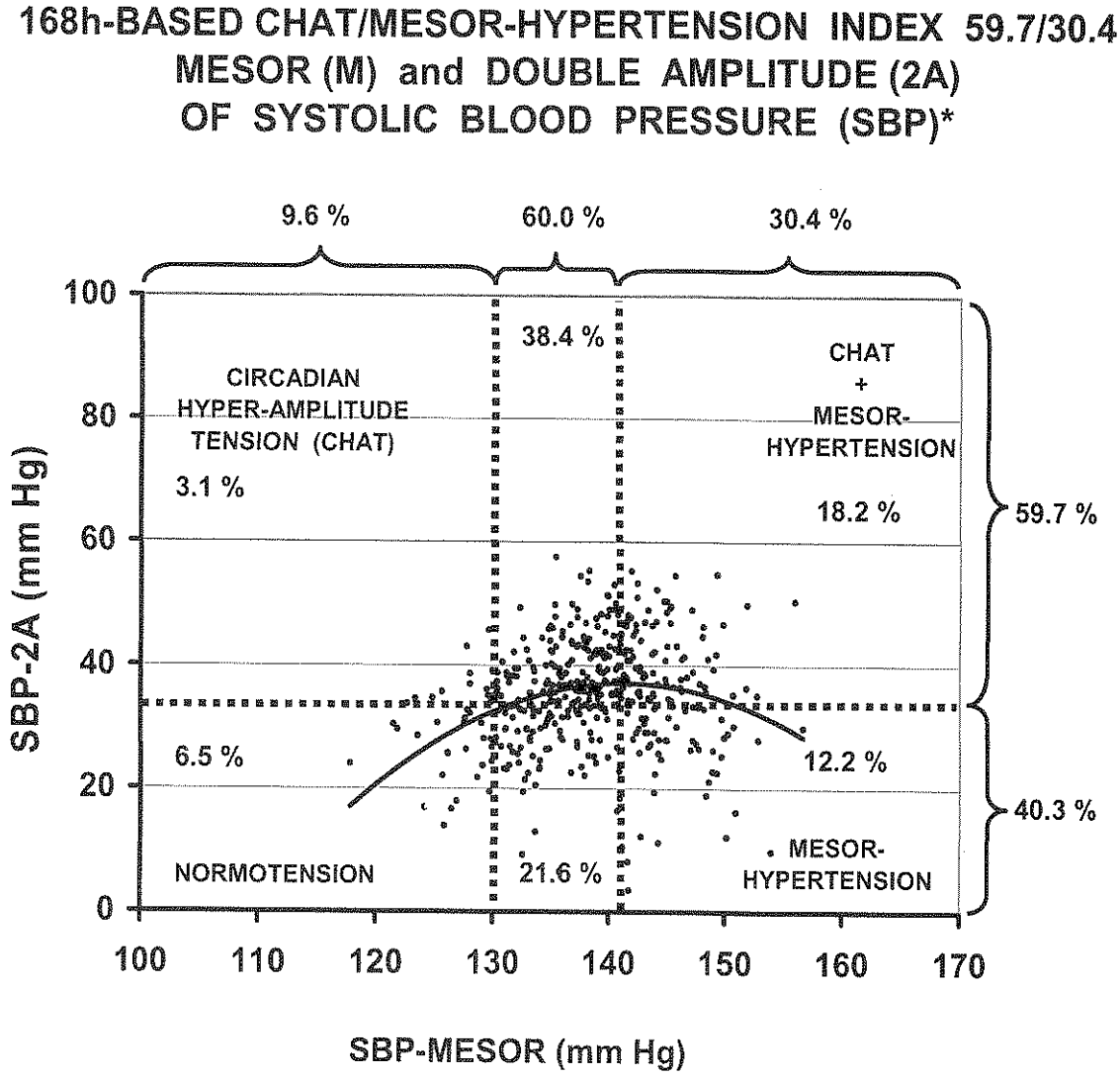
* Results from non-overlapping 7-day intervals in serial sections on half-hourly around the clock data; GK (M, 72-80 y) on varying treatments. ** MH = MESOR-Hypertension, CHAT = Circadian Hyper-Amplitude Tension.

Fig.4b



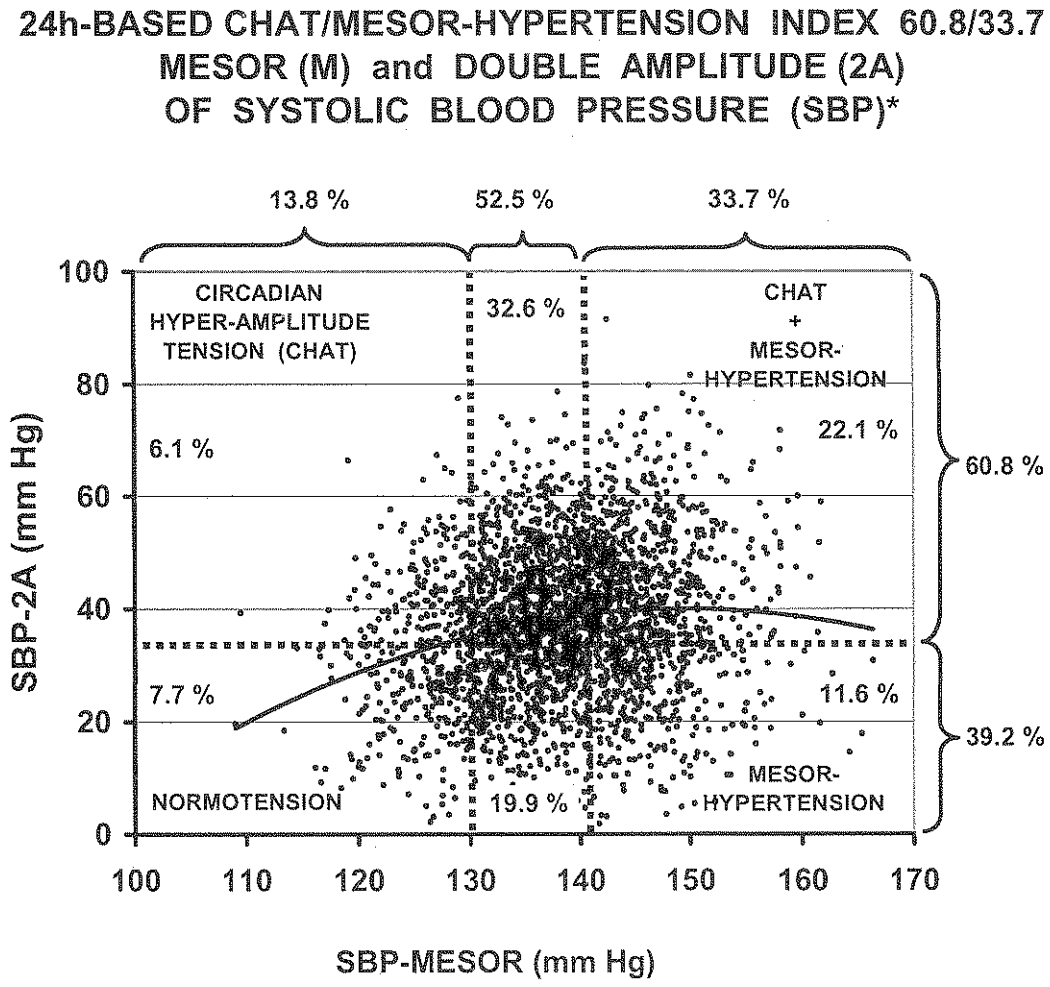
* Results from non-overlapping 1-day intervals in serial sections on half-hourly around the clock data; GK (M, 72-80 y) on varying treatments. ** MH = MESOR-Hypertension, CHAT = Circadian Hyper-Amplitude Tension.

Fig. 4c



* GK (M, 72 - 80 y in 1998-2006) on different treatments varied in dosing and timing.
Results from non-overlapping (fractionated) serial sections over weekly intervals on half-hourly around the clock measurements analyzed. Weekly records with fewer than 224 values discarded.

Fig.4d



* GK (M, 72 - 80 y in 1998-2006) on different treatments varied in dosing and timing.
Results from non-overlapping (fractionated) serial sections over daily intervals on half-hourly around the clock measurements analyzed. Daily records with fewer than 36 values discarded.

LESSONS ABOUT "LOADS" LEARNED WHILE DETECTING AND GREATLY REDUCING RESIDUAL MESOR-HYPERTENSION AND CHAT

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INTRODUCTION

Chronotheranostics, a chronomic (time structural) combination of diagnosis and therapy, may eventually involve beat-to-beat monitoring and responses by a drug pump to abnormal instantaneous values, in the light of both a circadian and extracircadian history, accumulated by repeated scans, as the time series grows, and involving as-one-goes sequential analyses of all parametric and nonparametric endpoints (1-3).
Aim. To examine, over nearly 16 years, the merits of adjusting the timing of medications in the treatment of coexisting vascular variability disorders on a weekly basis as a step complementing daily and longer-span-based summaries, and to search for dividends both in health care and in science.

METHODS

Subject. FH is a treated MESOR-hypertensive physiologist, who himself had had two sets of CABGs performed years earlier.
Measurement FH wore an automatic ambulatorily functioning device around the clock with gaps. Data were summarized in both daily and weekly analyses. The midline-estimating statistic of rhythm, or MESOR, is determined by the fit of a cosine curve; the same fit can provide estimates of the double amplitude, 2A, gauging the extent of predictable periodic change, and of the acrophase, gauging the timing of change at each period, characterizing the data.

RESULTS

FH's 24-hour BP summaries collected under a closely (weekly) self-supervised treatment, every so often show MESOR-hypertension and, on many days over 16 years, circadian hyper-

amplitude-tension, CHAT. If we summarize his experience in 24-h profiles, he has MESOR-hypertension for 12.1% of the time. With the relatively successful treatment of his M, if not for other unknown reasons, he also exhibits circadian overswing, CHAT, 49.9% of the time, if 36 or more measurements/day are analyzed and records with greater gaps are discarded.
In weekly summaries, however, the percentage of MESOR-hypertension is less than half of what it was in daily summaries, and % CHAT has also been reduced from 45.9 to 26.9%. Treatment of FH is associated with a practically normal M and an acceptable 2A nearly 3/4 of the time, by contrast to another case monitored half-hourly for 8.5 years, whose residual CHAT was present 3/4 of the time. A completed longevity study on groups in the perspective of 28 years ascertained that when all but one who had CHAT had died, of those still alive all but the one with CHAT, had an acceptable 2A (6).
Weekly summaries could be the routine diagnostic basis, but are best complemented by daily ones, so that daily CHAT is not altogether ignored, and if it persists, an attempt can be made to reduce it by whatever methods, notably relaxation procedures, are available, and helpful.
Since both an excessive MESOR and an excessive circadian double amplitude are high risks of severe disease, an attempt seems warranted to eliminate most if not all residual abnormality, to whatever extent possible. This was possible in FH despite self-experimentation, but with apparent benefit. On many occasions, in addition to attempting to optimize his own treatment, e.g., by reducing both the M and 2A of BP by timing his hypotensive medication, by adjusting the timing of other treatment, such that of the anti-arrhythmic sotalol or of the use of Flomax for prostatic hypertrophy, he also attempted to ascertain both the undesired and the desired timing in FH (thereby unduly inflating the incidence of CHAT reported above). All these procedures and his longevity are viewed in the context of the substantial gain in longevity by those without CHAT (6), indicating that self-monitoring, a long tradition in biomedical research and education as a basis for self-experimentation, can be a dividend from "not flying blind" in self-health care. Notwithstanding privacy considerations (nor, when desired, only by coding, to safeguard anonymity), it seems mandatory to make records available to the public, so that new findings such as associations with the solar wind, a dividend of FH's endeavor (4, 5), can be tested by subtraction and addition (remove-and-replace) approaches.

DISCUSSION

As an aside and as a basis for a potential load (or strain, rather than "stress") test, data were analyzed from a span when FH's greatly loved daughter, herself a physician, visited for several days from out of town. His BP during what to him at the time appeared to be a friendly discussion of his professional legacy, bracketed by a prior and a succeeding day, for several hours, exceeded by far the upper limit of a chronodesm, a 95% prediction interval, and appears to be very unusual (just as it was in discussion with a dear friend, when it also exceeded the elevation during a tornado watch at a tennis match [7]). Consecutive values exceeded 200 mm Hg systolic BP. This seemingly great response already loses somewhat in prominence when more days bracketing the discussion are displayed. With bracketing by months, years or the 16-year record as a whole, the discussion-associated rise becomes just one event among others occurring in everyday life, not identified by any association. This picture of BP changes with time may be compared with effects of emotions brought about at the time of a given event that fade away as time goes by, in keeping with the adage that time has the power to heal. The point that life is made of a series of events that can all bring about non-trivial physiological changes makes it the more desirable to monitor BP in real life rather than making a decision, often for a lifetime, based on only one or a few BP measurements

taken in the office under standardized but artificial conditions. Most interesting is that blood pressure alone reveals subconscious changes that can be of much greater extent than conscious ones. Thus, it is documented by another self-study of FH, monitoring while undergoing sonography and a rather painful prostatic biopsy. It took a statistical tour de force, however, to validate relatively small differences in mean (8).

There is no question that pain and/or emotions can raise the BP. (Equally clearly, but not shown here, instantaneous very high values, when a monitor records them beat-to-beat, can be single or very few high values, without the subject being aware of any emotion.) To support the point of a subject's unawareness of BP change, before getting off the examination table after a routine, noninvasive colonoscopy, FH was again surprised to see that the nurse had recorded a systolic BP >200 mm Hg while he was happy since on the screen he had witnessed a clean colon with no more than a few diverticuli. The use of BP monitoring to gauge known and in particular unknown loads may be pursued along lines also noted elsewhere (9).

Support: MSM0021622402

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CHRONOTHERANOSTICS OF MESOR-NORMOTENSION VS. CIRCADIAN OVERSWING, I.E., CHAT

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INTRODUCTION

A consensus meeting (1) recognizing that CHAT, as compared to MESOR-hypertension, can be a greater risk of stroke and nephropathy (2), advocated the treatment of both conditions. This case report illustrates the problem encountered and the lessons learned in so doing.
Aim. To know whether, and if so when, we trade MESOR-normotension for more frequent circadian hyper-amplitude-tension, i.e., CHAT, so that eventually something can be done about undue residuals of both conditions, in the face of conventionally seemingly acceptable results.

METHODS

Subject GK, a male physician-morphologist known to be hypertensive and treated for this condition since his 30s, monitored automatically from his 70s on at half-hour intervals around the clock, with very few gaps, with a weekly analysis of his BP and changes in treatment made accordingly. GK wore an automatic ambulatory functioning device around the clock with gaps. Data were summarized in both daily and weekly analyses. The midline-estimating statistic of rhythm, or MESOR, is determined by the fit of a cosine curve; the same fit can provide estimates of the double amplitude, 2A, gauging the extent of predictable periodic change, and of the acrophase, gauging the timing of change at each period, characterizing the data.

RESULTS

Results over 8.5 years of around-the-clock blood pressure (BP) and heart rate (HR) surveillance are summarized in this presentation. When they occurred, the extent of excess in BP MESOR (midline-estimating statistic of rhythm) and/or circadian amplitude (CHAT,

circadian hyper-amplitude-tension, or circadian overswing) was smaller in weekly than in daily summaries. When 24-hour intervals were summarized, some of the smoothing by overall weekly analyses was lost, and in particular a great variability in double amplitude (2A) became apparent, BP-2A reaching occasional high values. Each of this subject's data set is also summarized yearly, again to compare the presence in a given subject of the two conditions considered herein. Invariably, some measurements indicate MESOR-hypertension, and others indicate circadian overswing. It was not possible to eliminate abnormal MESORs (Ms) and 2As, not even from all the weekly summaries of the data, many adjustments of treatment notwithstanding (3). In this subject, the fit of a second-order polynomial to the 2As plotted as a function of the corresponding MESORs suggested, only after smoothing, that CHAT was more frequent at intermediate values, as found in a population (4). When daily summaries were examined, MESOR-hypertension was "controlled" two-thirds of the time and CHAT barely more than one-third of the time. A weekly summary was the best overall interpretation, and we find, as in the case of another subject (FH) (5), that GK had perhaps traded some CHAT, that is an excessive BP-2A (and higher risk [1, 2]) for a lesser M.

DISCUSSION

A 24-h profile corresponds to a single circadian cycle. Others have pointed out, as have we (6, 7), that a 24-hour profile of blood pressure and heart rate is equivalent to taking the pulse for one cardiac cycle, i.e., for one second. The variability at hand from day to day has been emphasized earlier, is particularly great in so-called borderline hypertension, and overall as well, it is hardly negligible. The question now revolves around the practicality of chronomic analyses and the instrumentation for data collection, in this order of importance. Self-measurements are practical and cheap, and chronomic analyses are offered free of charge from corne001@umn.edu, until a Phoenix Project (8) provides user-friendly software to all comers. Continuous self- or automatic monitoring gains in importance when our perspectives broaden, taking into account alterations of not only the circadian A and (based on at least weekly and preferably longer-term - yearly and transyearly summaries) but also of the period and waveform and of the same characteristics at all extracircadian periods mapped thus far as well as of trends with age. Chaos, the third element of chronomes has also found physiologic and clinical uses, notably when used in combination with rhythmometry (9,10).

Support: MSM0021622402

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OCCASIONAL TRANSIENT CHAT OCCURS IN THE MESOR-NORMOTENSIVE INDIVIDUAL

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INTRODUCTION

CHAT lasting for one day has been described in the context of 1-week monitoring (1) and has been followed as a transient condition for years (2, 3). It was tacitly assumed that it is a rare yet occasional occurrence when monitoring covers many weekly spans and that it occurs rarely and not for a week, an impression (1) here documented by a case report.
Aim. To describe, in a case report, transient and rare circadian overswing (CHAT, circadian hyper-amplitude-tension) occurring in the absence of MESOR-hypertension, with its mildness and physiological nature being compatible with the condition that it is present only in a very few daily, not in weekly summaries in a record covering 2 years, with gaps.

METHODS

Subject OS, a pediatrician, after coronary artery bypass grafting (CABG), aortic valve replacement, and two hip replacement surgeries, taking atenolol because of occasional cardiac arrhythmia, had a history of acceptable blood pressures (BP) since she wrote her doctoral thesis in medicine on BP.

Measurement
OS wore an automatic ambulatory functioning device around the clock with gaps. Data were summarized in both daily and weekly analyses. The midline-estimating statistic of rhythm, or MESOR, is determined by the fit of a cosine curve; the same fit can provide estimates of the double amplitude, 2A, gauging the extent of predictable periodic change, and of the acrophase, gauging the timing of change at each period, characterizing the data.

RESULTS

Subject OS BP MESOR (midline-estimating statistic of rhythm, M), a rhythm-adjusted mean, and double circadian amplitude, 2A (measure of the predictable extent of daily change), are acceptable in the light of a summary of analyses of week-long data intervals.
The picture of a clean bill of BP health when 168-hour intervals are summarized does not appreciably change when 24-hour data intervals are analyzed, for M. An occasional circadian blood pressure overswing is, however, seen on a number of days as values of 2A cross the upper limit of the 95% prediction interval, during spans when no CHAT was apparent in the corresponding weekly summaries. In daily records, OS is never MESOR-hypertensive, but on a few occasions has circadian overswing. With weekly summaries, she has 0% abnormality of either M or 2A.

DISCUSSION

CHAT has sometimes been shown to be present in clinical health, but usually only for a few days at a time, presumably under emotional loads (and the 24-h record in the 7-day perspective can actually serve as a load [stress] test) (4). Circadian overswing, however, must not be diagnosed based on records of 24 hours, dubbed transient CHAT. In the case examined, perhaps the mildest category of transient CHAT, no treatment seems indicated. For the current surveillance of BP, the chronomic analysis, carried out in the Halberg Chronobiology Center, is available for all comers. Data are obtained by monitoring during very different spans (from 1 day to many weeks and longer). These data are analyzed for differing total spans; if so, however, the results are not comparable. The problem of standardizing interval lengths for analyzing BP series for CHAT detection is to be considered and standardized at international meetings, and is here proposed for consensus discussions on such occasions.

CONCLUSION

We suggest that a week be a bare minimum to rule in BP health, but not to rule out either CHAT or MESOR-hypertension, when they occur on occasion, as CHAT does in OS in a few daily data, but in no weekly summaries.

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Chronomics* (*the study of time structures, chronomes) detects altered vascular variabilities constituting risks greater than hypertension: with an illustrative case report. In: Mitro P, Pella D, Rybar R, Valocik G, editors. Proceedings, 2nd Congress on Cardiovascular Diseases, Kosice, Slovakia, 25-27 April 2002. Bologna: Monduzzi Editore; 2002. p. 223-258.

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NEED TO STANDARDIZE DATA COLLECTION AND REFERENCE VALUES

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INTRODUCTION

Several cases document with measurement series covering decades that at or near the end of life, blood pressure (BP) in the presence or absence of MESOR (midline-estimating statistic of rhythm)-hypertension can gradually drop, just as it increases early in life, and that in so doing, the relative prominence of extracircadian vs. circadian rhythms changes. That BP varies with age at both extremes of life, early and late, as well as in-between, has been thus described time structurally (chronomically) (1). Once diagnosed as normotensive or as hypertensive in terms of the BP MESOR (M), a given person need not have that characteristic for the rest of his/her life. Some treated MESOR-hypertensives, in particular with systolic values around 200 mm Hg, can become untreated MESOR-hypotensives with systolic values near 100 mm Hg within a decade. BP also varies around the scale of decades, and in most people varies greatly along the scale of hours and days and further during weeks and months (2), so that during the same monitoring span of a few weeks, there can be both hyper- and hypotensive values. BP and HR variability disorders also differ, whether they are treated or untreated (3-6). We must not fly blind (7) to these variations.

Disorders include alterations of the BP M, double amplitude (2A) or acrophase, of the standard deviation (SD),circadian and other, including a number of infradian rhythms, as nonphotic aspects of BP and HR variability. Lasting CHAT (short for circadian hyper-amplitude-tension) can represent a risk greater than a high BP (2).

Aim. To plan for the long-term care of people with blood pressure disorders by starting the systematic collection of reference values for extracircadian as well as circadian characteristics, validated by lifelong studies, while we summarize lessons from the monitoring of those who have contributed longitudinal data thus far.

METHODS

For the current surveillance of BP, the sphygmochron analysis carried out in the Halberg Chronobiology Center is available for all comers.

RESULTS

Data are obtained by monitoring during very different spans, from 1 day to many weeks and longer, up to decades. These data are analyzed for differing total spans; if so, however, the results are not comparable. The problem of standardizing interval lengths for analyzing BP series for circadian hyper-amplitude-tension (CHAT) detection is to be considered and standardized at international meetings, and is here proposed for consensus discussions on such occasions.

DISCUSSION

7-day monitoring and both daily and overall analyzes are recommended, with the urgent task of collecting international reference standards in health starting with medical students and including high school students, each followed up for a lifetime to retain the records for reference values only of those who remain healthy for their lifespan. The relative merits of tolerance intervals (8) vs. prediction intervals (9, 10) and the need to age-qualify reference intervals, preferably based on clinically healthy "test pilots" monitored starting at birth, are also major issues. Most difficult is the educational task of conveying the mountains of evidence on the merits of replacing conventional reference values that allow interpretations of single values and are the same for men and women above a certain age. The single values ignore variability disorders of necessity and thus fail to detect severe vascular disorder risks greater than hypertension (2), leaving them silent to both care recipient and caregiver and thus untreated, until a hard event occurs.

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CHRONOBIOLOGIC SERIAL SECTIONS COMPLEMENT SPECTRA TO SEEK SOCIAL VS. PHYSICAL SIGNATURES IN HUMAN HEART RATE CIRCASEPTANS

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INTRODUCTION

When ordering significance of any approximation of oscillations in a man's heart rate in chronobiologic serial sections with different trial periods remains ambiguous, reference to a control serial section at a spectral minimum may be useful, yielding information on any nonstationarities and/or any violations of underlying assumptions such as serial correlation.
Aim. To complement, by chronobiologic serial section analyses in the time-varying phase domain, earlier global analyses in the frequency domain.

METHODS

Subject GK, 72 years of age at start of half-hourly monitoring from April 1998 to August 2006, with very few gaps.
Measurement GK wore an automatic ambulatory functioning device around the clock with gaps. Data were summarized in both daily and weekly analyses. The midline-estimating statistic of rhythm, or MESOR, is determined by the fit of a cosine curve; the same fit can provide estimates of the double amplitude, 2A, gauging the extent of predictable periodic change, and of the acrophase, gauging the timing of change at each period, characterizing the data.

RESULTS

Results from long lasting cardiovascular monitoring (Table 1) shows ordering significance at $P \leq 0.01$ from serial sections with the number of intervals as a function of the fitted period. If the spectral components drift or jump, one of them can transiently have more than one tested "period length". The 14.3% incidence at $P \leq 0.001$ is a control, since it corresponds to a valley in a spectral window (not here shown) and need not be all false positive. Moreover, the 99.5%

incidence of "significance" at P≤0.05, albeit qualified by restricting focus to P≤0.001, requires explanation. Could it be that a transient 7-day synchronization is missed in the global spectral window because of circaseptan heterophasing, in response to different timed single stimuli, so that varying phase relations during different subspans cancel out the corresponding differently phased 7.00-day synchronized social circaseptans, and allow resolution of a much weaker but not necessarily trivial effect of the solar wind, validated beyond congruence by subtraction and addition documented by concomitant monitoring in time of solar and biologic near- but not precise weekly circaseptans (1, 2)?

Table 1: Ordering statistical significance in chronobiologic serial sections of components investigated

		N	Percentage¶ of		
CSS	τ	of intervals		intervals with:	
NP	(days)	analyzed	P<0.05	P<0.01	P<0.001
1	6.772*	400	59.5	46.5	33.5
2	7.000**	387	99.5	53.7	33.9
3	7.011*	387	75.7	52.7	34.4
4	7.447***	364	51.1	31.3	14.3

*Ordering significance of peaklets in global spectral windows not shown: P<0.001, 6.772 days is natural circaseptan period found in the entire record on the speed of the solar wind, available at the time of analysis (~42 years) and in the geomagnetic indices Kp and aa for longer records up to >100 years (for aa).
**Ordering significance in global spectral window (in which it was not a peak) (P<0.001). This rthythm is analyzed because of possible synchronization of HR by the social week, but a linear regression line fitted to acrophases of non-overlapping yearly data intervals shows a statistically significant delaying trend in the fit of a 7.00-day rthythm, in keeping with the 7.011-day rthythm, but the same result can also be interpreted as a phase jump by attempts of the social schedule to lock-in the natural 7.011-day component. There is no statistically significant trend in acrophases with the rthythms of 6.772 and 7.011.
***which was a trough in the spectral window (P=0.980) analyzed as a "control" for spurious significance.

DISCUSSION

Regression diagnostic tests should be routinely carried out to check on the presence of any serial correlation, normality of residuals, and homogeneity of variance, apart from the stationarity of the parameters of the component under investigation. Further investigation is needed to reduce any violation of underlying assumptions and thus to assess the extent to which results at different trial rthythms represent a lasting and stable circaseptan component. Data transformation prior to regression diagnostic tests may be indicated, but such transformations can alter the actual time structure. Whether one or the other component is a false positive result awaits, from a statistical viewpoint, robust tests that do not rely on assumptions underlying regression. At the time of this writing, the fact that a period of 6.77 days was found in the record of solar wind speed as a whole and that a very close period was found in a longer record of Kp, and in an even longer record of another geomagnetic index, aa, is a validation within physics of the reality of the 6.77-day component, which gains

tremendously from the trans-disciplinary validation when it is also found in human heart rate and when such congruence is found in a given subject at other non-photic frequencies as well.

CONCLUSION

In the absence of robust inferential statistical procedures, the search for intra- and trans-disciplinary congruence of aeolians combined with subtraction and addition approaches is indicated.

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TIME COURSE OF BLOOD PRESSURES OVER 18 YEARS ANALYZED SEPARATELY BY DAY AND BY WEEK

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INTRODUCTION

24 hour monitoring of BP by ambulatory functioning devices is a gold standard, reserved for special cases of high BP, left uninterpreted in terms of its time structure. General reliance upon a single measurement (or a single 24-hour profile) of BP, however, has been dubbed "flying blind" (1) and is at variance with the documented (2, 3) need to meet requirements, stated repeatedly for over a century by opinion leaders, i.e., that we must evaluate periodic BP variations before a patient is examined. This proposition, at the turn of the 20th century, suggested by a leader at NIH as well (5), is greatly facilitated by modern hardware and software in the new millennium (6, 7).
The aim of the study was to map the systolic blood pressure daily with weekly oscillations and to determined MESORs, M (a midline-estimating statistic of rhythm) and circadian double amplitudes, 2A, computed by the fit of a single 24-h cosine curve of a clinically healthy subject as a function of age and as an indication of any need for intervention.

METHODS

Subject
YW, a cardiologist, currently in his 19th year of monitoring, used the Colin ABPM first and an A&D instrument thereafter to monitor at mostly half-hourly intervals around-the-clock. *Measurement* YW wore an automatic ambulatory functioning device around the clock with gaps. Data were summarized in both daily and weekly analyses. The midline-estimating statistic of rhythm, or MESOR, is determined by the fit of a cosine curve; the same fit can provide estimates of the double amplitude, 2A, gauging the extent of predictable periodic change, and of the acrophase, gauging the timing of change at each period, characterizing the data.

RESULTS

Weekly summaries of MESORs initially consist mainly of acceptable values with few exceptions over the first 13 years. Thereafter, there are greater fluctuations and more values above the upper limit of an acceptable MESOR, in the light of reference standards from gender- and age-matched peers.
In weekly summaries, YW's circadian double amplitude exceeds only on few occasions its limit of acceptability. By contrast, in the daily summary over the same time span, wider swings of the MESOR as well as of the double amplitude are seen, revealing the dangers of basing a diagnosis of CHAT in particular, but also of MESOR-hypertension, on a single 24-hour record.

DISCUSSION

Many more acceptable 24-hour records can follow several abnormal consecutive records and whether either abnormality is transient or lasting must be observed with more than even 48-hour monitoring before one starts possibly unwarranted treatment, perhaps for a lifetime, for a condition that persisted only for a relatively short time and recurred only briefly at long intervals. Thus, already early in his monitoring a week-long data summary would have supported the diagnosis of MESOR-hypertension and, in current conventional practice, based on single measurements or at best upon 24-hour profiles, a week-long abnormality might indeed constitute a finding prompting treatment. But the abnormal one-week span in YW is followed by MESOR-normotension for weeks, years and almost two decades and validates the proposition that a week-long monitoring can be transient and is an indication for continued monitoring for at least another week or longer, depending on results. This finding must not be misinterpreted as validating the conventional clinical custom to ask the patient to return in a month; we do not recommend only another spotcheck (that unknowingly to care provider or receiver could be done on a roller coaster in some cases).
Clinical trials that show benefit from treating "spotcheck" pressures above 120 mmHg come to mind (8). Necessarily, they include many false positives at entry and false negatives at their end and must not be taken to constitute an indication to treat what has been mislabeled "pre-hypertension" (9). A chronobiologic pre-hypertension, a gradual increase in amplitude prior to any lasting increase in M, was not (yet) seen in YW.
Until trials are based on at least week-long monitoring, they are not applicable to the individual, e.g., to YW. A decision whether a slightly increasing trend prompts starting hypotensive medication is the more complicated in this case, since there was also a change in monitors coincidental with a change in MESOR toward the end of the record and a possibly slightly increasing trend with time is confounded by the change of instrumentation. Relaxation treatment is indicated and practiced.
For YW, when incomplete records are discarded and the analysis is assessed only based on those weeks that are documented by a minimum of 224 values (/week), the abnormality seems rarer, apart from the sparser record, of course. Artifactual CHAT can come about more frequently when records with 116 values/week were accepted than in the case when records with fewer than 224 values/week (greater decimation, fewer artifacts) were discarded. The role of the density of the record in diagnosing CHAT is emphasized.
The coexistence of CHAT and MESOR-hypertension is seen in 2.3% of the days investigated. Overall MESOR-hypertension is present in 13.3% of the monitored days considered and CHAT overall is rarer yet, only seen in 7%. When weekly summaries are made, keeping all

records with 116 or more values or only those with 224 values/week, the incidence of MESOR-hypertension decreases to 7.5 or 3.7% and that of CHAT to 0.6%.

CONCLUSION

While monitoring continues and is done for health self-care it also contributes substantially to both biomedical and broader science (10-29).

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BLOOD PRESSURE AND HEART RATE VARIABILITY IN PATIENTS WITH CARDIAC TRANSPLANTATION

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INTRODUCTION

Cardiac transplantation results in complete afferent and efferent denervation of the donor atria and ventricles. This denervation includes both sympathetic and parasympathetic division of the autonomic nervous system. Although functional reinnervation of both sympathetic and parasympathetic fibres to the heart has been demonstrated in the canine transplant model within six months after transplantation (1), only limited functional reinnervation has been demonstrated in humans (2,3). The absence of parasympathetic control of heart rate after human orthotopic cardiac transplantation was studied (4) and the authors showed that arterial baroreflex gains for the donor sinus node were also depressed (early 0.1±0.2ms/mmHg, late 0.2±0.2 ms/mmHg) compared with controls (14.9±1.8 ms/mmHg). This data suggest that parasympathetic influences of the donor heart rate are absent in the majority of patients up to 96 months after cardiac transplantation. Mancia et al. found that baroreflex sensitivity is inversely related to blood pressure variability and positively related to heart rate variability (5).
The aim of the present study was to compare low frequency blood pressure variability in patients after orthotopic cardiac transplantation (OCT) with healthy controls.

METHODS

Subjects

We examined 7 cardiac transplant patients (age 55.7±9.7 years) after 2-8 years after cardiac transplantation. Cardiac transplant patients were without significant epicardial coronary artery disease and had normal left ejection fraction. Cardiac allograft rejection was excluded by right ventricular endomyocardial biopsy, usually obtained before the examinations started. All transplant patients were receiving cyclosporine, all vasculoactive medications were stopped 24 hours before the study. Nobody was treated with beta adrenergic blocking agents. The results were compared with the examination of the group of 7 healthy subjects (C) of similar age (50.0±2.8 years). Control subjects were free of organic heart disease as determined by history and physical examination.

Measurements

ECG, blood pressure (BP) and thoracic impedance were recorded beat-by-beat during 20 minutes (Task Force Monitor, CNSystem, Austria, Fig. 1) in supine position during spontaneous breathing (5 min) and breathing controlled by metronome (5 min, 0.33 Hz). Using thoracic impedance measurements we determined stroke volume index (ml/m^2), in cardiac index ($l/min.m^2$) and in total peripheral resistance index ($dyn.s.m^2/cm^5$).

The study protocol was approved by the local ethical committee and written informed consent was obtained from all participants.
The results are reported as a mean ± standard deviation, comparison between healthy subjects and cardiac transplant patients was performed by using Wilcoxon´s test.

RESULTS

Resting values of heart rate, systolic and diastolic blood pressure in healthy subjects and patients after cardiac transplantation are not different (Fig.2,3,4).
Using thoracic impedance measurements stroke volume index (ml/m^2), in cardiac index ($l/min.m^2$) and in total peripheral resistance index ($dyn.s.m^2/cm^5$) were determined and we have not found any differences between healthy subjects and patients after cardiac transplantation (Fig.5,6,7). We analyzed heart rate variability spectra (ms^2) and we have found the decrease in LF heart rate variability (ms^2) in patients after cardiac transplantation in comparison with healthy subjects ($p<0.01$, Fig.8). Diastolic blood pressure variability is presented in Fig. 9. Low frequency diastolic blood pressure variability was not different in patients after cardiac transplantation in comparison with healthy subjects.

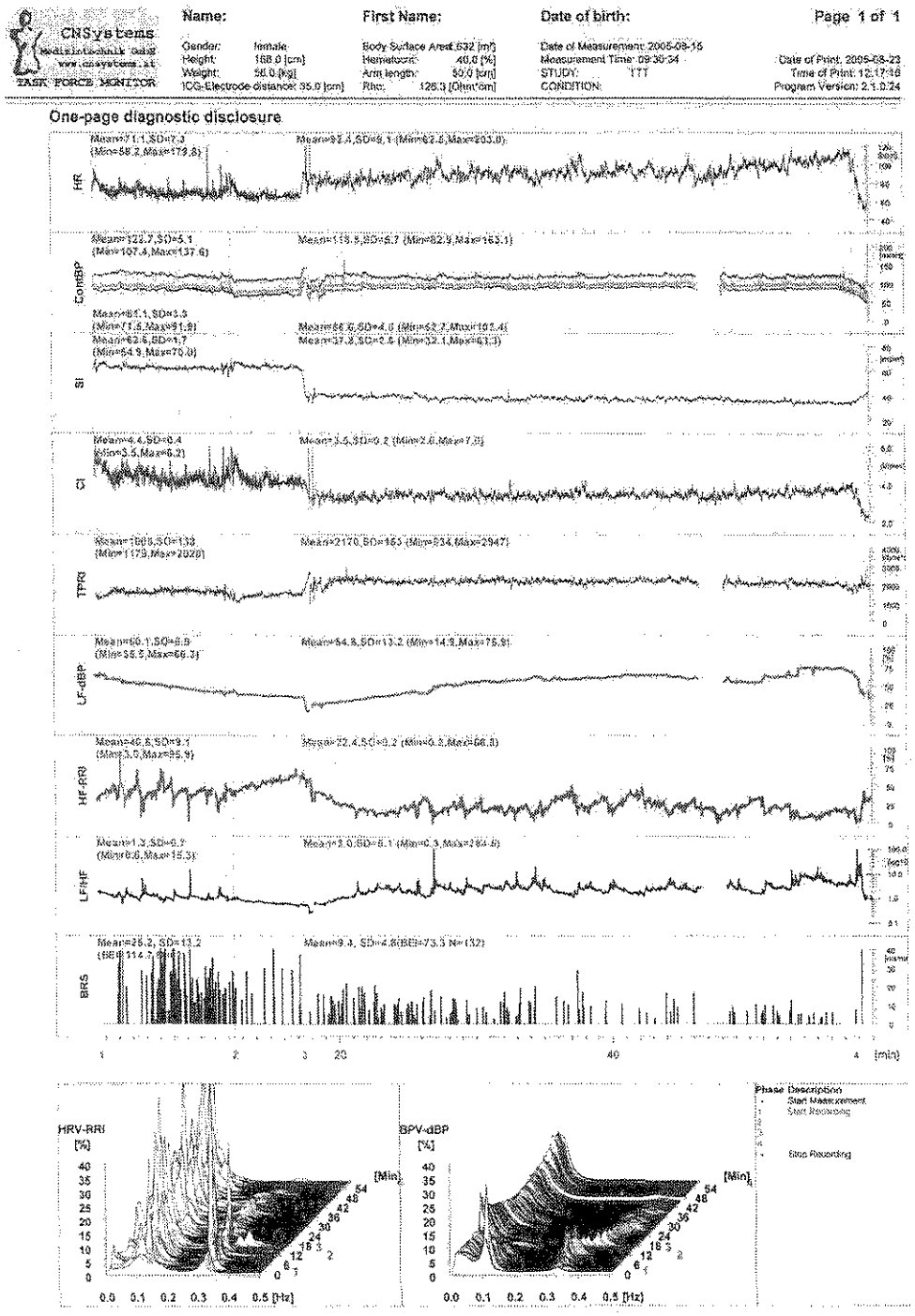

Fig.1 Example of CNSystem record

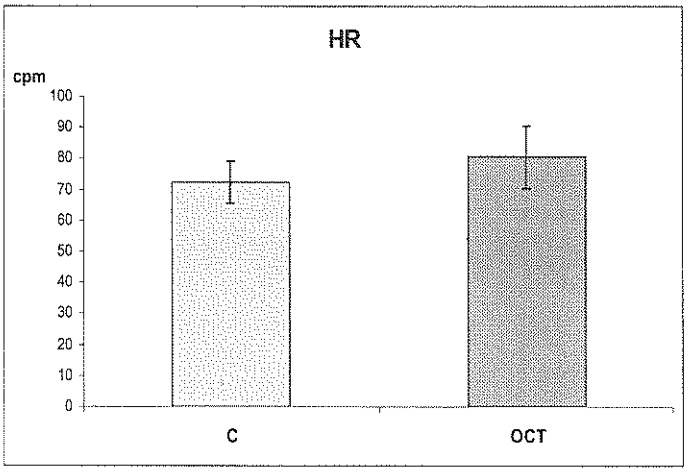

Fig. 2 Heart rate in healthy subjects and patients after cardiac transplantation (mean±SD).

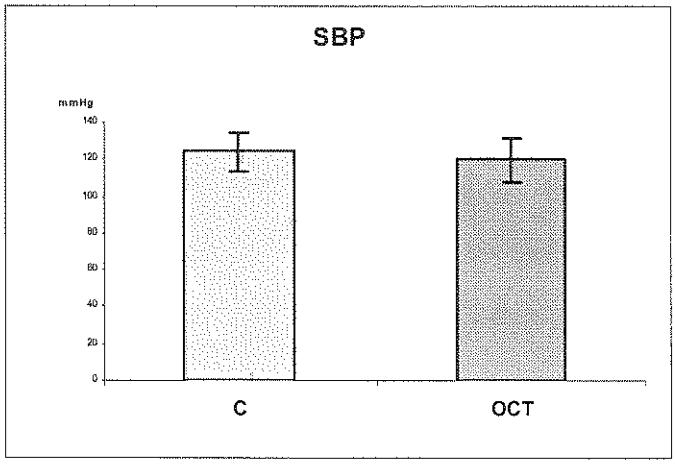

Fig. 3 Systolic blood pressure in healthy subjects and patients after cardiac transplantation (mean±SD).

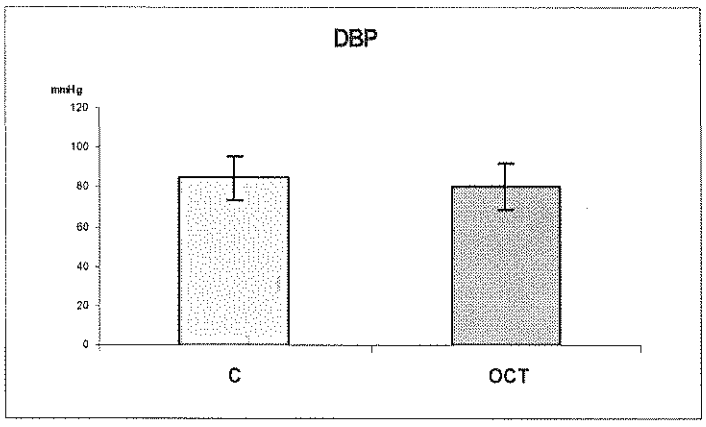

Fig. 4 Diastolic blood pressure in healthy subjects and patients after cardiac transplantation (mean±SD).

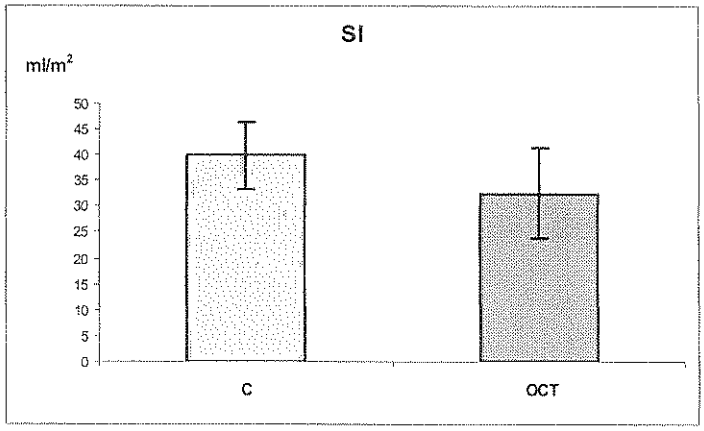

Fig.5 Stroke volume index in healthy subjects and patients after cardiac transplantation (mean±SD).

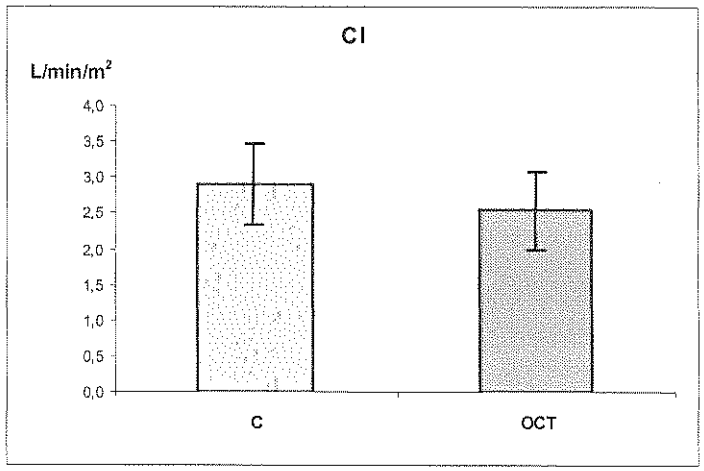

Fig. 6 Cardiac index in healthy subjects and patients after cardiac transplantation (mean±SD).

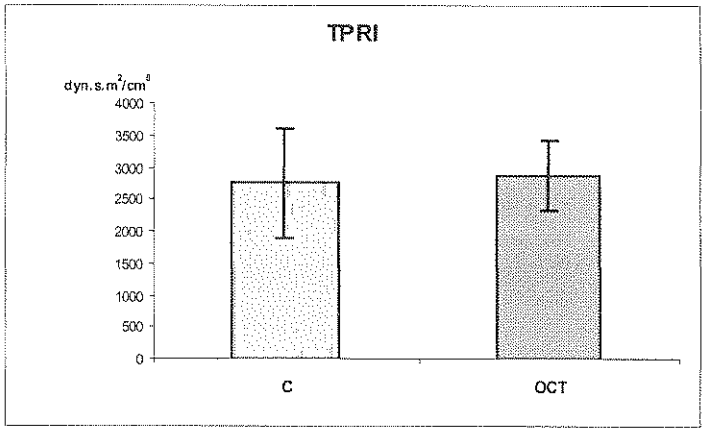

Fig. 7 Total peripheral resistance index in healthy subjects and patients after cardiac transplantation (mean±SD).

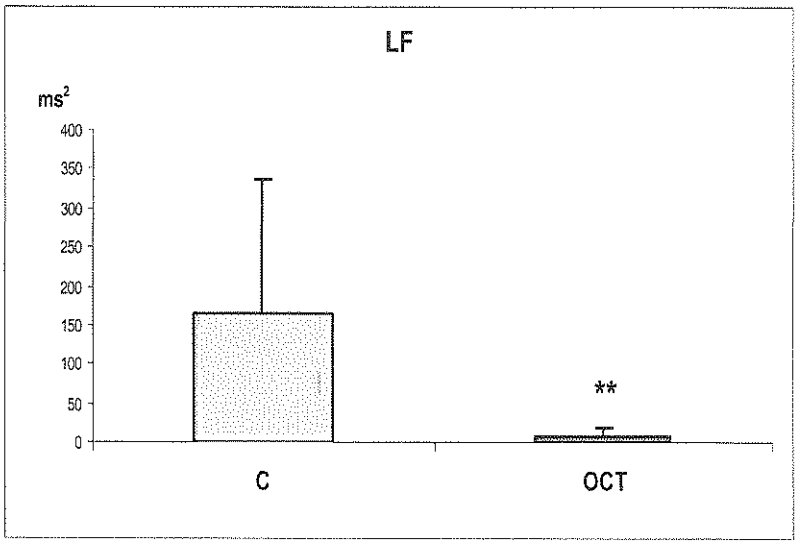

Fig 8. LF heart rate variability in healthy subjects and patients after cardiac transplantation (mean±SD).

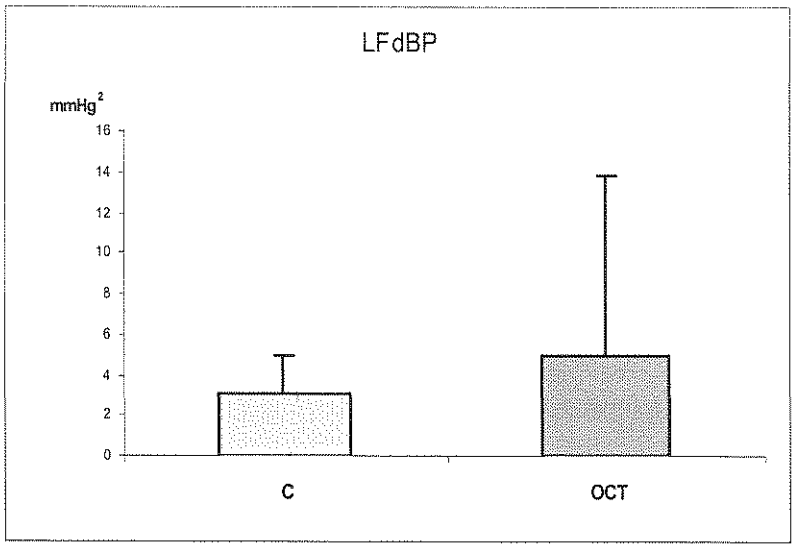

Fig.9 LF diastolic blood pressure variability in healthy subjects and patients after cardiac transplantation (mean±SD).

We can conclude our results by stating that both groups did not differ (OCT versus C, mean ± SD) in heart rate (80.4±10.8 versus 72.2± 6.9 beats/min), in systolic (119.4±11.8 vs. 124.9±11.0 mmHg) and diastolic BP (80.6±10.3 vs. 85.7±8.3 mmHg), in stroke volume index (32.6±8.9 vs. 39.9±6.6 ml/m^2), in cardiac index (2.54±0.55 vs. 2.90±0.58 l/min.m^2) and in total peripheral resistance index (2863±552 vs. 2754±845 dyn.s.m^2/cm^5). On the other hand, heart rate variability spectra (ms^2) were decreased in OTC (LF heart rate variability:

8.43±12.09 vs.164.29±171, $p<0.01$). No difference was seen in diastolic BP variability spectra ($mmHg^2$): LF dBP (5.00±8.82 vs.3.10±1.94, n.s.).

DISCUSSION

Spectral analysis of instantaneous heart rate and blood pressure is widely used to investigate the normal and pathological cardiovascular control system on the basis of the manifestation of autonomic activity in the respective power spectra. The power spectra of both haemodynamic parameters exhibit two distinctive peaks, corresponding to fluctuations at different frequencies. Oscillations at frequencies of 0.1 Hz are usually described as the low-frequency peak (LF) and are associated with sympathetic and parasympathetic activity.

Cardiovascular control is fundamentally altered after heart transplantation because of surgical denervation of the heart. The main goal of the scientific work of Toledo et coauthors (6) was the noninvasive characterization of cardiac rate control mechanisms after heart transplantation. They studied heart rate variability using power spectral analysis. They found similar spectral pattern of power spectra, but the power was markedly reduced compared to healthy subjects. The mere existence of a low frequency peak in heart rate spectra was believed to be a sign of reinnervation (6). However, Bernardi et al. (7) proved the existence of a mechanical coupling between respiration and the heart, in addition to the well known neural one.

It is important to note that the spectral analysis of cardiovascular parameters in heart transplantation patients does not yield knowledge regarding their autonomic activity, as opposed to the normal system. Rather, it serves as a powerful tool for characterization of the control mechanisms (6).

We have not found an increased LF DBP variability despite of a dramatic decrease of LF HRV contrary to Mancia et al. finding in healthy subjects (5). The Mancia et al. results can be explained by two alternative hypotheses: 1. The increased baroreflex heart rate sensitivity results in increased heart interval fluctuation elicited by blood pressure fluctuation and this increased heart interval fluctuation by changes in cardiac output suppresses the fluctuation of blood pressure. 2. The increased baroreceptor sensitivity causes the increased fluctuation of heart rate on the one hand and the suppression of blood pressure fluctuations by means of total peripheral resistance changes on the other hand. The later hypothesis is supported by our results.

CONCLUSION

It is concluded that LF diastolic blood pressure variability is unchanged in patients after orthotopic heart transplantation despite of the denervation of the heart.

Support: MSM0021622402

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STROKE IN THE CZECH REPUBLIC

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INTRODUCTION

Yearly mortality data from stroke in the Czech Republic, recorded from 1950 to 1999, were analyzed. About 50- and 21-year cycles are taken into account, either all data are considered or they are analyzed for men and women separately. After detrending, a self-starting cumulative sum (CUSUM) control chart finds an increase in stroke deaths to have taken place around 1997. These results are in keeping with similar findings in four other geographic locations. They warrant a renewed effort toward stroke prevention. Ambulatory monitoring of blood pressure and heart rate of the population at large is useful to detect and correct certain abnormalities of the circadian pattern of these variables, which have been associated with large increases in stroke risk, even in conventionally normotensive subjects.

Morbidity and mortality from stroke and other cardiovascular events have long been shown to follow non-random circadian and circannual patterns (1-13). Most epidemiological studies reveal a morning peak in onset and a higher occurrence in winter than in summer in temperate regions. About-weekly and half-weekly patterns in stroke incidence have also been documented (14; see also 12, 15-22). Differences in timing have been reported in relation to different etiologies (15). For instance, the incidence of strokes associated with subarachnoidal hemorrhage differs in its circadian and circaseptan timing from that of lacunar infarctions and other kinds of strokes (15). The incidence of strokes associated with a cardiac embolus also differs in its circannual timing from that of strokes associated with large vessel disease (15). Overall, strokes tend to occur preferentially on Mondays (14).

To study longer cycles, the data from the Czech Republic on overall stroke mortality and for each gender separately were analyzed by least-squares spectra (23), with frequencies in the range of one to 11 cycles per 52.2 years. In view of a prominent about 50-year cycle, analyses were repeated on the residuals from this long-term trend and from a third-order polynomial. Components corresponding to spectral peaks were further assessed by nonlinear rhythmometry (23-26). The analysis revealed the presence of 50-year periodicity (cycle duration: 54.3 years; 95% confidence: 50.6, 58.7 years) and of 20-year periodicity (cycle duration: 21.4 years; 95% confidence 16.8, 27.9 years).

The aim of the present paper was the spectral analysis of the stroke mortality data from the Czech Republic using calculations of autocorrelation functions according to Blackman-Tuckey method. Calculation of autocorrelation functions enables to determine the rhythm in signal and the noise in signal.

MATERIALS AND METHODS

Yearly mortality from stroke in the Czech Republic was recorded from 1950 to 1999. Only total mortality data were analyzed and not deaths in subcategories such as subarachnoid

vs. intracerebral hemorrhage or occlusion of cerebral arteries, in view of changes in disease classification during the span covered. The autocorrelation functions and power spectral densities were calculated from the data on overall mortality. In view of a prominent about 50-year cycle, analyses were repeated on the residuals from this long-term trend and from a third-order polynomial.

RESULTS

Original stroke mortality data are seen in Fig. 1. The calculated autocorrelation curve is seen in Fig. 2.

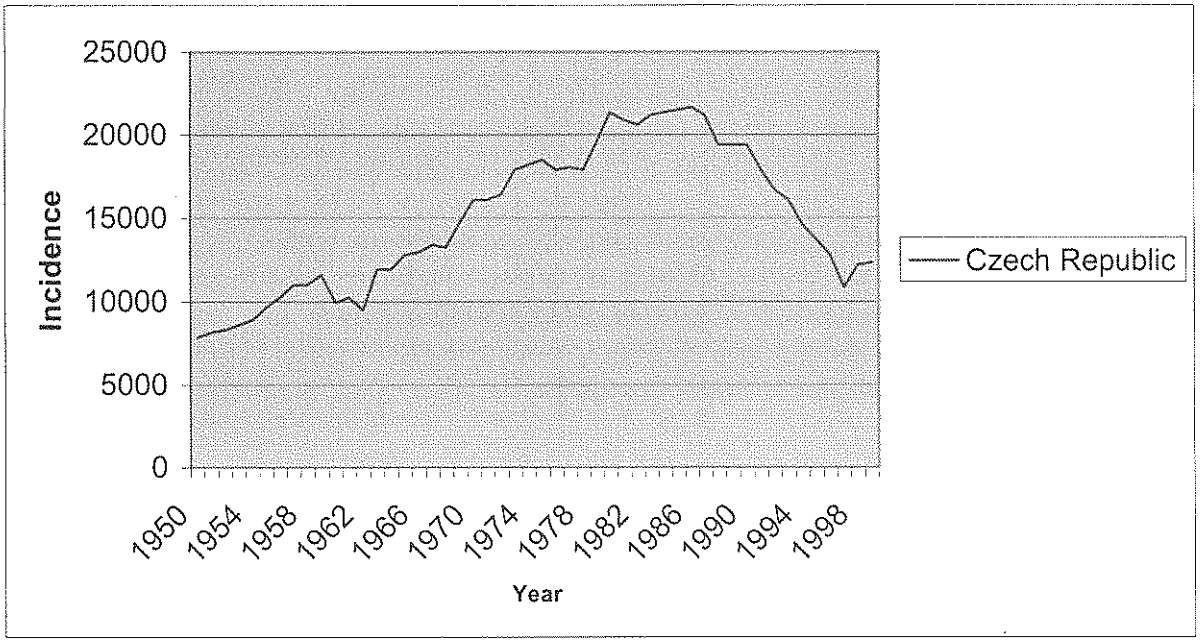

Fig. 1 Stroke mortality in Czech Republic in the period of 50 years

Autocorrelation function has the sinusodial character, and it has minimum of 23 years. While minimum corresponds to a half of the cycle, the duration of the whole cycle is about 50 years. The fact that the correlation coefficient at the value 23 years is approaching -1, supports the hypothesis of statistical significance of 50-year cycle $p<0.01$.

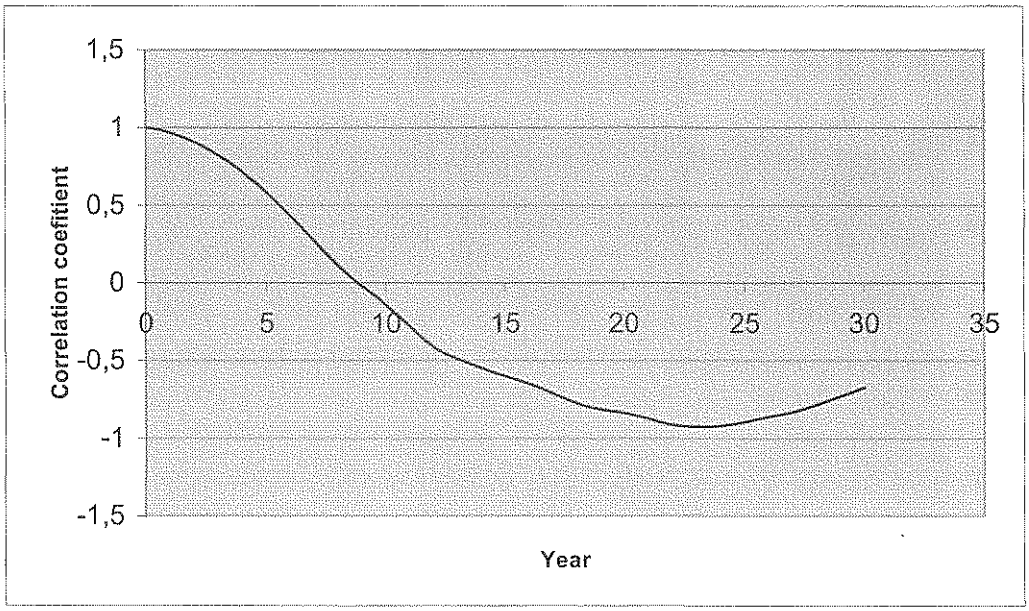

Fig. 2 Autocorrelation function of stroke mortality

Amplitude of about fifty-year cycle was 2123 deaths per year. In the original record the death numbers were: 1950 - 8 000 per year, 1985 – 22 000 per year, 1995 – 11 000 per year. Regarding the nonsinusoidal character of the fifty.year cycle, the trend, expressed by polynomial of 3rd degree, was removed and the residual record (Fig. 3) was analyzed again. The results of spectral analysis are seen in Fig. 4. We determined the amplitude of the fifteen-year cycle to be 384 deaths per year.

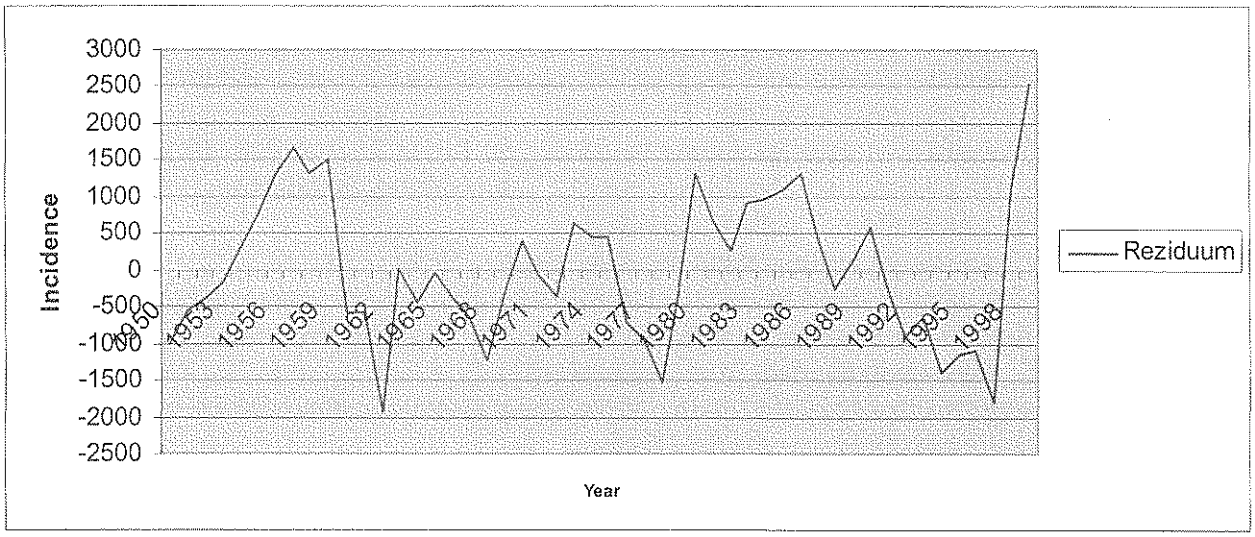

Fig. 3 Residual record of stroke mortality

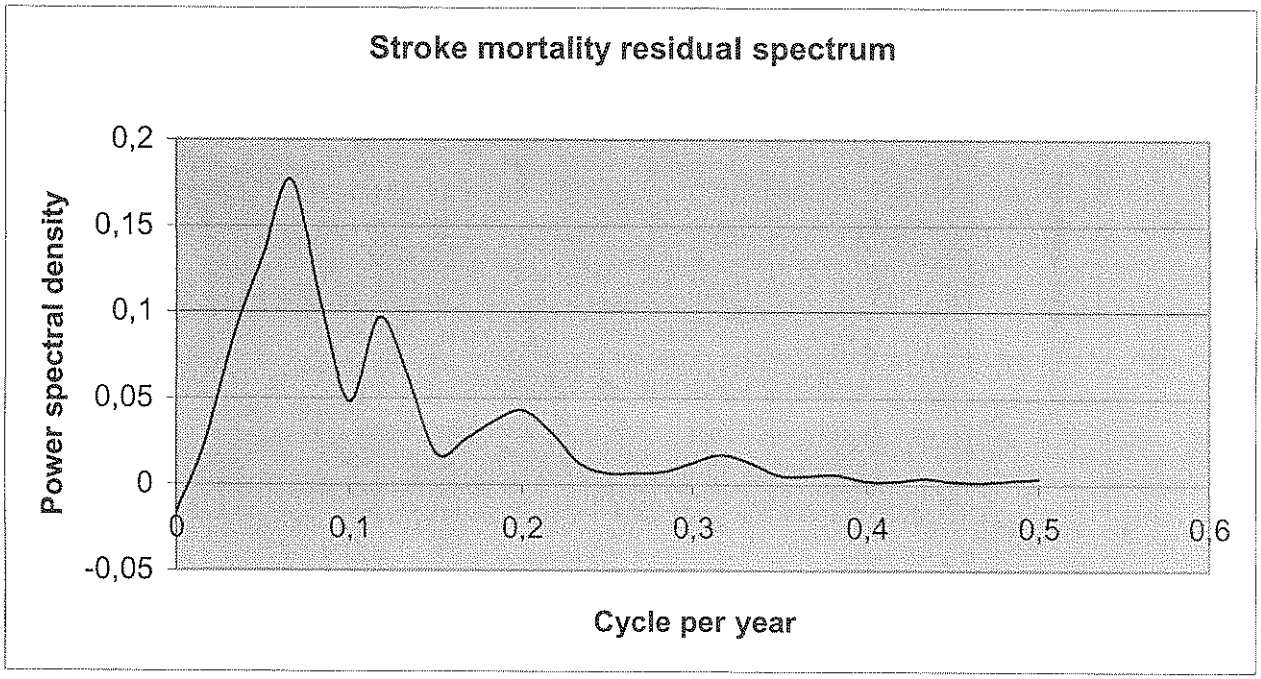

Fig. 4 Spectral analysis of residual record of stroke mortality

Results of spectral analysis determine fifty-year cycle ($p < 0.01$) and about fifteen-year cycle ($p < 0.05$) in the record of stroke mortality in men and women.

DISCUSSION

With the qualification that there have been changes in the classification of mortality from stroke, a non-monotonic trend over the past 50 years has been documented both in the Czech Republic and in Minnesota (24, 28). This result raises the question whether the decline in stroke during the past two decades cannot be accounted for, at least in part, by a natural about 50-year cycle. Of course, one should not use 50 years of data to discuss an about 50-year periodicity (28), unless there is collateral evidence.

In the case of a recent increasing trend in stroke deaths, there is corroborating evidence from other studies. An upward trend in stroke mortality was observed in most recent years not only in the Czech Republic and in Minnesota, but also in Slovakia (29), in Lund, Sweden (30), and with Paul W.C. Johnson in the data from Arkansas (27).

Our analysis suggests that the time course of the stroke death is influenced by socio-economic development and by cyclic environmental factors.

While treatment and public education are very important to limit the incidence of strokes, the decrease seen after 1985 may not only be a response to changes in patient management but may represent in part a response to environmental influences characterized by very low-frequency components, such as a circasemicentennial cycle that needs replications not only in different geographic locations, but also over several longitudinal cycles before qualifying as a rhythm. The recent identification of an excessive circadian blood pressure amplitude, as well as of a deficit in heart rate variability, as independent additive features of a risk syndrome for stroke and other vascular morbidity (24, 31, 32) should prompt systematic monitoring of the population.

CONCLUSION

Yearly mortality due to stroke in the Czech Republic had been recorded from 1950 to 1999. The data on overall mortality were processed by spectral analysis. In view of a prominent about 50-year cycle, analyses were repeated on the residuals from this long-term trend and from a third-order polynomial. Amplitude of about 50-year cycle in total mortality data was 2123 deaths per year (corresponding original data are as follows: 1950 – 8000 deaths per year, 1985 - 22000 deaths per year, and 1995 – 11000 deaths per year). In view of the non-sinusoidal waveform of the about 50-year cycle, a third-order polynomial was fitted to the data and the amplitude of about 15-year cycle was assessed to be 384 deaths per year. The time course of the stroke death is influenced by socio-economic development and by cyclic environmental factors.

Support: MSM0021622402

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IMPACT OF EXERCISE THERAPY ON CARDIOVASCULAR AUTONOMIC FUNCTION IN OBESE PATIENTS

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INTRODUCTION

Abdominal obesity and arterial hypertension, together with other pathological conditions (insulin resistance, dyslipidaemia, diabetes mellitus type 2) are included within the metabolic syndrome having the important role in the development of cardiovascular disease. Visceral obesity and the metabolic syndrome have been described as a neuroendocrine disorder characterized by dysregulation of the hypothalamic – pituitary – adrenal axis and parallel sympathetic nervous system activation; it has also been proved to contribute to the risk of cardiovascular complications (1,2). Depressed values of heart rate variability (HRV) and a depressed value of baroreflex heart rate sensitivity (BRS) indicate an increased sympathetic nervous activity (3).

OBJECTIVE

The study was designed to analyze the impact of exercise training on heart rate variability (HRV), baroreflex sensitivity (BRS) and aerobic fitness in obese patients with and without hypertension.

PATIENTS AND METHODS

We examined 27 obese patients (**OB,** age 56.6 years, BMI 34.6 men, 21 women, 11 patients with DM type 2).
The aerobic fitness, HRV, BRS and anthropometric values were evaluated in the whole group OB and in the two subgroups - with hypertension (**OBH,** n = 15, age 57 years, BMI 34.3) and without hypertension (**OBN**, n = 12, age 56.1 , BMI 33.6) .
After the standard internal examination (medical history, physical examination, resting ECG, basic laboratory examination) all patients were subjected to the initial bicycle spiroergometry (Cardiovit CS-10 Schiller, gas analyser Medgraphics), heart rate variability (HRV) and baroreflex sensitivity (BRS) examination.
Heart rate variability (HRV) was determined by spectral analysis of short-term heart rate record (Varia Puls TF3) in supine position with metronome-controlled breathing (0.33 Hz). We evaluated the frequency domain variable - spectral power (SP) of HRV :

total power - TP (ms^2), low frequency band - LF (ms^2), high frequency band - HF (ms^2) and ratio LF/HF – LF/HF.

Baroreflex sensitivity (BRS) was determined by spectral analysis of spontaneous fluctuations of systolic blood pressure (SBP) and cardiac intervals (CI) by Peňaz method (5) (Finapres Ohmeda). We used 5-minute record of SBP and HR at metronome-controlled breathing at frequency 0.33Hz. The value of cross-spectral power density of CI and SBP fluctuation was divided by the value of power spectral density of systolic blood pressure fluctuation at 0.1Hz. The modulus of the transfer function between variation in blood pressure and heart rate is considered to be the measure of BRS (ms/mm Hg).

Aerobic fitness (VO_{2max} /kg, W_{max} /kg) was determined by spiroergometry, the protocol with a workload increasing up to the symptom-limited maximum was selected. Spiroergometry was used also for the determination of anaerobic (ventilatory) threshold (AT) and expressed it in the heart rate value for determining safe exercise training intensity.

Exercise therapy

All patients were involved in the exercise therapy programme for 12 weeks. It consisted of controlled aerobic exercise training (twice a week 60 minutes) and encouragement of increasing of habitual physical activity (walking at least three times a week for 30 to 60 min). All subjects followed former recommendation of energy intake restriction to 2000kJ /day.

Spiroergometry, BRS and HRV examinations were performed after 12 weeks of the training programme as well as anthropometric parameters by the same method as that used at the beginning.

The study protocol was approved by the local Ethics Committee. A written informed consent was obtained from each subject prior to their participation.

The spectral power values are expressed in ln (ms^2), where ln is the natural logarithm of the absolute values.

The data obtained were processed by Microsoft Excel 97. Statistical analysis was carried out by the Wilcoxon test for paired values at the significance level of 0.05 (*) or $p < 0.01$(**).

RESULTS

The BRS values both in OB and OBH group increased significantly. Significance of increase in OBN was borderline (Tab. 1); as well the parameters of physical fitness VO_{2max}/kg, W_{max}/kg significantly increased (Fig. 1).

Concerning HRV, in OB group we found out boundary decrease of the LF/HF ratio and significant increase in HF band; in OBH favourable trend in HF was present as well as in OBN in LF/HF ratio (Tab. 2).

The body weight, BMI and waist circumference decreased significantly in all groups (Tab. 3).

Tab. 1 Baroreflex sensitivity before and after exercise therapy

	BRS (ms/mm Hg)		SBP (mm Hg)		DBP (mm Hg)	
	before	after	before	after	before	after
OB (n = 27)	5.3 ± 2.8	6.7 ± 3*	124 ± 17	124 ± 17	74 ± 12	69 ± 13 *p=0.05*
OBH (n = 15)	5.4 ± 2.8	7.1 ± 3.1*	129 ± 15	127 ± 15	74 ± 11	70 ± 13
OBN (n = 12)	5.2 ± 2.9	6.2 ± 2.90 *p = 0.05*	116 ± 16	121 ± 18	75 ± 12	68 ± 12

Legend : BRS – baroreflex sensitivity; SBP – systolic BP; DBP – diastolic BP

Tab. 2 Heart rate variability before and after exercise therapy

	TP (log ms^2)		**LF (log ms^2)**		**HF (log ms^2)**		**LF/HF ratio(log)**	
	before	**after**	**before**	**after**	**before**	**after**	**before**	**after**
OB (n = 27)	**5.8±1.0**	**6.0±0.9**	**4.9±1.0**	**5.0±0.9**	**5.1±1.2**	**5.5±0.9***	**-0.2±1.1**	**-0.49±0.90** *p=0.05*
OBH (n = 15)	**5.8±0.8**	**6.0±0.9**	**4.9±0.9**	**5.0±0.9**	**5.2±1.0**	**5.5±0.8** *p=0.06*	**-0.25±1.0**	**-0.41±0.7**
OBN (n = 12)	**5.8±1.3**	**6.1±0.9**	**4.9±1.1**	**5.0±0.9**	**5.0±1.6**	**5.6±1.2**	**-0.12±1.4**	**-0.59±1.2** *p=0.09*

Legend : TP (ms^2)- total power ; LF (ms^2) - low frequency band; HF (ms^2) - high frequency band

Tab. 3 Anthropometric parameters before and after exercise therapy

	BMI		Waist circumference (cm)		Body weight (kg)	
	before	after	before	after	before	after
OB (n = 27)	34±4.5	32±3.7**	106.1±13.3	103.5±12.7**	89.6±13.4	86.9±13.2**
OBH (n = 15)	34.3±3.7	33.2±3.1*	103.8±13.5	102.2±12.7**	90.2±11.8	87.3±11.2**
OBN (n = 12)	33.6±5.5	31.9±4.4*	106.8±16.9	102.8±16.6*	88.9±15.8	86.3±15.9*

DISCUSSION

Metabolic syndrome including abdominal obesity is associated with increased sympathetic activity that increases the cardiovascular risk (especially the risk of sudden death and life-threatening arrhythmias); therefore, the evaluation of cardiovascular autonomic functions is reasonable in these patients. Both reduced HRV and reduced BRS indicate an increased risk of mortality in patients with ischemic heart disease. Altered autonomic regulation has been proposed as one of the factors predisposing patients with metabolic syndrome to adverse cardiac events; as well low physical fitness is an important element of cardiovascular risk (4). Abdominal obesity is accompanied in the majority of patients by the development of insulin resistance (IR). IR appears to be a key factor in the development of other pathological conditions involved in the metabolic syndrome, therefore the main therapeutic objective in these patients is to decrease both IR and sympathetic tone. Physical activity is also one of the non-pharmacological. therapeutic means, however, lack of data in patients with obesity or metabolic syndrome exists. The favourable influence of endurance training on autonomous

cardiovascular functions has been reported both in experiments with dogs with myocardial ischaemia (6) and in our patients with ICHS (7). After 12 weeks of endurance training, Howorka et al. (8) found a significant increase in the total spectral power of heart rate variability in obese diabetic patients with moderate form of cardiovascular autonomic neuropathy.

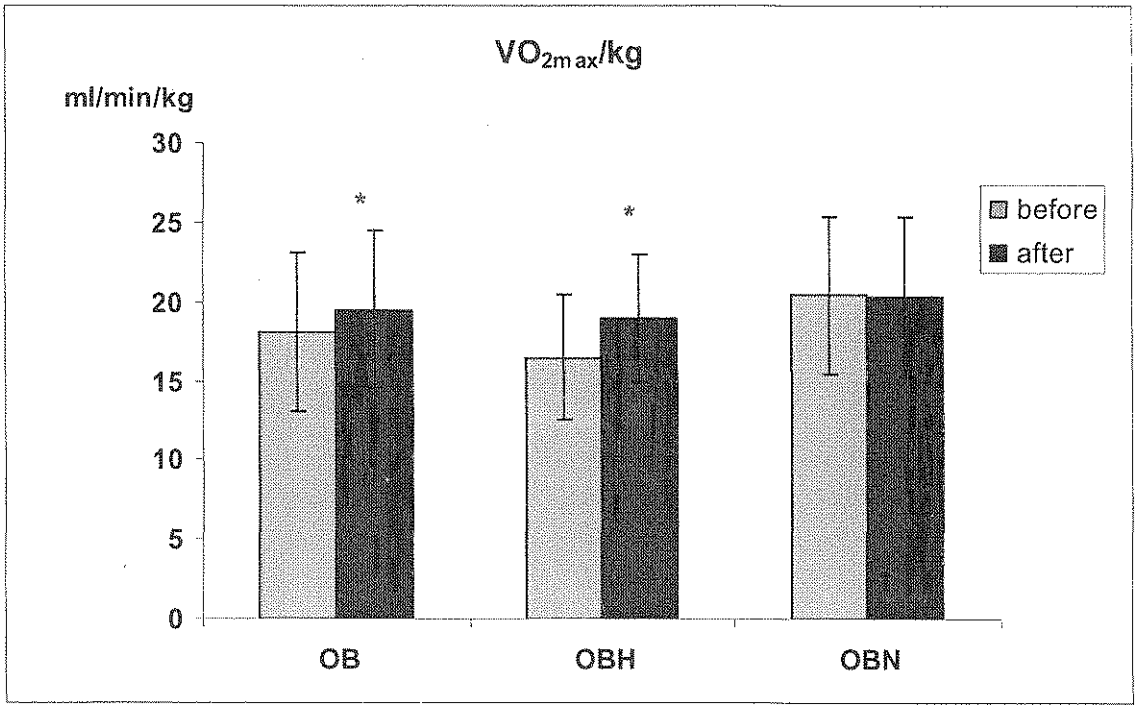

Fig. 1 Physical fitness (VO_{2max}/kg) before and after exercise therapy

CONCLUSIONS

In obese patients regular physical training significantly improves baroreflex sensitivity and aerobic fitness; anthropometric values (BMI, body weight and waist circumference) were also favourably influenced. In HRV parameters the trend to improvement of sympathovagal balance was found.
The results suggested beneficial effect on autonomic regulation in obese subjects with other abnormalities included in metabolic syndrome. This favourable effect was more strongly demonstrated in the subgroup of obese patients with hypertension.

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COMBINED TRAINING IN WOMEN WITH ISCHEMIC HEART DISEASE: EFFECTS OF EIGHT-WEEK REHABILITATION PROGRAM

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INTRODUCTION

The principal goal of cardiac rehabilitation is to restore physical and psychosocial function in cardiac patients (11,12,21). Traditionally, these programs emphasized aerobic (dynamic) exercise, whereas resistance exercise was assumed to be hemodynamically hazardous. During the past two decades, there has been ample evidence to suggest that resistance exercise training for cardiac patients may be less dangerous than was it was claimed, especially in low-moderate risk (1,5,6,8,9,11,13,15,19,20).
Resistance training has become increasingly important component of cardiovascular rehabilitation. When appropriately prescribed and supervised, it has favourable effects on bone mineral density, body composition, muscular strength and endurance, glucose metabolism, selected coronary risk factors, and other health-related variables (19).
Cardiovascular rehabilitation of outpatients is known to be the most important factor in the ischemic heart disease prevention and in changes of the lifestyle (2).

Aim of the study
This study examined the effects of combined training (aerobic and resistance training) in outpatients on aerobic capacity, functional capacity and maximal attained load in one-repetition-maximum (1-RM) test in women with ischemic heart disease.

METHODS

Subjects
Fourteen women with ischemic heart disease (mean age 64,5 ± 9 years) with mean ejection fraction 51 ± 8,8 % participated in this study.
Inclusion criteria: documented coronary artery disease 3-5 months after myocardial infarction (MI). The diagnosis of MI was assessed in the Department of Cardio-angiology, St. Anna´s Teaching Hospital.
Exclusion criteria: instable angina, manifest heart failure, hemodynamically significant heart valve defect, smoking.
There were no changes in medication during the rehabilitation program. Informed consent was obtained from all subjects.

Undergone examinations:

- Symptom-limited spiroergometry before entering and after finishing the rehabilitation program (anaerobic threshold assessment).

- Isometric test („handgrip") and one-repetition-maximum test before starting the resistance training, after 4 weeks of resistance training and after finishing the rehabilitation program.

Experimental protocol:
Our program was arranged as the 8-week outpatient supervised program. Patients exercised 3-times a week. The exercise unit consisted of warm-up phase (10 minutes), aerobic phase (25 minutes), resistance training (15 minutes) and relaxation phase (10 minutes).
The program started as aerobic training alone (first 2 weeks), than the program continued as combined training.

- Aerobic phase: 25 minutes on bicycle ergometer (Ergoline REHA E900, software ErgoSoft+ for Windows). Training load and heart rate were on anaerobic threshold value.
- Resistance training: The exercises were composed as follows: bench press, leg extension, pull down (TK-HC COMPACT) and abdominal muscle training. The training started on 30 % of 1-RM in the first week, 40 % in the second week, 50 % in the third week and 60 % in the fourth week (3-5 sets of 10 repetitions, 30-60 seconds of rest between the sets). Than the 1-RM test was repeated and resistance training continued on new 60 % of 1-RM till the end of the program.
  All patients were instructed on the proper form and breathing technique.

Statistical analysis
The values are displayed as mean ± SD. The effects of combined training were assessed using the Wilcoxon test. The statistical significance was set at $P < 0,05$.

RESULTS

After the 8-week rehabilitation program the maximal achieved aerobic capacity significantly increased (Table 1).
Maximal achieved load in 1-RM test increased in all exercises (Table 2).
Spiroergometry does not show any change in maximal achieved load, only trends to increase were found (Table 3).

Table 1. Symptom-limited aerobic capacity.

	Before RHB	After RHB	p
$VO2_{SL}$ ($ml.min^{-1}$)	1155 ± 150.6	1292 ± 179.2	0.02
$VO2_{SL}.kg^{-1}$ ($ml.min.kg^{-1}$)	16.2 ± 4.06	17.8 ± 4.10	0.03

Table 2. Maximal 1-RM load.

	1-RM test		p
	Before RHB	After RHB	
Bench press (kg)	18.8 ± 4.06	21.6 ± 3.99	0.01
Leg extension(kg)	18.0 ± 4.06	22.6 ± 3.16	0.03
Pull down (kg)	18.9 ± 4.47	23.7 ± 4.07	0.001

Table 3. Symptom-limited performance.

	Before RHB	After RHB	p
W_{SL} (W)	79.6 ± 18.55	84.3 ± 17.30	NS
$W_{SL}.kg^{-1}$ ($W.kg^{-1}$)	1.1 ± 0.40	1.2 ± 0.35	NS

DISCUSSION

It was demonstrated that many cardiac patients lack the physical strength or confidence to perform common daily tasks, (9,14,21)it is critical that they gain a minimum level of strength (20). Our results are in accordance with studies, which demonstrate that patients engaging in resistance exercise can perform strenuous daily activities with less relative exertion, diminished effort perception, and decreased injury risks, resulting in enhanced functional capacity (3,10,14,20).

For some women, especially for women of higher age, the exercise with men in mixed groups could be a problem. (2). A cardiac rehabilitation program offers groups intended exclusively for women focusing not only on physical exercise, but also on social skills training, which might encourage women to participate (4). Some studies indicate that about 25 % of women do not exercise at all and only 48 % of women are exercising for only 3 months (16).

Women who undergo rehabilitation programs are generally older, have lower self-efficacy scores, more cardiac risk factors, lower VO2 maximum, severe cardiovascular disease, and have lower adherence to the program than men (17). Women also have the same benefit from cardiovascular rehabilitation programs as men (2).

CONCLUSION

After the 8-week combined training the maximal aerobic capacity and maximal strength of trained muscle groups was significantly increased. No cardiovascular complications during the resistance and aerobic training appeared. This rehabilitation program contributed to higher quality of life and well-being of our women patients.

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CARDIOPULMONARY FUNCTIONS AND BAROREFLEX SENSITIVITY BEFORE AND AFTER EXERCISE TRAINING LASTING 8 WEEKS IN PATIENTS WITH CHRONIC ISCHEMIC HEART DISEASE

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INTRODUCTION

Increased sympathetic nervous activity at resting conditions can be considered to be a sign of cardiovascular autonomic dysfunction. The non-invasive determination of increased sympathetic activity is the measurement of heart rate variability and baroreflex heart rate sensitivity (BRS, 1-5). Several studies have demonstrated that depressed BRS and HRV are strong independent risk factors for sudden cardiac death in patients after myocardial infarction (6-8) and some studies have later demonstrated a favourable impact of exercise on sympathetic overactivity and improvement of patients´ prognosis (9). The present study was designed to evaluate whether a specific programme of exercise training at anaerobic threshold level may be sufficient to improve cardiopulmonary functions and BRS of patients with chronic heart disease.

METHODS

We examined 32 patients with chronic ischemic heart disease (cardiography, coronarography, NYHA I-II, stable therapy, body weight of 86±6 kg, age of 63±8 years).

Criteria of inclusion:

1. Presence of at least one haemodynamicly significant coronary stenosis (more than 50% of the diameter of lumen).
2. Objective evidence of ischaemia is present (positive SPECT or positive ECG response at exercise testing).
3. Patient´s signature of informed consent after approval by ethics committee.

Criteria of exclusion:

1. CABG in the last 6 months
2. PTCA in the last 3 months
3. Manifest heart failure
4. Unstable angina
5. Haemodynamicly significant heart valve defect
6. Disease which contraindicates performing of training
7. Diabetes mellitus treated by insuline

Experimental procedure

The symptom-limited spiroergometry was provided before and after the training (maximal attained work load $W_{max,}$ peak VO_2/kg, MET).We evaluated the reached maximal exercise workload (W_{max}), maximal consumption of oxygen (VO_2. kg^{-1} body weight) and maximal consumption of oxygen expressed in metabolic units (MET). There was also assessed the anaerobic threshold for the determination of intensity of the training. Symptom-limited spiroergometry was performed before and after 8-week training period. The patients were subjected to the 8-week intensive aerobic training (at anaerobic threshold level, 20 min three times a week). Functional examinations of lungs were carried out using Pulmonary Function System 1070 (MedGraphics, USA). We evaluated FVC, FEV_1/VC, RV, RV/TLC, DLCO, PEF before and after 8-week training period. BRS was determined by spectral analysis of the pulse interval (PI), systolic (SBP) blood pressure (5 minutes lasting beat-to-beat non-invasive monitoring of blood pressure – Finapres Ohmeda, Peňáz, 1973, metronome-controlled breathing 0.3 Hz) before and after the training period (Siegelová et al.1995, Al-Kubati et al.1997). The study was approved by the ethics committee of the Masaryk University in Brno and all subjects gave their written informed consent. The results presented in this paper are expressed as mean values of subjects and patients with standard deviations. Statistical significances of observed differences were calculated using ANOVA and Wilcoxon test, only p values lower than 0.05 being considered as significant.

RESULTS

The results of PI (ms), SBP (mmHg), DBP (mmHg), BRS ($ms.mmHg^{-1}$), W_{max} (W), peak VO_2 ($ml.min^{-1}.kg^{-1}$), MET are given in the following table (mean±SD) before (B) and after (A) the training. All data are presented as means ± standard deviation (SD) and are given in Table 1 and Table 2. We have not found any significant differences in FVC, FEV_1/VC, RV, RV/TLC, DLCO, PEF before and after 8-week training period. The significant increase of W_{max} ($p<0.05$, Wilcoxon) indicates the improvement of fitness. The significant prolongation of PI ($p<0.05$) and increase of BRS ($p<0.05$) indicate the increase of parasympathetic and/or decrease of sympathetic nervous activity.

TABLE 1 Pulse interval (PI), systolic (SBP) and diastolic blood pressure (DBP), maximal exercise workload (W_{max}), maximal consumption of oxygen (VO_2 . kg^{-1} body weight) and maximal consumption of oxygen expressed in metabolic units (MET).

	PI	SBP	DBP	BRS	W_{max}	VO_2	MET
B	852±163	124±19	66±12	2.9±0.9	139±31	20±4	6.1±1
A	926±126*	131±16	67±9	3.9±1.1*	156±32*	21±3	6.3±1

TABLE 2 Functional examinations of lungs

	FVC	FEV_1	FEV_1/VC	DLCO	PEF	RV
B	4.18±0.91	3.29±0.8	78.8±4	10.2±2.1	9.3±2.6	2.69±1.0
A	4.07±1.03	3.39±0.9	78.8±4	10.0±1.8	10.7±1.9	2.64±1.0

DISCUSSION

The assessment of baroreflex sensitivity was introduced to clinical practice by Smyth, Sleight and Pickering in 1969. They found out and documented that intravenous administration of phenylephrin induces an increase of blood pressure and as a reaction to it there is a decrease of heart rate. Baroreflex sensitivity is then expressed as extension of the pulse interval (in ms) per 1 mm Hg rise in systolic blood pressure. Impaired (decreased) baroreflex sensitivity is an indicator of increased risk of sudden cardiac death in patients after myocardial infarction. Conclusions of ATRAMI study showed that analysis of baroreflex sensitivity and heart rate variability (independently of left ventricular function or other non-invasive risk markers) after myocardial infarction provides a significant prognostic value in the assessment of autonomic tone and in the risk stratification after myocardial infarction (6,8). Effect of exercise training in patients with chronic ischemic heart disease on heart rate variability showed an improvement of sympathetic overactivity (10, 11) and our results with the determination of baroreflex sensitivity brought similar findings in this study.
From this point of view the increase of BRS due to 8-week training is important for the further prognosis of patients with chronic coronary artery disease.

CONCLUSION

It is concluded that 8-week exercise training at anaerobic threshold level increased pulse interval, baroreflex sensitivity and maximal attained workload in patients with coronary artery disease.

This study was supported by the grant MSM0021622402

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LUNG VOLUME REDUCTION SURGERY OF EMPHYSEMA PULMONUM: LUNG FUNCTION EXAMINATIONS

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INTRODUCTION

Volume reduction surgery of pulmonary emphysema (LVRS) is used in therapy in the end stage of disease (1,2,3). The aim of the study was to evaluate lung functions in patients with LVRS before and 6 months after the surgical therapy.

METHODS

Patients

Eleven patients with end stage of emphysema pulmonum in the age of 60 to 70 years were examined (ten men, one woman).

Inclusion criteria:

- diagnosis of emphysema pulmonum -end stage
- computer tomography of lungs
- NYHA III and IV classification
- 6 months without smoking
- ability of physiotherapy

Lung functional tests:

- irreversible pulmonary obstruction. FEV_1 20-35%
- hyperinflation and air–trapping: RV>250% of ref. values, TLC >125% of ref. values
- DLCO<50% of ref. values
- blood gases pCO^2 <7.3 kPa

Exclusion criteria:

1. chest surgery
2. need of artificial respiration
3. asthma bronchiale
4. bronchitis chronica
5. bronchiectasia
6. ischemic heart disease
7. ejection fraction of left ventricle lower than 50%
8. pulmonary hypertension (PAP over 35 mmHg)
9. age over 75 years
10. long lasting therapy with corticoids (prednisone over 15 mg per day)

The study protocol was approved by local ethical committee and patients signed informed consent.

Study protocol

Lung function tests were carried out on MedGraphics, USA- pulmonary function system 1070 (4). Blood gases were determined using equipment AVL (4). Quality of life was analyzed using the questionnaire for determination of quality of life (SGRQ).

Surgery procedure

Surgery was performed using video-assisted thoraco-scopic surgical approach in 9 cases, in two patients thoracotomy was used to reduce lung volume. In 9 patients the procedure was carried out only on one side of the chest, in two cases in both sides of the chest. The amount of lung tissue was 30-98g. The histological examination of the lung tissue proved the diagnosis of emphysema pulmonum.

RESULTS

The results of lung function tests before and six months after LVRS surgery are presented for 7 patients in Table 1 and Fig 1-5.

Table1. Lung function tests before and six months after LVRS surgery in 7 patients with emphysema pulmonum

	Before	**After**
FEV_1 % ref. values	32.7±11.7	48±9.5*
TLC % ref. values	122.3±13.7	113±12.1
DLCO % ref. values	39.8±13.5	41±17.1
RV % ref. values	198.0±43.8	155±41*
RV/TLC % ref. values	60.0±6.7	48±13*

$p<0.05$, Wilcoxon

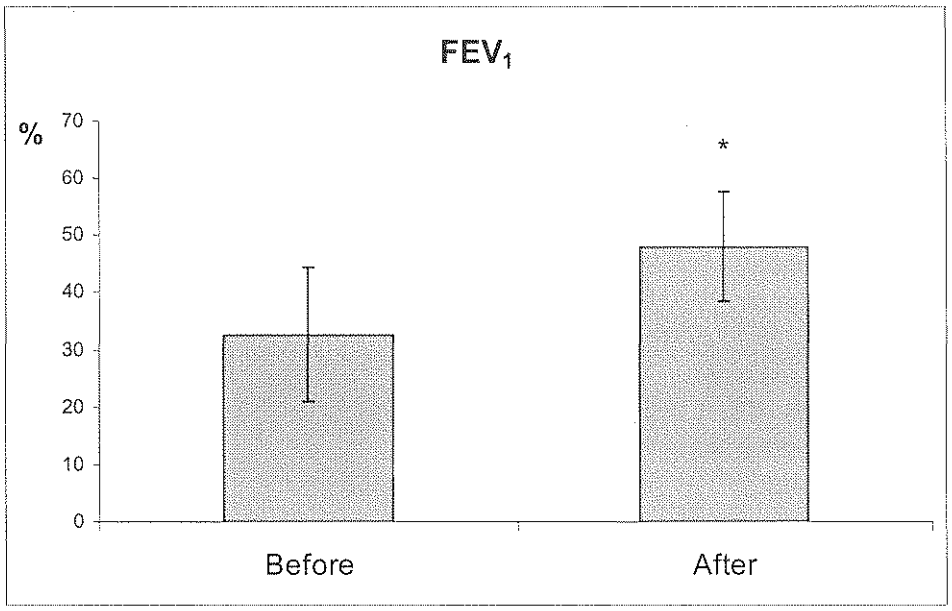

Fig. 1 Forced expiratory volume in one second (FEV_1) before and after LVRS

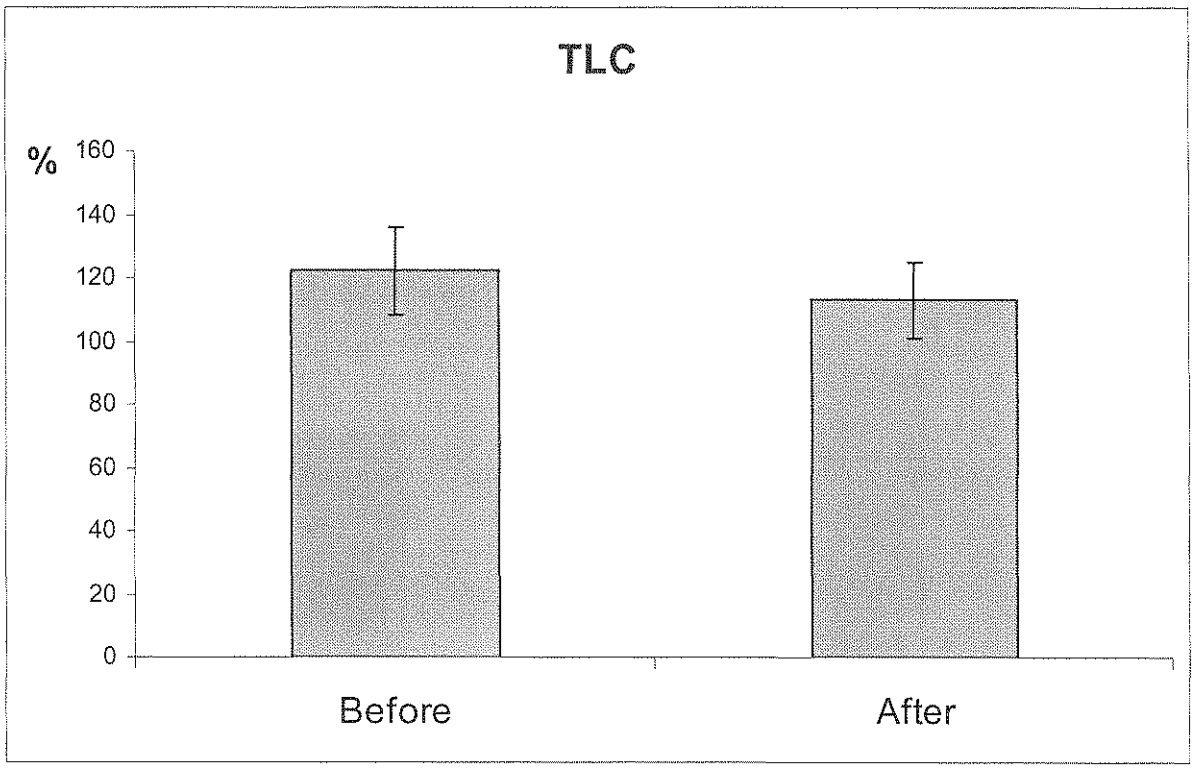

Fig. 2 Total lung capacity (TLC) before and after LVRS

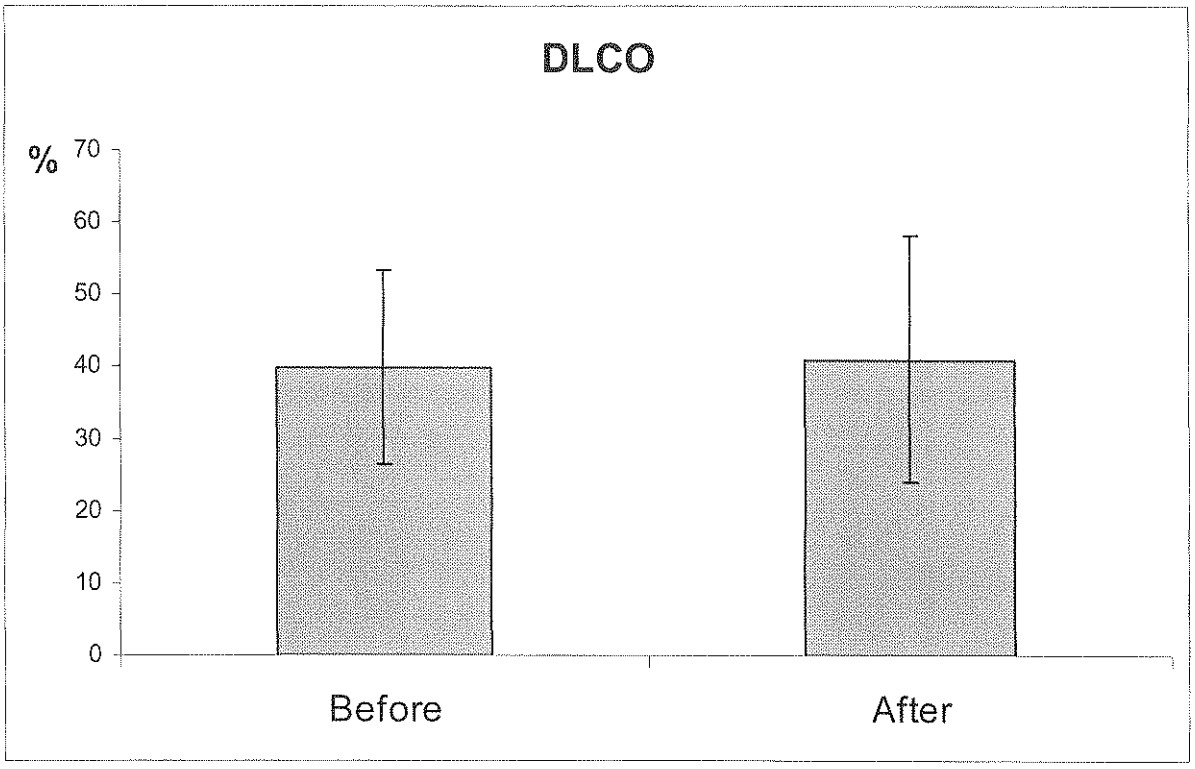

Fig. 3 DLCO before and after LVRS

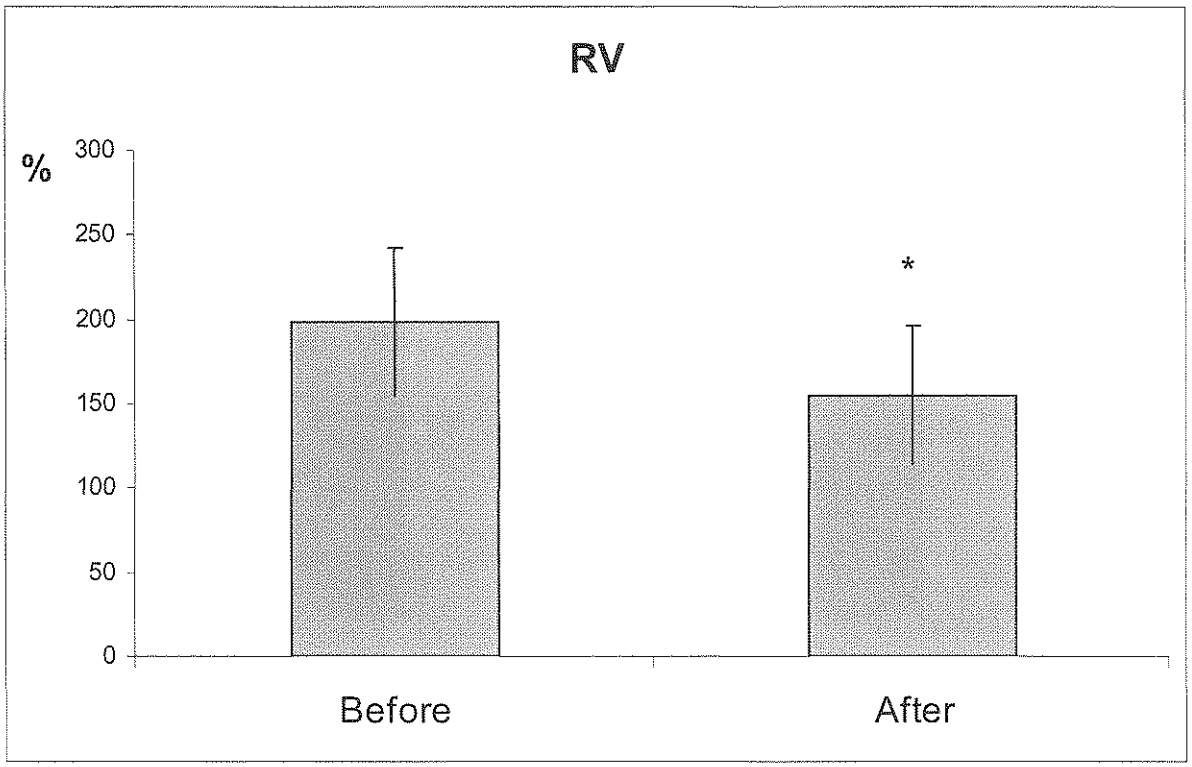

Fig. 4 Residual volume (RV) before and after LVRS

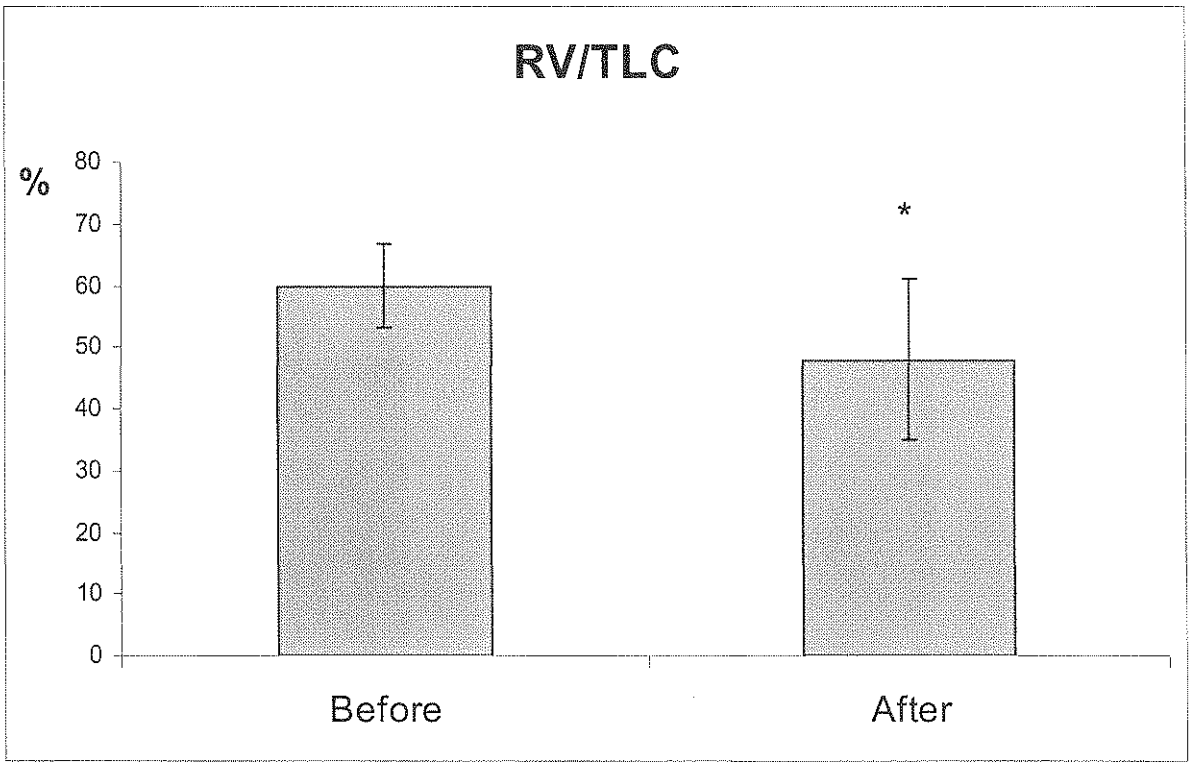

Fig. 5 Ratio RV/TLC before and after LVRS

The results of lung volume reduction surgery of pulmonary emphysema in seven patients, who survived 6 months after surgery, showed increase in forced expiratory volume in one second (FEV_1), decrease in residual volume (RV) and ratio RV/TLC ($p<0.05$, Wilcoxon). The quality of life was improved in accordance with the improvement of lung functions.
From the group of 11 patients 3 patients died, the mortality was 27 %. In one patient the tumor of pancreas appeared and he leaved the study for this reason.

DISCUSSION

Lung volume reduction surgery of pulmonary emphysema is indicated in patients with end stage of emphysema pulmonum. Lung volume reduction surgery of pulmonary emphysema is performed to reduce the number of large bulges (vesicles, plebs) of lung tissue, to decrease residual volume of lungs, to decrease increased total lung volume capacity. Our results of lung function examinations in seven patients showed similar results. The age limitation of 75 years is not accepted in all studies (3). The progression of the disease of emphysema pulmonum is in the long time survival of patients also some limitation of the use of this therapy as well as the complication of surgical procedure. In our group, we detected pneumonia in four patients and in two cases pneumothorax.

Support: MSM0021622402

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EXERCISE TRAINING AND SYMPATHETIC NERVOUS ACTIVITY IN PATIENTS WITH HEART FAILURE

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INTRODUCTION

It was proved that a regular physical activity could modify the sympathetic nervous activity. The indicator of increased sympathetic activity is heart rate variability and low heart rate variability (HRV) correlates with increased risk of sudden cardiac death after myocardial infarction in patients with chronic heart failure (CHF) (*1, 2*). However, most of the training methods including the rehabilitation protocols used also in our previously published studies are based on aerobic exercise (*3, 4*), and until now there is a lack of valid information from actual bibliography concerning the effects of resistance or combined long-term training on the heart rate variability parameters (HRV). Classical methodology for evaluating the benefits of physical training is based on cardiopulmonary exercise testing. This examination is time-consuming and could be potentially life-threatening. The examination of HRV is comfortable for the patient and without any risk. The aim of this study was to investigate if HRV testing can be useful for determination of the influence of 8-week combined exercise training on the heart rate variability expressed in frequency domain parameters in the group of patients with CHF.

METHODS

Ten patients (mean body weight 85 ± 12 kg; mean age 61 ± 13 years) with chronic heart failure were selected according to the inclusion criteria listed below. The treatment regimen of all selected patients was optimised to ensure that the patients were symptomatically stable. Standardised pharmacological treatment at the beginning and in the end of the 8-week period included administration of angiotensine converting enzyme inhibitors (ACEI), β-blockers, diuretics and digitalis in varying combinations. Inclusion criteria were as follows: age over 18 years, symptomatic chronic congestive heart failure NYHA class II-III determined for at least 3 months, and stable for at least 6 weeks; left ventricular ejection fraction < 40 % (assessed by 2D-echocardiography); symptom-limited spiroergometry showed symptom-limited oxygen consumption (VO_{2SL}) < 20 ml.kg.min^{-1}. Before the inclusion to the study all the subjects signed the Informed Patient's Consent; the study was approved by the local Ethical Committee and conforms to the principles outlined in the Declaration of Helsinki and to GCP guidelines of European Community.

Heart rate variability was registered by the system Varia-Pulse TF-3. A short-time evaluation of the heart rate variability was done using the beat-to-beat non-invasive monitoring of ECG, spontaneous and metronome-controlled breathing at 0.33Hz before and after the training period of 8 weeks. HRV frequency-domain parameters were determined by spectral analysis of pulse interval (PI).

Combined exercise training was realized at the Department of Functional Diagnostics and Rehabilitation 3 times a week. Resistance training elements were included into the exercise protocol only after 2 weeks of aerobic training. One exercise session lasted 60 min and included the following periods: warm-up period (10 min), period of aerobic exercise on bicycle ergometer with load intensity at the level of anaerobic threshold (20 min), period of fitness (or resistance) training performed on combined training machine (20 min), and relaxation period (10 min). In the period of fitness (resistance) training all the subjects started to exercise at 30% level of 1-RM (one repetition maximum), and after 2 weeks they continued at 60% level of 1-RM. The rehabilitation programme was performed by the patients for eight weeks.

Standard exercise spiroergometry (Blood Gas Analyser, MedGraphics, USA) up to the maximum limited by symptoms was carried out before and after 8 weeks of training to assess symptom-limited oxygen consumption (VO_{2SL}), maximal workload (W_{max}), metabolic equivalents (METs) and maximal heart rate (HR_{max}). The first spiroergometry test was applied also to determine the anaerobic threshold (ANP) in order to decide the individual training intensity.
Results are expressed as mean ± SD; Wilcoxon paired test Statistical analysis of functional data was performed using the Wilcoxon paired test, the Chi-2 test, the Friedmann test, and analysis of variance ANOVA. The P value < 0.05 was considered as significant.

RESULTS

Improvement of physical performance

Table 1 Results of registered functional parameters assessed by bicycle spiroergometry testing before and after 8 weeks of combined exercise training. Results are expressed as mean ± SD; Wilcoxon paired test

Functional parameters	W_{max} (watts)	$W_{max}.kg^{-1}$ (watts. min^{-1})	VO_{2SL} ($mlO_2.min^{-1}$)	$VO_{2SL}.kg^{-1}$ ($mlO_2.min.kg^{-1}$)	**METs**
Before	93 (± 17)	1.0 (± 0.2)	1399 (± 284)	15.2 (± 3.4)	4.3 (± 1.0)
After	*** 110** (± 20)	*** 1.2** (± 0.2)	*** 1551** (± 261)	*** 16.9** (± 2.8)	*** 4.7** (± 0.9)

W_{max} – maximal workload; $W_{max}.kg^{-1}$ – maximal workload per kg; VO_{2SL} – symptom-limited oxygen uptake; $VO_{2SL}.kg^{-1}$ – symptom-limited oxygen uptake per kg; METs – metabolic equivalents; * $P < 0.05$

Spiroergometry testing after 8 weeks of the training showed a significant increase of W_{max} (110 ± 20 W; *$P < 0.05$), and also a significant increase of VO_{2SL} values (1551 ± 261 $mlO_2 .min^{-1}$; *$P < 0.05$); the increase of both values was approximately +20 % compared to the initial values (*Fig. 1* and *2*). Table 1 summarizes the results of all evaluated functional parameters.

Spectral analysis of HRV

Spectral analysis of HRV parameters was evaluated and is presented in *Table 2*. They are pulse intervals (PI; ms), total power – TP; ms^2, the power of low-frequency component (LF; 0.04-014 Hz/ms^2), the power of high-frequency component (HF; 0.15-04 Hz/ms^2) and ratio of LF power to HF power (LF/HF). Spectral analysis revealed a significant increase of the total power (TP) of HRV after 8 weeks of combined exercise training (2829 ± 2600 ms^2; * $P < 0.05$) as well as HF (2573±2435 ms^2; * $P < 0.05$) in comparison with the TP and HF initial values (Fig *3*). An increase of other HRV parameters was also observed, but it is without statistical significance.

The results of HRV spectral analysis and the results of functional performance testing indicate that HRV parameters could be useful for the evaluation of the effectiveness of physical training.

Table 2 Results of the spectral analysis of registered HRV frequency-domain parameters before and after 8 weeks of combined exercise training. Results are expressed as mean ± SD; Wilcoxon paired test

Functional parameters	**PI** (ms)	**TP** (ms^2)	**LF** (Hz/ms^2)	**HF** (Hz/ms^2)	**LF/HF**
before	1016 (± 137)	891 (± 1011)	191 (± 178)	665 (± 820)	1.01 (± 1.11)
after	1046 (± 124)	* **2829** (± 2600)	256 (± 214)	***2573** (± 2435)	0.80 (± 1.12)

PI – pulse interval; TP – total power; LF – low-frequency component, HF – high-frequency component; LF/HF – LF to HF ratio; * $P < 0.05$

DISCUSSION

In the last 20 years the decreased heart rate variability has been shown to be a significant sign of sudden death risk in patients after myocardial infarction (*5*), and the predictive value of decreased heart rate variability is comparable to the ejection fraction volume in the risk stratification of patients after myocardial infarction (*6*).

The autonomic nervous system is permanently influenced by a variety of stimuli of the inner or outer origin. Age and health status belong to the inner stimuli, whereas climatic conditions, day (night) period, actual psychic and physical workload, or changes of the body position are the stimuli of the outer origin (*7*). For an easier interpretation of the results of HRV examination a test (supine – standing – supine position) was introduced in which the vagal activity increases in supine position, whereas the sympathetic tone is increased in standing position. Moreover, after repeated supine position an overshoot of the spectral power of the high-frequency component of the heart rate spectral analysis appears. Thus, in order to analyze the data of vagal activity with maximal precision, an analysis of spectral parameters after repeated supine position is recommended (*8*).

With regard to the fact that the amplitude of respiration arrhythmia is predominantly dependent on the frequency and depth of breathing (without breathing frequency control), the variability at high frequency can be submitted to non-predictable changes. A deep and slowed respiration to 6 breath cycles per minute shifts the top of respiratory spectra in the area of 0.1Hz and so can imitate an increase of sympathetic tone modulation of cardiac rhythm (*9*). In our present study we evaluated 5min intervals of HRV using metronome-controlled breathing at 0.33Hz.

The adaptation of cardiovascular system in resistance exercise training is different from the adaptation in dynamic exercise training. Heart muscle in resistance training shows signs of concentric hypertrophy, whereas the heart muscle adaptation in dynamic training is characterized by the increase of heart cavities and only a limited heart wall thickening. In that case the hypertrophy is considered as eccentric (*10*). In contrast to the resistance exercise the aerobic (or dynamic) training is more efficient for the decrease of heart rate and systolic blood pressure at rest, and also for the increase of stroke volume at rest and during the exercise (*11*). Thus, it is possible to suppose that various types of exercise influence the HRV in a different manner. The results of our study showed statistically significant differences in TP.

Up to the present the influence of combined training on the patients' performance and the autonomic nervous system has not been fully explained. Our results have shown that 8 weeks of combined training led to the increase of functional capacity in patients with chronic heart failure and to the increase of total spectral power. This study contributes to the knowledge about rehabilitation training importance in patients with chronic heart failure.

Abbreviations used

CHF – chronic heart failure, HF – high-frequency component, HR_{max} – maximal heart rate, HRV – heart rate variability, NYHA – New York Heart Association, LF – low-frequency component, PI – pulse interval; LF/HF – LF to HF ratio, VO_{2SL} – symptom-limited oxygen uptake, VO_{2AT} – oxygen uptake at anaerobic threshold, TP – total power, W_{max} – maximal workload

This study was supported by the grant MSM0021622402

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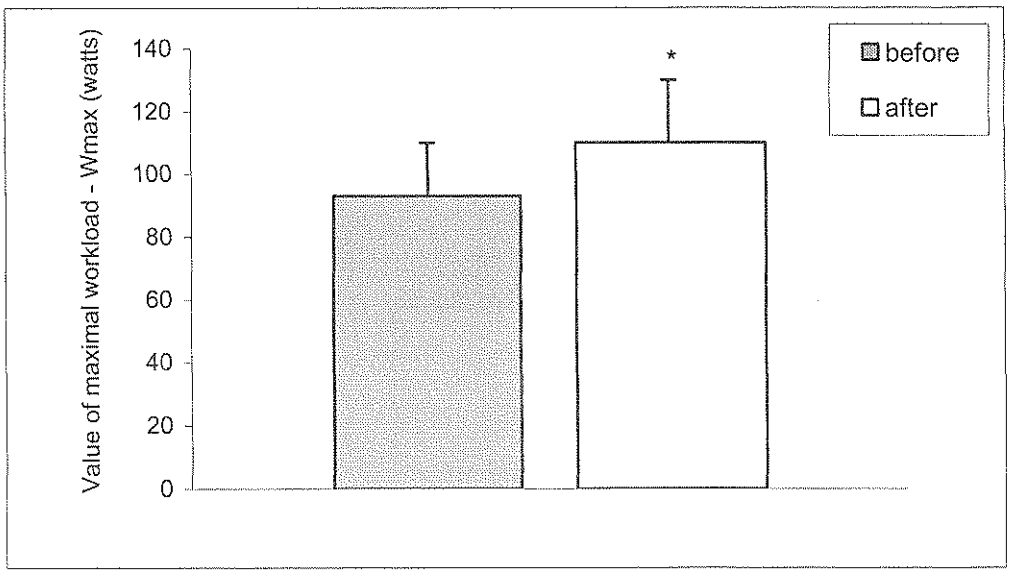

Fig. 1 Comparison of the values of maximal workload (W_{max}) before and after 8 weeks of combined exercise training. Results are expressed as mean ± SD (* $P < 0.05$; Wilcoxon paired test).

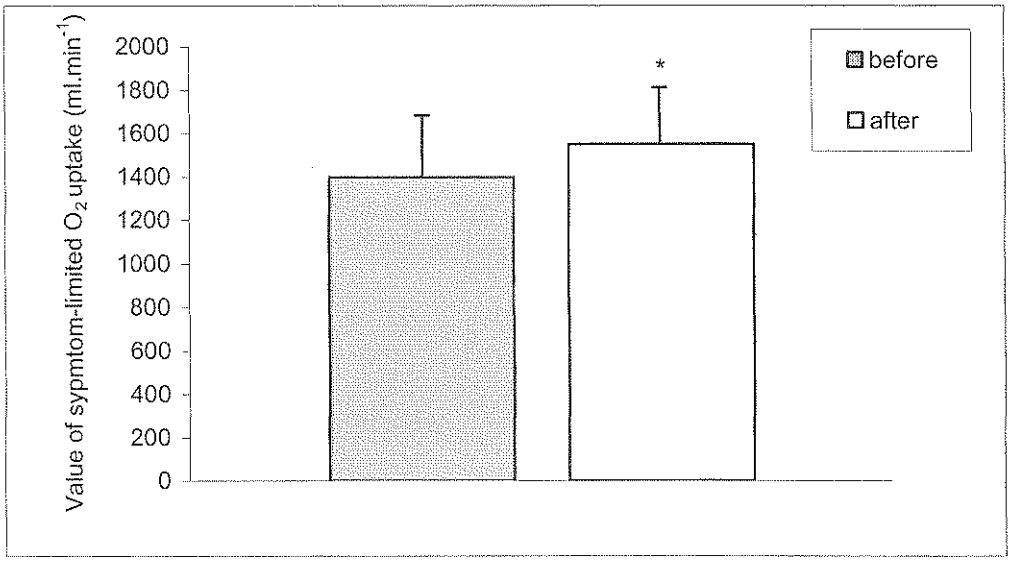

Fig. 2 Comparison of the values of symptom-limited oxygen uptake (VO_{2SL}) before and after 8 weeks of combined exercise training. Results are expressed as mean ± SD (* $P < 0.05$; Wilcoxon paired test).

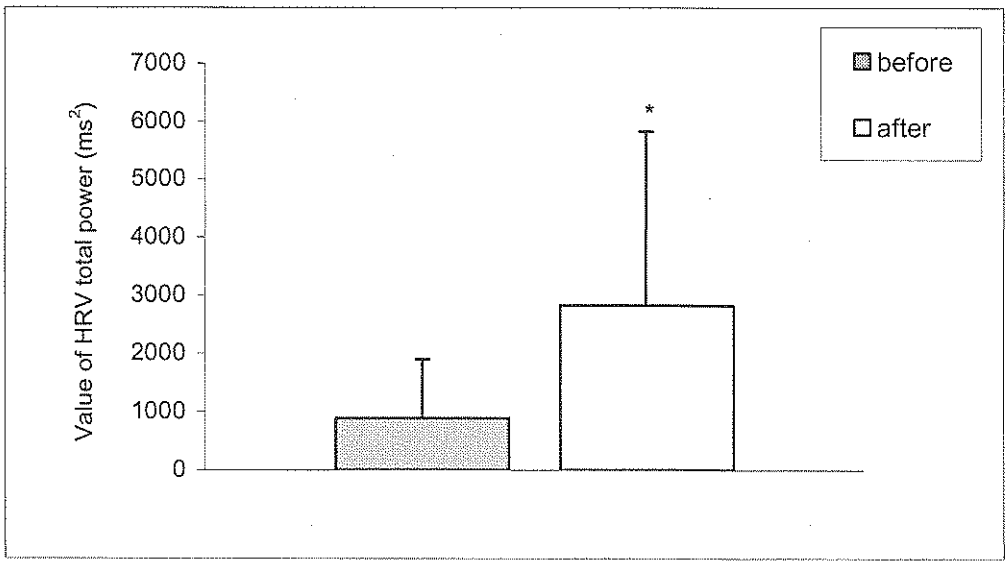

Fig. 3 Comparison of the values of spectral analysis of HRV - Total Power (ms^2) before and after 8 weeks of combined exercise training. Values are expressed as mean ± SD (* $P < 0.05$; Wilcoxon paired test).

FUNCTIONAL IMPAIRMENT IN CHILDREN WITH CEREBRAL PALSY

Drlíková L.[1], Pospíšil P., Konečný L., Chludilová V., Siegelova J., Fiser B., Pochmonova J., Erajhi A.A, Abais F.H., Hashim M.K.A, Al-Fadhli A., Al-Mahmodi N.A.I., Vank P.

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INTRODUCTION

Several studies have already focused on groups of cerebral palsied children and assessed their functions in relation with therapy (1,2,3). Cerebral palsy (CP) is a non-progressive damage of brain in an early period of its development that is characterized by pathologies in muscle tone and coordination of movements. The brain was affected in an early stage of development in prenatal, perinatal or postnatal period. The status of disease is relatively stable, the impairment is determined by the development and plasticity of the brain (4). The aim of the study was to evaluate functional impairment in a group of children suffering from cerebral palsy using Gross Motor Function Measure and Barthel index.

METHODS

Subjects

We have examined a group of 10 CP children 5 to 15 years old suffering from different kinds of CP. The average age was 11.7 years. The group consists of 6 boys and 4 girls. The neurogical examinations showed mainly spastic forms of CP, one of the patients suffered from combination of ataxia and spasticity. We used classification according to Bobaths (4). The group of CP patients is presented in Table 1.

Measurement

The group was tested according to Gross Motor Function Measure (GMFM) that is designed for children from the age of 5. The GMFM enables quantitative assessment of their gross motor skills. 5 years old child must be able to prove all the items included in this measure. GMFM is divided in 5 parts according to the tested positions: A - lying and rolling, B - sitting, C - crawling and kneeling, D - standing, E - walking, running and jumping (5). We can calculate the score for each dimension in percents, the total score and goal total score.

The GMFM were supplemented with Barthel index evaluating activities of daily living ADL (6). The test consists of 10 most important items of ADLs. The maximum score is 100 points (%), that means complete independency (6).

The study protocol was approved by local ethical committee and the patient or parents signed informed consent.

The results are presented as a mean ± standard deviation.

RESULTS

The Gross Motor Function Measure (GMFM) shows the individual results in Table 2, the mean values are in Table 3. The total goal score, expressed in percentage, is presented in Tables 2 and 3. Our results show an individual variability and different impairment according the age and severity of the disease.

Table 1. The age (years) and neurological examination of patients with cerebral palsy

	Age	CP form
1	7,1	spastic quadruplegia
2	7,6	spastic quadruplegia
3	5,4	ataxia with spasticity
4	11,6	spastic diplegia
5	10,3	spastic diplegia
6	13,6	spastic diplegia
7	15,75	spastic quadruplegia
8	15,25	spastic quadruplegia
9	15,6	spastic diplegia
10	14,6	spastic hemiplegia

Table 2. GMFM in patients with cerebral palsy

	GMFM A	GMFM B	GMFM C	GMFM D	GMFM E	TOTAL SCORE	GOAL SCORE
1	96	92	69	18	18	59	35
2	69	35	2	0	0	21	35
3	100	100	98	90	86	95	88
4	94	80	43	15	11	49	29
5	90	58	21	0	0	34	40
6	100	100	95	82	71	90	83
7	84	75	33	0	0	38	64
8	90	20	7	0	0	23	20
9	90	90	83	77	60	80	60
10	96	97	88	74	93	90	84

Table 3. GMFM in group of patients with cerebral palsy

	GMFM A	GMFM B	GMFM C	GMFM D	GMFM E	TOTAL SCORE	GOAL SCORE
Mean	83	69	48	30	28	51	50
SD	±26	±32	±36	±37	±36	±30	±27

Barthel index of activities of daily living (ADL) in every individual patient is presented in Table 4 and the mean values (±SD) in Table 5.

Table 4. Barthel index of ADL in patients with cerebral palsy in percentages

	%
1	45
2	20
3	85
4	35
5	35
6	95
7	35
8	25
9	70
10	100

Table 5. Barthel index of ADL in group of patients with cerebral palsy in percentages

	%
Mean	48
SD	±30

Our participants obtained 20 to 100 points in the test, mean value is 48 ± 30. The correlations between GMFM goal score and Barthel index is high ($r=0.962$) and is significant ($p<0.01$); it can be seen in Fig. 1.

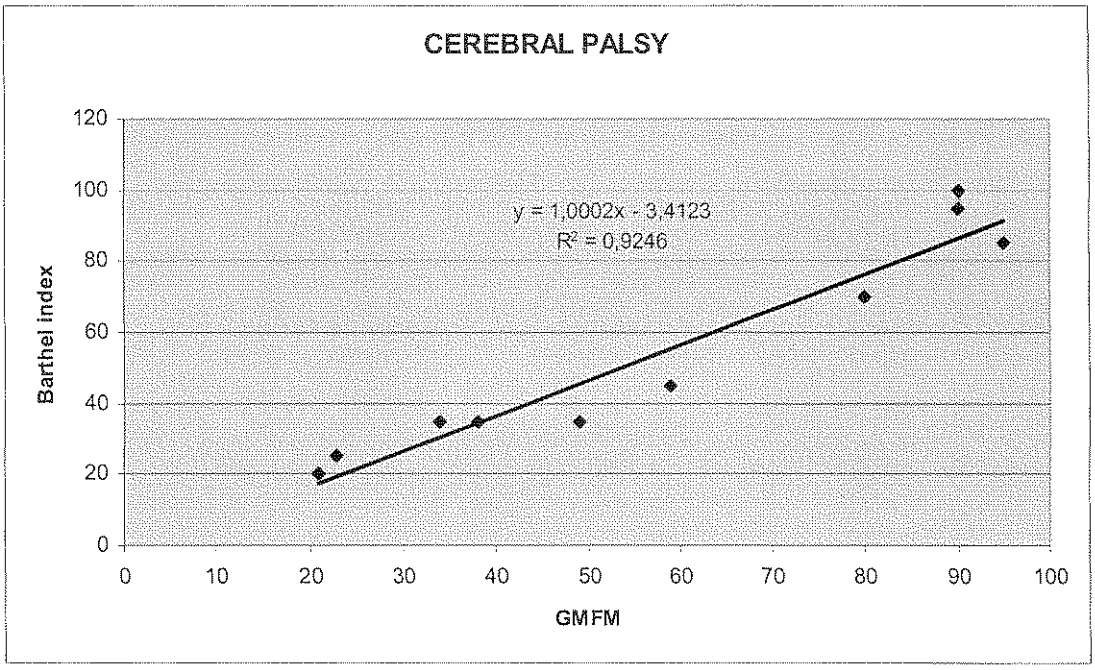

Fig. 1 Correlations between GMFM goal score and Barthel index

DISCUSSION

The study showed the different functional impairment in the group of CP patients. Spastic forms are represented in the same rate as in the population of CP patients (1,4). Both results - of Gross Motor Function Measure and Barthel test – are in accordance with other studies (1,2,3). The results of therapy are controversial. The Greek study proved effects of Neurodevelopment treatment in their group (3), other studies were not successful and do not bring any evidence of effects (1,2). In our institute we treat the patients with different techniques of physiotherapy (Neurodevelopment treatment according to Bobath, the method according to Vojta and other non-neurological approaches) and the continuous evaluation of possible progress is necessary. High correlation between GMFM values and Barthel index indicates that both methods are suitable for this task.

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