PIONEERING TECHNOLOGY: BREAKTHROUGH DIAGNOSTICS IN CARDIOLOGY
CARDIOMETRY

Basic and applied research.
Theory, practice, therapy, engineering, philosophy & methodology.
ISSN 2304-7232 e-Journal
www.cardiometry.net

Editorial board

EDITOR-IN-CHIEF
Prof. V. Zernov, RUS

EXECUTIVE EDITORS
Prof. M. Rudenko, RUS

EDITORIAL ADVISORY BOARD

Prof. Y. Gulyaev, RUS
Prof. R. Baevsky, RUS
Prof. S. Chefranov, RUS
Dr. S. Kolmakov, FIN
Prof. J. Moreno-López, SWE
Prof. V. Polikarpov, RUS
Prof. G. Stupakov, RUS
Prof. V. Tyutyunnik, RUS
Prof. B. Leonov, RUS
Prof. Mohammad Aleem, EGY
Dr. Alberto Alfie, ARG
Dr. Pablo Avanzas, ESP
Dr. Marko Banovic, SRB

Prof. H.R. Horvitz, USA
Prof. P. Mansfield, GBR
Dr. C. Müller, AUT
Dr. O. Voronova, RUS
Prof. V. Vecherkin, RUS
Prof. S. Zaguskin, RUS
Dr. Zied ben El hadj, TUN
Dr. Marwan Refaat, LBN
Dr. Chandra Mani Adhikari, NPL
Dr. Saad Al Bugami, SAU
Prof. Alejandro Barbagelata, USA
Dr. Nancy Aggeli, GRC
Prof. Dimitrios Karakitsos, USA
CARDIOMETRY

No.5 November 2014

Goran Krstacic

New points on ECG: a new valuable source of information
Mikhail Y. Rudenko

Michael Nobel has become Honorary Professor of Russian New University and met the Head of Russian Academy of Sciences

Our congratulations!

Review of papers presented at the ESC Congress 2014 in Barcelona
Dmitry F. Makedonsky

Hagen-Poiseuille flow linear instability
Sergey G. Chefranov, Alexander G. Chefranov

The effects of long-term microgravity on autonomic regulation of blood circulation in crewmembers of the international space station
Roman M. Baevsky, Irina I. Funtova, Elena S. Luchitskaya, Anna G. Chernikova

Noninvasive investigation of the body functional state during night sleep in microgravity
Irina I. Funtova, Elena S. Luchitskaya, Irina N. Slepchenkova, Anna G. Chernikova, Roman M. Baevsky

Paroxysmal atrial fibrillation in 5 months old Afro-Caribbean
Sandra Williams-Phillips

Efficacy of enhanced external counterpulsation: our experience
Chandra Mani Adhikari, Dipanker Prajapati, Suman Thapaliya, Man Bahadur KC

Spotlight on management of hypertrophic cardiomyopathy
Mohammed El-Assaly

Cardiometry: going from theory to praxis. Training
Dear readers!

It is the matter of fact that not only our reading audience has significantly expanded recently, but more important, we note an increasing number of physicians among our readers who successfully apply theory in practice. At the same time it should be stated that a problem of medical education becomes acute. Knowledge obtained by physicians and based mainly on empirical evidence in cardiology hinders their logical way of thinking. That is the reason that our current issue is devoted to the presentation of the key concepts in cardiometry as they can support a practitioner to learn more about capabilities offered by the new science for application in practice.

Cardiometry confirms its status of the new science. Its laws (they are already six now) laid the groundwork for the axiomatic system and furnish a clue to most complicated problems in cardiology one has to face in the research process. Actually, the results obtained from the basic proof and the logical apparatus provide scientists with the unique keys to interpreting new issues occurring in investigations. This makes cardiometry unique in practical use efficacy: a single examination of a patient supported with express diagnostics is quite enough to make a diagnosis, identify the primary cause of changes in the cardiovascular system performance and provide well-defined recommendations how to tackle a problem, if any, by adequate treatment. Moreover, there is a possibility to monitor efficacy of treatment. But at the same time the above advantages conflict with the generally accepted principles of evidence-based diagnostics and therapy in the conventional cardiology. The existing guidelines in the present-day cardiology accompanied by lack of incentives to introduce new educational programs in the system of the medical professional training impede the proper understanding of the cardiac cycle phase analysis logic.

However cardiometry accelerates the rate of its development. It offers more and more new opportunities our journal regularly describes. This release contains not only conceptual papers, but also some practical materials which might be useful for time-saving mastering of innovative diagnostic technologies based on cardiometry.

Good luck!

Cardiometry Editorial Board
Conference Report


Goran Krstacic*, MD, PhD, FESC, ESC WG e-Cardiology Chairperson 2014-2016

1 Director of Institute for Cardiovascular Diseases and Rehabilitation Zagreb, 10000, Croatia, Zagreb, Draskovicva 13

* Corresponding author phone: +385 (1) 4612 290, e-mail: goran.krstacic@zg.t-com.hr

The European Congress on e-Cardiology & e-Health took place in Bern, Switzerland. There were 250 participants from 23 countries and 90 speakers presented papers. The Congress was devoted to the latest advancements in e-Cardiology, e-Health and telemedicine. Scientists and cardiologists could get acquainted with a great variety of papers and participate in discussions. Here I would like to make some general conclusions whilst avoiding detailed considerations of each paper.

Nowadays, the factual evidence available to practitioners is used in information technologies and telemedicine methodologies. Practitioners’ decision-making is limited to the goal to do no harm to patients’ health. Such statements were insufficient for the health care experts who participated in this Congress.

But it is urgently required that data obtained by physicians should allow prediction and modeling of patients’ health. Unfortunately this is not the case today. Such an approach becomes possible in cases where the relevant data on a patient is accumulated and stored automatically in the patient’s records in accordance with the applicable data protection acts. It allows modeling of his actual health state and prediction of outcomes with the use of the accumulated data. To accumulate data from birth till extreme old age is the best option. Modern technologies can provide these options nowadays, but clear standards should be laid down for this purpose. Such standards do not currently exist.

Congress Director Prof. Hugo Saner said in his report that nowadays a huge amount of the information recorded by smartphones and smart e-Health devices does not reach your doctor and data cannot be used in the proper way for decision-making in health care. Preventive cardiology and health care system experts are interested in predicting health. Therefore there is a vast field to be developed by e-Cardiology and e-Health.

I do very much hope that the Congress participants share my opinion. We look forward to learning more about new achievements in effective cardiovascular system monitoring at future Congresses.
Editorial

New points on ECG: a new valuable source of information

Mikhail Y. Rudenko¹*

¹ Russian New University, 105005, Russia, Moscow, 22 Radio St.
* Corresponding author phone: +7 (8634) 312-403, e-mail: cardiocode@mail.ru

Submitted: 12 September 2014
Accepted: 10 October 2014
Published online: 14 November 2014

Keywords

ECG • Cardiac cycle • QRS complex • Point Z • Point L • Point S • Point M1 • Point M2

Imprint

Mikhail Y. Rudenko. New points on ECG: a new valuable source of information; Cardiometry; No.5; November 2014; p.7-11; doi:10.12710/cardiometry.2014.5.711
Available from: www.cardiometry.net/no5-november-2014/new-points-on-ecg

This is an overview aimed at a detailed interpretation of the concept of identification of boundaries in each cardiac cycle, and first it is directed to justification of an introduction of new points on an ECG curve, namely, point L as the end of the blood rapid ejection phase and point Z as the moment of reaching energy balance of myocardial muscle contraction determining the ECG isoline.

The issues associated with the L point have been already described in our journal [1]. Fig.1 exhibits an ECG where all points corresponding to each cardiac cycle phase in accordance with our cardiac cycle phase analysis concept are marked.

Figure 1. Letter designations for identification of boundaries in each cardiac cycle phase on ECG including new points L and Z introduced by the developers of the cardiometry theory

A detailed description of the process of the ECG shape formation has been already presented by us [2]. Here we just intend to demonstrate how the ECG segment sequence is generated (Fig.2). In our opinion, the QRS complex is shaped for the purpose of the initial generation of the proper blood
flow structure. In this case, all heart valves are closed. The SL segment is a phase of pre-loading and can be considered to be a QRS complex, too, but showing lower amplitude since we deal in this interval with the total static tension of the myocardial and septal muscles. At the point L, the pressure level in the ventricle and that in the aorta become equal, and the aortic valve opens. A rheorgam shows this phenomenon as the initial point of a blood pressure rise.

The form of the Lj phase segment follows the shape of the QRS complex, but the j point reflects the start of the slow ejection phase [3-17]. In this case, we can say that the blood pressure applied to the heart muscle fibers starts to drop, and therefore the Lj phase amplitude is low [2].

Of particular interest is an ECG curve of an athlete recorded during heavy lifting and holding for 12 sec. overhead (s. Fig.3 below) [18]. Under the said conditions, a QRS complex is found even after the j point. Our research has shown that the Lj phase and its further repeated manifestations in case of intensive physical load are determined by phosphocreatine processes. To be more exact, it is attributable to those energy resources which are responsible for ATP recovery, and the energy resources are limited. Fig. 3 below shows a decrease in the oscillations after the j point from cycle to cycle. In the classical physics, it is explained according to the well-known concept of oscillatory circuit energy.

Figure 2. ECG segment sequence generated by blood pressures applied to SA and AV nodes which operate as baroreceptors
Based on the above considerations, the authors hereof have introduced new definitions, namely, the next, the second and the third QRS complexes. These QRS’s can be found only in case of significant physical loading during sharp accelerations by athletes. Therefore, a complete ECG curve should contain points and segments as given below (Fig. 4):

The introduction of letter designations for new ECG points according to our original interpretation concept is both of scientific and historical importance. The developers of the original ECG interpretation concept have decided to use initial letters of their last and first names for that purpose. As a result, we obtain the following list of those who made a significant contribution thereto:

Point Z is named after Zernov Vladimir.
Point L is named after Larissa Rudenko.
Point S is referred to by the name of Sergey Rudenko who has first identified the location of this point.
Point M1 is named after Mamberger Konstantin.
Point M2 is named after Makedonsky Dmitry.
Of course, it was not our idea of making ECG points personalized, but the above researchers have made a considerable contribution to the scientific investigations and may be honored by introduction of letters of their names to the new points on ECG as these points is a new information source produced by ECG digital processing.

The foundation of the cardiometry theory is a pioneering mathematical model of hemodynamics. The model describes the conceptual principles of the heart performance which are consistent with the evidence delivered by practice. In actual practice, the mathematical equations [18-20] are used to calculate phase-related volumes of blood on the basis of the respective measured the cardiac cycle phase duration linear values. These equations were named hemodynamic equations by G. Poyedintsev - O. Voronova after their originators.

Cardiometry has already offered a lot of novelties in science, and the authors hereof are sure that every future discoverer has a chance to give his or her name to future detectable laws and phenomena, why not?

References


Michael Nobel has become Honorary Professor of Russian New University and met the Head of Russian Academy of Sciences

Russian New University (RosNOU) chancellor Vladimir Zernov, the President of the Russian Nobelistics Center Vyacheslav Tutunnik, scientists and other members of RosNOU and other universities took part in the conference.

The conference participants discussed the present condition and the prospectives of the Russian science, the Nobel family’s contribution to the development of the Russian science and industry in the XIX – the beginning of the XX centuries (Michael Nobel is the great-grandson of the engineer and manufacturer Ludwig Nobel, the brother of Alfred Nobel – the inventor of dynamite and the founder of the Nobel Prize).

In conclusion to the conference Vladimir Zernov awarded Michael Nobel the RosNOU honorary professor degree on wording 'For the contribution to Russian research and innovation activities abroad'.

On the same day Russian Academy of Sciences held a meeting in which the Academy’s President Vladimir Fortov, the head of RosNOU Vladimir Zernov, the President of the Russian Nobelistics Center Vyacheslav Tutunnik and the Ex-President of the Nobel Family Association and the founder of the Nobel Charitable Endowment, RosNOU’s Honorary Professor Michael Nobel took part.
During the meeting the participants discussed Russia’s contribution to the development of the world’s science, the problems of the positioning of the Russian science in the world and the ways of cooperation between Russian Academy of Sciences and the representatives of the Nobel movement.

Vladimir Fortov expressed thanks to Michael Nobel for his interest in the Russian science and gratitude to the Nobel Committee for their attention to the discoveries of our compatriots.

The participants of the meeting emphasized the fact that it’s the development of science that will determine the state and function of the economy of this or that country for the world leaders in the post-industrial epoch.
Our congratulations!

We are pleased and honored to inform that one of our most prominent authors Mr. Goran Krstacic, MD, PhD, Director of the Institute for Cardiovascular Diseases and Rehabilitation, Zagreb, Croatia, has been elected the Chairperson 2014-2016 of the ESC Working Group on e-Cardiology.

A great deal of this success, in our opinion, must be directly attributed to his strong leadership and the sense of direction that he provides.

Mr. Krstacic, please accept our heartiest congratulations and best wishes for your continued success in your new position!

We expect that this post growing will inspire further scientific cooperation between the CARDIOMETRY Journal and the WG e-Cardiology members within the framework of the ESC activities.

Once again many congratulations and all the best for future growth!
As usual, the Congress of European Society of Cardiology attracted many experts and visitors. 4597 abstracts were presented. It was reported that more than 30000 cardiologists participated there. 15 Clinical Trials Updates, 19 Registry studies and 4 new Guidelines on cardiovascular disease treatment were presented in Barcelona: [http://www.escardio.org/about/press/press-releases/esc14-barcelona/Pages/best-of-esc-congress-2014.aspx](http://www.escardio.org/about/press/press-releases/esc14-barcelona/Pages/best-of-esc-congress-2014.aspx)

Experts highlight new recommendations on myocardial revasculization prepared by the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) in 2014. Several most significant and major researches presented at ESC Congress 2014 should also be noted. Analyzing them we can conclude that they are devoted to new heart failure drugs and medication.

Our experts were more interested in hemodynamics research. We hoped to see some abstracts showing data obtained with the use of the unique capabilities of CARDIOMETRY.

We noted that all the abstracts on hemodynamics were presented in the BLOOD PRESSURE MONITORING AND HAEMODYNAMICS section. However, all the 6 abstracts were devoted to arterial pressure monitoring. The term “hemodynamics” was mentioned neither in the titles nor the texts of the abstracts.

After the detailed analysis, we detected 2 abstracts containing the term “hemodynamics” in its title:


2. Arterial stiffness is a better predictor of left ventricular hypertrophy than the Framingham Risk Score and central hemodynamics: insights from 1,141 never-treated hypertensives. P1092 – P. Xaplanteris, C. Vlachopoulos, N. Ioakeimidis, D. Terentes-Printzios, I. Dima, G. Vyssoulis, C. Stefanadis (Athens, GR)

The papers were presented in the CARDIAC AND ARTERIAL REMODELLING IN HYPERTENSION section. Nevertheless, the characteristic parameters of hemodynamics such as stroke and minute volumes of blood were even not mentioned in them.

It can be concluded that CARDIOMETRY, i.e., the science based on the hemodynamics description, is still not widely discussed at major forums. Firstly, the reason is that the proper hemodynamic data can be obtained using the device Cardiocode only. The above researchers still do not use it.

We hope the topics of hemodynamics will be discussed more thoroughly at the future ESC Congress in London.
**Report**

**Hagen-Poiseuille flow linear instability**

Sergey G. Chefranov, Alexander G. Chefranov

1 Obukhov Institute of Atmospheric Physics of RAS, 119017, Russia, Moscow, Pijevskii str.3

2 Eastern Mediterranean University, Famagusta T.R. North Cyprus via Mersin 10, Turkey

* Corresponding author phone: +7 (916) 947-63-58, e-mail: schefranov@mail.ru

Submitted: 21 July 2014
Accepted: 15 August 2014
Published online: 14 November 2014

**Abstract**

In the suggested here linear theory of hydrodynamic instability of the Hagen-Poiseuille flow it is counted the possibility of quasi periodic longitudinal variations, when there is no separation of the longitudinal and radial variables in the description of the disturbances field. It is proposed to use the energetic method and the Galerkin approximation method that takes into account existence of different values of longitudinal variability periods for different radial modes corresponding to the equation of evolution of extremely small axially symmetric velocity field tangential component disturbances and boundary condition on the tube surface and axis. We found that even for two linearly interacting radial modes the HP flow may have linear instability, when $\text{Re} > \text{Re}_{th}(p)$ and the value $\text{Re}_{th}(p)$ very sensitively depends on the ratio $p$ of two longitudinal periods each of which describes longitudinal variability for its own radial mode only. Obtained from energetic method for the HP flow linear instability realization minimal value $\text{Re}_{th,\text{min}} \approx 704$ (for $N=600$ radial modes) and from Galerkin approximation $\text{Re}_{th,\text{min}} \approx 448$ (for $N=2$ modes with $p=1.516$) which quantitatively agrees with the Tolmin-Shlihting waves in the boundary layer arising, where also the threshold value $\text{Re}_{th} = 420$ is obtained. We state also the agreement of the phase velocity values of the considered in our theory vortex disturbances with the experimental data on the fore and rear fronts of the turbulent “puffs” spreading along the pipe axis.

PACS: 47.20.Ft, 47.27.Cn, 47.27.nf

**Keywords**

Linear hydrodynamic instability • Spiral vortex flow • Pipe flow

**Imprint**

Sergey G. Chefranov, Alexander G. Chefranov. Hagen-Poiseuille flow linear instability; Cardiometry; No.5; November 2014; p.17-34; doi:10.12710/cardimetry.2014.5.1734
Available from: www.cardiometry.net/no5-november-2014/flow-linear-instability
Introduction

Fundamental and applied problem of defining of the turbulence arising mechanism for the Hagen-Poiseuille (HP)\(^1\) flow more than century is left mysterious because of the linear stability paradox of the flow with respect to extremely small by amplitude disturbances for any Reynolds number value
\[ \text{Re} = \frac{V_{\text{max}} R}{\nu} \]
(where \( V_{\text{max}}, \nu, R \) are the maximal HP flow near axis velocity, kinematic viscosity coefficient, and pipe radius respectively) [1-4]. Obvious contradiction with experiments corresponding to the paradox now is used to be coped with based on an assumption of permissibility of the HP flow instability with respect to disturbances having sufficiently large finite amplitude strict non-linear mechanism only [5-10]. The basis for such the assumption (see [3, 4]) gives one side interpretation of experiments [11] in which many-fold increase of the threshold Reynolds number value \( \text{Re}_{th} \) up to 100000 is achieved due to the increase of the level of smoothness of the streamlined pipe surface. In this interpretation, only correlation between the surface smoothness increase and resultant decrease of the average amplitude of the original disturbances is taken into account. At the same time, noted even by O. Reynolds [1] extremely high sensitivity of the value of \( \text{Re}_{th} \) to the initial disturbance does not exclude possibility of impact on \( \text{Re}_{th} \) of not only amplitude but also space-time characteristics of the disturbances also caused by non-ideal smoothness of the streamlined surface. Actually, for example in the experiment [12], it is found that under the fixed amplitude of artificially excited disturbances, instability of the HP flow emerges only in some definite narrow range of the disturbances’ frequencies.

In the present work, we show that possibility of linear absolute (i.e., non-convective [4]) instability of the HP flow is defined by the value of complementary to the Reynolds number \( \text{Re} \) control parameter \( p \), which characterizes frequency-wave features of the disturbances and determines the value of the threshold Reynolds number \( \text{Re}_{th}(p) \) independently from the amplitude of the initial disturbances. Such complementary parameters are easily introduced in all known HP flow modifications – in the cases of the flow in the pipe with the existence of near-axis cylinder [13], in the pipe with elliptic cross section [14], in the rotating pipe [15, 16], and even for a flow transferring particles of finite size in a pipe [17]. In all these examples, there already exists complementary to the Reynolds number control parameter \( p \) and the linear stability theory paradox is absent. This examples show that “circumvention” (see [5]) of the HP flow linear stability paradox due to the consideration of strict finite amplitude only mechanism of instability of the flow “hardly can satisfy anybody” [18].

Introduction of such a complementary parameter \( p \) for the HP flow is already not as obvious as for the HP flow modifications in [13–17]. It however is performed below on the base of pointed by O. Reynolds [1] (and then by W. Heisenberg also for the flat Poiseuille flow, see in [4, 6]) concept of dissipative instability mechanism\(^2\) of the HP flow related with the action of molecular viscosity \( \nu \) near the very solid boundary. According to [1], the mechanism manifests itself in the form of

---

\(^1\) HP flow is by definition a laminar stationary flow of the uniform viscous fluid along the static straight linear and unbounded in length pipe with round same along the whole pipe axis cross section

\(^2\) Such a mechanism is naturally realized in the systems having disturbances with negative energy [19-22], for example, for threshold emergence of vortexes (rotons) in the flow of super-fluid helium in a capillary [19].
spontaneous one-step emergence for \( \text{Re} > \text{Re}_{th} \) of vortexes having character size \( L_v \), «...that is already not growing as it was expected with the growth of the velocity amplitude [1]». That is why, the value \( L_v \) must significantly differ also from the length scale \( l_v = \nu / V_{\text{max}} \) that leads to the Reynolds number defining as \( \text{Re} = R / l_v \) and explicitly depending on the stream velocity maximal amplitude value. Such scale \( L_v \) seemingly related also with the level of the streamlined pipe surface smoothness, may together with the of radius \( R \) define not amplitude only but also frequency-wave initial disturbance parameters, for example, their longitudinal along the pipe axis (axis \( z \)) spatial periods. The ratio of the periods \( p = \frac{L_v}{R} \) as it is shown below is a new complementary parameter defining the HP flow linear instability threshold with respect to extremely small by amplitude vortex disturbances. Note that for any Reynolds number value, \( p \) can vary in vast range from \( p<<1 \) to \( p>>1 \).

It is suggested here to use disturbance structure representation in the form of two radial modes each of which having its own period of longitudinal variability differing from that of the other mode. Such representation corresponds to the observed conditionally periodic Tolmin-Shlihting (TS) waves emergence of which (caused also by near-boundary action of the molecular viscosity) precedes blow-like emergence of the turbulence in the near-boundary layer [23-25]. Besides that, even in [2, 26], it is noted that usually considered in the linear stability theory “normal” periodic by \( z \) disturbances fields obviously don’t correspond to the structures observed in the experiments, for which different longitudinal periods for different radial modes are characteristic.

In the present work, it is shown that leaving off the assumption of separation of the longitudinal and radial variables defining spatial disturbance variability leads now to the finite value of the minimal threshold Reynolds number \( \text{Re}_{th} = 448 \ ( p \approx 1.53..) \). Close to it threshold Reynolds number value is characteristic also for the observed threshold for the transition from the laminar resistance law to another one [2, 27] and for the conditions of excitation of TS waves in a boundary layer [25]. We have conducted comparison of the considered theory with the experimental data for the flow in the pipe [28-30] and also with the conclusions of the stability theory (Tolmin-Shlihting and Lin) and experimental data on the stability of laminar near-boundary layer [31]. We obtained correspondence not only of the quantitative values of the critical Reynolds number for linear exponential instability for the HP flow and for TS waves excitation (where also \( \text{Re}_{th} = 420 \)), but also similar shapes of instability regions (bounded by the curves of neutral stability). This also confirms expected above similarity of their viscous dissipative realization mechanisms.
Materials and methods

1. The statement of the problem

Let us consider known (see [4]) representation of the HP flow in the cylindrical reference frame 
\((z,r,\phi)\): 
\[ V_{0r} = V_{0\phi} = 0, V_{0z} = V_{\text{max}}(1 - \frac{r^2}{R^2}) \],
where 
\[ V_{\text{max}} = \frac{R^2}{4\rho \nu} \frac{\partial p_0}{\partial z} \],
the fluid density \( \rho = \text{const} \), \( \frac{\partial p_0}{\partial z} \) is the constant value of the pressure gradient \( p_0 \) along the axis of the pipe of radius \( R \), and \( \nu \) is the coefficient of kinematic fluid viscosity.

The linear stability of this flow is considered for the more simple case, when there exist only extremely small disturbances of tangential component of velocity and the stability to the “normal” pure periodic longitudinal disturbances is easy to determine at all Reynolds numbers. We demonstrate here that, when instead of this “normal” form, it is taken into consideration quasi periodic longitudinal variability of disturbances, it is possible for HP flow to be linear unstable for the finite Reynolds numbers larger than some threshold value.

In the axially symmetric case (i.e. for extremely small disturbances not depending on the angular coordinate \( \phi \)) linear instability of the HP flow can be defined by the tangential velocity component \( V_\phi \) only, which meets the following equation in dimensionless form (when \( y = r/R, z = z/R, \tau = t\nu/R^2; \text{Re} = V_{\text{max}} R/\nu \)) and corresponding boundary condition on the rigid surface of the tube at \( y=1 \) and at the axis of the tube at \( y=0 \):

\[
\frac{\partial V_\phi}{\partial \tau} + \text{Re}(1 - y^2) \frac{\partial V_\phi}{\partial x} = \Delta V_\phi - \frac{V_\phi}{y^2}; \Delta = \frac{1}{y} \frac{\partial}{\partial y} y \frac{\partial}{\partial y} + \frac{\partial^2}{\partial x^2};
\]

\[ V_\phi(y = 1) = 0; V_\phi(y = 0) = 0 \]  

(1)

where the value \( V_\phi \) in (1) is also dimensionless (normalized on \( V_{\text{max}} \)).

When other components of velocity disturbances are absent in this axially symmetric case the equation and boundary conditions (1) are also useful to describe evolution of finite amplitude disturbances, not only extremely small ones. The solution of equation (1) must be found with boundary condition \( V_\phi = 0 \) at \( y=0 \) because the angular velocity of rotation on the axis of the tube must be finite. It is useful to represent the solution of equation (1) satisfying boundary condition of (1) as follows:

\[
V_\phi = e^{i\lambda \tau} V; V = \sum_{n=1}^{N} A_n(x) J_1\left(j_{1,n} y\right); J_1\left(j_{1,n}\right) = 0; \lambda = \lambda_1 + i\lambda_2; A_n = A_{1n} + iA_{2n},
\]

(2)

In (2), \( J_1 \) is the Bessel function of the first order and the value \( N \) must be considered as infinite for obtaining the exact solution of (1) with mentioned in (1) and (2) boundary conditions on \( y \) and \( x \).
Thus, instead of the traditional “normal” periodic form (which coincides with (2), when in (2) \( T_n = T = \text{const} \) for all \( n \)) we introduce in (2) the new definition of individual periodic boundary condition along the infinite tube for each radial mode with number \( n=1,2,\ldots,N \).

The statement of the problem (1), (2) for the longitudinal quasi periodic disturbances \( n=1, 2,\ldots, N \), is different from previously used in linear theory of hydrodynamic stability, where the pure periodic conditions along the tube are considered. In the experimental data [2, 26], from the other side, only quasi periodic variations take place and (2) is better complying to them than traditional “normal” periodic form of disturbances.

2. Energy consideration

Let us consider, on the base of (1), (2), evolution of the average energy (on the unit of mass):

\[
E = \frac{\langle V_x V_x^* \rangle}{2} = e^{2\lambda t} \frac{\langle V V^* \rangle}{2};
\]

\[
I_0 = \frac{\langle V V^* \rangle}{2} = 2 \int_0^1 dy y \frac{1}{T_{\text{max}}} \int_0^{T_{\text{max}}} dxVV^*.
\]

For example, in (3), we may take \( T_{\text{max}} = 1/j_{1,1} \).

From (1), it is possible to obtain the following equation for the exponential index \( \lambda_i \) of energy growth (for \( \lambda_i > 0 \)) or fall (if \( \lambda_i < 0 \)) in time:

\[
2\lambda_i I_0 = \text{Re} I_1 - I_2; I_2 = \left\langle V^* (\Delta V - \frac{V}{y^2}) + V (\Delta V^* - \frac{V^*}{y^2}) \right\rangle.
\]

\[
I_1 = -\left(1 - y^2\right) \frac{d}{dx} \left(\frac{\partial (VV^*)}{\partial y}\right) = \frac{1}{T_{\text{max}}} \sum_{n=1}^{N} \sum_{m=1}^{N} q_{nm} (A_n(T_{\text{max}})A_m^*(T_{\text{max}}) - A_n(0)A_m^*(0)) - I_{11},
\]

\[
I_{11} = \sum_{n=1}^{N} J_2^2 (j_{1,n}) (A_n(T_{\text{max}})A_n^*(T_{\text{max}}) - A_n(0)A_n^*(0)),
\]

\[
q_{nm} = q_{mn} = 2 \int_0^1 dy y^3 J_1 (j_{1,n} y) J_1 (j_{1,m} y);
\]

\[
I_2 = \sum_{n=1}^{N} J_2^2 (j_{1,n}) \frac{1}{T_{\text{max}}} \int_0^{T_{\text{max}}} dx \left[ 2 j_{1,n}^2 A_n A_n^* - A_n \frac{d^2 A_n^*}{dx^2} - A_n^* \frac{d^2 A_n}{dx^2} \right] > 0,
\]

where \( J_2 \) is the Bessel function of the second order.

Let’s consider a special case, when in (2)–(4), \( A_n(x) = A_{n0} \exp(i2\pi\alpha_n x + i2\pi\beta_n) \), and, from (4), we have:

\[
I_2 = 2 \sum_{n=1}^{N} \left( j_{1,n}^2 + 4\pi^2 \alpha_n^2 \right) A_{n0}^2 J_2^2 (j_{1,n}); I_0 = \sum_{n=1}^{N} A_{n0}^2 J_2^2 (j_{1,n});
\]

\[
I_1 = -2\alpha_i \sum_{n=1}^{N} \sum_{m=1}^{N} q_{nm} A_{n0} A_{m0} \sin(\pi|p_n - p_m|) \sin(\pi|p_n - p_m| + 2\pi|\beta_n - \beta_m|),
\]
where \( p_n = \alpha_n / \alpha_1 \) (\( p_1 = 1; p_2 = \alpha_2 / \alpha_1 \equiv p; p_3 = \alpha_3 / \alpha_1 \) and so on). For the convergence of sums in (5), (6) in the limit of \( N \to \infty \), the following inequality for amplitudes shall hold: \( A_{0n} < 1 / j_{n,k}^{1+\delta}, k > 0 \).

For \( A_{0n} = A_0 / j_{1,n}^{1+\delta} \) when \( k>0 \) and \( \beta_n = \beta = const \) for all \( n \), from (5), (6), we can obtain the following criterion of the HP flow linear instability (only for the cases with \( c>0 \) in (7)):

\[
\text{Re} > \text{Re}_{Eh}^{min} = \frac{2ab}{c}. \tag{9}
\]

In (9), for the limit of \( N \to \infty \), if \( p_n = \alpha_n / \alpha_1 = j_{1,n} / j_{1,1}, n=3,4,\ldots \), there is only one free continuous parameter \( p \) on which \( \text{Re}_{Eh}^{min} (p) \) can be minimized. It allows determining of the threshold Reynolds number absolute minimum \( \text{Re}_{thabs}^{min} = 704 \) when \( p=0.481 \) and \( k=0.7 \) (minimization was made over \( p \) and \( k \)). Dependence of the right hand side of (9) on \( p \) is presented in Fig.1d for \( N=600, k=0.7 \).

Thus, only when \( \nu \neq 0 \) in (1), it is possible to expect realization of the HP flow viscous dissipative instability for some above threshold Reynolds numbers, \( \text{Re} > \text{Re}_{th}^{*} \). Actually, when \( \nu = 0 \), the right-hand side of (1) also turns to zero (if considering (1) in its original dimensional form). In that case, only convective disturbance transfer without change of its form and amplitude in time takes place. From (4), it follows that instability of the HP flow obviously is not realizable also in the case of the pure periodic variability of \( \phi \) along the pipe (see also (24.7) in [2]) when \( I_i = 0 \) and \( \lambda_i < 0 \) in (4). If to refuse from that, so called "normal", periodic form for the disturbance field in (1), as we do in (2), it is possible to obtain another result from (4) allowing to realize the conditions, when in (6)-(8), the value of \( I_i \) is positive, \( I_i > 0 \), and, under condition (9), exponential growth of the disturbance energy with \( \lambda_i > 0 \) takes place.

Let’s also note that due to the consideration in (1) of only velocity field tangential component disturbances, conservation of the mass stream through the cross section of the pipe for the superposition of the main flow and disturbance field is provided identically. Natural emergence of such disturbances in an axially symmetrical stream really may be hindered although it can’t be fully excluded due to the possibility of presence of corresponding randomly-non-uniform smoothness of
the streamlined pipe surface. In the laboratory simulation of the HP flow such disturbances can be easily artificially created (see [12]). Let’s note also that combination of the main stream and considered disturbance field has non zero value of integral helicity.

For the disturbance representation in the form (2), on the boundary at $y=1$, only vortex field radial component $\omega_r = -\frac{\partial V_y}{\partial x}$ shall turn to zero. The value of the longitudinal vortex field component $\omega_z = \frac{1}{y} \frac{\partial (yV_y)}{\partial y}$ on the boundary at $y=1$ has already non zero value that corresponds to the character of forming of the vortex disturbances due to interaction of the stream with the solid pipe wall caused by viscosity forces.

In the considered energy theory, we have used for amplitudes $A_n$, characterizing different radial modes, only restrictions related with the necessity of convergence of the sum $I_\tau$ in (5).

3. The Galerkin–Kantorovich and Bubnov-Galerkin methods

On the base of using the Galerkin–Kantorovich method, for the coefficients $A_n$, characterizing amplitudes of the linearly interacting disturbance field radial modes, from (1), (2), we get the following system of equations in dimensionless form:

$$\frac{\partial A_m}{\partial \tau} + f^2_{m,n,m} A_m - \frac{\partial^2 A_m}{\partial x^2} + \text{Re} \sum_{n=1}^{N} P_{nm} \frac{\partial A_n}{\partial x} = 0,$$

where $m=1,2,3,\ldots$. In (10), constant coefficients $P_{nm}$ have the form

$$P_{nm} = \frac{2}{J^2_{j_{1,m}}(j_{1,m})} Q_{nm}; \quad Q_{nm} = \int_0^1 dy y(1-y^2)J_1(j_{1,n}y)J_1(j_{1,m}y),$$

where $J_2$ are the Bessel functions of the second order and the linear with respect to $y$ term under the integral sign yields in $P_{nm}$ the contribution in the form of unity matrix $\delta_{nm} = \begin{cases} 1, n = m \\ 0, n \neq m \end{cases}$. For $N = 1$ in (10), the last term can be excluded by Galileo transformation and hence for $N = 1$, there is no opportunity of the global absolute instability of the HP flow. In that relation, we shall consider (10) in the simplest non-trivial case $N = 2$, that allows already to resolve the HP flow linear stability paradox and leads to the conclusions quantitatively agreeing with the experimental data [29, 31].

As it was already noted, observed in the experiments field structures do not correspond to strictly periodic along the pipe axis disturbances changes (see above and [2, 26]). More over, in [26], it is noted that different radial modes (defining dependence of the disturbances on the radial coordinate) have corresponding differing each from the other variability periods along the pipe axis. This behavior of the observed disturbances change can be modeled with the help of the use in the representation of the system (10) solution an assumption on the difference of the longitudinal periods along the pipe axis for radial modes with different values of index $m$. Such a requirement corresponds to the introduction for each of these modes of its own, independent from the other
modes, periodical boundary condition on $x$. In the result, there emerges necessity in the use of the adequate to the pointed boundary conditions Galerkin’s approximation of the system (10) solution. Let in (10), for $N=2$, amplitudes $A_1$ and $A_2$ have the form of the running waves with different periods along the pipe axis:

$$A_1 = \sum_{n=1}^{M} A_{n10} e^{\lambda \tau + i x 2 \pi n}, \quad A_2 = \sum_{n=1}^{M} A_{n20} e^{\lambda \tau + i x 2 \pi n},$$  

(12)

where $A_{n10}$ and $A_{n20}$ are the constant values. Meanwhile, complementary to the Reynolds number $Re$ control parameter can be defined as $p = \frac{\alpha}{\beta}$ for any $\alpha$ and $\beta$. Using (12), from (10) when $N=2$, we get on the base of using of Bubnov-Galerkin weighed differences method the following system for $2M$ unknown constant coefficients appearing in (12) under the symbols of summation:

$$A_{n10}(\lambda + j_{11}^2 + 4 \pi^2 \alpha^2 m^2 + i 2 \pi \alpha n P_{11} Re) + \sum_{n=1}^{M} i 2 \pi \beta n P_{21} Re I_1(n,m) A_{n20} = 0;$$

$$\sum_{n=1}^{M} i 2 \pi \alpha n P_{22} I_2(n,m) Re A_{n10} + A_{n20}(\lambda + j_{12}^2 + 4 \pi^2 \beta^2 m^2 + i 2 \pi \beta n P_{22} Re) = 0;$$

$$I_1 = \alpha \int_0^{1/\alpha} dx \exp(i 2 \pi \alpha (\beta - \alpha)); I_2 = \beta \int_0^{1/\beta} dx \exp(i 2 \pi \alpha (\alpha - \beta)); I_1 I_2 = -\frac{p \sin(\pi p) \sin(\pi / p) e^{i \pi (p+1)/ p}}{\pi^2 (1 - p)^2},$$

(13)

For simplicity, let’s consider the case $M=1$ in system (12) (i.e., farther, we shall use $A_{110} \equiv A_{10}; A_{120} \equiv A_{20}$).

In the result, the system (13) is transformed into a uniform system with constant coefficients for the unknown values $A_{10}$ and $A_{20}$. From the condition of solvability of this system for the non zero $A_{10}$ and $A_{20}$, we define the value of the exponent $\lambda = \lambda_1 + i \lambda_2$ depending on dimensionless parameters Re, $p$ and $\beta$ (see (A.1) and (A.2) in Appendix).

It is interesting also to consider more general cases with $N>2$ and $M>1$. Here we note only permissibility of the very fact of existence of linear exponential (not algebraic, with the power law of growth with time) instability of the HP flow stated in the present work. Let’s note that even if in the system (10), to turn the kinematic viscosity coefficient to zero, then this does not exclude as for (1) possibility of the HP flow linear instability realization. It is related with the fact that already the very
inference of (10) from (1) and (2) for \( N>1 \) is based on the finiteness of the kinematic viscosity coefficient in (1).

The condition of existence of linear exponential instability has the form (A.3). For \( \text{Re} \gg 1 \), (A.3) may be reduced to (A.4). Meanwhile, the value \( \beta \), defined in (A.5), minimizes the expression for \( \text{Re}_{th} \) in (A.4) and defines the following condition of the HP flow linear instability condition (giving the estimate from below of the exact value \( \text{Re}_{th} \) defined from (A.3)):

\[
\text{Re} > \text{Re}_{th} = \frac{\pi^2 (1-p)^2 F}{P_{12} P_{21} p^2 |S|}^{1/2},
\]

where:

\[
S = \sin \frac{\pi}{p} \sin \frac{\pi}{p} \sin \left( \frac{1}{p} + p \right),\quad B = \frac{S}{|S|} (p P_{11} - P_{22}),
\]

\[
F = (j_{1,2}^2 + j_{1,1}^2)(1+p^2)A^2 + (j_{1,2}^2 - j_{1,1}^2)(1-p^2)B^2 + 2AB(j_{1,2}^2 - p^2 j_{1,1}^2),
\]

\[
A^2 = B^2 - \frac{4SP_{12}P_{21}p^2 \ctg \pi (p + \frac{1}{p})}{\pi^2 (1-p)^2} \quad \text{for} \quad P_{11}, P_{22}, P_{12}, P_{21} \text{ from (11)},
\]

because for any \( p \), inequality \( A^2 > 0 \) holds.

In the condition (14), providing realization of the HP flow linear instability realization Reynolds number threshold value can tend to infinity \( \text{Re}_{th} \rightarrow \infty \) only for such \( p \), for which the denominator in (14) turns to zero. It takes place for \( S = 0 \), when the value of the ratio of longitudinal periods is equal to one of the following irrational numbers \( p = k/p_k = k, \quad p = p_{1/k} = \frac{1}{k} \), or equals to one of the irrational numbers defined by the following equality \( p = k/\sqrt{k} = \frac{k + 1 + \sqrt{(k+1)^2 - 4}}{2} \) for any integer \( k \). For \( p \), related to the intervals of variability \( p \) between any two neighboring values \( p_k, p_{1/k}, p_{\sqrt{k}} \), the value \( \text{Re}_{th} \) in (14) is a function of \( p \), having one local minimum on each of the mentioned intervals (see Fig. 1,b). And the value of the absolute minimum \( \text{Re}_{th}^{\min} \approx 442 \) in (14) is reached for \( p \approx 1.53.. \), close to the value of the “golden” ratio \( p_g = \frac{1 + \sqrt{5}}{2} \approx 1.618.. \) (i.e., the limit of the infinite sequence of the ratios of two neighboring Fibonacci numbers each of which is equal to the sum of two previous numbers: 1, 2, 3, 5, 8, 13, 21, etc.). For the same \( p \), from the exact condition (A.3), we get close value of the absolute minimum \( \text{Re}_{th}^{\min} \approx 448 \) (see also Table in the Appendix where conclusions on the base of (A.3) and (14) are compared).
Results and Discussion

The comparison with experimental data and results of TWs (travelling waves) numerical simulation

1. Found value $\text{Re}_{th}^{\min} \approx 448$ corresponds to the interval of values $\text{Re} \in 300 \div 500$, noted in experimental observation of the threshold transition of the laminar resistance law (for a flow in the pipe) to another already non laminar (but yet not obviously turbulent) resistance mode [2, 27] and for Tolmin-Shlihting (TS) waves in the near wall region of the boundary layer [25]. Observed in [1] and other experiments (see references in [29, 30]) unusual sensitivity of the value $\text{Re}_{th}$ to the initial disturbances, actually, corresponds to the obtained in (14) dependency of $\text{Re}_{th}$ on $p$, when, for example, $\text{Re}_{th}$ in (14) changes nearly 600 times only when $p$ changes from the value 0.12 to the value 0.11. Neighboring local minima of $\text{Re}_{th}$ in (14) also may significantly differ each from the other. For example, for the value $p \approx 2.23$, we have in (14) $\text{Re}_{th} \approx 1982$, and for the value $p \approx 3.86$, already we get $\text{Re}_{th} \approx 84634$. In the scaled form, fragments of the neutral curve, corresponding to the condition (14) (see Fig. 1b), are given on Fig. 1a) in the form of dependency of the value $1/2p$ on $\text{Re}$. They are plotted on the taken from the paper [31] Fig.12, on which theoretical (of Lin and Shlihting) neutral curves and respective experimental data, related with the determining instability emergence threshold in a boundary layer, are given. Obvious correspondence of the results following from Fig. 1a) allows us making the conclusion also about similarity of the linear dissipative instability mechanisms realized for the HP flow (when meeting the condition (14) or (A.3)), as well as for Tolmin-Shlihting waves excitation in a boundary layer.

2. Conditionally periodic with respect to $x$ structure of the initial disturbances field $V \phi$ in the representation of the solution (1) in the form (2), (12) agrees with the observed (in [29]) wave velocity field tangential component disturbances changes along the pipe axis. It is especially obvious near very turbulence dying threshold for $\text{Re} \approx 1750$, when on Fig. 5d in [29], it is possible to recognize pairs of characteristic longitudinal variability periods ratios of which are close to the values $p \approx \frac{8}{5} = 1.6$ and $p \approx \frac{13}{8} = 1.625$ which are close to the value of the “golden” value of the periods ratio $p_g = 1.618...$

3. On the Fig. 2a) (where Fig. 4 from [30] is used as a basic), dependency on $\text{Re}$ of the turbulent spot rear front constant velocity observed for the flow in a pipe is given as well as respective experimental data from [28], scaled by the average flow velocity. There, data are given from [28], corresponding to the turbulent spot rear front velocity description (blue triangles), as well as that of the fore front (light triangles). Also, there, results are given following from the TW in the pipe non-
linear theory [8], and also conclusions of the present work for the phase velocity

$$V_p = -\frac{\lambda_2 V_{\text{max}}}{2\pi \beta \text{Re}}$$

(scaled by the HP flow average velocity: $V_{av} = \frac{V_{\text{max}}}{2}$). The value of the phase velocity is defined in (A.6) from $\lambda_2$ in (A.2) for the neutral curve (i.e. under condition $\lambda_1 = 0$). In the present theory, the estimates $V=1.4$ and $V=0.8$ for the velocities of the fore (leaving the average stream behind) and rear (remaining behind the average stream) fronts of the vortex disturbance in the units of the HP flow average velocity. Experimental data [28, 30] give respective values $V = 1.2$ and $V= 0.75$, and numerical calculations on the base of the non-linear theory [8] yield the possibility of the change of $V$ from 1.55 to 0.95. In the result, conclusions of the present linear theory lead to the better agreeing with the experimental data compared with those of the non-linear theory [8], especially in the estimate of the rear front velocity which for the present work is $0.2V_{av}$, for the experiment is $0.25V_{av}$, and for the non-linear theory is $0.05V_{av}$.

Thus, conducted comparison of the suggested theory with the observation data and results of the non-linear theory shows that the data and the conclusions of the present HP flow linear instability theory satisfactory quantitatively and qualitatively agree.

Conclusions

The obtained in the present work new conclusion on possibility of the proof of existence of linear instability for the HP flow is based on the analysis of the system (10) inferred from the initial equation (1) for the evolution of the velocity field tangential component disturbances under condition that the right hand side of (1) is non-zero due to the finiteness of the kinematic viscosity coefficient. Otherwise, when the coefficient is equal to zero, from (1), in principle, it is not possible to get evolution equations for linearly interacting each with the other radial modes and come to the conclusion of the HP flow linear instability. That is why, the mechanism of the found out HP flow linear instability can be called dissipative, and the very instability to consider as the dissipative instability.

Earlier, such hydrodynamic instability dissipative mechanism was considered in the works of L. Prandtl (1921-22) when investigating laminar boundary layer stability, and also of W. Heisenberg (1924) and Lin C. C. (1944-45) when establishing flat Poiseuille flow linear instability (see also [23] and references therein). Qualitative explanation of the physical sense and possibility of appearance of dissipative instability in the problems of hydrodynamic stability are discussed in [18] on the base of elementary accounting of the delay effects on example of an oscillator with the friction linear with respect to velocity. Substantial understanding of the phenomenon of the dissipative instability for HP and other flows near solid boundary surface may also be obtained using a method similar to the one suggested by L.D. Landau in [19] for estimation of the critical velocity of motion of the super-fluid liquid in a capillary. In [19], from the condition of negativity of the energy of an elementary vortex disturbance when for the velocities exceeding that critical value due to the viscous interaction of the
stream with the capillary wall, there emerges a vortex disturbance (roton) destroying the laminar super-fluid state of the liquid motion. For the HP flow, for example, also it is interesting to conduct similar to [19 – 22] research aiming defining conditions for realization of the dissipative instability related with the threshold character of the emerging vortex disturbance energy becoming negative valued (in an appropriate inertial reference frame) when exceeding some definite critical Reynolds number.

Let us note, however, that in the present work, to get for the HP flow the conclusion on linear instability, accounting of finiteness of the viscosity is important only on the stage of getting, from the equation (1), the system (10) that defines evolution with time and along the pipe axis, for \(N>1\), of the linearly interacting radial disturbance modes. Already in (10) it is possible to consider the limit of infinitely large values of \(Re\), corresponding to the ideal liquid with zero viscosity. Meanwhile, it is important only to preserve the suggested above consideration of the linear hydrodynamic stability problem for the very case of the boundary conditions individually defined for each of the both considered (for \(N=2\)) radial disturbance modes. Only in that case, it is preserved the obtained conclusion about possibility of the HP flow exponential instability but now instead of two control parameters, \((Re, p)\), defining the instability region (depending on the wave number \(\beta\)), in the limit of zero viscosity, there will be left only the parameter \(p\). In the present work, such a limit of zero viscosity for the system (10) was not considered. Such an investigation on the base of the linear system of interacting radial modes (10) for \(N=2\) may be interesting in relation with available works on simulation of the processes of instability formation in the flow in a pipe based on the use of the concept of ideal (non-viscous) disturbances describing non-linear pair-wise interacting TWs with small but finite amplitude [32-34]. At the same time, we show in the present work that for the finite value of the kinematic viscosity coefficient, consideration of the limit \(Re>>1\), yielding the formula (14) for estimation of the minimal threshold Reynolds number gives not large difference in the value of the estimate (since it was obtained the value \(Re_{th} = 442\)) from the exact formula (A.3), where \(Re_{th} = 448\).

Let us note that the considered double vortex-wave structure of the spatial disturbance field variability is in the qualitative agreement with the data of laboratory [35] and numeric [36, 37] experiments in the pipe. This is witnessed also by the conducted in the previous paragraph comparison of the conclusions of the present theory with the experimental data and results of numerical modeling of instability development for the flow in the pipe. And in [36], for example, there were obtained estimates of the turbulent spot phase velocity \(V=0.9\) and \(V=1.1\) (in the units of the flow in the pipe average velocity), similar to the presented above.

The radial modes have differing each from the other longitudinal variability periods that corresponds to the use of representation (12) for them. And according to (14), linear exponential instability is found to be possible not only for almost all irrational values of ratios of such longitudinal periods \(p\), but also for the rational values of \(p\), not coinciding with \(p = \frac{k}{pp} = k\) or \(p = \frac{1}{k}\) for integer \(k (k=1, 2, 3..)\). An exemption from all possible irrational values \(p\) constitute only defined from (14).
irrational numbers $p = p\sqrt{k} = \frac{k + 1 \pm \sqrt{(k + 1)^2 - 4}}{2}$, $k = 1, 2, \ldots$, for which, vice versa, $\text{Re}_{th} \to \infty$ in (14) and the HP flow linear instability can’t be realized.

For $p$ not equal to the noted above values $p_\sqrt{k}$, such an integral helicity can exponentially grow with time when realizing HP flow linear instability for $\text{Re} > \text{Re}_{th}$, where the threshold Reynolds number value $\text{Re}_{th}$ is defined in (14) and (A.3).

The conclusions of the present work allow filling the well-known gap in the non-linear theory [7, 8], when instead of the linear exponential instability up to now it was necessary to consider the stage of the seed algebraic instability (where small initial disturbances can only locally in time grow tending to zero for $t \to \infty$).

Let us note also that it is reasonable to revise also the mentioned above problems on linear stability for the flat Couette flow and the flat Poisuisse flow on the base of accounting of the obtained in the present work conclusion about possibility of the HP flow linear exponential instability due to the consideration of differing from the “normal” longitudinal quasi-periodic disturbances. Meanwhile, longitudinal disturbances quasi-periodicity is not by itself important but formation of it due to the longitudinal periods distinctions for different basic (in that case, radial) modes existing only for the non zero fluid viscosity.

Appendix

1. From (10) and (13) for $N = 2$ and $M=1$ in (12) we get for $\hat{\lambda} = \lambda_1 + i\lambda_2$:

$$\begin{align*}
\lambda_1 &= -j_{1,1}^2 - 4\pi^2 \beta^2 p^2 - \frac{1}{2} (a_1 \pm \frac{1}{\sqrt{2}} D_1^{1/2}) , \\
\lambda_2 &= -2 \pi \beta p_0 \text{Re} - \frac{1}{2} (a_2 \pm \frac{1}{\sqrt{2}} D_2^{1/2}) ,
\end{align*}$$

(A.1)

where $D_1 = d_0^{1/2} + l$, $D_2 = d_0^{1/2} - l$, $l = a_1^2 - a_2^2 + 4c_1 \text{Re}_1^2$

$$\begin{align*}
a_1 &= j_{1,2}^2 - j_{1,1}^2 + 4\pi^2 \beta^2 (1 - p^2) , \\
a_2 &= 2 \pi \beta \text{Re}(p_{22} - p_0 p_{11}) ,
\end{align*}$$

and

$$\text{Re}_1^2 = \frac{\text{Re}_0^2 p_{11} p_{22} \beta^2}{(1 - p)^2} , \\
d_0 = l^2 + 4(a_1 a_2 - 2 \text{Re}_1^2 d_1^2) , \\
d_1 = -4S ,
$$

$$c_1 = -4Sctg \pi (p + \frac{1}{p}) ,$$

and $S$ is defined in (14).
The condition $\lambda_1 > 0$ leads to the inequality

$$(a \text{Re} + b)^2 > c + \frac{d}{\text{Re}^2} \quad (A.3)$$

where $a = \frac{4P_{21} P_{12} p^2 \beta^2 S}{(1 - p)^2}$, $b = \pi \beta (P_{22} - p P_{11}) a_1$, $d = a_2^2 (j_{1,1}^2 + 4 \pi^2 \beta^2 p^2) (j_{1,2}^2 + 4 \pi^2 \beta^2)$,

$$a_3 = j_{1,2}^2 + j_{1,1}^2 + 4 \pi^2 \beta^2 (1 + p^2), c = a_2^2 \beta^2 (\pi^2 (P_{22} - p P_{11})^2 - 4 \frac{P_{12} P_{21} p^2 S \text{ctg} \pi (p + \frac{1}{p})}{(1 - p)^2}).$$

2. In the limit $\text{Re} >> 1$, inequality (A.3) with $c > 0$ is reduced to the inequality

$$\text{Re} > \text{Re}_{th} (\beta) = \frac{\sqrt{c - b} \cdot S}{|S|} \quad (A.4)$$

In (A.4), the function $\text{Re}_{th} (\beta)$ takes minimal value (given in (14)) for

$$\beta = \beta_0 = \frac{1}{2\pi} \left[ \frac{A(j_{1,2}^2 + j_{1,1}^2) + B(j_{1,2}^2 - j_{1,1}^2)}{A(1 + p^2) + B(1 - p^2)} \right]^{1/2}, \quad (A.5)$$

where $A$ and $B$ are defined in the main text (see (14)) for $A^2 > 0$.

3. On the neutral curve with $\lambda_1 = 0$ (i.e. when equality $\text{Re} = \text{Re}_{th} (\beta, p)$ in (A.4) holds), the phase velocity $V_\beta / V_{cp}$ has the form

$$V_\beta / V_{cp} = p P_{11} + P_{22} \pm \left( \frac{D_{21/2}}{2\sqrt{2\pi \beta \text{Re}}} \right)^{1/2} \beta = \beta_{1,2} \quad (A.6)$$

where $\beta = \beta_{1,2} (\text{Re}, p)$ corresponds to replacing of inequality in (A.4) by equality. For such a replacement in (A.4), we get a quadratic equation with respect to $\beta$. Its solution is

$$\beta = \beta_{1,2} = \frac{\text{Re} \pm \sqrt{\text{Re}^2 - \text{Re}_{th}^2}}{2\pi \delta_i} \quad (A.7)$$

for $\text{Re} \geq \text{Re}_{th}$, where $\text{Re}_{th}$ from (14), when $\beta_{1,2} = \beta_i$ for $\text{Re} = \text{Re}_{th}$, and

$$\delta_i = \pi ((p^2 + 1)\sqrt{1 - 4S^2} - (1 - p^2) \frac{S b_1}{|S b_1|} |b_1| (1 - p^2) \frac{S^2 P_{22} - P_{11}}{S^2 P_{22} P_{11}}, b_i = P_{22} - p P_{11}, \delta = \frac{p^2 P_{22} P_{12}}{(1 - p)^2 \pi b_i^2} \text{ctg} \pi (p + \frac{1}{p}).$$

4.
Figure 1. a) Family of the six curves of neutral stability (with $\lambda_1 = 0$), according to (14) and (A.5); the instability regions bounded by lines 2 and 3, respectively, correspond to $\beta_0 = 0.463$ (at $p=1.527$) and $\beta_0 = 1.099$ (at $p=2.239$). b) Curves 1-3 from panel a) in a magnified scale together with Fig.12 from [31] under the condition of the coincidence of the dimensionless parameters $1/2p = \alpha \delta^*$, where $\alpha$ is the wavenumber of the disturbance, and $\delta$ is the shift of the boundary layer in the flow around the thin plate [31]. The points and dashed curves correspond to the experiment reported in [31], and thin solid curves I and II are Shlihting and Lin theories, respectively. c) For $N=2$, Galerkin approximation (blue, labeled by 1) and energy theory (black, labeled by 2), integer values of $p$ are excluded from calculations; d) Energy theory for $N=2$, 10, 100, 600 (numbered 1 to 4 respectively for one set of curves).
5. Table of values $Re_{th}$ and $\beta_0$, obtained by (A.3) and (14) for $p$, corresponding to the local minima $Re_{th}$ in the approximate formula (14)

<table>
<thead>
<tr>
<th>$p$</th>
<th>$\beta_0$ (from (A.3))</th>
<th>$Re_{th}$ (from (A.3))</th>
<th>$\beta_0$ (from (A.5))</th>
<th>$Re_{th}$ (from (14))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,527</td>
<td>0,471</td>
<td>448,455</td>
<td>0,463</td>
<td>442,278</td>
</tr>
<tr>
<td>0,674</td>
<td>1,124</td>
<td>680,307</td>
<td>1,101</td>
<td>678,482</td>
</tr>
<tr>
<td>0,447</td>
<td>1,368</td>
<td>1095,455</td>
<td>1,358</td>
<td>1093,824</td>
</tr>
<tr>
<td>2,239</td>
<td>1,100</td>
<td>1983,171</td>
<td>1,099</td>
<td>1981,838</td>
</tr>
<tr>
<td>2,791</td>
<td>0,220</td>
<td>13095,398</td>
<td>0,219</td>
<td>13095,285</td>
</tr>
<tr>
<td>0,359</td>
<td>1,114</td>
<td>23816,499</td>
<td>1,114</td>
<td>23816,488</td>
</tr>
</tbody>
</table>

**Figure 2.** a) Results of the experiment [28] (for the velocity of the rear edge of a turbulent spot, blue rectangles, and for the velocity of the fore edge, light triangles) and [30] (rectangles and circles, for the velocity of the rear edge). The phase velocity of the wave solutions [8] (numbers 1-5 denote the level of azimuthal symmetry of the corresponding travelling wave). The velocities are normalized by the stream in the pipe volumetric/average velocity. Also the result of calculations of the phase velocity according to (A.6) is given. The top “straight” line corresponds to sign plus in (A.6), and the bottom one to sign minus for $p \approx 1.53, \beta = 0.471$ (that corresponds to the absolute minimum $Re_{th} = 448.5$ according to (A.3). b) Zoomed representation of the bottom “straight” line from Fig.2,a according to (A.6) (the upper brunch on Fig.2,b corresponds to sign plus in (A.7), and the lower to sign minus).
Statement on ethical issues
Research involving people and/or animals is in full compliance with current national and international ethical standards.

Acknowledgements
We are grateful to S.I. Anisimov, G.S. Golitsin, V. P. Goncharov, E.A. Novikov, and N.A. Inogamov for useful comments and interest to the work.

Conflict of interest
None declared.

Author contributions
All authors prepared the manuscript and analyzed the data, S.G.C. drafted the manuscript. All authors read the ICMJE criteria for authorship and approved the final manuscript.

References


19. Landau LD. JETP. 1941;11:592. [in Russian]


The effects of long-term microgravity on autonomic regulation of blood circulation in crewmembers of the international space station

Roman M. Baevsky¹, Irina I. Funtova¹, Elena S. Luchitskaya¹, Anna G. Chernikova¹*

¹ Institute of Biomedical Problems of the Russian Academy of Sciences, 123007, Russia, Moscow, 76A Khoroshevskoye Ch.

* Corresponding author phone: +7 (499) 193-62-44, e-mail: anna.imbp@mail.ru

Submitted: 05 September 2014
Accepted: 26 September 2014
Published online: 14 November 2014

Abstract

The article presents the results of space experiment "Pneumocard". The investigation involved all 25 Russian members of the ISS crew. The total of 226 sessions were made including 130 aboard the ISS, 50 prior to launch and 46 on return from mission.

The objective was to study effects of the spaceflight factors on autonomic regulation of blood circulation, respiration and cardiac contractility during long-duration mission. The purpose was to secure new research data that would clarify our present view of adaptation mechanisms.

Registered were the following signals: electrocardiogram, impedance cardiogram, seismic cardiogram, pneumotachogram, finger photoplethysmogram. A set of hard- and software was used.

Autonomic regulation of blood circulation by HRV analysis was investigated. It was shown that at the onset of a space mission parasympathetic involvement in regulation increases typically with subsequent mobilization of additional functional reserve. It guided the development of a functional states mathematical model incorporating the established types of autonomic regulation.

Our data evidence that the combination of HRV analysis, pre-nosology diagnosis and probabilistic estimate of the pathology risk can reinforce the medical care program in space missions.

Keywords

Cardiorespiratory system • Autonomic regulation • Adaptation mechanisms • Heart rate variability • Functional reserve • Strain degree • Stroke volume • Probabilistic assessment • Risk category

Imprint

Roman M. Baevsky, Irina I. Funtova, Elena S. Luchitskaya, Anna G. Chernikova. The effects of long-term microgravity on autonomic regulation of blood circulation in crewmembers of the international space station; Cardiometry; No.5; November 2014; p.35-49 ; doi: 10.12710/cardiometry.2014.5.3549
Available from: www.cardiometry.net/no5-november-2014/long-term-microgravity
Introduction

One of the main targets of space microgravity is the cardiovascular system. The major underlying reason is liquids displacement toward the upper part of the body and consequent increase of relative blood volume in the pulmonary circulation and cerebral vessels. Concurrent reductions in energy expense and afferent signaling complicate blood circulation regulation and, consequently, sufficient blood supply to organs and tissues in this situation. Adaptive reactions of organism in space flight are much dependent on the functioning of the cardiovascular system and its controls. Studies of heart rate regulation performed by IBMP investigators with participation of cosmonauts onboard the orbital stations “Salyut” and “Mir” gave the initial insight into the paths autonomic regulation of blood circulation chooses to adapt to in long-duration space flight. Already then it was found out that shifts occur in autonomic balance and segmental and suprasegmental activities rearrange to secure successful functional adaptation of organism to microgravity [1, 2]. The recent advance in understanding autonomic regulation of the cardiovascular system in microgravity has been made owing to research experiments “Pulse” and “Pneumocard” onboard the International space station (ISS) [3]. Experiment “Pulse” (ISS missions 5 - 13) was focused on autonomic regulation of blood circulation and respiration during long stay in microgravity. Registered were ECG, pneumotachogram, and peripheral pulse with the help of a finger photoplethysmography sensor [4,5]. Experiment “Pneumocard” was started in ISS mission 14; sessions were performed by Russian crewmembers every month over 5 years (from March, 2007 till end of 2012) [6]. In this experiment, seismic cardiography and impedance cardiography were added. Concurrent synchronous recording of five parameters and implementation of a series of functional tests made it possible to assess autonomic regulation of circulation simultaneously with cardiac contractility and central hemodynamics, and to judge straight about adaptability of organism in different mission periods. In fact, “Pneumocard” was the first research in space that furnished abundant information about multiple cardiac parameters used in assessing the functional state of cosmonaut’s organism and estimating the risk of pathology.

Experiment “Pneumocard” had the objective to acquire new data that would expand our knowledge of the mechanisms by which the cardiovascular system adapts to the conditions of long-duration space mission.

Materials and methods

The following physiological signals were recorded in the experiment:

- Electrocardiogram (ECG);
- Impedance cardiogram (ICG) according to the classic Shramek technique using 8 disposable electrodes (four on the neck (one pair on the right and the other on the left side) and four electrodes on the thorax (one pair on the right and the other on the left side);
- Seismic cardiogram (SCG);
- Pneumotachogram (PTG);
- Finger plethysmogram (FPG).
Investigations onboard the ISS employed a set of hard- and software called “Pneumocard” (patent for “Compact mobile device for investigation of the cardiovascular system of cosmonauts aboard space vehicle” RF № 77783 dated 03 July, 2008). The Pneumocard set with electrodes and sensors was attached to the breast belt of cosmonaut and did not cause any discomfort during experimental sessions in microgravity. Logged signals were stored in board PC and downlinked via the Internet; besides, data files were copied to flashcards which returned to Earth with the crew.

Preparation for experimental session consisted of donning the breast belt; care was taken to position the SCG sensor (linear acceleration - voltage converter) in the area of heart projection. Pneumocard recorder was fastened to the belt also. The photoplethysmographic sensor (tissue optical density - voltage converter) was applied to the left long finger. The pneumotachographic sensor or a thermister (ambient temperature - resistance converter) was attached to nostrils. Figure 1 shows an ISS cosmonaut making preparations for the Pneumocard session.

![Figure 1. An ISS cosmonaut making preparations for the Pneumocard session](image)

Experimental session included recording at rest (5 minutes), functional testing at a fixed breathing rate (10 breaths per a minute over 3 minutes; 6 breaths per a minute over 3 minutes) and with maximal in- and expiration breath-hold. Standing test was performed additionally before launch and after landing.

Fragment of a record is illustrated in fig. 2. Below is an example of cardiac intervalogram recorded for heart rate variability analysis (HVR) in all the experimental sessions. The results were analyzed for determination of a large number of parameters, HRV parameters first and foremost as...
guides to the autonomic regulation of functions. This technique is broadly used in space medicine since the early piloted missions [7].

HRV analysis is an integral approach to the assessment of mechanisms regulating physiological functions in organism of human and animal; specifically it comprises investigation of total regulation activity, neurohumoral regulation of the heart, and sympathetic-parasympathetic ratio in the autonomic nervous regulation. Actual status of the sympathetic and parasympathetic activities is a result of a multicircuit and multilevel cardiovascular reaction; the blood circulation system keeps adjusting own parameters till it finally achieves the optimum heralding successful adaptation of the whole organism [8, 9, 10]. The method is based on identification and measurement of time intervals between ECG R-waves (R-R intervals), construction of cardiac interval dynamic series (cardiac intervalograms) and ensuing analysis of numeric series with the use of mathematical methods.

Figure 2. Example of a Pneumocard-recorded physiological signal. Top-down: ECG, impedance CG, first ICG derivative, seismic CG, finger photopletysmography, pneumotachography. Below – HRV at rest, at fixed breathing rate, and during in- and expiration breath-hold.

Advanced approaches were applied to analyze and assess information obtained in the space experiment. Space medicine has framed a fundamentally new concept of health evaluation with reference to the present-day postulates of the theory of adaptation and homeostasis teaching [11]. The concept asserts that health is a process of continuous adjustment of organism to ambient conditions; measure of health is organism adaptability. Degradation from health to disease is linked to reduction of the adaptive potential, loss of the ability to respond adequately to socio-occupational and everyday stresses. On the borderline between health and disease many transitory states known
as pre-nosology may develop [12, 13]. Results of investigations are considered in terms of pre-
nosology diagnosis concerned with the states in-between the norm and pathology. The staple method 
of pre-nosology diagnosis is heart rate variability analysis (HRV). It served as a cornerstone for 
mathematical modeling of the functional states of organism in which the states plane is specified by 
two main parameters: DT (degree of tension) and FR (functional reserve). The mathematical model 
inspired the development of the probabilistic approach to pathology risk estimation [14].

Results and Discussion

A. Cardiovascular system adaptation to microgravity

Role of autonomic regulation

Adaptation processes are aimed at setting equilibrium between organism and environment. The 
processes are stipulated by mechanisms of autonomic regulation; type of regulation is deduced from 
dynamics of the heart rate variability (HRV) parameters. Figure 3 (A, B, C, D) gives an example of 
specific autonomic regulation changes in a cosmonaut in different periods of a long-duration ISS 
mission. One can see that in orbit heart rate (HR) was 5-10 beats/min slower compared with the 
pre-launch measurement; HR on the landing day was equal to pre-launch. During the first half of the 
mission SDNN demonstrates a strong trend upward (from 26 ms to 39 ms) and then goes down till 
return to initial values at the end of mission. Yet, a more detail analysis of the in-flight autonomic 
balance reveals rather complex dynamics.

In the pre-flight investigation, the cosmonaut was characterized by a high sympathetic tone. Stress index values (SI) amounted to 189-306 conventional units remaining 184 conv. units on 
mission day 17. As figure 3B shows it, further in mission SI made a decrease against a distinct rise in 
pNN50. For instance, on MD-102 SI decreased to 135 conv. units which was necessitated massive 
mobilization of the functional reserve of regulation.

Figure 3C presents curves for TP (HRV total power) and IC (regulation centralization index) 
according to which the total spectral power tripled on MD-102 in comparison with pre-launch values. 
At the same time, centralization index (CI) almost halved.
Also, the maximum in absolute value calculated for HRV low-frequency power (LF) was the result of blood pressure regulation (fig. 3D).

On MD-128, regulation by the subcortical vascular center persisted as it is apparent from still high absolute, and maximal LF relative values (fig. 3D) reaching 75%. In its turn, CI rises to 7.8 in relative units due to the high LF value.
Figure 3. Changes in HRV parameters in a cosmonaut in the course of ISS mission. HR (heart rate) and SDNN; SI (stress index) and pNN50; TP (total spectral power) and IC (index of centralization); Involvement of specific parts of the autonomic regulation system (HF – parasympathetic regulation; LF - sympathetic regulation of the vascular tone; VLF - segmental and suprasegmental regulation of energy metabolism).
Looking closely into the vascular tone regulation on MD 102 and 128 it can be noted that HR and SI had relatively normal values in the cosmonaut. In this context, we should turn our attention to dynamics of the ultralow-frequency HRV spectrum (ULF) presented in figure 4. On MD-102, the parameter was at its maximum (435 ms$^2$ versus 102 ms$^2$ before launch) which is attested by high activity of the suprasegmental centers in the brain. Consequently, there is good reason to tie up these changes in vascular regulation with hypothalamo-pituitary involvement, i.e. mobilization of the higher autonomic centers. These phenomena can be caused by fatigue, poor sleep or psycho-emotional strain.

By the end of mission (MD-148) stress-index is again on the rise (up to 238 conv.units) while pNN50 drops sharply (fig. 3B); very low frequency power (VLF) grows as high as 219 ms$^2$ in comparison with 78 ms$^2$ before launch. It means that sympathetic regulation becomes more influential because of the need to mobilize the functional reserve. Abrupt reduction of the functional reserve by the mission end reveals itself by the conspicuous stress reaction in the post-landing period. From figure 3 (B-C) it is evident that after landing stress index grew to 335 conv. units and that index of centralization reached 11.4.

**Figure 4.** HRV ultralow-frequency power (ULF) dynamics in an ISS cosmonaut.
The above character of autonomic regulation dynamics essentially depends on individual peculiarities of the regulation mechanism. Table 1 provides data on individual patterns of autonomic regulation in Russian members of ISS crews in different mission periods. Based on these data, there is no direct correlation between the results of pre-launch investigations and those obtained in and post flight. However, cosmonauts’ reactions have similarity with the extreme types of autonomic regulation. For instance, K-10 and K-13 who exhibited the highest pre-launch heart rate and SI values both had high HR post flight (112 and 85, respectively); besides, K-10 had the highest SI (915). At the same time, although pre-launch HR in K-6 was the lowest (52), his post-landing PR also measured very high (84).

Values of HRV total spectral power (TP) that characterize level of the regulation functional reserve are in no way predictors. For instance, in K-16 TP values were the highest during mission (2200-6000) and relatively high before launch (3480), whereas in K-14 TP was the highest before launch (8000) but no metamorphosis was observed in autonomic regulation either during or after mission. These observations instigated the development of alternative methods of functional state assessment with account of type of autonomic regulation.
Table 1. Individuality of autonomic regulation in cosmonauts in different ISS missions periods (experiment “Pneumocard”)

<table>
<thead>
<tr>
<th>ISS cosmonauts</th>
<th>Heart rate variability parameters</th>
<th>Before launch</th>
<th>In mission</th>
<th>After mission</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HR</td>
<td>SI</td>
<td>TP</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>71</td>
<td>177</td>
<td>2735</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>63</td>
<td>65</td>
<td>2270</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>67</td>
<td>165</td>
<td>835</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>66</td>
<td>98</td>
<td>1130</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>63</td>
<td>77</td>
<td>1550</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>52</td>
<td>23</td>
<td>3860</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>70</td>
<td>101</td>
<td>1670</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>59</td>
<td>64</td>
<td>2100</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>56</td>
<td>66</td>
<td>2030</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>85</td>
<td>400</td>
<td>360</td>
</tr>
<tr>
<td>11</td>
<td></td>
<td>58</td>
<td>100</td>
<td>1200</td>
</tr>
<tr>
<td>12</td>
<td></td>
<td>68</td>
<td>105</td>
<td>1300</td>
</tr>
<tr>
<td>13</td>
<td></td>
<td>89</td>
<td>270</td>
<td>1000</td>
</tr>
<tr>
<td>14</td>
<td></td>
<td>65</td>
<td>25</td>
<td>8000</td>
</tr>
<tr>
<td>15</td>
<td></td>
<td>55</td>
<td>130</td>
<td>450</td>
</tr>
<tr>
<td>16</td>
<td></td>
<td>60</td>
<td>26</td>
<td>3480</td>
</tr>
<tr>
<td>17</td>
<td></td>
<td>75</td>
<td>190</td>
<td>720</td>
</tr>
<tr>
<td>18</td>
<td></td>
<td>70</td>
<td>88</td>
<td>1700</td>
</tr>
<tr>
<td>19</td>
<td></td>
<td>68</td>
<td>90</td>
<td>2140</td>
</tr>
<tr>
<td>20</td>
<td></td>
<td>67</td>
<td>124</td>
<td>1600</td>
</tr>
<tr>
<td>21</td>
<td></td>
<td>72</td>
<td>65</td>
<td>1980</td>
</tr>
<tr>
<td>22</td>
<td></td>
<td>71</td>
<td>47</td>
<td>1800</td>
</tr>
<tr>
<td>23</td>
<td></td>
<td>58</td>
<td>114</td>
<td>1200</td>
</tr>
<tr>
<td>24</td>
<td></td>
<td>57</td>
<td>98</td>
<td>1500</td>
</tr>
<tr>
<td>25</td>
<td></td>
<td>67</td>
<td>77</td>
<td>1800</td>
</tr>
</tbody>
</table>
B. Pathology risk estimation

Risk of pathology development in the course of mission was estimated using a mathematical model of the functional states of organism built on the generalized results of heart rate variability analysis in all Russian cosmonauts who had made long-term missions to the ISS [15].

The model represents a system of two discriminant function equations; one equation describes strain degree of regulation straining (SD) and the other, regulation functional reserve (FR). Magnitudes of SD and FR are calculated from HR, pNN50, SI and HF, %. Besides, consideration is given to individual type of autonomic regulation. SD and FR values are used to form a phase plane as a two-dimensional space of the functional states. Each of four quadrants in the space corresponds to one of four functional states: physiological norm, pre-nosology, premorbidity and pathology.

![Phase plane trajectory for cosmonauts](image)

**Figure 5.** Functional state dynamics in four cosmonauts on space missions (phase plane trajectory). Abscissa – FR (functional reserve), ordinate – DT (degree of tension).
During every investigation the actual functional state is determined as a point with coordinates SD and FR; variations in the functional state in the course of mission are displayed as a phase plane trajectory. Figure 5 illustrates the functional state trajectory in four ISS cosmonauts during mission. As zone. By the mission end the pre-nosology character of functional state becomes even more evident reaching the pre-launch level and moves to the premobidity borderline after landing.

Following every experimental session, functional states probability was calculated from DT and FR values with consideration of a person-specific type of autonomic regulation. Each point in the states space has continuation in the future and, therefore, can be estimated using methods of the mathematical probability theory. The actual functional state is the most probable one, and yet it is also possible to judge about probability of functional state evolution down to pathology.

To assess the risk of pathology, a risk classification system was set up by IBMP investigators [14]. The rating scale has reference to 10 risk categories. The first three categories lie within a relatively safe zone of the functional states, categories 4-5 suggest presence of debilitating factors, categories 6-7 call for urgent measures to be taken to optimize living and labour conditions; category 8 and above indicate the necessity of nondelayed risk mitigation. Figure 6 presents risk categories established for K-17 at different time points of the investigation. According to these data, his functional state was unfavorable prior to and after mission, and on mission day 148.

Table 2 tabulates the results of functional state assessment in all Russian cosmonauts who participated in the Pneumocard experiment aboard the ISS. From the table it follows that before launch pre-nosology (PN) was diagnosed in 9 out of 25 cosmonauts and premorbidity (PM) in one cosmonaut. There were 16 pre-nosology episodes during missions. On return from orbit, pre-nosology was observed in 13 cosmonauts; functional state of 5 cosmonauts was qualified as premorbid. From this follows the conclusion that the overall stress-effect of the spaceflight factors on human organism is rather detrimental, for pre-nosology was diagnosed 1.5 times more frequently on mission than earlier on the ground and 20% of cosmonauts exhibited premorbidity after return from the ISS. Mean risk categories were equal to 2.08, 3.04 and 3.36 before, in and after mission, respectively. Based on this evidence, combination of HRV analysis with the probabilistic approach and application of the methods of pathology risk estimation can be advantageously adopted by the system of spacecrew health monitoring.

![Figure 6. Risk categories established for K-17 at different time points of the investigation](image-url)
Table 2. Functional state of the ISS cosmonauts according to the “Pneumocard” data

<table>
<thead>
<tr>
<th>ISS cosmonauts</th>
<th>Before launch</th>
<th>During mission</th>
<th>After return</th>
<th>Risk category</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>4-3-3</td>
</tr>
<tr>
<td>2</td>
<td>N</td>
<td>N-PN -N</td>
<td>PN</td>
<td>1-4-6</td>
</tr>
<tr>
<td>3</td>
<td>N</td>
<td>N</td>
<td>N-PM</td>
<td>3-3-7</td>
</tr>
<tr>
<td>4</td>
<td>N</td>
<td>N-PN</td>
<td>PM</td>
<td>1-6-9</td>
</tr>
<tr>
<td>5</td>
<td>N</td>
<td>PN-N</td>
<td>PN</td>
<td>1-4-3</td>
</tr>
<tr>
<td>6</td>
<td>N</td>
<td>PN-N</td>
<td>PN-N</td>
<td>1-5-3</td>
</tr>
<tr>
<td>7</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>3-2-1</td>
</tr>
<tr>
<td>8</td>
<td>N</td>
<td>N</td>
<td>N-PN</td>
<td>2-3-3</td>
</tr>
<tr>
<td>9</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>2-1-1</td>
</tr>
<tr>
<td>10</td>
<td>PN</td>
<td>PN</td>
<td>PM</td>
<td>4-4-8</td>
</tr>
<tr>
<td>11</td>
<td>PN</td>
<td>PN</td>
<td>PN</td>
<td>2-4-2</td>
</tr>
<tr>
<td>12</td>
<td>PN</td>
<td>N-PN</td>
<td>PN</td>
<td>3-3-4</td>
</tr>
<tr>
<td>13</td>
<td>PM</td>
<td>PN</td>
<td>PN</td>
<td>5-2-2</td>
</tr>
<tr>
<td>14</td>
<td>N</td>
<td>N-PN -N</td>
<td>N</td>
<td>1-4-1</td>
</tr>
<tr>
<td>15</td>
<td>PN</td>
<td>PN</td>
<td>PN</td>
<td>2-3-2</td>
</tr>
<tr>
<td>16</td>
<td>N</td>
<td>N</td>
<td>PN -N</td>
<td>1-2-4</td>
</tr>
<tr>
<td>17</td>
<td>PN</td>
<td>PN</td>
<td>PN</td>
<td>4-4-4</td>
</tr>
<tr>
<td>18</td>
<td>PN</td>
<td>PN -N</td>
<td>N</td>
<td>1-2-1</td>
</tr>
<tr>
<td>19</td>
<td>N – PN</td>
<td>N – PN</td>
<td>PM -PN</td>
<td>2-2-4</td>
</tr>
<tr>
<td>20</td>
<td>PN</td>
<td>PN</td>
<td>PN</td>
<td>2-3-2</td>
</tr>
<tr>
<td>21</td>
<td>N</td>
<td>PN N-PN</td>
<td>PN - PM</td>
<td>1-2-4</td>
</tr>
<tr>
<td>22</td>
<td>N</td>
<td>N</td>
<td>PN - N</td>
<td>1-1-3</td>
</tr>
<tr>
<td>23</td>
<td>N</td>
<td>N – PN</td>
<td>N</td>
<td>3-4-2</td>
</tr>
<tr>
<td>24</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>1-2-2</td>
</tr>
<tr>
<td>25</td>
<td>N</td>
<td>N – PN</td>
<td>PN -N</td>
<td>1-3-3</td>
</tr>
</tbody>
</table>

Conclusions

Space experiment “Pneumocard” made a milestone in the advance of space medicine, space cardiology specifically. First and foremost, this was not a one-off experiment but a great series of systematic purposeful investigations of the cardiorespiration system scheduled for every month and continued by the ISS cosmonauts over more than 5 years. We should emphasize the unprecedented nature of the experiment. Its findings gained acceptance at many Russian and international symposia and conferences [2, 3, 4, 5, 16, 17, 18, 19, 20, 21]. Their theoretical significance arises from demonstration of the role played by autonomic regulation in providing cardiovascular homeostasis.
in long-duration space mission. The experiment enabled elicitation of mechanisms through which autonomic balance rearranges in different periods of long exposure to microgravity, and setting the criteria of autonomic regulation assessment based on HRV analysis. Finally, the experiment evidenced that to a large degree adaptation of human organism to microgravity is dependent on individual type of autonomic regulation.

Applicative implications of the results of our investigation are determined by two outcomes: 1) successful testing of the technique for identification of individual type of autonomic regulation in spacecrew members; 2) development of the probabilistic approach to estimation of the risk of pathology in the conditions of long-duration space mission as an instrument for predicting functional state degradation in crewmembers. Both outcomes have the potential to gain footing as in space medicine, so in different fields of applied physiology delving into the adaptive reactions of human organism to extreme environments. Space medicine is committed to promotion of cutting-edge space technologies to healthcare and, at the same time, to integration of the latest achievements of medical sciences into the system of spacecrew medical care and life support.

Statement on ethical issues

Research involving people and/or animals is in full compliance with current national and international ethical standards.

Conflict of interest

None declared.

Author contributions

All authors prepared the manuscript and analyzed the data, A.G.C. drafted the manuscript. All authors read the ICMJE criteria for authorship and approved the final manuscript.

References

4. Baranov VM, Baevsky RM, Drescher J, Tank J, et al. Investigations of the cardiovascular and respiratory systems on board the international space station: Experiments “Puls” and “Pneumocard. 53rd Congress IAF; 2002 October; Houston, USA.


17. Baevsky RM, Funtova II, Diedrich A, Chernikova AG, Drescher J, Baranov VM, Tank J. Cardiac function measured by impedance cardiography is maintained during long term space flight. 59 IAC; 2008; Glasgow, Scotland.

18. Funtova II, Chernikova AG, Fedorova IN, Baranov VM, Tank J, Baevsky RM. Some results of scientific experiment “Pneumocard” onboard the ISS. 17th IAA Humans in Space Symposium; 2009 June 7-11; Moscow, Russia. [in Russian]

19. Chernikova AG, Baevsky RM, Funtova II. Assessment of the functional state of ISS crewmembers by heart rate variability analysis. 17th IAA Humans in Space Symposium; 2009 June 7-11; Moscow, Russia. [in Russian]


21. Chernikova AG, Baevsky RM, Funtova II. The probability approach to an estimation of risk of a pathology at cosmonauts according to analysis HRV. ISHNE-2011; 2011 April; Moscow, Russia.
Noninvasive investigation of the body functional state during night sleep in microgravity

Irina I. Funtova, Elena S. Luchitskaya, Irina N. Slepchenkova, Anna G. Chernikova, Roman M. Baevsky

1 Institute of Biomedical Problems of the Russian Academy of Sciences, 123007, Russia, Moscow, 76A Khoroshevskoye Ch.

* Corresponding author phone: +7 (499) 193-62-44, e-mail: anna.imbp@mail.ru

Submitted: 09 September 2014
Accepted: 30 September 2014
Published online: 14 November 2014

Abstract

The Sonocard experiment purpose was a noninvasive physiological signal recording from sleeping humans. In 2007-2012 the experiment was made by 22 Russian members of 17 missions to the International space station. Of the overall 302 experimental sessions 47 were performed pre, 215 in and 40 after flight.

The seismographic technique was used to pick up cosmonaut’s body microoscillations induced by cardiac beats, respiration and motor activity. The flight Sonocard model is a midget device fitting into the T-shirt pocket. Heart rate variability analysis (HRV) was the major method of securing conclusive evidence on stress level and blood circulation autonomic regulation. We were first to trace reorganization of the autonomic regulation at the night time on different phases of long-duration space mission and pioneered a systematic investigation of the human body functional state during sleep. It was shown that in the absence of work loads and emotional stresses the central mechanisms of circulation regulation tend to increase their activities. The characteristic subsidence of breathing waves (HF) and growth of the vascular center (LF) portion within the HRV total spectrum by the end of flight were observed.

Sleep quality in the course of long-duration missions was assessed. We succeeded in the first ever sleep assessment following operations in open space.

The noninvasive physiological signal recording was recommended for use in spacecrew medical monitoring and ground-based experiments.

Keywords

Noninvasive physiological signal recording • Recovery of the functional reserve • Body microoscillations • Sleep • Seismocardiography • Autonomic regulation • Heart rate variability • Sleep quality • Straining degree

Imprint

Irina I. Funtova, Elena S. Luchitskaya, Irina N. Slepchenkova, Anna G. Chernikova, Roman M. Baevsky. Noninvasive investigation of the body functional state during night sleep in microgravity: Cardiometry; No.5; November 2014; p.50-65; doi:10.12710/cardiometry.2014.5.5065
Available from: www.cardiometry.net/no5-november-2014/night-sleep-in-microgravity
**Introduction**

Studies of the human sleep-wakefulness cycle in the unusual environment of long stay aboard space vehicles are of high practical significance. The reason is that the particular biological role of sleep among vital activities of the organism is the recovery phase. Though sleep in space flight has been the objective of a large number of investigations [1], assessment of recovery completeness in these conditions is a fundamentally new task. It is well known that organism recovery during sleep occurs with the autonomic balance shifting toward prevalence of the parasympathetic regulation. The process can be controlled by the instrumentality of the methods of heart rate variability analysis [2,3].

Till recently autonomic balance in orbiting cosmonaunts has been investigated only during workday hours. Simultaneously with the influence of the specific factor of microgravity cosmonaut’s organism is also affected by “factors of production” such as mental and emotional straining and physical loads of daily exercises. Effects of microgravity per se can be studied in sleep only. This being so, the theoretical aspect of the investigation implies filling the gap in the knowledge of microgravity effects on autonomic regulation of human physiological functions in the course of long-duration mission. The practical aspect consists in exploring the possibility to assess sleep quality in microgravity and, therefore, effectiveness of the recovery process as staples of the human ability to work and functionality in general. In this context, it was crucial to develop a simple and comfortable procedure sleep studies other than present-day cumbersome polysomnography, which, because of placement of numerous sensors and electrodes and complex data analysis is unsuitable for the space flight environment.

**Materials and methods**

**Procedure**

Noninvasive signal recording, a simple, comfortable and physiologically seamless method of investigation imparted uniqueness to space experiment Sonocard. The patented space-oriented device with the same name is an original development of Russian engineers [4]. It was delivered onto the International space station in September of 2007. The first record was made on October 19, 2007 by a Russian member of ISS crew-16.

Inside the midget device (210x140x18 mm) there are an accelerometer-type sensor, amplifier-transformer, memory box, and controllers for communication with external PC and power supply.
Before going to bed, cosmonaut put Sonocard in the T-shirt pocket and got into the sleeping bag (fig. 1). After waking-up, cosmonaut was to copy the night records into the board PC memory. The records were downlinked via the Internet at the first opportunity; on the eve of landing, the records were copied to PCMCIA for more careful analysis in laboratory.

The active sensor detects microoscillations of the chest wall caused by mechanic work of the heart. In parallel, it captures all other oscillations associated with breathing, motor activity or external factors (fig. 2). Since amplitudes of irrelevant oscillations may be many times over the magnitude of heartbeat signals, total records are subject to special processing in order to isolate useful information.

Specialized software Corr serves to recognize and measure continuous dynamic series of cardiac interval durations over the entire period of investigation (night sleep). The choice fell on the method of standards, i.e. construction of the cross-correlation function between a current signal and a selected typical seismic or ballistic cardiocomplex. Software executes digital filtration of signals to facilitate recognition of individual complexes and measurement of time intervals between them.

In addition to the priority objective of constructing cardio intervals along the night record, Corr also permits prompt isolation and measuring time of interferences, mostly due to motor activity (MA). MA parameters are calculated automatically on the analysis of signal power. Besides, software is capable to isolate and measure breathing movements by way of low-frequency filtration of a seismic or ballistic cardiogram. The snap analysis function provides immediate data on subject’s heart rate, breathing rate and motor activity while he or she was asleep.

In 2007-2012, space experiment Sonocard was performed by 22 cosmonauts in 17 ISS missions. The overall number of experimental investigations is 302 including 47 pre launch, 215 in and 40 after mission. Every cosmonaut was investigated 2 or 3 times before launch; during ISS missions 17 - 28 the investigations were scheduled twice a month; starting from ISS mission-28 they were made once a month and twice after return.
Figure 1. Implementation of experiment Sonocard onboard the ISS (left) and signal analysis program (right).

A) a fragment of signal with heartbeat-related complexes

B) a fragment of signal recorded at the moment of in-sleep movement

C) a fragment of signal with breathing-induced envelope

Figure 2. Fragments of signals reflecting different physiological processes.
Data processing

Heart rate variability (HRV) constitutes the core of the noninvasive physiological records analysis. Corr identifies 5-minute fragments clean of motor activity and artifacts for ensuing calculation of the HRV standard time and frequency parameters. Analysis and physiological interpretation of HRV parameters were performed with consideration of the recommendations given by a group of Russian experts [5] and standards of the European Society of cardiologists and North American Society of electrostimulation and electrophysiology [6]. Heart rate variability analysis is modern methodology and technology of investigating and evaluating the functional state of organism and specific components of the autonomic nervous system. Space medicine was one of the disciplines and practical areas where HRV analysis was used as a source of new information and a tool of medical monitoring humans exposed to extreme environments [7, 8, 9, 10, 11]. Since systematic investigations of organism functions during sleep in long-term microgravity have not been attempted in the past, attention was focused on person-unique features of autonomic regulation.

Results and Discussion

1. Dynamics of mean values of the set of physiological parameters during sleep on different flight phases

Table 1 presents mean values of the main HRV parameters in experiment Sonocard. From these data it follows that mission average changes in heart rate were significantly lower in orbit and reliably higher in the post-landing period. Analysis points to statistically significant shifts in the autonomic balance during flight. Parasympathetic regulation declines (HF), the subcortex sympathetic vascular center (LF) builds up its activity while power of the energy metabolism regulation (VLF) goes down.

Table 1. Mean values of the main HRV parameters in experiment Sonocard

<table>
<thead>
<tr>
<th>Flight phase</th>
<th>HR</th>
<th>SI</th>
<th>pNN50</th>
<th>HF %</th>
<th>LF %</th>
<th>VLF%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before flight</td>
<td>58.18</td>
<td>90.90</td>
<td>18.66</td>
<td>27.15</td>
<td>42.65</td>
<td>29.8</td>
</tr>
<tr>
<td>In flight</td>
<td>55.81*</td>
<td>91.5</td>
<td>18.2</td>
<td>23.9*</td>
<td>48.55*</td>
<td>27.5*</td>
</tr>
<tr>
<td>After flight</td>
<td>68.55**</td>
<td>150.14**</td>
<td>9.73**</td>
<td>18.36**</td>
<td>50.31**</td>
<td>31.26**</td>
</tr>
</tbody>
</table>

* p<0.05    ** p<0.01
These changes sum over the data from all 22 ISS cosmonauts and evidence common trends. Post-landing changes reveal distinct and of greater reliability growth in heart rate and shifting of autonomic balance toward sympathetic tone regulation (rise in SI, LF % and VLF%, reduction in pNN50 and HF %).

Table 2. Nighttime average HRV parameters in space experiment Sonocard.

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>SDNN</th>
<th>pNN50</th>
<th>SI</th>
<th>TP</th>
<th>HF, %</th>
<th>LF,%</th>
<th>VLF,%</th>
<th>BR</th>
<th>MA</th>
<th>MA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before flight -1</td>
<td>M</td>
<td>56.44</td>
<td>59.17</td>
<td>25.64</td>
<td>78.85</td>
<td>2848.56</td>
<td>27.93</td>
<td>42.77</td>
<td>29.26</td>
<td>13.79</td>
<td>9.21</td>
</tr>
<tr>
<td></td>
<td>σ</td>
<td>7.39</td>
<td>18.49</td>
<td>16.27</td>
<td>55.38</td>
<td>1529.60</td>
<td>10.18</td>
<td>8.06</td>
<td>8.23</td>
<td>1.77</td>
<td>4.16</td>
</tr>
<tr>
<td></td>
<td>m</td>
<td>1.79</td>
<td>4.48</td>
<td>3.95</td>
<td>13.43</td>
<td>370.98</td>
<td>2.47</td>
<td>1.96</td>
<td>2.00</td>
<td>0.43</td>
<td>1.20</td>
</tr>
<tr>
<td>Before flight -2</td>
<td>M</td>
<td>58.31</td>
<td>56.28</td>
<td>20.18</td>
<td>93.40</td>
<td>2963.26</td>
<td>26.98</td>
<td>41.95</td>
<td>29.69</td>
<td>13.84</td>
<td>9.59</td>
</tr>
<tr>
<td></td>
<td>σ</td>
<td>6.95</td>
<td>18.78</td>
<td>14.23</td>
<td>61.98</td>
<td>1938.85</td>
<td>8.61</td>
<td>6.86</td>
<td>7.70</td>
<td>2.35</td>
<td>4.38</td>
</tr>
<tr>
<td></td>
<td>m</td>
<td>1.52</td>
<td>4.10</td>
<td>3.11</td>
<td>13.53</td>
<td>423.09</td>
<td>1.88</td>
<td>1.50</td>
<td>1.68</td>
<td>0.51</td>
<td>1.09</td>
</tr>
<tr>
<td>1-st months of flight</td>
<td>M</td>
<td>54.95*</td>
<td>54.85</td>
<td>21.99</td>
<td>83.40</td>
<td>2683.17</td>
<td>25.16</td>
<td>43.56</td>
<td>29.60</td>
<td>11.37*</td>
<td>9.45</td>
</tr>
<tr>
<td></td>
<td>σ</td>
<td>7.83</td>
<td>19.23</td>
<td>13.82</td>
<td>60.34</td>
<td>1551.43</td>
<td>11.07</td>
<td>11.06</td>
<td>9.23</td>
<td>2.67</td>
<td>5.18</td>
</tr>
<tr>
<td></td>
<td>m</td>
<td>1.34</td>
<td>3.30</td>
<td>2.37</td>
<td>10.35</td>
<td>266.07</td>
<td>1.90</td>
<td>1.90</td>
<td>1.58</td>
<td>0.49</td>
<td>1.13</td>
</tr>
<tr>
<td>2-nd months of flight</td>
<td>M</td>
<td>56.46</td>
<td>56.65</td>
<td>21.69</td>
<td>80.57</td>
<td>2752.74</td>
<td>23.45</td>
<td>46.41</td>
<td>28.59</td>
<td>12.17*</td>
<td>7.67*</td>
</tr>
<tr>
<td></td>
<td>σ</td>
<td>7.78</td>
<td>18.81</td>
<td>14.44</td>
<td>48.25</td>
<td>1367.29</td>
<td>8.56</td>
<td>9.72</td>
<td>7.77</td>
<td>1.77</td>
<td>3.81</td>
</tr>
<tr>
<td></td>
<td>m</td>
<td>1.33</td>
<td>3.23</td>
<td>2.48</td>
<td>8.27</td>
<td>234.49</td>
<td>1.47</td>
<td>1.67</td>
<td>1.33</td>
<td>0.32</td>
<td>0.78</td>
</tr>
<tr>
<td>3-rd months of flight</td>
<td>M</td>
<td>56.04</td>
<td>53.11</td>
<td>21.86</td>
<td>85.19</td>
<td>2413.19</td>
<td>24.76</td>
<td>45.18*</td>
<td>27.22</td>
<td>12.02*</td>
<td>7.46*</td>
</tr>
<tr>
<td></td>
<td>σ</td>
<td>7.08</td>
<td>18.41</td>
<td>13.62</td>
<td>46.20</td>
<td>1266.62</td>
<td>9.14</td>
<td>10.18</td>
<td>7.46</td>
<td>1.82</td>
<td>3.62</td>
</tr>
<tr>
<td></td>
<td>m</td>
<td>1.25</td>
<td>3.25</td>
<td>2.41</td>
<td>8.17</td>
<td>223.91</td>
<td>1.62</td>
<td>1.80</td>
<td>1.32</td>
<td>0.33</td>
<td>0.83</td>
</tr>
<tr>
<td>4-th months of flight</td>
<td>M</td>
<td>56.14</td>
<td>54.23</td>
<td>19.92</td>
<td>81.81</td>
<td>2574.84</td>
<td>23.49</td>
<td>46.38*</td>
<td>27.72</td>
<td>11.66*</td>
<td>8.02</td>
</tr>
<tr>
<td></td>
<td>σ</td>
<td>7.31</td>
<td>17.59</td>
<td>12.20</td>
<td>43.36</td>
<td>1270.73</td>
<td>10.60</td>
<td>9.87</td>
<td>7.31</td>
<td>2.27</td>
<td>3.35</td>
</tr>
<tr>
<td></td>
<td>m</td>
<td>1.20</td>
<td>2.89</td>
<td>2.01</td>
<td>7.13</td>
<td>208.91</td>
<td>1.74</td>
<td>1.62</td>
<td>1.20</td>
<td>0.38</td>
<td>0.68</td>
</tr>
<tr>
<td>5-th months of flight</td>
<td>M</td>
<td>55.54</td>
<td>55.78</td>
<td>20.41</td>
<td>80.38</td>
<td>2942.53</td>
<td>21.51*</td>
<td>47.53*</td>
<td>28.65</td>
<td>11.30*</td>
<td>8.68</td>
</tr>
<tr>
<td></td>
<td>σ</td>
<td>7.08</td>
<td>17.69</td>
<td>12.61</td>
<td>49.72</td>
<td>1533.27</td>
<td>6.53</td>
<td>8.96</td>
<td>6.06</td>
<td>2.97</td>
<td>3.99</td>
</tr>
<tr>
<td></td>
<td>m</td>
<td>1.21</td>
<td>3.03</td>
<td>2.16</td>
<td>8.53</td>
<td>262.95</td>
<td>1.12</td>
<td>1.54</td>
<td>1.04</td>
<td>0.52</td>
<td>0.89</td>
</tr>
<tr>
<td>6-st months of flight</td>
<td>M</td>
<td>56.24</td>
<td>58.19</td>
<td>23.13</td>
<td>77.52</td>
<td>2860.02</td>
<td>22.93*</td>
<td>45.03*</td>
<td>29.87</td>
<td>11.42*</td>
<td>6.11*</td>
</tr>
<tr>
<td></td>
<td>σ</td>
<td>7.13</td>
<td>19.70</td>
<td>13.47</td>
<td>49.67</td>
<td>1734.79</td>
<td>7.91</td>
<td>7.28</td>
<td>8.18</td>
<td>2.23</td>
<td>1.87</td>
</tr>
<tr>
<td></td>
<td>m</td>
<td>1.46</td>
<td>4.02</td>
<td>2.75</td>
<td>10.14</td>
<td>354.11</td>
<td>1.62</td>
<td>1.49</td>
<td>1.67</td>
<td>0.46</td>
<td>0.66</td>
</tr>
<tr>
<td>After Flight-1</td>
<td>M</td>
<td>68.70*</td>
<td>46.43*</td>
<td>11.16*</td>
<td>157.65*</td>
<td>2013.33*</td>
<td>17.00*</td>
<td>51.00*</td>
<td>33.69</td>
<td>14.58</td>
<td>10.57</td>
</tr>
<tr>
<td></td>
<td>σ</td>
<td>11.25</td>
<td>20.74</td>
<td>13.71</td>
<td>105.99</td>
<td>1441.85</td>
<td>6.58</td>
<td>10.27</td>
<td>9.79</td>
<td>2.60</td>
<td>5.28</td>
</tr>
<tr>
<td></td>
<td>m</td>
<td>2.65</td>
<td>5.03</td>
<td>3.33</td>
<td>25.71</td>
<td>349.70</td>
<td>1.60</td>
<td>2.49</td>
<td>2.37</td>
<td>0.63</td>
<td>1.52</td>
</tr>
<tr>
<td>After Flight-2</td>
<td>M</td>
<td>64.03*</td>
<td>46.64*</td>
<td>10.49*</td>
<td>131.28*</td>
<td>2175.42*</td>
<td>21.52*</td>
<td>48.72*</td>
<td>29.77</td>
<td>14.13</td>
<td>9.80</td>
</tr>
<tr>
<td></td>
<td>σ</td>
<td>8.33</td>
<td>14.96</td>
<td>9.34</td>
<td>79.33</td>
<td>1302.20</td>
<td>5.17</td>
<td>5.84</td>
<td>6.83</td>
<td>1.86</td>
<td>3.39</td>
</tr>
<tr>
<td></td>
<td>m</td>
<td>2.15</td>
<td>4.00</td>
<td>2.50</td>
<td>21.20</td>
<td>348.03</td>
<td>1.38</td>
<td>1.56</td>
<td>1.83</td>
<td>0.50</td>
<td>0.94</td>
</tr>
</tbody>
</table>
Table 2 presents night average values of all main parameters on specific flight phases (prior to launch, in every mission month, after landing).

Before launch, measurements were fulfilled twice (at L-2 months and L-2-3 weeks). According to the table, differences between the first and second measurements of all parameters were statistically insignificant. Results of the second, close to launch measurements, were used for comparison with in- and post-flight data.

In orbit, night average values of many parameters did not change to the degree of statistical significance. In the first month of life in microgravity night-time heart rate reduces fiducially and breathing rate increases (breathing cycle grows short). The only reliable change on the second month is only reduction in motor activity during sleep. From month 3 till mission end there is a significant growth in relative power of the HRV low-frequency spectrum controlled by the sympathetic vascular center [5]. Breathing rate gets markedly rapid after 4 months on mission.

Considerable weakening of relative high-frequency power on months 5 and 6 points to a more active sympathetic involvement. Motor activity of sleeping cosmonaut becomes reliably less on mission month 5.

After return to Earth, virtually all parameters exhibit considerable changes. Heart rate increases already on days 1 to 4 of landing. Shifting of autonomic regulation toward sympathetic regulation declares itself by decreased pNN50 values and rise of stress index paralleled by significant reduction in HRV total spectral power (TP). Obvious changes in high- (HF) and low-frequency (LF) relative power are an additional indication of the domination of sympathetic regulation.

In summary, the nighttime average data obtained in long-duration space missions evidence that microgravity produces a statistically reliable activation of the sympathetic autonomic regulation and a slight increase in breathing rate. Motor activity of sleeping cosmonauts gradually decreases testifying indirectly relaxation of the neuromuscular tension. However, individual adaptive reactions of cosmonauts on mission are characterized by a large diversity depending on type of autonomic regulation.
2. Individual patterns of autonomic balance

Table 3 contains mean HRV parameters before, in and after space flights in five groups of cosmonauts differing in the type of autonomic regulation.

**Table 3.** Mean HRV parameters in cosmonauts differing in type of autonomic regulation in the course of space flight

<table>
<thead>
<tr>
<th>Type of autonomic regulation</th>
<th>HR</th>
<th>SI</th>
<th>pNN50</th>
<th>HF %</th>
<th>LF %</th>
<th>VLF%</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before flight</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V (vagotonic)</td>
<td>52.6</td>
<td>80.6</td>
<td>22.83</td>
<td>26</td>
<td>45</td>
<td>29</td>
<td>6</td>
</tr>
<tr>
<td>In Flight</td>
<td>47.6*</td>
<td>64.8*</td>
<td>21</td>
<td>21*</td>
<td>49.4*</td>
<td>29.8</td>
<td>6</td>
</tr>
<tr>
<td>After Flight</td>
<td>63.4*</td>
<td>104.8*</td>
<td>12.8*</td>
<td>17.4*</td>
<td>47.2</td>
<td>35.2*</td>
<td>6</td>
</tr>
<tr>
<td>NV (normal-vagotonic)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before flight</td>
<td>57.5</td>
<td>73.8</td>
<td>20.2</td>
<td>28.2</td>
<td>40.4</td>
<td>31.2</td>
<td>8</td>
</tr>
<tr>
<td>In Flight</td>
<td>54*</td>
<td>65.3</td>
<td>22.5</td>
<td>26.5</td>
<td>48</td>
<td>25.4*</td>
<td>8</td>
</tr>
<tr>
<td>After Flight</td>
<td>63.3*</td>
<td>94.8*</td>
<td>15*</td>
<td>19.5*</td>
<td>50.8</td>
<td>29.5</td>
<td>8</td>
</tr>
<tr>
<td>N (normotonic)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before flight</td>
<td>63</td>
<td>134.1</td>
<td>11.1</td>
<td>26.6</td>
<td>43.3</td>
<td>28.6</td>
<td>6</td>
</tr>
<tr>
<td>In Flight</td>
<td>61</td>
<td>124.3</td>
<td>12</td>
<td>25.3</td>
<td>48</td>
<td>26.3</td>
<td>6</td>
</tr>
<tr>
<td>After Flight</td>
<td>75.4*</td>
<td>240*</td>
<td>8.2*</td>
<td>19*</td>
<td>51.6</td>
<td>29.4</td>
<td>6</td>
</tr>
<tr>
<td>NS (normal-sympathotonic)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before flight</td>
<td>58</td>
<td>48</td>
<td>28</td>
<td>36</td>
<td>41</td>
<td>23</td>
<td>1</td>
</tr>
<tr>
<td>In Flight</td>
<td>69</td>
<td>121</td>
<td>8</td>
<td>22</td>
<td>51</td>
<td>27</td>
<td>1</td>
</tr>
<tr>
<td>After Flight</td>
<td>97</td>
<td>363</td>
<td>0</td>
<td>10</td>
<td>56</td>
<td>34</td>
<td>1</td>
</tr>
<tr>
<td>S (sympathotonic)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before flight</td>
<td>68</td>
<td>72</td>
<td>18</td>
<td>19</td>
<td>44</td>
<td>37</td>
<td>1</td>
</tr>
<tr>
<td>In Flight</td>
<td>75</td>
<td>234</td>
<td>0.5</td>
<td>13</td>
<td>49</td>
<td>38</td>
<td>1</td>
</tr>
<tr>
<td>After Flight</td>
<td>73</td>
<td>202</td>
<td>3</td>
<td>20</td>
<td>50</td>
<td>30</td>
<td>1</td>
</tr>
</tbody>
</table>

As viewed in table 4, the majority of 22 ISS cosmonauts (n=8) belonged to the group with normal vagotonic (NV) regulation. Groups with vagotonic (V) and normal tonic (NT) regulation consisted of six participants in the experiment each; one cosmonaut had normal sympathotonic (NS) and also one sympathotonic (S) regulation. Table 5 contains mean HRV parameters in different mission periods for each type of autonomic regulation.

As is evident from these data, reaction to prolonged microgravity varied in cosmonauts with different types of regulation. Those who have regulation of the vagotonic type displayed substantial
reductions of heart rate, index of tension and relative high-frequency power (HF %). The low-frequency power (LF %), on the contrary, showed a significant growth. Cosmonauts with NV regulation were found to slow down heart rate and to reduce relative HRV power in the very low-frequency spectrum (VLF%) considerably. Cosmonauts with NT regulation did not change the HRV parameters significantly during space flight. To sum up, the trend in adaptive reactions in all groups was identical; however, it was the strongest in cosmonauts with vagotonic regulation.

Preliminary assignment to the groups was made with consideration of individual heart rate values averaged for the entire period of life in microgravity (table 4).

Table 4. Determination of the type of autonomic regulation by the criterion of heart rate averaged over the entire period of life in microgravity

<table>
<thead>
<tr>
<th>Type of autonomic regulation</th>
<th>Mean heart rate in microgravity (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>V (vagotonic)</td>
<td>50 or less</td>
</tr>
<tr>
<td>NV (normal-vagotonic)</td>
<td>51-60</td>
</tr>
<tr>
<td>N (normotonic)</td>
<td>61-65</td>
</tr>
<tr>
<td>NS (normal-sympathotonic)</td>
<td>66-70</td>
</tr>
<tr>
<td>S (sympathotonic)</td>
<td>Above 70</td>
</tr>
</tbody>
</table>

Cosmonauts with normal sympathotonic and sympathotonic regulation exhibited same trend of reaction as the other groups but the reaction per so was sharper with the values SI, pNN50, HF % and LF % suggesting high activation of the sympathetic nervous system.

In the post-landing period, all cosmonauts displayed identical reactions though of different strength. The reaction was the strongest in cosmonauts with normotonic regulation.

3. Functional reserve recovery during sleep in microgravity
Quality of sleep and completeness of the functional reserve recovery can be assessed by comparison of data recorded at the first and last sleep hours. Even HR changes are enough to see that difference values of the parameters furnish important information about sleep quality (fig. 3). Heart rate variability parameters are particularly informative. It is well known that sleep is the kingdom of vagus. In sleep, parasympathetic structures take over dominance, owing to which the functional
reserve of the organism restores and is spent minimally. The defensive-recovery function of the parasympathetic system is vital for those whose occupation is associated with exposure to stressful environments. That is why it is so interesting to find out how autonomic regulation changes in sleeping cosmonauts in different periods of space flight.

To be certain that sleep quality can be indeed assessed by difference values of the HRV parameters, special comparative studies with the use of polysomnography were performed [12].

We studied cross-correlation between polysomnographic data and results of HRV analysis. The following polysomnography parameters were considered: sleep index, falling asleep time, wakefulness, time, sleep effectiveness, duration of rapid eye movement sleep and number of sleep cycles. HRV analysis results were used to calculate HR SDNN, pNN50 and SI difference values. The highest correlation was established between polysomnography data and sympathetic (SI) and parasympathetic (pNN50) regulation activities.
Figure 3. Evening and morning HR, SDNN, SI and pNN50 values measured in crew member (K1) in different periods of space flight.

This seems to be linked with the fact that their parasympathetic segment of the autonomic nervous system (pNN50) is very active and reacts to inhibitory processes in the brain cortex controllers of the falling asleep quicker than other segments.

To sum up, analysis of sleep quality in ISS cosmonauts by HRV difference values allows quantify to what degree sleep in microgravity recovers functional reserve of the organism. It should be mentioned that subjective sleep assessment by cosmonauts coincides with objective data in no more
than 70-80 %. However, as a rule, when a cosmonaut said that he had not slept well his words were supported by objective data.

4. “SONOCARD” as an instrument of assessing recovery from open space operations
It is well known that sleep is crucial for restoration of the functional reserve of organism. This explains the importance of assessing the quality of cosmonauts’ sleep after heavy flight duties. One of the most demanding spaceflight operations is egress into open space and extravehicular activities (EVA) on outer surface of the International space station. These operations challenge cosmonauts physically and psychoemotionally. That is why it is essential to know the reserve potential of organism before cosmonaut goes out and when he returns into the station. The latter needs to be known as for assessment of cosmonaut’s fatigue and energy cost of planned operations, so prediction of fitness for next EVAs. Practical aspects of this approach were validated on the ISS by the instrumentality of device “SONOCARD” [13, 14, 15].

One investigation was scheduled 3 to 10 days prior to preplanned EVA and the other, on the night following open space operations. Three Russian crewmembers (К1, К2 и К3) were investigated. The very first investigation was performed on November 15, 2010 with two cosmonauts (К1 and К3). К3 made three egresses in a mission. K2 went out in open space twice.

Tables 5 and 6 present night average values of the main HRV parameters following EVA performed by K2 and K3. Six days before the EVA (mission day 33) K2 developed moderate bradycardia (night average heart rate = 47.1 /min) and had slightly increased LF (52.4 %). On the night following the first EVA his heart rate rose to 54.2 /min and LF made up 63.5%. Functional straining was testified also by reductions in pNN50, TP and HF, and growth in the stress index (SI).

By his second EVA (mission day 62) all means of the HRV parameters were back within the ranges identified on the eve of the first egress. After the second EVA, the pattern of HRV changes was analogous to what had been observed previously; pNN50, TP and SI underwent more significant changes. It should be noted that degree of regulation straining after the working in open space was more obvious following the second EVA as compared with the first one.

So, already the first investigation showed that work in open space involves high straining of the regulatory systems and costs gross expenses of the functional reserve. Subsequent investigations reinforced this conclusion and demonstrated that repeated participation in EVA causes fatigue accumulation and every next egress becomes more demanding for the regulatory systems.
Table 5. Changes in mean HVR parameters in К2 on the night following EVA

<table>
<thead>
<tr>
<th>Period</th>
<th>Mission day</th>
<th>HR</th>
<th>pNN50</th>
<th>SI</th>
<th>TP</th>
<th>HF</th>
<th>LF</th>
<th>VLF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before EVA-1</td>
<td>33</td>
<td>47.1</td>
<td>38.6</td>
<td>31.9</td>
<td>5090</td>
<td>22.5</td>
<td>52.4</td>
<td>25.1</td>
</tr>
<tr>
<td>After EVA-1</td>
<td>39</td>
<td>54.2*</td>
<td>16.4*</td>
<td>64.7*</td>
<td>2932.6*</td>
<td>13.9*</td>
<td>63.5*</td>
<td>22.5</td>
</tr>
<tr>
<td>Before EVA-2</td>
<td>62</td>
<td>46.8</td>
<td>28.9</td>
<td>34.5</td>
<td>4973.8</td>
<td>18.4</td>
<td>49.6</td>
<td>32</td>
</tr>
<tr>
<td>After EVA-2</td>
<td>64</td>
<td>52.8</td>
<td>12.9*</td>
<td>94.3*</td>
<td>1891*</td>
<td>19.3</td>
<td>53.4</td>
<td>27.3</td>
</tr>
</tbody>
</table>

*- statistically significant change (p < 0.05)

Table 6 contains similar data from К3 who made three egresses onto the ISS outer surface over his 6-month mission. HRV analysis following the first EVA found no other changes except a considerable LF increase and VLF reduction in comparison with baseline values collected 9 days prior to EVA. The second EVA produced a somewhat moderate LF increase and VLF reduction. Obvious signs of the functional straining, i.e. SI growth and TP reduction, appeared only following the third EVA.

Table 6. Changes in the night average HVR parameters in К3 on the night following EVA

<table>
<thead>
<tr>
<th>Period</th>
<th>Mission day</th>
<th>HR</th>
<th>pNN50</th>
<th>SI</th>
<th>TP</th>
<th>HF</th>
<th>LF</th>
<th>VLF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before EVA-1</td>
<td>32</td>
<td>47.1</td>
<td>13.3</td>
<td>102.4</td>
<td>1370</td>
<td>27.8</td>
<td>36.7</td>
<td>35.6</td>
</tr>
<tr>
<td>After EVA-1</td>
<td>40</td>
<td>46</td>
<td>15.8</td>
<td>95.8</td>
<td>1650.2</td>
<td>20.9</td>
<td>50.4*</td>
<td>28.7*</td>
</tr>
<tr>
<td>Before EVA-2</td>
<td>102</td>
<td>46.1</td>
<td>12.9</td>
<td>97.6</td>
<td>1405.7</td>
<td>32.4</td>
<td>38.8</td>
<td>28.8</td>
</tr>
<tr>
<td>After EVA-2</td>
<td>106</td>
<td>47.5</td>
<td>11.5</td>
<td>112</td>
<td>1460.4</td>
<td>27.6</td>
<td>41.2</td>
<td>31.2</td>
</tr>
<tr>
<td>Before EVA-3</td>
<td>129</td>
<td>47.9</td>
<td>10.7</td>
<td>95</td>
<td>2220.8</td>
<td>19.3</td>
<td>46.8</td>
<td>33.9</td>
</tr>
<tr>
<td>After EVA-3</td>
<td>132</td>
<td>46.9</td>
<td>8.41</td>
<td>132.8*</td>
<td>942.8*</td>
<td>23.7</td>
<td>44.8</td>
<td>31.5</td>
</tr>
</tbody>
</table>

*- statistically significant change (p < 0.05)

Table 7. Results of K1 pre and post EVA data analysis (investigations with the use of “Sonocard”)

<table>
<thead>
<tr>
<th>HRV parameter</th>
<th>12 d. prior to EVA</th>
<th>Second night post EVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR, beats/min</td>
<td>57.7</td>
<td>69.2*</td>
</tr>
<tr>
<td>pNN50,%</td>
<td>15.6</td>
<td>7.8*</td>
</tr>
<tr>
<td>SI, stand.unit</td>
<td>71.7</td>
<td>121.4*</td>
</tr>
<tr>
<td>TP, ms2</td>
<td>2356.3</td>
<td>1342.6*</td>
</tr>
</tbody>
</table>

*- statistically significant change (p < 0.05)
Table 7 presents the results of K1 investigations. He made one egress on mission day 153; implementation of this EVA at the end of his six-month mission could have affected the results. On the second night following EVA the pronounced increase of the degree of functional straining was manifested by significant rises in HR and SI and reductions in pNN50 and TP. Functional straining due to depletion of the functional reserve of organism was developed in all cosmonauts though to a variable extent. Apparently, much depends on individual functional potential which is subject to gradual depletion as mission continues. It may be that functional straining is a function of the length of stay in microgravity.

Conclusions

Implementation of experiment “Sonocard” aboard the ISS furnished important scientific and practical results. First of all, the unique technique of noninvasive physiological signal recording for sleep investigations in long-duration piloted missions was developed. The simple and comfortable technique provides high quality data recording all night through. Five years of the research experiments on the ISS demonstrated steady reliability of device “Sonocard”. Software products for in-sleep seismocardiogram analysis ensure acquisition of valuable data about quality of cosmonauts’ night sleep during space flight [16]. We should also point out the possibility to assess sleep quality which is essential for judging about completeness of the functional reserve recovery and adjustment of cosmonaut’s work/rest cycle, if necessary. The series of investigations scheduled on the eve and soon after operations in open space showed the utility of this approach for estimating degree of organism straining and ability to recover, and energy cost of these operations [17]. The unprecedented systematic physiological signal recording during sleep in space is the best argument for advocating this technique as an enabling instrument for the system of spacecrew medical monitoring.

Results of experiment Sonocard rationalized the development of concrete recommendations for continuation of the investigations and research data application. Specifically, the new technique should be integrated into the system of medical monitoring of crew members in orbital and future remote space missions. Other fields of application of the in-sleep signal recording are clinical and rehabilitation medicine and applied physiology.
The experimental use of the Sonocard technique in the Mars-500 project (simulation of a mission to Mars) testified its validity in ground-based investigations with simulation of the effects of space factors on human organism.

Statement on ethical issues
Research involving people and/or animals is in full compliance with current national and international ethical standards.

Conflict of interest
None declared.

Author contributions
I.I.F., E.S.L., I.N.S. defined the aim of research and supervised the implementation. I.N.S., A.G.C., R.M.B. prepared the manuscript and analyzed the data, R.M.B. drafted the manuscript. All authors read and met the ICMJE criteria for authorship. All authors read and approved the final manuscript.

References


15. Funtova II, Baevsky RM, Luchitskaya ES, Slepchenkova IN. The flight experiment Sonocard on board the International Space Station (ISS) - the contactless study of autonomic cardiovascular regulation during sleep in long term space flight. 19th IAA Humans in Space Symposium; 2013; ID: 55.

16. Slepchenkova IN. Assessment of the functional state организма of organism under the action of spaceflight factors according to data of noninvasive physiological signal recording in the night period. 2010; Moscow. 24 p. [in Russian]

Case report

Paroxysmal atrial fibrillation in 5 months old Afro-Caribbean

Sandra Williams-Phillips* MD, FESC, FAHA, FASE

1 Andrews Memorial Hospital, TAI Wing, 27 Hope Road, JMAAW08, Kingston 10, Jamaica, West Indies

* Corresponding author phone: +(876) 881-78-44, e-mail: sandrap@cwjamaica.com

Submitted: 15 July 2014
Accepted: 14 August 2014
Published online: 14 November 2014

Abstract

Congenital paroxysmal Atrial Fibrillation in infants is a rare occurrence requiring a high index of suspicion. The majority have a Pre-excitation syndrome which may be concealed. It may be associated with specific structural congenital cardiac lesions. This Index case had only paroxysmal atrial tachyarrhythmia with no predisposing condition that subsided spontaneously and is the first case documented in an Afro-Caribbean infant.

Learning objective

This Case Report documents a rare Paroxysmal Atrial Fibrillation in an infant with spontaneous remission. This has never been documented in the English Medical Literature in an Afro-Caribbean.

Keywords

Atrial fibrillation • Wolff-Parkinson-White syndrome • Beta-blockers • Flecainide

Imprint

Sandra Williams-Phillips. Paroxysmal atrial fibrillation in 5 months old Afro-Caribbean; Cardiometry; No.5; November 2014; p.66-70; doi:10.12710/cardiometry.2014.5.6670
Available from: www.cardiometry.net/no5-november-2014/paroxysmal-atrial-fibrillation

Introduction

Congenital paroxysmal Atrial Fibrillation in infants was noted in only ten patients over seventeen years between 1958 and 1975 by Radford et al [1]. The rarity and findings have been well documented by Andersen et al (1953) and Clint et al in 1972. [2,3]. Simcha et al had thirty nine cases isolated cases in seventeen years. Agarwala et al in 1980 confirmed that the diagnosis has become more frequent with the use of Foetal and Neonatal electrocardiographic monitoring [4,5]. Campa et al has classified these patients using the age of onset in three groups with a direct clinically significant correlation. The onset occurs in the foetus in group one, in the first month of life in group two and group three with occurrences of atrial dysrhythmia, between one month and twelve months of age. Group one had episodic episodes with slower heart rates, Group two had a greater occurrence of
cardiac decompensation [6]. In most of the cases mentioned by Simcha et al, Campa et al and Radford et al about one-third has complete cessation before a year of age and up to 70% of cases had Wolff-Parkinson Syndrome which was either overt or concealed, on resting electrocardiography (ECG) [4,6]. The signs of Pre-excitation may post date the onset of arrhythmia and was associated with a greater recurrence when confirmed [1-4, 6].

Atrioventricular re-entry tachycardia (AVRT) was noted more in infants with atrio-ventricular bypass tracts as compared to atrio-ventricular node re-entry in adolescents as the underlying mechanism of the atrial tachyarrhythmia [7,8]. The statistically significant structural cardiac lesions associated with paroxysmal atrial tachycardia were noted to be Ebstiens anomaly but it also occurred in patients with atrial septal defects, ventricular septal defects, transposition of the great arteries, endocardial fibroelastosis, coarctation of the aorta and dextrocardia [6-8]. The index case had none of these structural lesions or any Pre-excitation syndrome or Ion channelopathy.

Case report
A five month old Afro-Caribbean female infant presented with intermittent respiratory distress and mother noticing intermittent episodes of palpitations associated with the respiratory distress. There was no preceding or concurrent fever, viral symptoms or signs, in caregivers or infant. She was the product of an uncomplicated pregnancy and delivery, who was feeding well with appropriate weight gain for age. There was no gestational diabetes or maternal autoimmune disorder. No family history of arrhythmia, pre-excitation syndrome, ion channelopathy, sudden infant death syndrome, sudden death or deafness.

Significant findings on examination were confined initially to the respiratory system with intermittent episodes of rhonchi. Heart rate was 160 beats per minute. There was no hepatomegaly or signs of congestive cardiac failure. Twenty four hour Holter assessment detected intermittent episodes of Atrial tachycardia (Fig.1), when the event button was pressed and at other times not noted by caregiver. The resting ECG and Transthoracic Echocardiogram were normal and Digoxin was given with cessation of symptoms. This was discontinued by caregiver despite advice after two months and there has not been a recurrence. Thyroid function tests were normal.
Discussion

The spontaneous remission of the Atrial Tachyarrhythmia in the absence of a structural congenital cardiac lesion and absence of Pre-excitation syndrome is consistent with the majority of cases reports with similar findings. The prophylactic treatment of one year where the likelihood of recurrences would be expected would have been optimal but the fortuitous discontinuing of medication helped to confirm the spontaneous cessation of the tachyarrhythmia [6-9].

The use of Digoxin with no overt accessory pathway was used with the caution that a concealed pathway could lead to exacerbation of symptoms. Beta-blocker, the drug of first choice for many centers was avoided because of the possibility of exacerbation of bronchospasm noted clinically [8-10].

The choice of medication is dependent on the initial presentation and the persistent and incessant nature of the arrhythmia. Treatments being used have changes over the past two decades with Adenosine now being used as drug of choice in some centers, instead of direct cardioversion for the incessant especially in Congestive Cardiac Failure. Medications recommended in order of preference varies among institutions, in the absence of cardiac decompensation are beta-blockers, flecainide, digoxin. Drugs control the most common cause of AVRT in different ways. Conduction via the accessory pathway is affected by beta-blockers and digoxin. Reductions of transmission via the accessory pathway are by use of flecainide and propafenone. Sotalol and amiodarone are used in incessant and resistant cases and affect conduction in both the atrioventricular node and the accessory pathway. All are consistent with avoidance of Verapamil in infancy which aggravates cardiac decompensation. Amiodarone is used as a last resort with a close watch for the myriad of complications associated with its use [9]. Incessant and uncontrollable cases have the potential to be
cured with Electrophysiological studies and Catheter ablation, preferred in the older child but can be used successfully in Infants when Atrial Tachyarrhythmia is uncontrollable [8-10].

The inadvertent early positive outcome with complete cessation, in this 5 month old female Afro-Caribbean, is the first case of paroxysmal Atrial Fibrillation documented in an Afro-Caribbean infant.

Statement on ethical issues
Research involving people and/or animals is in full compliance with current national and international ethical standards.

Conflict of interest
None declared.

Author contributions
The author read the ICMJE criteria for authorship and approved the final manuscript.

References


**Original research**

**Efficacy of enhanced external counterpulsation: our experience**

Chandra Mani Adhikari†, Dipanker Prajapati†, Suman Thapaliya†, Man Bahadur KC†

† Department of Cardiology, Shahid Gangalal National Heart Centre, 11360, Nepal, Bansbari, Kathmandu

* Corresponding author phone: +977 (1) 437-13-22, e-mail: topjhap@hotmail.com

Submitted: 29 August 2014
Accepted: 23 September 2014
Published online: 14 November 2014

**Aims**
Enhanced external counterpulsation therapy is a non-invasive, non-pharmacological outpatient treatment option for refractory angina pectoris. Our aim is to evaluate its efficacy in Nepalese refractory angina pectoris patients.

**Materials and methods**
It was single centre prospective study conducted from 2010 August to 2013 December. All thirty one (n=31) consecutive patients, referred for and received 35 hours of treatment were included in this study. The distance covered in six minute walk test before and after the treatment was recorded and compared. Patients were followed each with the questionnaires about their anginal symptoms before and after the treatment.

**Results**
In our study 19(61.3%) were male and 12(38.7%) female. The mean age was 65.7±9.3 years. Most patients had multi vessel disease. Twelve patients had previous history of revascularization. In 6 minute walk test there was significant difference in mean distance covered before and after the treatment. Most patients experienced decrease in the angina symptom. They had decreased in severity and frequency of angina, resulting in decreased use of sublingual nitrates.

**Conclusion**
EECP can be safe and effective treatment option for patients with RAP.

**Keywords**
Enhanced external counterpulsation • Refractory angina pectoris

**Imprint**
Chandra Mani Adhikari, Dipanker Prajapati, Suman Thapaliya, Man Bahadur KC.
Efficacy of enhanced external counterpulsation: our experience; Cardiometry; No.5; November 2014; p.71-77; doi:10.12710/cardiometry.2014.5.7177
Available from: http://www.cardiometry.net/no5-november-2014/external-counterpulsation

**Introduction**
Enhanced external counterpulsation (EECP) therapy is a non-invasive, non-pharmacological outpatient treatment option for chronic stable angina that is refractory to optimal anti-anginal medical therapy and without options for revascularization, commonly referred to as refractory
angina pectoris (RAP) [1]. EECP can improve exercise tolerance; ameliorate symptoms [2, 3] and quality of life [4] in patients with RAP [5]. EECP has been given IIa Class of Recommendation in the 2013 European Society of Cardiology (ESC) Guidelines on the Management of Stable Coronary Artery Disease [6] for RAP patients. In December 2013 The Food and Drug Administration (FDA) issued a final order to reclassify EECP for treatment of RAP, which is a preamendments class III device, into class II [7].

Our aim is to evaluate the efficacy of EECP in RAP patients in Shahid Gangalal National Heart Centre, Kathmandu, Nepal.

Materials and methods

It was single centre prospective study conducted from 2010 August to 2013 December in Shahid Gangalal National Heart Centre (SGNHC), Kathmandu, Nepal. The study protocol was approved by the Ethics Committee of SGNHC. Informed consent was taken from patients and patient party. Unless for emergency purpose medical therapy was not changed during the EECP treatment.

Thirty one (n=31) consecutive patients, referred for EECP were included in this study. Before patients were included all the contraindication of EECP therapy were ruled out. One patients was excluded from that study as the treatment was stopped due to frequent ventricular ectopic. Patients’ data, which had been recorded prior to treatment, included age, gender, past history of diabetes mellitus (DM), hypertension, dyslipidaemia, tobacco consumption, previous angiographic data (angiographic score as Single (SVD)-, double (DVD)-or triple (TVD)-vessel disease) and previous revascularization therapy. A six minute walk test was performed under the same circumstances for all the patients at baseline and at the end of the treatment. The distance covered in six minute was recorded and compared. Each patient were followed with the questionnaires about their anginal symptoms before and after the treatment.

EECP equipment was supplied by Vamed Company (Guangzhou, China). The equipment consists of an air compressor, a console, a treatment table and two sets of three cuffs. Before a treatment session, cuffs are wrapped around the patient's legs, one set on each leg. Using compressed air, pressure (260–350mmHg of external pressure) was applied via the cuffs to the patient’s lower extremities in a sequence synchronized with the cardiac cycle. In early diastole, pressure was applied sequentially from the lower legs to the lower and upper thighs to propel blood back to the heart. At end-diastole, air was released instantaneously from all the cuffs to remove the externally applied
pressure, allowing the compressed vessels to reconfirm, thereby reducing vascular impedance. Daily one hour treatment sessions were administered for a total treatment course of 35 hours.

The two-tailed paired t-test was used to evaluate the significance of improvement in the distance covered in six minute walk test before and after the treatment.

Results

Thirty one patients completed 35 hours of treatment within 7 weeks. Demographic and clinical characteristics of the patients are shown in Table 1 below. The mean age was 65.7±9.3 years. Among the 31 patients were included in this study 19(61.3%) were male and 12(38.7%) female. Twenty three (74.1%) patients had TVD, 8 (25.9%) with DVD in coronary angiogram. Seven (22.5%) patients had undergone Coronary Artery Bypass Graft (CABG), four (12.9%) individuals had undergone percutaneous coronary intervention (PCI) with stenting and one (3.2%) patient had undergone CABG as well as PCI. Among risk factors for Coronary artery disease, hypertension was present in 26(83.8%) cases, diabetes mellitus in 12(38.7%) individuals, and 12 (38.7%) were tobacco consumers. Low LVEF defined as LVEF≤ 40% was present in two (6.4%) patients.

Table 1. Baseline demographic and clinical characteristics: N= 31 (%)
In 6 minute walk test there was significant difference in mean distance covered before and after the treatment. Compared to baseline, 29 patients noted an increase in the 6 min walk test distance by more than 150 feet. Though there was an increase in the distance covered in 6 minute walk test distance in all patients, 30 patients experienced decrease in the angina symptom. Based on the questionnaires, except one patient, all patients noticed the decrease in severity and frequency of angina, resulting in decreased use of sublingual nitrates. Table 2 shows, as compared to the baseline, there was a significant improvement in distance covered in 6 min walk test.

**Table 2.** Comparison in 6 min walk test distance covered mean±standard deviation

<table>
<thead>
<tr>
<th></th>
<th>Pre EECP</th>
<th>Post EECP</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 min walk test distance</td>
<td>817.2±362.4</td>
<td>1053.4±346.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Though three patients developed blisters in the legs, two developed ecchymosis during the treatment, treatment was completed.

**Discussion and Conclusions**

Our study shows that EECP can be effective in RAP patients. The decrease in the angina symptoms, severity, intensity and nitrates use proves its efficacy in these patients. In the first and also the only multicentre, prospective, randomized, blinded, placebo controlled trial, Multicentre Study of Enhanced External Counter Pulsation (MUST-EECP), patients undergoing active counter-pulsation had a significant decrease in angina episodes, but there was no significant improvement in the duration of the exercise test [8].

In an EECP consortium, among 2 284 patients, an improvement was reported in up to 74% of patients by one or more CCS functional classes. The younger patients had a greater likelihood of improvement [8]. Patients who were younger, male, without multi-vessel coronary or non-cardiac vascular disease and non-smokers were likely to have higher diastolic augmentation and greater reduction in angina class after EECP. [9]

As in our study, efficacy of EECP was proven by numerous studies done in the US [10, 11, 12], Sweden [13] and Iran. [14] EECP has shown to provide long-term symptom relief and improved quality of life in a heterogeneous group of patients with ischaemic heart disease. [15] Though tobacco
use and previous myocardial infarction were associated with early relapse in angina in spite of an initial response other baseline factors studied did not affect the outcome of EECP treatment. [16]

EECP increases diastolic aortic pressure, reduces systolic pressure and enhances venous return, thus resulting in increased cardiac output. [17] However, the mechanisms by which these hemodynamic effects lead to a reduction of angina are poorly understood, although the acute effect is similar to IABP. [18] There is accumulating evidence suggesting that EECP treatment improves endothelial function, which may contribute to the clinical benefit. [5] EECP treatment is associated with an immediate increase in blood flow in multiple vascular beds including the coronary arterial circulation. [18] This increase in blood flow may result in increased endothelial shear stress which enhances endothelial function by stimulating the release of the vasodilatory mediator nitric oxide and reduces the release of the vasocontractile endothelin-1. [17, 20, 21, 22] Furthermore, besides the release of metabolites from ischemic regions, an increase in endothelial shear stress is considered a major stimulus for collateral blood vessel development and recruitment. This suggests that EECP treatment may exert its clinical beneficial effect by enhancement of coronary collateralization. EECP therapy has been associated with the release of angiogenic factors, such as vascular endothelial growth factor [23], basic fibroblast growth factor and hepatocyte growth factor. [22]

Our study limitations are single centre, non-randomized study with a small number of patients.

Our study demonstrates, EECP can be effective in decreasing the severity and intensity of angina pain. It is also helpful in improving the effort tolerance and the quality of life in patients with RAP.
Statement on ethical issues

Research involving people and/or animals is in full compliance with current national and international ethical standards.

Conflict of interest

None declared.

Author contributions

All authors contributed to the writing of the manuscript and analyzed the data, C.M.A. drafted the manuscript. All authors read and met the ICMJE criteria for authorship, agree with manuscript results and conclusions and approved the final manuscript.

References


Review

Spotlight on management of hypertrophic cardiomyopathy

Mohammed El-Assaly1*

1 Cardiology registrar, Heartland hospital, Bordesley Green, B95SS, Birmingham-UK

* Corresponding author phone: +44 (0) 7780-001-016, e-mail: mohammed.elassaly@heartofengland.nhs.uk

Submitted: 4 September 2014
Accepted: 23 September 2014
Published online: 14 November 2014

Abstract

Hypertrophic cardiomyopathy (HCM) is the commonest inherited cardio-myopathy. Prevalence 1/500 individuals. The disease has variable expressivity and penetrance, which leads to a diverse phenotypical expression. The aim of this review paper is to shed light on management of HCM.

Keywords

Cardiac magnetic resonance imaging • Left ventricular outflow tract obstruction • Hypertrophic cardiomyopathy • Left ventricular hypertrophy • Sudden cardiac death

Imprint

Mohammed El-Assaly. Spotlight on management of hypertrophic cardiomyopathy; Cardiometry; No.5; November 2014; p.78-88; doi:10.12710/cardiometry.2014.5.7888
Available from: www.cardiometry.net/no5-november-2014/hypertrophic-cardiomyopathy

Introduction

Dr. Robert Donald Teare, a pathologist at St George's hospital in London, described HCM more than fifty years ago. Sudden cardiac death (SCD) may be the first presentation hence the need to identify potential inheritants who may benefit from SCD preventive strategy. Incidence of sudden cardiac death is 2% to 4% per year in adults [1]. The emergence of cardiovascular magnetic resonance imaging (CMR) as an imaging modality aids diagnosis and prognostication.

A cardiomyopathy is:
“A myocardial disorder in which the heart muscle is structurally and functionally abnormal, in the absence of coronary artery disease, hypertension, valvular dis-ease and congenital heart disease sufficient to cause the observed myocardial ab-normality.” [2]

The heart muscle hypertrophy is the cause of the disease and not a sequala of an-other cardiac (like aortic stenosis) or extra-cardiac pathology (for example acro-megaly).

Genetics:
It is typically autosomal dominant. Autosomal recessive, X-linked, and mito-chondria patterns of inheritance also occur. About 50-60% of patients with a high index of clinical suspicion for HCM will have a mutation identified in at least 1 of 9
sarcomeric genes. In HCM there is no sex or race predilection. New molecular & genetic techniques allow identifying patients & family members with HCM. It can also identify genotypically positive phenotypically negative patients (carrier of the gene without clinical manifestation yet).

Diagnosis:
High index of suspicion is mandatory although may lead to false positive diagnosis of HCM. Causes of false positive diagnosis of HCM are:

Conditions simulating LVH/ASH:

1. Sigmoid septum of elderly.
2. Oblique sections of ventricular walls (off axis views).
3. Left ventricular false tendons.

LVH due to:

1. Infiltrative cardiomyopathy.
2. Anderson-Fabry disease (Skin manifestations may be a clue and enzymatic as-says confirms deficiency of alpha-galactosidase).
3. Hypertension with LVH and inferior myocardial infarction.

LVOT gradient is present due to LVH or haemodialysis.

HCM may present with symptoms of Exertional syncope, pre-syncope, palpita-tions or dyspnea in absence of another disease which could account for the symp-tom. More fortunate individuals from the diagnosis point of view are those asymptomatic detected during screening.

Hypertrophic obstructive cardiomyopathy (HOCM) may cause Pulsus bisferiens (double peak pulse) due to dynamic left ventricular outflow tract obstruction (LVOTO). Aortic stenosis or sub-valvular aortic membrane (fixed LVOTO) gives low pulse volume, Pulsus parvus et tardus.

A systolic murmur in left parasternal edge increases with valsalva. In con-trast to other causes of LVOTO the systolic murmur is decreased with valsalva due to decreased preload.

LVOTO is caused by septal hypertrophy, SAM and anterior displacement of mitral valve apparatus.

ECG showing LVH usually triggers imaging modality like trans-thoracic echocardiography (TTE) for the first instance. Cardiac imaging demonstrates asymmetrical septal hypertrophy (ASH), systolic anterior motion of mitral valve (SAM), left ventricular cavity obliteration and/or blood flow acceleration. Up to 42% of HCM cases show symmetrical (concentric) hypertrophy with no regional wall preference.

Risk Stratification:
The aim is to identify individuals in whom pre-emptive implantation of AICD is warranted to prevent SCD due to VF/VT.
Major risk factors for SCD are:

- Left ventricular hypertrophy (LVH) ≥30 mm or more.
- Previous cardiac arrest.
- Fall of systolic blood pressure on symptom limited ETT.
- First degree relative with SCD.
- Unexplained syncope or pre-syncope (non vasovagal).
- Non-sustained ventricular tachycardia (NSVT) on ECG monitoring.

NSVT:
Is defined as 3 or more consecutive beats arising below the atrio-ventricular node with a rate >120 beats/min and lasting less than 30 seconds.

NSVT can be precipitated by vasodilatation, dynamic LVOTO, myocardial ischemia driven by epicardial coronary artery stenosis and/or small vessel disease.

The stimulus may be atrial and/or ventricular non malignant arrhythmia. VT is maintained via reentry. Programed electrical stimulation rarely induces VT hence EP is of benefit in ablating atrio-ventricular accessory pathway if present.

LVH≥30 mm:
Any myocardial segment can be involved. LVH of HCM is 15 mm or more usually involving inter-ventricular septum or ratio of septum to lateral wall 1.3 or more. A septal to posterior wall thickness ratio >1.5 can point towards diagnosis of HCM in hypertensive patients.

However Maron et al. [3] stated that virtually any LV wall thickness can be consistent with the presence of an HCM-causing mutant gene.

CMR usually quantifies LV mass accurately.

Abnormal blood pressure response to exercise (ABPR):
ABPR is failure of blood pressure to rise, or a fall in blood pressure during exer-cise. Patient should not be on any cardio-active medications for 5 pharmacokinetic half lives. The mechanism of ABPR in patients with HCM is still debated. Counihan et al. and Frenneaux et al. [4] reported that excessive fall in systemic vascular resistance during exercise occurs due to a peripheral vasodilatory mechanism. Yoshida N, Ikeda H, Wada T, et al [5] suggested sub-endocardial ischemia in patients with HCM causes decline in LV systolic function and ABPR.

ABPR can be detected in 25% of HCM patients and thus it is positive pre-dictive accuracy for sudden death is low. It is a more sensitive indicator of SCD risk in younger patients (< 40 year old).

Family history of first degree relative with SCD (FHSCD):
SCD is defined as unexpected natural death from a cardiac cause within a short time period, generally <1 hour from the onset of symptoms, in a person without any prior condition that would appear fatal.
FHSCD is fulfilled as a major risk factor if:

1. First degree relative <50 years of age died suddenly whether or not had the diagnosis of HCM and/or:
2. First degree relative with diagnosis of HCM died suddenly at any age.

The diagnosis of HCM may be suggested by postmortem examination. Causes of unexplained syncope and pre-syncope are as follows: a broad differential diagnosis should be considered including vasovagal syncope, atrial tachyarrhythmias with rapid ventricular response with or without accessory pathway, VT, bradyarrhythmia and atrio-ventricular nodal block. LVOTO, orthostatic hypotension or carotid sinus hypersensitivity may cause syncope or presyncope.

The utilization of ambulatory ECG monitoring and ambulatory blood pressure (ABP) recording may reveal diagnosis and guide subsequent therapy. PPM can be used for treatment of bradyarrhythmias. Radiofrequency (RF) ablation used to ablate accessory pathway. AICD is indicated if NSVT is revealed. If syncope or pre-syncope cannot be explained it is best regarded as a major risk factor for SCD and AICD is warranted.

Previous cardiac arrest:
History taking may be rewarding if there is family history of diagnoses of HCM. The first presenter in any family poses the greatest challenge. Once diagnosed the rest of first degree relatives will be under medical surveillance.

Factors associated with increased risk of SCD in HCM are as listed below:

- Young age;
- Left ventricular outflow tract obstruction;
- Atrial fibrillation;
- Myocardial ischemia;
- Genetic mutations.

CMR in cardiomyopathy:
Whether ischemic cardiomyopathy (ICMP) or non-ischemic cardiomyopathy (NICMP), CMR provides an imaging modality which is quite unique: no ionizing radiation is available, it is non-invasive, independent of patient habitus and significant operator variability.

In CMR the contrast agent used is gadolinium. Caution is advised if estimated glomerular filtration rate (eGFR) is less than 30 due to increasing incidence of nephrogenic systemic fibrosis. Limitations include claustrophobia, which may be managed by prone positioning of patient. The presence of non-MRI compatible cardiac device or metal clips remains a hurdle. CMR scan usually takes 40 to 60 minutes according to protocol. When clinical suspicion of HCM is present HCM protocol is utilized.
CMR in HCM [6, 7]:

Resting cardiac functions:
Breath-holding cine steady state free precision (SSFP) imaging is the gold standard for accurate non-operator depended quantification of cardiac volumes, mass and biventricular systolic function.

Mostly the presence of LVH is the cornerstone of consideration of the diagnosis of HCM. In end stage HCM LV exhibits dilatation, LVH may be absent.

LVH may be asymmetrical commonly affecting inter-ventricular septum (ASH). Sometimes concentric hypertrophy is noted but out of proportion to loading conditions. LVH>15 mm even in presence of afterload increasing disease argues strongly for diagnosis of HCM. Systolic anterior motion of mitral (SAM) valve apparatus participates in left ventricular out flow tract obstruction (LVO-TO).

CMR can quantify accurately LV mass and localize hypertrophied segments.

Maximal LV thickness ≥30 mm is a major risk factor for SCD. LV maximal hypertrophy may be under appreciated by transthoracic echocardiography (TTE). The increase of LV mass points towards progression of HCM. A reduction of LV mass and LV dilatation in an established diagnosis of HCM could mean end stage HCM.

Right ventricular hypertrophy (RVH) and apical HCM can be readily identified by CMR yet pose an imaging challenge to trans-thoracic echocardiography.

A hyper-contractile LV is usually present. Accurate quantification of LV ejection fraction is needed for follow up of HCM patients. Cavity obliteration and flow acceleration are readily demonstrated by CMR. LVOT gradients, whether dynamic or resting, are accurately quantified by echocardiography. Resting cardiac functions evaluating end diastolic (EDV) and end systolic (ESV) volumes are used to monitor progression of HCM. Abnormality of mitral valve apparatus and SAM is easily demonstrated by CMR along with mitral regurgitation for which TTE is validated for quantification.

In up to 42 % of HCM cases concentric LVH is present, which should be more meticulously differentiated form other causes of concentric LVH.

Apical HCM:
It is more common in Japan. Apical wall thickness of > 15 mm gives imaging feature of HCM. A ratio of apical LVH to basal LVH ≥ 1.3–1.5 is another imaging clue. The characteristic spade like configuration of the left ventricular cavity initially described in angiographic studies is well appreciated on left ventricular vertical long-axis views on MRI. Right ventricular apical ventricular hypertrophy is well demonstrated by CMR paving the way to picking right ventricular involvement in HCM. RVH may lead to RVOTO and RV diastolic dysfunction.
Non-contrast tissue characterization

T2-weighted sequence, Short-Tau Inversion Recovery (STIR):
It is a sensitive sequence to detect myocardial edema. Although myocardial edema was first noticed on STIR for ICM it has been extended to NICP as well. As it suppresses the signal from flowing blood and fat it enhances sensitivity to tissue fluid. There is growing interest in myocardial edema which acts as a substrate to facilitate re-entry mechanism that sustains arrhythmias in HCM.

T1 mapping in HCM a histopathological sample of the myocardium:
T1 mapping without contrast shows myocardial cells versus extracellular volume (ECV). ECV is the space in the myocardium not occupied by myocytes. In non-ischemic myocardial insult T1 mapping is superior to LGE in quantifying extra-cellular matrix expansion (ECM). ECV can detect subtle myocardial fibrosis not necessary detected by LGE. Hence CMR evidence of subclinical HCM may be demonstrated by T1 mapping enabling initiation of management.

Contrast tissue characterization:
Mid wall T2 late gadolinium enchantment of LV myocardium points to myocardial fibrosis. Disarray of myocyte and fibrosis leads to delayed wash out of Gadolinium and hyper-enhancement. In HCM commonest site of LGE is in the ventricular septum and LV free wall. A less frequent pattern of LGE is restricted to the LV free wall or septum only. A less common pattern is LGE at RV insertion into the ventricular septum. Lastly LGE confined to the LV apex. It is uncommon to find LGE without LVH in HCM, although this is usually the case in pre-clinical HCM. Anecdotal data correlating extent of LGE and severity of LVEF re-duction exist. Extent of LGE is associated with cardiac mortality.

In HCM late gadolinium enhancement of LV myocardium is not subendo-cardial nor transmural. LGE is not restricted to a coronary artery territory. In HCM LGE is typically mid-wall and mid-segment enhancement. Sub-endocardial LGE is present if myocardial infarction occurs due to coexisting epicardial coronary artery stenosis leading to myocardial infarction. Thromboembolic led epicardial coronary occlusion usually causes myocardial infarction in apical LV segments. Increasing amount of LGE in comparison to previous CMR is an indicator of progression of HCM. Progression of LGE is not yet validated as a major risk factor for SCD.

Stress perfusion study:
Adenosine is used to induce hyperaemia which demonstrates hypo-perfusion in myocardial segments. In HCM hypo-perfusion may co-localize to segments of maximal hypertrophy. Stress induced perfusion may be due to epicardial to en-docardial gradients because of micro vascular dysfunction. Rest perfusion defect is due to micro-vascular disruption as a result of myofibril disarray and fibrosis. Mixed defects may exist.

Pharmacological therapy:
Diastolic and possibly systolic dysfunction is present in HCM. Beta blockers (BB) can increase diastolic time and allow LV more time for filling. If BB do not provide full symptomatic improvement in way of dyspnea non-dihydropyridine calcium channel blockers (CCB) such as verapamil can be added. Amiodarone can be used as a sinus rhythm maintain drug after AF cardioversion. Pharmacological antiarrhythmic are not a replacement for AICD when indicated.
Careful use of diuretics may also relieve symptoms of pulmonary venous congestion. Judicial use of diuretics is needed to avoid decreasing preload and increasing LVOT gradient.

Aspirin can be used for thromboprophylaxis in patients not known to have atrial fibrillation/flutter. Warfarin is needed if AF is diagnosed regardless of type of AF, (paroxysmal, persistent, longstanding persistent or permanent). Patients with HCM tolerate tachyarrhythmias poorly due to reduced diastolic time. Chemical or DC cardioversion is needed for atrial fibrillation/flutter.

The major risk factors for SCD are used to decide which patient need AICD to guard against VT/VF induced SCD [8]. During AICD implantation a challenge in testing for VF threshold may arise. VF threshold may be increased by amiodarone and BB.

Single chamber ICD is usually preferred especially in young patients. Patients should be well informed about possibility of inappropriate shocks (around 25%), restriction on driving and occupational implications. Anti tachycardia pacing is usually effective in terminating VT. Device therapy is not without complications among which cardiac device related infective endocarditis and device mal-function (inappropriate shocks, failure of sensing or capturing, pacemaker mediated tachycardia).

Disopyramide is a class IA anti arrhythmic with sodium channel blocking effect and a weak calcium channel blocking activity. It can be used to reduce symp-toms of LVOTO [9]. Disopyramide may be used to maintain sinus rhythm after cardioversion of A.fibrillation/A/flutter. Pollick and coworkers reported a decrease in LVEDP in response to intravenous disopyramide in their patients with HOCM. In 10 patients with HCM (6 with HOCM), Fifer et al reported intravenous disopyramide caused a universal increase in LVEDP. τ (the relaxation time constant), an index for the active diastolic LV properties, was unchanged. Mastubara and coworkers demonstrated LVEDP lowering effect of disopyramide along with shortened τ in patients with LVOT obstruction but raised LVEDP and lengthened τ in patients without LVOT obstruction.

Interventional measures to reduce LVOTO:
In absence of LVOT obstruction, LV systolic pressure = systolic arterial blood pressure.

In HCM LVOT gradient may be resting or on provocation. It can vary from beat to beat and with respiration.

LVOT obstruction is defined as a resting LVOT gradient of ≥30 mmHg. Severe obstruction is defined as ≥50 mmHg [10].

Septal reduction commonly performed for severely symptomatic patients in spite of optimal medical therapy with severe obstruction ≥30 mmHg at rest or ≥50 mmHg with provocation.
Alcohol septal ablation (ASA) [11-13]

Criteria for selection:
Symptoms of LVOTO that interfere with lifestyle despite optimal medical therapy; (2) Septal thickness ≥15-16 mm; (3) LVOT gradient ≥30 mm Hg at rest or ≥50 mm Hg on provocation; (4) accessible septal branch(es); and (5) absence of intrinsic abnormality of the mitral valve and of proximal left anterior descending coronary artery stenosis or severe coronary artery disease.

Complications include CHB requiring PPM. Large volume of alcohol injection, female sex and age >55y are associated with CHB. Among the criteria, found is presence of LBBB on pre-intervention ECG as a strong predictor of development of post ASA CHB.

Surgical myomectomy [14-16]:
may be misrepresented as a high risk treatment modality if compared to ASA. In North American centers 0 % post-operative mortality was reported for >1500 consecutive isolated myomectomy operations.

Meta-analysis of three retrospective studies demonstrated that surgical myomectomy and ASA showed comparable results on septal hypertrophy and NYHA class improvement.

Dual chamber pacing [17]:
Backed by subjective symptom improvement reported by the patients. It is ar-gued against by lack of consistent objective reduction of LVOT gradient suggest-ing symptom improvement may be a placebo effect. Cardiac catheterization la-boratory studies showed that a decrease in the outflow gradient produced by temporary A-V sequential pacing could be detrimental to ventricular filling and cardiac output.

Advantage of dual chamber pacing was demonstrated in patients receiving dual chamber ICD permitting more aggressive pharmacological intervention without fear of bradyarrhythmia. To obtain best results dual chamber pacing should be carried out in centers highly experienced in both pacemaker therapy and HCM.

Life style modification:
Competitive sports should be discouraged, patients should be educated to report change in severity of shortness of breath or the appearance of red flags like symptoms of pre-syncope or syncope.

Psychological aspect of HCM:
1,297 patients with HCM over period of 16 months reported emotionally trig-gered:
- Chest pain (60%).
- Syncope/lightheadedness 50%.
- Dyspnea 54%.

Females reported emotion-triggered symptoms more than males (50% vs 35% in males, P < 0.001).
As with any chronic disease, especially if life threatening, anxiety and depression should not be overlooked.

Infective endocarditis:
Is largely confined to those patients with LV outflow tract obstruction (resting or provoked), with intrinsic mitral valve disease or cardiac device related. The AHA recommendation 212 for antibiotic prophylaxis should be applied at the time of dental or selected surgical procedures.

Family screening:
Family screening for HCM poses a challenge. The customary strategy utilizes 12 lead ECG and TEE on a 12- to 18-month basis, usually beginning at age of 12 years. If no LVH is demonstrated at the age of about 18 to 21 years reassurance that HCM is likely to be absent.

Nevertheless being a disease of variable expressivity and penetrance late on-set HCM can be missed. Extending diagnostic serial transthoracic echocardiogram into mid-life for those family members with a normal echocardiogram and ECG may be advised.

Statement on ethical issues
Research involving people and/or animals is in full compliance with current national and international ethical standards.

Conflict of interest
None declared.

Author contributions
The author read the ICMJE criteria for authorship and approved the final manuscript.

References
2. ESC Working Group on Myocardial Pericardial Diseases (Elliott P et al. EHJ 2007)


Lesson 1

Subject 1. Substantiation of the principle of the single lead ECG recording of aorta with synchronous rheogram recording using ECG electrodes. Placing the electrodes on the patient’s body.

1. Substantiation of the principle of the single lead ECG recording of aorta.

The aim of the existing multi-lead ECG is to obtain data on the performance of various heart segments. The conventional ECG representing the total of all multi-lead signals is equivalent to a single lead ECG of the ascending aorta. This original single-lead ECG reflects the entire performance of all the heart segments in the most adequate way. This technology offers the possibility to obtain such the resulting signal in case of placing the ECG electrodes in the area of aorta and apex of heart as it is shown in Fig. 1 below.

![Figure 1. Placing the ECG electrodes in the area of aorta and apex of heart](image)

The upper electrode is fixed to the body surface in the aortic area as shown in the above Figure. It is convenient to fix it there. The lower electrode is fixed below the xiphoid process of the sternum in the soft tissue area. It is 5 cm below the xiphoid process. The both electrodes are placed on the anterior median line.
It is technically much simpler than the conventional multi-lead ECG recording. Besides, the obtained data volume is significantly larger as it is the case with using multi-leads. Fig. 2 demonstrates the correspondence between the data from different multi-leads vs. the single lead recorded of the ascending aorta. Each channel corresponds to a certain cardiac cycle phase. Thus, the atria performance is reflected in the atrial systole phase, the interventricular septum (IVS) performance is demonstrated in the IVS contraction phase, the myocardium is in the myocardial contraction phase, etc. Moreover, it becomes possible to analyze the processes in S-T segment that has never been done before. New definitions of the rapid ejection phase L-j boundaries are introduced.

**Figure 2.** The correspondence between the data containing in different leads of multi-lead system and the cardiac cycle phases of the single-lead ECG recorded of the ascending aorta. Transition from multi-lead ECG to single-lead ECG of the ascending aorta.

Modern engineering capabilities allow improving this technology by simultaneous recording of rheogram of aorta from the same ECG sensors. Fig. 3 demonstrates the placing of additional electrodes of a rheograph generator. There are no strict regulations where to place them. They are placed close to the signal electrodes as it is shown in the Figure below. Fig. 3 demonstrates electrode 5 that is connected to the common bus of the device (ground connection). It is placed in the lower part of the body.
Such a simple electrode placing scheme allows their easy fixing on the patient’s body and start running the device avoiding any inconveniences for patient or doctor.

Thus, the general scheme of the device connection to the electrodes is shown in Fig. 4. Fig. 5 demonstrates the scheme of recording of two signals, i.e., the ECG and the rheogram, using for this purpose the same pair of electrodes.

Fig. 6 shows a cardiac cycle phase structure which reflects all the processes of cardiovascular system performance.

**Figure 3.** Expanding of ECG information capability owing to the synchronous rheogram recording using the same electrodes. Another electrode is added to each ECG signal electrode. The signal of the RHEO generator is fed to the electrodes. One more electrode is fixed below to be connected to the device ground for noise suppression.
**Figure 4.** Connection of the device to the electrodes

**Figure 5.** Scheme of obtaining the two signals, i.e., ECG and rheogram signals, using the same pair of electrodes.
Figure 6. Cardiac cycle phase structure of ECG and rheogram
Subject 2. Orthostatic Test.
Orthostatic test is principally important to be carried out. After the first recording in lying position it is necessary to help a patient to sit and carry out the second record. Mitochondrial cardiomyopathy can be diagnosed only by the orthostatic test. The sitting position is shown in Fig.7.

Figure 7. Sitting position when carrying out the orthostatic test.
Lesson 2

Case topics: Location of cardiac cycle phases on ECG and their accurate identification using the first order derivative (mathematical graphical differentiation)

1. Cardiac cycle structure on ECG

Each cardiac cycle consists of 10 phases (Fig.1). In each phase, the contraction of the strictly defined cardiac muscle fibers occurs.

![Cardiac cycle structure on ECG](image)

**Figure1.** Cardiac cycle structure on ECG
Energy is consumed to provide the muscle contraction. This energy is generated by biochemical reactions. The efficiency of the operation of each phase determines changes in the respective muscle contraction rate. The energy is being changed from phase to phase showing its highest and lowest levels which correspond to the muscle contraction and relaxation, respectively. We can see the so-called transition of the energy consumption when the curve shows zero-crossings that may be compared with rising and falling of sea waves. Locations of the zero crossings can be precisely identified by the first order derivative as the derivative maxima and minima. On ECG, these crossings are found by the respective derivative maxima and minima which correspond to the cardiac cycle phase boundaries in the most precise manner (Fig.2).

Figure 2. ECG curve and the associated first order derivative. The derivative extrema correspond to the cardiac cycle phase boundaries (except R point).

Mathematical differentiation can be used for an analysis of any process. Several derivatives can be obtained sequentially. When analyzing an ECG it is quite reasonable to use only the first order derivative since just maxima and minima of the latter strictly correspond to the changes in the muscle contraction energy.

Every signal can be represented in terms of simple harmonic oscillations. Fig.3 demonstrates such an oscillation, namely, a sinusoidal oscillation.

![Figure 3. Sinusoidal oscillation curve and its derivative](image)

In the classical physics, curves of this sort describe oscillations of a pendulum moving left to right and reaching its extreme positions. These extreme positions correspond to the energy changing from its highest level to its lowest one. In Fig.3 we can find such a transition of the first curve crossing the time axis from the positive region to the negative one and vice versa. Each crossing point corresponds to the respective maximum or minimum on the second graph. These points are also called extrema.

If to differentiate an ECG, the extrema on its derivative correspond to the cases of the respective phase transitions of energy consumptions. It is just the criterion used to identify the cardiac cycle phase boundaries.
3. ECG as a sequence of simple harmonic oscillations
An ECG can be represented as a sequence of simple harmonic oscillations (Fig.4 below). In doing so, we can see that each oscillation segment corresponds to one phase. The boundaries of the elementary segments of these oscillations correspond to the phase boundaries. They are just the boundaries on the ECG which can be determined using the derivative.

![Figure 4. ECG as a sequence of simple harmonic oscillations](image)

4. Cardiac cycle phase boundary identification with the use of the first order derivative (graphical differentiation)

4.1. Identification of the boundaries of P-Q phase of atrioventricular valve closure.
The closure of the atrioventricular valves starts at the beginning of this phase. It corresponds to the P point on an ECG. The valves are completely closed at point Q. The P point corresponds to the inflection point of the P wave trailing edge. It is determined as a minimum of the P wave trailing edge derivative (Fig.5).

The Q point also corresponds to a derivative minimum, but this minimum is the first if to move left referred to the QRS complex (Fig.5). The Q point is the end of diastole (or the beginning of systole).

4.2. Identification of the boundaries of S-L phase of myocardium muscle fiber tension.
The phase is required to create the proper heart muscle fiber tension and increase a pressure applied to the blood volume in the ventricles that is necessary for opening the aortic valve. At the beginning of the phase, at point S, the muscle fibers start their tensioning. At point L, the created pressure in the ventricles is high enough in order to open the aortic valve and initiate the process of blood rapid ejection into the aorta.
Figure 5a.

Figure 5b.
Figure 5c.

Figure 5d.
Figure 5e.

**Figure 5.** Exemplary cases of identification of cardiac cycle phase boundaries using the first derivative of ECG.

Let us note that the point L identifying the tension phase end is introduced by the authors hereof for the first time. This phase has never been identified and described before. But it has a very important diagnostic value. It is described in detail in the training course of cardiac cycle phase analysis.

The point S corresponds to the derivative maximum (Fig.5).

The point L corresponds to the first maximum of the derivative locating right referring to the S point (Fig.5).

4.3. Identification of point j.

The j point corresponds to the inflection point of the rheogram leading edge (Fig.6). This point is identified as a maximum of the first derivative of the rheogram. It is located close to the T wave onset on an ECG.
4.4. T point identification.

In the phase analysis, the T point corresponds to the systole end (or diastole beginning). It is identified as a minimum of the derivative of the T wave tailing edge (Fig.5).