ECG + RHEO =

measuring of phase related volumes of blood

+ analysis of performance of cardiovascular system (compensatory mechanism)

+ biochemistry data of myocardium
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. Y Gulyaev, RU

EXECUTIVE EDITORS
Prof. V. Zernov, RU  Prof. M. Rudenko, RU

EDITORIAL ADVISORY BOARD
Prof. R. Baevsky, RU  Prof. H. R. Horvitz, US
Prof. S. Chefranov, RU  Prof. P. Mansfield, GB
Dr. S. Kolmakov, FI  Dr. C. Müller, AT
Prof. J. Moreno-López, SE  Dr. O. Voronova, RU
Prof. V. Polikarpov, RU  Prof. V. Vecherkin, RU
Prof. G. Stupakov, RU  Prof. S. Zaguskin, RU
Prof. V. Tyutyunnik, RU
The J wave: why so many contradictions and confusion in interpretation of its diagnostic value?  
Mikhail Y. Rudenko

New philosophy of validation and verification for cardiology: classical proof theory imported from natural sciences  
Mikhail Y. Rudenko, Goran Krstačić

Our new tornado-compatible aortic valve prosthesis: notable results of hydrodynamic testing and experimental trials  

Linear Eckman friction in the mechanism of the cyclone-anticyclone vortex asymmetry and in a new theory of rotating superfluid  
Sergey G. Chefranov

Our book is in Book Citation Index (Web of Science) now  

Occurrence of HLA- and Non-HLA Antibodies after Heart Transplantation are Associated with Cardiac Allograft Vasculopathy  
Maja-Theresa Dieterlen, Jens Garbade, Robert Riede, Stefan Dhein, Friedrich W. Mohr, Hartmuth B. Bittner, Markus J. Barten

Familial arrhythmogenic right ventricular dysplasia in afrocaribbeans: treadmill stress test the key to early diagnosis  
Sandra Williams-Phillips

Phase characteristics of rheograms. Original classification of phase-related changes of Rheos  
Mikhail Y. Rudenko

International Scientific Symposium CRO-e-CARDIOLOGY 2014
Cardiometry: pioneering experience in assessment of the heart performance and evaluation of fatal arrhythmia risks in intensive care unit patients

Vladimir V. Chepenko

Join the ESC Working group e-Cardiology
Dear readers!

The current issue of our journal has been published. Since the previous issue CARDIOMETRY has been making rapid strides. It is important to note that the journal's papers have served not only the purpose of formulation of new scientific problems, but also the purpose of their solutions. Despite the complexity of the problems and the fundamental consequences of application of the original results in practice, we can say with reasonable confidence that the offered solutions are simple enough. We mean the possibility of noninvasive measurements of heart muscle acid-alkaline balance parameters. It has not been discussed before, but it is just CARDIOMETRY that has stated this problem and solved it in the most efficient way. It is also the case with an assessment of ageing of the cardiovascular system performance. Identified are the mechanisms of sudden cardiac death; general evaluation of the coronary arteries blood filling is offered; the mechanisms of triggering of various arrhythmias are revealed, and the arterial pressure regulation mechanism is detected. These problems have long resisted solution by ordinary means. Nowadays CARDIOMETRY becomes a reliable diagnostic tool that can be used both for identifying various cardiac diseases & disorders and effectively eliminating them.

In the present issue of the journal we are reporting on a cardiologist who has defined the criteria of prediction of the heart performance resource within the accuracy of several hours with the use of CARDIOMETRY.

Herein you can also find papers of some authors who justify scientifically their new approaches to solutions using CARDIOMETRY principles. An example is a paper in our journal where our authors describe their new cardiac valve prosthesis that is capable of maintaining a specific blood flow structure similar to the biological elevated fluidity mode.

The growing popularity of the journal should also be mentioned. It is read in more than 95 countries in the world.

But we also have to note some problems the practitioners face studying the publications in the CARDIOMETRY journal. First of all, understanding of the new science is connected with the system of their education. Observed is a conflict between the knowledge acquired by the medical staff at the classical medical universities and the concepts offered in CARDIOMETRY. Primarily, it is hard for them to understand logics, axiomatics and computations which are found in CARDIOMETRY. We are taking into account all these problems and trying to explain difficult questions in a more simplified way. For this purpose, developed are the new methodological recommendations for practical
application which should assist the medical staff to rapidly master the unique capabilities of the new diagnostic method in practice.

Verification of new methods remains a great problem for practitioners. This problem is reflected in the first article of the journal issue. A new methodology of verification in medicine based on the classical principle of proving that is used in natural sciences is proposed therein. Physicists and mathematicians will find nothing innovative in it, but for the medical experts it is really a revolution. Therefore our journal will continue discussing this problem in the next issues.

We do very much hope our journal will be not only an academic one, but it will be able to support every practitioner in using the new science theoretical potential in full.

Looking forward to your feedback letters!

With best regards,

Cardiometry Editorial Board
There has been a significant interest in recent times in discussing how to properly interpret the diagnostic value of the point J on ECG. At first sight, it might appear to be a rather simple issue, but till now no consensus in its interpretation has been reached. Volume 46 of Journal of Electrocardiology No. 5, September/October 2013 is fully devoted to the above mentioned topics. A lot of publications in various journals and conference reports supply us with a great variety of concepts treating this problem [1-4].

Referring to our studies in the field of the cardiac cycle phase analysis, we would like to suggest our opinion on this issue.

There is a paradox that up to the present the phase-structured cardiac cycle is not understood in a proper manner. After the comprehensive research, we have identified that the J point corresponds to the end of the rapid ejection phase [5,6]. In this connection, a question arises: where is the beginning of this phase? It should correspond to the time of the beginning of the aortic valve opening that is recorded as the onset of a rheogram upslope segment. This issue has not been described in scientific literature, and therefore we have introduced a new point on ECG: it is point L that corresponds to the beginning of the rapid ejection phase. These topics were considered in details in a number of our papers and monographs. According to our concept, the cardiac cycle phase structure appears as follows (Fig. 1)[5].
Figure 1. A new concept developed by us: cardiac cycle phase structure.
Firstly, let us note that the above mentioned phase cannot shift and overlap the preloading S-L phase. It is just the matter that seems confusing for many authors and many minds and that makes them think that it is exactly the shifting of the phase that is the pathological onset of the early repolarization (ER). The repolarization can be initiated if and only if the blood pressure at the AV node is released, i.e., in case of depressurization at the AV node. Therefore, it is always the rule without exception that the repolarization begins with the end of the T wave [7].

Answering the question about the diagnostic value of the ECG segment in the phase being studied, it should be noted that the L-j phase reflects the amplitude of the third repeated septal and myocardial muscle contraction in the background of the general tension of all muscles that occurs in the S-L phase. Actually, we deal with the third QRS complex within the same cardiac cycle. This case has been already detailed by us in our papers [5].

Let us consider some real records to better illustrate our approaches. Fig. 2 below exhibits two synchronously recorded curves: an ECG and a Rheo of the ascending aorta, when changing the muscle diaphragm position caused by a mechanical force generated by an expansion in the abdominal volume. The specific feature of these curves is that the first part of the recordings corresponds to the starting of the abdominal volumetric expansion that leads to shifting of the heart electrical axis, and the second portion of the records reflects traveling of the heart electrical axis without such volumetric expansion. Fig.3 shows the respective responsiveness in detail.

Cardiac cycles are numbered below from 9 to 31. Both the shift of the heart’s electrical axis and the associated alteration in the S wave amplitude from its normal value up to its full disappearing are caused by an abdominal expansion in the volume that reduces the pressure on the diaphragm and contributes to the S wave formation.
The measured basic parameters of hemodynamics given in Fig.4 below unambiguously indicate the stability of all processes in each cardiac cycle regardless of the ECG shape. Such is the case for the stroke volume (SV) that remains stable and reaches 55,1 ml in cycles from 11 to 15. When assessing the stroke volume in the other cycles, it is evident that this parameter is not significantly larger in cycles 27-31 and accounts for 55,3 ml. The same is the case with the rest of the phase volumes. This proves the fact that the j point does not change its position, and therefore there are no grounds to speak about the early polarization.
Figure 4. Hemodynamic parameters derived from the ECG shown in fig. 2.

The basic hemodynamic parameters SV- stroke volume, MV-minute volume, PV1, PV2, PV3, PV4, PV5 and HR are indicated herein.

<table>
<thead>
<tr>
<th></th>
<th>SV</th>
<th>MV</th>
<th>PV1</th>
<th>PV2</th>
<th>PV3</th>
<th>PV4</th>
<th>PV5</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Средн.</td>
<td>53.7</td>
<td>4.3</td>
<td>31.8</td>
<td>22.0</td>
<td>31.9</td>
<td>21.8</td>
<td>8.3</td>
<td>79.4</td>
</tr>
<tr>
<td>1</td>
<td>55.1</td>
<td>4.6</td>
<td>31.2</td>
<td>23.9</td>
<td>32.7</td>
<td>22.4</td>
<td>8.4</td>
<td>83.5</td>
</tr>
<tr>
<td>2</td>
<td>47.2</td>
<td>3.9</td>
<td>26.3</td>
<td>20.9</td>
<td>28.0</td>
<td>19.2</td>
<td>7.5</td>
<td>82.6</td>
</tr>
<tr>
<td>3</td>
<td>55.1</td>
<td>4.5</td>
<td>33.0</td>
<td>22.1</td>
<td>32.7</td>
<td>22.4</td>
<td>8.4</td>
<td>81.7</td>
</tr>
<tr>
<td>4</td>
<td>55.1</td>
<td>4.4</td>
<td>33.1</td>
<td>22.0</td>
<td>32.7</td>
<td>22.4</td>
<td>8.4</td>
<td>80.3</td>
</tr>
<tr>
<td>5</td>
<td>55.1</td>
<td>4.4</td>
<td>32.9</td>
<td>22.3</td>
<td>32.7</td>
<td>22.4</td>
<td>8.4</td>
<td>79.5</td>
</tr>
<tr>
<td>6</td>
<td>55.3</td>
<td>4.4</td>
<td>32.5</td>
<td>22.8</td>
<td>32.8</td>
<td>22.5</td>
<td>8.5</td>
<td>79.9</td>
</tr>
<tr>
<td>7</td>
<td>55.3</td>
<td>4.4</td>
<td>32.3</td>
<td>23.0</td>
<td>32.8</td>
<td>22.5</td>
<td>8.5</td>
<td>80.3</td>
</tr>
<tr>
<td>8</td>
<td>47.2</td>
<td>3.8</td>
<td>27.2</td>
<td>20.0</td>
<td>28.0</td>
<td>19.2</td>
<td>7.5</td>
<td>80.8</td>
</tr>
<tr>
<td>9</td>
<td>55.1</td>
<td>4.4</td>
<td>32.0</td>
<td>23.1</td>
<td>32.7</td>
<td>22.4</td>
<td>8.4</td>
<td>79.9</td>
</tr>
<tr>
<td>10</td>
<td>55.3</td>
<td>4.4</td>
<td>32.3</td>
<td>23.0</td>
<td>32.8</td>
<td>22.5</td>
<td>8.5</td>
<td>80.3</td>
</tr>
<tr>
<td>11</td>
<td>55.1</td>
<td>4.5</td>
<td>32.3</td>
<td>22.8</td>
<td>32.7</td>
<td>22.4</td>
<td>8.4</td>
<td>81.7</td>
</tr>
<tr>
<td>12</td>
<td>55.1</td>
<td>4.5</td>
<td>31.5</td>
<td>23.6</td>
<td>32.7</td>
<td>22.4</td>
<td>8.4</td>
<td>80.8</td>
</tr>
<tr>
<td>13</td>
<td>55.1</td>
<td>4.4</td>
<td>31.8</td>
<td>23.3</td>
<td>32.7</td>
<td>22.4</td>
<td>8.4</td>
<td>80.3</td>
</tr>
<tr>
<td>14</td>
<td>55.3</td>
<td>4.4</td>
<td>32.3</td>
<td>23.0</td>
<td>32.8</td>
<td>22.5</td>
<td>8.5</td>
<td>80.3</td>
</tr>
<tr>
<td>15</td>
<td>55.1</td>
<td>4.5</td>
<td>32.6</td>
<td>22.5</td>
<td>32.7</td>
<td>22.4</td>
<td>8.4</td>
<td>81.2</td>
</tr>
<tr>
<td>16</td>
<td>55.1</td>
<td>4.4</td>
<td>33.2</td>
<td>22.0</td>
<td>32.7</td>
<td>22.4</td>
<td>8.4</td>
<td>80.3</td>
</tr>
<tr>
<td>17</td>
<td>55.6</td>
<td>4.3</td>
<td>33.9</td>
<td>21.7</td>
<td>33.0</td>
<td>22.6</td>
<td>8.6</td>
<td>77.4</td>
</tr>
<tr>
<td>18</td>
<td>55.6</td>
<td>4.4</td>
<td>32.8</td>
<td>22.9</td>
<td>33.0</td>
<td>22.6</td>
<td>8.6</td>
<td>78.2</td>
</tr>
<tr>
<td>19</td>
<td>55.6</td>
<td>4.5</td>
<td>31.9</td>
<td>23.7</td>
<td>33.0</td>
<td>22.6</td>
<td>8.6</td>
<td>80.8</td>
</tr>
<tr>
<td>20</td>
<td>54.9</td>
<td>4.5</td>
<td>30.6</td>
<td>24.3</td>
<td>32.6</td>
<td>22.3</td>
<td>8.3</td>
<td>82.6</td>
</tr>
<tr>
<td>21</td>
<td>47.6</td>
<td>3.8</td>
<td>27.1</td>
<td>20.5</td>
<td>28.2</td>
<td>19.4</td>
<td>7.7</td>
<td>79.5</td>
</tr>
<tr>
<td>22</td>
<td>55.1</td>
<td>4.4</td>
<td>31.1</td>
<td>24.0</td>
<td>32.7</td>
<td>22.4</td>
<td>8.4</td>
<td>80.3</td>
</tr>
<tr>
<td>23</td>
<td>55.6</td>
<td>4.4</td>
<td>31.4</td>
<td>24.3</td>
<td>33.0</td>
<td>22.6</td>
<td>8.6</td>
<td>79.5</td>
</tr>
<tr>
<td>24</td>
<td>54.9</td>
<td>4.4</td>
<td>31.7</td>
<td>23.3</td>
<td>32.6</td>
<td>22.3</td>
<td>8.3</td>
<td>80.8</td>
</tr>
<tr>
<td>25</td>
<td>56.0</td>
<td>4.4</td>
<td>32.5</td>
<td>23.5</td>
<td>33.2</td>
<td>22.8</td>
<td>8.7</td>
<td>78.6</td>
</tr>
<tr>
<td>26</td>
<td>55.1</td>
<td>4.5</td>
<td>31.0</td>
<td>24.2</td>
<td>32.7</td>
<td>22.4</td>
<td>8.4</td>
<td>81.7</td>
</tr>
<tr>
<td>27</td>
<td>55.3</td>
<td>4.4</td>
<td>31.5</td>
<td>23.8</td>
<td>32.8</td>
<td>22.5</td>
<td>8.5</td>
<td>79.5</td>
</tr>
<tr>
<td>28</td>
<td>55.6</td>
<td>4.4</td>
<td>33.0</td>
<td>22.7</td>
<td>33.0</td>
<td>22.6</td>
<td>8.6</td>
<td>79.0</td>
</tr>
<tr>
<td>29</td>
<td>55.3</td>
<td>4.4</td>
<td>31.4</td>
<td>23.8</td>
<td>32.8</td>
<td>22.5</td>
<td>8.5</td>
<td>79.5</td>
</tr>
<tr>
<td>30</td>
<td>55.3</td>
<td>4.3</td>
<td>32.0</td>
<td>23.3</td>
<td>32.8</td>
<td>22.5</td>
<td>8.5</td>
<td>78.6</td>
</tr>
<tr>
<td>31</td>
<td>55.3</td>
<td>4.4</td>
<td>32.5</td>
<td>22.7</td>
<td>32.8</td>
<td>22.5</td>
<td>8.5</td>
<td>79.9</td>
</tr>
</tbody>
</table>
Another example is an ECG curve given in Fig. 5 below. It was recorded in a patient with a lower body mass index. The so-called j-wave is marked clearer on this ECG. It is obvious that the S-L and L-j phases on the resting ECG demonstrate no changes in their durations. A more detailed examination of 2 cardiac cycles shows that we deal with a variation in the ECG shapes. Fig. 6 below illustrates that a sudden change in the stroke blood volume (SV) is recorded during the sharp ECG shape alteration that corresponds to the time of the j wave disappearance. The SV parameter in cycle 13 is 45.3 ml, while the same parameter accounts for 38 ml in the previous and the next cycle. It is only evidence of the responsiveness of the cardiac cycle phases which are included as variables in the hemodynamic equations by Poyedintsev-Voronova used for the blood phase volume calculation [5-10].

*Figure 5 The cyclically changing j wave on the curve for vertical patient body position. No symptoms of disease are reported. No patient's complaints are available.*
In this case, the following common feature should be highlighted: the j wave appears only in the event that a significant decrease in the QRS amplitude in general is observed. Nowadays it is still impossible to exactly define what processes may cause a drop in the potential on an ECG. In our research, we have detected sudden sharp changes in the electrical potential in one cycle in a patient due to his emotional stress. But today there are still no definitive answers to this question. Another issue of significance is to investigate how a high level protein input can influence the electrical potential of the heart muscle. We believe we are capable of solving all these issues within the nearest future.

In summary it may be said the following:

1. The recorded j wave cannot be considered as a criterion of pathological changes in the heart performance.

2. Hereby we confirm that we fully accept the statements by Prof. Victor Froelicher on the necessity to develop more profound methods for further investigations of the j wave phenomenon in
accordance with the considerations given by us herein that should be supported by the utilization of the cardiac cycle phase analysis.

3. It should be noted that we share Prof. Macfarlane’s opinion on the complexity of computerization in studying the J wave phenomenon.

References


New philosophy of validation and verification for cardiology: classical proof theory imported from natural sciences

Mikhail Y. Rudenko¹, Goran Krstačić² *

¹ Russian New University, 105005, Russia, Moscow, 22 Radio St.
² Institute for Cardiovascular Diseases and Rehabilitation, 10 000, Croatia, Zagreb, Draskovic eva 13
* Corresponding author phone: +385 (1) 461-23-46, e-mail: goran.krstacic@zg.t-com.hr

Submitted: 10 April 2014
Accepted: 22 April 2014
Published online: 30 May 2014

Aims
Problems of validation and verification are very critical in medicine. The absence of adequate models describing biophysical processes in the organism leads to using only practical evidence for these purposes that hinders innovations. But advances in medicine require new effective ways to solve these problems. Cardiometry as a new field in cardiology offers a new philosophy of validation and verification based on the classical proof theory borrowed from natural sciences. The aim hereof is to provide a new methodology for validation and verification for cardiovascular diagnostics.

Materials and methods
Axiomatic concepts based on new laws and rules allow applying direct and indirect methods of proof for validation and verification in medicine.

Results
The formulated laws of cardiometry provide reliable tools for verification of the correspondence between the cardiac signals and the real biophysical processes in the cardiovascular system.

Conclusion
The proposed methodology for verification of the correspondence between the ECG shapes and the relevant biophysical processes has been successfully developed exclusively as a result of creation of the comprehensive theory of cardiac cycle phase analysis being the basis of cardiometry. Progress in cardiology is badly affected by the absence of an adequate cardiac cycle phase concept so that a lot of inconsistencies have been accumulated therein. It has been just the logics imported to the theoretical analysis methods of cardiology and supported by a new knowledge of the cardiac cycle phase structure that allows us to originally apply the natural science proof philosophy to cardiology.

Keywords
Evidence-based medicine • Verification • Validation • ECG • Metabolic processes • Cardiometry • Cardiology • Scientific research philosophy • Science methodology

Imprint
Mikhail Y. Rudenko, Goran Krstačić. New philosophy of validation and verification for cardiology: classical proof theory imported from natural sciences; Cardiometry; No.4; May 2014; p.16-30; doi: 10.12710/cardiometry.2014.4.1630. Available from: http://www.cardiometry.net/no4-may-2014/verification
Introduction

The word “verification” is defined in a philosophical dictionary as follows: *verus* in Latin means *true*, and *facĕre* means *to make*, so considering all together it denotes evidence that establishes or confirms the accuracy or truth of something. A supposition (hypothesis) may be verified, i.e., its validity can be proved either empirically or by a consistent logical proof.

The given definition offers two ways for finding the truth: the first way is an empirical method of proof, and the second one is based on a logical proving procedure.

In general, in medicine, including cardiology, verification is based on empirical data, i.e., experimentation evidence only. It is connected with the fact that cardiology deals exclusively with anatomical evidence [1-7]. The theoretical basis of the existing cardiology that explains the functioning of individual segments of the cardiovascular system shows significant contradictions and inconsistencies, and sometimes even false ideas about physical processes prevail therein. Thus, the classical interpretation of the fluid flow pattern in the laminar regime used for the conventional description of blood circulation is based on a wrong concept that all fluid particles in blood move always in parallel to walls in a pipe where the flow occurs [8,9]. However, it is impossible to find such a hypothetic concept anywhere in physics, since, by definition, under the laminar conditions, all particles are concentrated in the center of the flow that finally results in a higher energy consumption to overcome an increased fluid flow friction. As shown in Table 1, the efficiency in the laminar flow is very low, and, therefore, the laminar regime cannot physically exist in the blood vessels. Besides, the pressure in the aorta under the laminar conditions would reach approximately 2 atmospheres that is not the case in reality: actually, the aortic pressure in a human body does not exceed 200 mm Hg. Therefore it should be stated that the classical approach thereto is not capable of providing any mathematics to describe hemodynamics in the proper way.

Table 1. Hemodynamic efficiency for hypothetic case of the laminar blood flow regime in blood vessels in a human body

<table>
<thead>
<tr>
<th>Vessels</th>
<th>Diameter, cm</th>
<th>Length, cm</th>
<th>Blood flow velocity, cm/sec.</th>
<th>Reynolds number</th>
<th>Hydraulic efficiency of blood vessels, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aorta</td>
<td>1,0</td>
<td>40</td>
<td>50</td>
<td>1670</td>
<td>39,4</td>
</tr>
<tr>
<td>Large arteries</td>
<td>0,3</td>
<td>20</td>
<td>13</td>
<td>130</td>
<td>3</td>
</tr>
<tr>
<td>Main arterial branches</td>
<td>0,1</td>
<td>10</td>
<td>8</td>
<td>27</td>
<td>0,42</td>
</tr>
<tr>
<td>Terminal arteries</td>
<td>0,06</td>
<td>1</td>
<td>6</td>
<td>12</td>
<td>1,1</td>
</tr>
<tr>
<td>Arterioles</td>
<td>0,002</td>
<td>0,2</td>
<td>0,3</td>
<td>0,02</td>
<td>3,15·10^-4</td>
</tr>
<tr>
<td>Capillaries</td>
<td>0,0008</td>
<td>0,1</td>
<td>0,07</td>
<td>0,002</td>
<td>2,5·10^-5</td>
</tr>
<tr>
<td>Capillary veins</td>
<td>0,003</td>
<td>0,2</td>
<td>0,07</td>
<td>0,007</td>
<td>1,6·10^-4</td>
</tr>
<tr>
<td>Terminal veins</td>
<td>0,15</td>
<td>1</td>
<td>1,3</td>
<td>6,5</td>
<td>1,5</td>
</tr>
<tr>
<td>Main vein branches</td>
<td>0,24</td>
<td>10</td>
<td>1,5</td>
<td>12</td>
<td>0,44</td>
</tr>
<tr>
<td>Large veins</td>
<td>0,6</td>
<td>20</td>
<td>3,6</td>
<td>72</td>
<td>3,4</td>
</tr>
<tr>
<td>Vena cava</td>
<td>1,25</td>
<td>40</td>
<td>33</td>
<td>1375</td>
<td>40</td>
</tr>
</tbody>
</table>
By adopting the above erroneous model of blood circulation, the classical cardiology fails to create an adequate theory for an acceptable logical analysis of the hemodynamic processes in the cardiovascular system in a human body.

Among other things, the problem of the necessity to specify signal filtering parameters for cardiac signal recording has never been discussed, when designing or developing various diagnostic devices. As a consequence, contradictions in the cardiac signal form analysis do not allow classifying the cardiac signal forms in a proper manner.

As a result, until recently, the verification of the cardiac signals has been carried out on the basis of clinical evidence only. And another very important fact is that it is very often the case that measuring the same parameter according to different technologies or with different devices gives inconsistent results which may show significant discordance.

It should be noted that the natural sciences do not come up against the above mentioned problems since any object is investigated by logical proof procedures that is the basis of scientific research methodology. At the same time, curricula of medical universities ignore methodological concepts of this sort at all. Therefore, the authors would like to outline the essence of the natural-science-based methodology borrowed from natural sciences [10-15].

**Materials and methods**

There are two methods for proving in a natural science: the method of direct proof and that of indirect proof.

The basis of the direct method of proof can be outlined as follows:

1. A mathematical description of the phenomenon to be investigated should be available.
2. Axiomatic logic statements for explanation of the process under study should be available. It is an axiomatic foundation for making logical conclusions. The axioms should be unambiguous.
3. Reproducibility: the phenomenon being investigated should be reproduced at least three times under different experimental conditions.
4. Modeling and predicting an influence of different conditions on the given phenomenon should be provided.

The indirect method (elimination method) of proof is based on the following:

1. Axiomatic logic statements used for constructing the system of logical negation and confirmation of arguments in favor of existence of the observed phenomenon should be available.
2. Recording of the phenomenon at least three times under different experimental conditions should be provided.

The most reliable way for proving is to combine the direct and indirect methods of proof. The above mentioned methods of proof form the basis of the proof theory and the scientific research philosophy & methodology in natural sciences that may be successfully imported to cardiology.
Let us note again that the verification principle in cardiology is based on empirical evidence speaking about correspondence between the forms of cardiac signals and the associated physiological processes that determine the said cardiac signals. But there is a disadvantage because there is no logical apparatus available required for describing the object being investigated, so it may produce a lot of disagreements in results obtained by different methods.

The weak points in the situation are as follows:

1. No unified logical theory of the performance of the cardiovascular system is available.

2. A plausible explanation for only particular, but not systemic characteristics of the cardiac signals is available.

Thus, the aim of this paper is to focus attention of the cardiology community on the fact that now we are facing the problem of quality in diagnostics in cardiology and that it is necessary to identify new ways to improve the existing situation. For proving the correspondence between the different forms of the cardiac signals and the relevant physiological processes, covering all cases within and beyond their norm, including extremely critical cases, it is necessary to adopt arguments that can be used as axioms in the proving procedure. For the purpose of establishing the correspondence, the logical proving system should meet the following requirements:

1. A database of various cardiac signals should be available.

2. The relevant axioms (arguments) including an adequate mathematical model of hemodynamics should be available.

3. At least three signs of changes in the cardiac signal form explained by the axioms (arguments) should be identified.

4. Logical justification of the relations between the cardiac signal forms and the relevant biochemical processes they are caused by should be at hand.

5. Theoretical prediction (modeling) of the process progression under various conditions should be available.

6. Recording of prognosticated changes in the cardiac signal forms upon influencing the biophysical process should be provided.

To improve the quality in diagnostics, the core concept of the theory of hemodynamics should be used as arguments. In doing so, we suggest six laws of hemodynamics as given below:
Law 1
The blood flow in the heart and the blood vessels is organized under the conditions of elevated fluidity (which is said to be the third mode of flow to differ from the laminar regime and turbulent mode), and the elevated fluidity is characterized by low friction due to the specific flow pattern formed by alternating rings of blood elements and plasma. This blood flow regime is defined by mathematical equations introduced by Poyedintsev-Voronova for hemodynamics.

Consequences
1) The entire human anatomy of the circulatory system is designed for the generation and the maintenance of the specific elevated fluidity regime.
2) Every cardiac cycle consists of ten phases, and each of the phases undertakes its own specified function to provide and maintain the proper hemodynamics.
3) Phase-related volumes of blood can be calculated by the above mentioned hemodynamic equations.
4) The quality of each function in the cardiac performance depends on amplitudes and intensity of contractions of the respective cardiac and vascular muscles.
5) There is a compensatory mechanism in the circulatory system muscle contractility that is responsible for maintaining hemodynamic parameters at their normal level. The operation of the compensatory mechanism is as follows: if a muscle group in the circulatory system demonstrates a decreased contractile function, one or more of the contiguous muscle groups within the circulatory system will automatically increase their contractile activity to compensate the loss of the contractility of the weakened muscle group.

Law 2
The SA and the AV nodes of the heart plus the aorta baroreceptors (AB) are neural centers which generate nervous impulses (action potentials) as soon as blood pressure at the said baroreceptors reaches a specified value [16-18].

Consequence
1) It is just the pressure applied to and sensed by the relevant baroreceptor that initiates generation of the nervous impulses (action potentials) and activates the mechanism of the contractile function of the cardiac and vascular muscle involved.

Law 3
The SA node is responsible for closure of atrioventricular valves.

Consequence
1) If the atrioventricular valves cannot complete their closing procedure at the end of the atrial systole phase in a cardiac cycle, the residual pressure in the atrium will act on the SA node and necessarily initiate another atrial contraction that will be reflected as the second P wave on ECG (which is the cause of atrial arrhythmia).
Law 4
The AV node controls three mechanisms responsible for the generation of the specific blood flow pattern. These mechanisms are as follows:

1. regulation of diastolic pressure in the aorta (carotid artery);
2. generation of vortex-type flows of blood before opening of aortic valve (carotid artery valve), and
3. opening of the aortic valve (carotid artery valve).

Consequences
1) The generation of the nervous impulse at the AV node in each cardiac cycle occurs three times that manifests itself on an ECG as the QRS-complex, the S-L interval and the L-j phase.
2) Under intensive physical exercise, nervous impulses of this sort can be generated up to seven times.

Law 5
The CABs (the carotid artery baroreceptors) undertake to maintain the generated specific blood flow pattern and drive blood in the elevated fluidity regime via the blood vessels throughout the body.

Consequences
1) Amplitude of the expansion of the aorta (carotid artery) depends on the blood pressure sensed by the CABs that is reflected as amplitude of the T-wave on ECG;
2) Amplitude of the aorta expansion regulates resistance to the blood flow.
Law 6
The ECG amplitude varies in direct proportion to the amplitude of the heart muscle contraction, and the ECG amplitude for the T wave varies directly as the expansion of the aorta.

Consequences
1) The ECG amplitude in each cardiac cycle phase depends on metabolic processes that determine the contraction and relaxation of the cardiac and vascular muscles.

On the basis of the above laws and the physical principles of fluid flow in a rigid pipe, it is possible to formulate a set of rules which can be utilized as arguments for an interpretation of the compensatory mechanism of cardiovascular system performance.
Results

The given laws are the most suitable tools for verifying any ECG shape by establishing its correspondence with the relevant biophysical processes which occur in the cardiovascular system. To illustrate this, let us consider some examples.

Example 1

Figure 2 displays an ECG curve with multiple P waves. This sort of ECG curves is classified by the classical cardiology as atrial arrhythmia.

Let us consider the given ECG shape using the logics of the proof methods imported from natural sciences as follows:

1. In this case, we consider an ECG curve of the ascending aorta to be the most informative graphics that is equivalent to summarized data produced by all conventional standard multi-lead systems.

2. To analyze the ECG shape, the above laws taken as arguments and assumed to be in correspondence with the axiomatic logical statements should be used.

3. Let us find 3 logically dependent manifestations. They are as follows:

   3.1 Manifestation 1: Weak myocardium muscle relaxation: no S-wave-effect is detected.

   3.2 Manifestation 2: The pressure at the SA-node (baroreceptor) remains the same owing to the weak relaxation; the second P wave is generated.

   3.3 Manifestation 3: The PQ phase is extended, since more time is required to compensate for weakness of myocardial muscle stretching.

4. Causes leading to the ECG shape changes are determined in terms of physics. The logics of the consideration should identify the primary cause of the changes.

   Each cardiac cycle phase is limited in its duration. In the given case, the impaired myocardial muscle relaxation cannot provide the proper filling of the ventricles with a sufficient blood volume and the proper closure of the atrioventricular valve (Law 3). Only upon the atrioventricular valve closure, the AV node can start generating the relevant action potential (Law 4). Thus, the SA node remains under the residual atrial pressure that leads to generation of the second P wave. The
There are no other ECG shape changes which may be associated with or linked to any other physical processes. In this case, we make a conclusion using the indirect method of proof, namely, the so-called elimination method. It contributes to strengthening the logics of the direct proof method.

Conclusion: the primary cause of the given ECG shape change is the weak myocardial muscle relaxation. It is pathology which is to be treated.

5. Modeling of process progression.

A prerequisite for modeling is that the primary cause of pathology has been properly identified. In the given case, the weak relaxation occurs due to low mitochondria energetic balance only and, first of all, due to low ATP energy. This energy is not high enough to supply the necessary amount of calcium to the cell to reach the required initial level. However, some problems in the coronary blood flow also might be the cause in the case under consideration.

Thus, two prediction cases may be discussed: what will happen if no treatment is performed and what will happen if the proper treatment is carried out?

If no treatment is performed, the weakness of the myocardium will be in further progress, and for the aorta it will be necessary to reduce the blood flow resistance that will be reflected as an increase in the T wave amplitude. It is an indicator of a reduction in the resistance owing to the aorta dilatation. But there are certain limitations in the aorta expansion. If this were the case, the situation would be critical.

- Prediction case one: Other processes cannot occur because there are no other causes for that from the point of view of physics (elimination method).

- Prediction case two: If to choose the proper treatment, one P wave only will appear on ECG, and the S wave amplitude will increase.

6. Under the real conditions, the patient with the above ECG curve has received therapy to recover the coronary blood flow. As a result, our prediction for the above mentioned ECG shape change has become true.

The given logical procedure for finding the primary cause of a disease that is reflected in the ECG shape has been tested in more than 2000 patients. Finally, we have successfully classified all the observed ECG curve variety based on the cardiac cycle phase analysis. Moreover, we have succeeded in predicting the lethal outcome in some patients several tens of minutes before full cardiac arrest. The developed methodology and the appropriate treatment allows for reducing in-hospital mortality by 40%.

It should be noted that additional data obtained by the cardiac cycle phase analysis like non-invasively measured phase-related blood volumes and synchronous point-type aorta rheography provides us with a new reliable tool of verification of every ECG shape change.
Example 2
An ECG curve showing the QRS complex of low amplitude and the P and T waves of large amplitudes is presented in Figure 3 below.

Taking into account the above detailed considerations, it is possible to simplify the descriptions following the logics of establishing the primary cause of a disease.

Figure 3. QRS complex of low amplitude and P and T waves of large amplitudes on ECG.

Considering the accepted axiomatics, it is possible to reveal three logically interdependent manifestations:

1. Small amplitude of QRS
2. Large amplitude of the T wave
3. Large amplitude of the P wave.

In our case, we can see one more manifestation which is as follows:

4. Large amplitude of S-L phase.

The low amplitudes of the QRS, the R wave and the S wave are indicators of weak energetic processes in mitochondria. There is no other interpretation available. The large P wave amplitude confirms the fact that the heart muscle relaxation is weak. The large T wave is responsible for the aorta expansion, and in the case under consideration it is providing for the reduction in the blood flow resistance in case of a weak heart.

The presence of the large amplitude in the S-L phase contributes additionally to the validation of the above conclusions. It is a marker of significant musculature tension in the phase of preloading that demonstrates the compensatory mechanism.

As a result, we can make a conclusion that the primary cause of the disease is an energetic weakness of ATP in mitochondria of heart muscles. The other cardiovascular functions are within the norm.
The aim of the therapy has been to normalize the function of oxygen transportation chain “serotonin - L carnitine” for oxygen delivery to mitochondria and enhance the Q coenzyme action.

Six months later, the stable therapeutic effect resulted in normalizing the ECG phase amplitudes has been reported for the patient.

Example 3
Some ECG curves recorded during orthostatic test are presented in Figure 4 below. In terms of the classical cardiology, these curve shapes are classified as His bundle conduction disorder. However, such a severe pathology cannot be “treated” by changing the body position only as evident from Fig.4. Therefore, the verification assumes a new significance.

![ECG curves in lying (a) and sitting (b) position](image)

**Figure 4. ECG of the aorta in lying (a) and sitting (b) position**
There are three logically interdependent manifestations on ECG as listed below:

1. A weak relaxation of myocardial muscles: no-S-wave effect.
2. Reverse of myocardium instead of contraction is observed: a dip at the R wave front edge on the ECG.
3. Certain symptoms are available: bursting pain in the left side in the area of the heart apex caused by the reverse of myocardium is reported.

Here, we are dealing with a rare case of the functioning of the interventricular septum (IVS). Before to properly contract, an adequate relaxation of the IVS should be provided by significant expanding of the septum that is recorded on ECG in the QR phase. This phenomenon is called by us “the reverse motion”. In this connection, a feeling of muscle pressure disorder in the area of the heart apex is reported. It confirms that the reverse motion of the muscles occurs. This phenomenon is not stable and depends on the body position. It appears only slightly on ECG when recording in the horizontal position, but it becomes significant when recording ECG in the vertical position. The only tool for the proper interpretation of the specific heart performance is the cardiac cycle phase analysis. The matter is that the blood flow pattern is generated during a QRS phase according to Law 1. In doing so, the valves are closed, but blood cannot stop circulating. If blood stops circulating, it cannot enter the aorta. Therefore, the R wave bifurcation is not a marker of QRS pathology, but it exhibits the compensatory mechanism in the heart performance.

Life expectancy of patients showing a phenomenon of this sort is usually long enough. From our experience, we report that we have never achieved normalizing of the reverse motion of the IVS in our patients.

**Discussion and conclusions**

The basic principles of logics for proof methods imported from natural sciences to cardiology are presented herein. It would serve no purpose to discuss herein the methodology in full. Each case requires its specific comprehensive knowledge. It is just the scientific research philosophy that is the core of successful activities in science.

We have pioneered in the verification by establishing the correspondence of the ECG shape with the relevant biophysical processes exclusively because of the application of the new theory of the cardiac cycle phase analysis [19-26]. A lot of contradictions have been accumulated in the existing cardiology due to the lack of an adequate theory. It is precisely these logical methods of the theoretical analysis and the new knowledge of the cardiac cycle phase structure that allow using the natural science principles of proving procedures in cardiology. Otherwise no success can be achieved.

It opens a new way for creating a principally new ECG classification [19-26] and using the scientific cognition logics for establishing of the primary cause of cardiovascular diseases. The characteristic feature of new potentials of this approach is a simplification of theory and practice cognition. It provides a new tool to make express diagnostics at any time, anywhere. In addition, the new express diagnostic technology is easy in use and cost-effective.
The further development of the logics in cardiology will be connected with expanding the ECG analysis capabilities. We think, first and foremost it might be applied to deriving data on metabolic processes in the cardiovascular system and evaluating psychoanalytic conditions.

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 authors read the ICMJE criteria for authorship and approved the final manuscript.

References


Original research

Our new tornado-compatible aortic valve prosthesis: notable results of hydrodynamic testing and experimental trials

Leo A. Bockeria1, Andrey V. Agafonov1, Gennady I. Kiknadze1, Victor O. Kuznetsov1, Ivan M. Krestininitch1, Shota T. Zhorzholiani1, Nadezhda O. Sokalskaya1, Alexander Y. Gorodkov1*

1 Bakoulev Scientific Center for Cardiovascular Surgery of the Russian Academy of Medical Sciences, 117931, Russia, Moscow, Leninsky Prospekt 8

* Corresponding author phone: +7 (495) 414-75-78, e-mail: agorodkov@bk.ru

Submitted: 11 March 2014
Accepted: 08 April 2014
Published online: 30 May 2014

Aims
A shortcoming common to all existing designs of mechanical cardiac valve prostheses is an increased trombogenicity caused, among other factors, by the lack of hydrodynamic compatibility between the luminal part of the prosthesis and the patterned blood flow. The aim of the study is to design and test our new mechanical aortic valve prosthesis to exclude life-long anticoagulation treatment.

Materials and methods
Standard hydrodynamic tests of the new prosthetic valve have been carried out for comparing with the other existing valve designs. A new method for the heart valve prosthesis testing in a tornado-like flow has been developed. The valve function has been verified in a swine excluding the anticoagulation treatment during the period of time exceeding six months.

Results
The significant advantage of the new prosthesis in the standard hydrodynamic tests has been demonstrated. The tests in the tornado-like flow have shown that only this prosthesis allows maintaining the pattern, the head and flow rate characteristics of the tornado-like jet. Upon implanting the new prosthesis in the aortic position in a swine, the good performance of the valve without anticoagulation therapy has been confirmed in the course of more than six months.

Conclusion
Obtained has been the evidence of the merits of the new mechanical aortic valve owing to the due consideration of the hydrodynamic peculiarities of the aortic blood flow and the creation of the design providing the proper hydrodynamic compatibility.

Keywords
Mechanical aortic valve prosthesis • Tornado-like vortex flow • Heart flow rate

Imprint
Introduction

A 50 year-long history of the development of mechanical prosthetic cardiac valves includes a great variety of original engineering concepts, but it should be noted that to the present day there has been no design of mechanical prostheses available which is really capable to completely replace the cardiac valve function and at the same time avoid aggressive anticoagulant therapy which affects quality of life of recipients [1,2].

The authors hereof assume that a conflict between a prosthetic cardiac valve and a recipient organism is provoked by a complex of causes, among which mentioned should be the following factors: inadequate (poor) quality of prosthetic valve materials, failure in cardiac contractility mechanics, provocation of hyperplasia on the prosthesis sewing ring and destruction of the specific hydrodynamic pattern of the blood flow. The latter manifests itself as a damage and activation of blood formed elements involved in coagulation cascade, along with a damage of endothelium due to high linear velocities and effects of flow splitting in separation and stagnation regions. In this case, none of the authors undertakes to identify the most critical factor among those listed above, since the mechanisms and developments of complications in cardiac valve replacement surgery are still imperfectly understood.

A preliminary assessment of functional properties of all mechanical prosthetic cardiac valves is provided with the use of hydrodynamic test benches both under stationary and pulsating turbulent water flow conditions. Test results reflect in every case those significant flow distortions which may occur on some valve components located within the flow core. It appears as a considerable increase in shear stresses and liner velocities, when flowing along the leaflets, as well as separation and stagnation regions within a space downstream of an artificial valve, and in the testing process all distortions take place to a variable degree for all existing models of the mechanical cardiac valve prostheses. We have succeeded in the development of a radically new mechanical prosthesis, which is designed with due consideration of the specific fluid dynamics pattern in the blood circulation segment between the left ventricle and the aorta, that determines the hydrodynamic compatibility of the offered prosthetic cardiac valve. Our new prosthetic valve has received the name Tornado-Compatible Aortic Valve Prosthesis (TCV).

Starting in 1992, the Bakoulev Scientific Center for Cardiovascular Surgery at the Russian Academy of Medical Sciences has been conducting research on the specific hydrodynamic pattern of the blood flow in the heart chambers and the aorta [3]. As a result, our suggestion has been proven that the blood flow generated in the left ventricle shows a structure of self-organizing tornado-like flows which are described by exact solutions to non-stationary equations in fluid dynamics published in 1986 for this sort of flows [4]. A tornado-like vortex represents an axially-symmetric structurally-organized swirl flow, the streamlines of which are directed along a converging spiral and do not intersect each other. Such a structural pattern is responsible for a laminar separation-free fluid flow, which may exist in a pipe with a curvilinear axis. This blood flow regime provides for integrity and intactness of blood cells and endothelial lining of blood vessels, while the biologically active systems in blood and the blood vessel walls (the coagulation and complement system) remain inactivated.

A flow of this class features high head and flow rate characteristics at a low hydrodynamic resistance because of the convergence, the specific organization of the labile three-dimensional
boundary layer and extra gradients which occur in the flow core due to its rotational movement. The self-organization of the flow appears subject to the necessary and sufficient conditions resulting from the exact solutions of the above mentioned equations. The said conditions imply the necessity to initiate longitudinal movement of fluid, the channel convergence along the streamlines, the mechanism of flow swirling and the availability of the conditions for the formation of the labile three-dimensional boundary layer to provide full contact of fluid with the channel wall or other fixed external surface. The tornado-like flows are stable by virtue of rotational inertia, but if an obstacle in the flow core appears, it causes local changes in structural parameters in the flow (the ratio between the longitudinal, radial and azimuthal components of the velocity) and leads to a partial or full disruption of the flow structure and transformation of the flow into a turbulent one with all associated unfavorable consequences as follows: an increase in its hydrodynamic resistance and shearing stresses as well as formation of separation and stagnation regions therein [5]. These phenomena in the blood flow initiate an activation of coagulation; they cause damages to the blood formed elements, induce increased shearing stresses at the blood vessel walls and start re-distribution of the blood stream through the branches located in the vicinity of the flow disturbance zone [6]. The totality of all above phenomena dictates the necessity to receive a long-life anticoagulation treatment for every patient who underwent an implantation of a cardiac prosthetic device, if its design ignores the specific organization of the blood flow.

A number of attempts have been made in order to adapt the geometry of the flowing channel of an artificial cardiac valve to that of the biological swirl blood flow. For this purpose, our engineering concept developed for the Cardiomed [7] and trileaflet heart valves with intraluminal disposition of the leaflets [8, 9, 16] has provided for the rotation of the paired leaflets about the channel axis, but we have faced the problem of a significant distortion of the flow structural pattern either due to the triangular shape of the lumen cross-sectional area with the valve open or due to placement of the leaflets within the flow that provides a hindrance to fluid stream. The Bakoulev Scientific Center for Cardiovascular Surgery has offered an absolutely new model of the mechanical aortic valve prosthesis (Patent RU 2434604 C1), the lumen of which is shaped as a circular-type cross-section throughout the full length of the flow-exposed prosthetic body portion and is free of any obstacles which might distort the blood flow pattern. The prosthetic valve consists of a body and three leaflets attached to the external body surface with the use of hinges (see Figure 1 below). The profile of the leaflets is designed so that the lumen cross-sectional area, as viewed from the flowing-through part, is of circular type with the valve open, and the other side of the leaflets has a contour following the curvature of the surface of the sinuses of Valsalva. This provides the proper matching of the aortic stream to the blood flow in the coronary arteries with the valve closed.
The aim of our study was to conduct comprehensive tests of the TCV developed by us and assess implantability of the valve in experiments without administration of anticoagulation therapy.

Methods and results

1. Standard hydrodynamic testing

The hydrodynamic bench tests were carried out in the Testing Laboratory operated by the Bakoulev Scientific Center for Cardiovascular Surgery. The test benches have been properly certified by the Russian National Agency ROSTEST, and the said test facilities have been found to be in full conformity with the requirements of the Russian National Standard GOST 26997-2003. The hydrodynamic testing of cardiac prosthetic devices was conducted under the conditions both of the stationary and pulsating flow. For the purpose of testing, water was used as the test medium. The testing conditions were in accordance with the Russian National Standard GOST 26997-2003 requirements.
a) Testing in stationary flow

<table>
<thead>
<tr>
<th>Model</th>
<th>Effective orifice area (mm²)</th>
<th>Leakages (l/min at 120 mm hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCV (Ø23)</td>
<td>340</td>
<td>1,0</td>
</tr>
<tr>
<td>Roscardics (Ø25)</td>
<td>310</td>
<td>1,2</td>
</tr>
<tr>
<td>NeoCor (Ø26)</td>
<td>230</td>
<td>0,1</td>
</tr>
<tr>
<td>CorBeat (Ø25)</td>
<td>305</td>
<td>1,0</td>
</tr>
<tr>
<td>CardioMed (Ø25)</td>
<td>290</td>
<td>&gt;&gt;1.0</td>
</tr>
<tr>
<td>LICS (Ø30)</td>
<td>310</td>
<td>0,6</td>
</tr>
</tbody>
</table>

Reference: applicable testing requirements according to the above GOST

b) Testing in pulsating flow

<table>
<thead>
<tr>
<th>Model</th>
<th>Stroke volume (ml/stroke)</th>
<th>Backflow leakage (ml/stroke)</th>
<th>Functional characteristics (visual examination)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCV (Ø23)</td>
<td>108</td>
<td>4,7</td>
<td>Sat.</td>
</tr>
<tr>
<td>MICS (Ø23)</td>
<td>100</td>
<td>2,5</td>
<td>Sat.</td>
</tr>
<tr>
<td>TriCardics (Ø23)</td>
<td>75</td>
<td>4,5</td>
<td>Sat.</td>
</tr>
<tr>
<td>CorBeat (Ø25)</td>
<td>105</td>
<td>2,5</td>
<td>Sat.</td>
</tr>
<tr>
<td>RosCardics (Ø25)</td>
<td>85</td>
<td>4,5</td>
<td>Sat.</td>
</tr>
<tr>
<td>NeoCor (Ø25)</td>
<td>102</td>
<td>2,5</td>
<td>Sat.</td>
</tr>
<tr>
<td>Cardiomed (Ø25)</td>
<td>96</td>
<td>5,5</td>
<td>Sat.</td>
</tr>
</tbody>
</table>

Reference: applicable test requirements according to the above GOST

b) Durability testing

The TCV item was tested on an accelerated life test bench in the Testing Lab responsible for testing of implantable CVP items at the Bakoulev Scientific Center for Cardiovascular Surgery. During the accelerated durability testing, 400 000 000 cycles were completed that corresponded to 10 years of the CVP performance in a patient body. Upon testing, no damages or wear of the prosthesis moving parts, which could result in a risk of disintegration of the valve or failure in its performance, were
reported. Upon testing completion, the prosthetic valve surfaces subject to friction were examined at magnification x40.

2. Testing in tornado-like flow

The type of the flow of the test fluid has a significant influence on hydrodynamic properties of the investigated mechanical cardiac valve prosthesis. Following the suggestion, L. Bockeria et al. [10] published their own data that an insertion of a vane consisting of inclined blades into the flowing-through channel of the stationary flow test bench provoked a non-systematic change in the measured functional properties of a tested object.

Therefore, the challenge of that stage of the study was designing a new test bench that should be capable of generating a stationary tornado-like jet stream.

The newly designed test bench comprises two vessels (a feeding vessel and a receiver) arranged one above another (see Figure 2 below). Water freely leaves the upper feeding vessel. A tested valve is to be inserted in line with the jet stream which is formed at the outlet nozzle of the vessel. The nozzle is designed as a confusor channel, the profile of which is computed in accordance with the exact solutions to the above mentioned equations. For the purpose of the computation, a bore diameter of the tested valve and the required ratio between the outlet size and the length of the channel to be equal to 1/5 are taken as initial parameters.

![Figure 2. Test bench for testing CVP in stationary tornado-like flow (left: external appearance; middle: attachment of confusor to bottom of feeding vessel; right: confusor channel).](image-url)
Water, upon leaving the feeding vessel, self-organizes into a tornado-like jet stream within the confusor channel. This jet stream differs from the turbulent one in the following: no surface disturbances are available; the jet shows glass-like transparency; no disturbances occur at the location of the water jet falling in the receiving vessel despite the fact that twisting of the jet stream is visually detected due to the fluid rotational motion in the receiving vessel. The visual characteristics of the tornado-like jet exhibit significant differences from those of the jet formed with the use of a pipe-like channel with the same cross-section and length parameters. An efflux time of a specified volume of fluid via the confusor channel is with certainty known to be less than it is the case with an efflux of the same fluid volume through a pipe (s. Figure 3 below).

![Figure 3. Glass-like transparent jet stream at outlet of confusor channel without valve inserted (left) vs. jet stream at outlet of the pipe with the same cross-sectional area (right).](image)

A comparative test of 5 major designs of the mechanical cardiac valve prostheses of the same size was carried out to cover the following items: a caged ball valve, a disc-type cardiac prosthesis (MICS), a bileaflet valve (Cardiomed), a trileaflet valve prosthesis (CorBeat) and a trileaflet TCV (tornado-compatible aortic valve prosthesis). The results of the comparative test are given in Figures 4 and 5 as well as shown in Table 3 below.

During the said experimental testing, 190 l water was made to flow from the upper into the lower vessel under a head pressure ranging from 50 to 5 mm hg.

For the purpose of a quantitative assessment of a degree of influence of the design of each valve on parameters of the exiting liquid, an efflux time of the same liquid volume between the two recorded heights of the liquid columns in the upper vessel was measured for different designs of the prostheses tested (s. Figure 6).
Figure 4. Destruction of tornado-like jet when flowing over the mechanical aortic valve body: top left: caged ball valve; top right: disc valve MICS; bottom left: bileaflet valve Cardiomed; bottom right: trileaflet valve CorBeat.

Figure 5. Maintenance of the tornado-like jet pattern at outlet of confusor channel with cardiac prosthetic device TCV inserted therein.
Table 3. Patterns of flow around a prosthetic aortic valve body by falling tornado-like jet stream

<table>
<thead>
<tr>
<th>Type of prosthetic valve</th>
<th>Front view</th>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caged ball valve CBV</td>
<td><img src="https://example.com/diagram1.png" alt="Diagram" /></td>
<td>Complete destruction of the swirl flow; backflows within the area under the ball and disintegration of the water jet stream.</td>
</tr>
<tr>
<td>Disc valve MICS</td>
<td><img src="https://example.com/diagram2.png" alt="Diagram" /></td>
<td>Complete destruction of the swirl flow; the water jet is attracted to the surface of the disc (the Coandă effect); the main jet stream shifts towards an inclination of a leaflet; the typical jet compression takes place in the area of the bottom edge of the body.</td>
</tr>
<tr>
<td>Bileaflet valve Cardiomed</td>
<td><img src="https://example.com/diagram3.png" alt="Diagram" /></td>
<td>Complete destruction of the swirl flow; the water jet is attracted to the surface of the leaflets (the Coandă effect); there is a flow separation between the leaflets; the main stream is shifted towards an inclination of the leaflets; the typical jet compression takes place in the area of the bottom edge of the body.</td>
</tr>
<tr>
<td>Trileaflet valve CorBeat</td>
<td><img src="https://example.com/diagram4.png" alt="Diagram" /></td>
<td>Complete destruction of the swirl flow; the water jet is attracted to the surface of the leaflets (the Coandă effect); there is a fragmentation of the flow and there are return flows within the hinge region; breaking-through diverging streams in the shape of a cone between the leaflets occur; the typical jet compression occurs in the area of the bottom edge of the body.</td>
</tr>
</tbody>
</table>
Complete destruction of the swirl flow; the water jet is attracted to the surface of the leaflets (the Coandă effect); the jet compression takes place in the area of the bottom edge of the body that is typical for a conical extension.

The flow pattern shown herein is observed because the TCV internal surface geometric shape is a perfect geometric extension of the surface of the swirling apparatus.

**Figure 6.** Efflux time of the same liquid volume between two recorded heights of the liquid columns: efflux via free confusor channel vs. efflux via flowing channel with inserted prosthetic devices of different designs.
As is evident from the above presented data, the maintenance of the pattern of the flow in its passage through the TCV does not produce an increase in the efflux time, and, consequently, it does not create any resistance to the out-streaming jet. Reported is that all the other designs of the prosthetic valves contribute to a resistance to the out-streaming jet to one degree or another.

During cardiac valve surgery, it is not infrequently the case when the internal architectonics of the left ventricular cavity is disrupted that leads to a destruction of the swirl flow, so that the aortic valve prosthesis is washed by a non-swirl flow.

We performed a study in order to establish how the swirl-free flow interacts with the same set of the cardiac prosthetic valves. For the purpose of the experimental study, instead of the confusor we installed a cylindrical extension piece with a diameter equal to that of the confusor outlet diameter, and the length of the extension was more than 5 diameters. Results of that hydrodynamic trial are given in Figure 7 below.

![Figure 7](image)

*Figure 7. Efflux time of the same liquid volume between the two recorded heights of the liquid columns: efflux via free pipe channel vs. efflux via channel with inserted valve prosthesis of different designs.*
During the above experimental study, it was reliably established that in case of the test with the TCV inserted, the resistance to outflow was considerably decreased, but not increased, that is evident from the data represented herein. The other valve models demonstrated their resistance to the flow to one extent or another.

The reported data unambiguously demonstrate that the stream jet pattern downstream of the TCV remains essentially intact that is the evidence for the hydrodynamic compatibility between the structural pattern of the intracardiac and the aortic blood flow and the tornado-like jet stream structure.

The offered testing methodology makes it possible to assess the behavior of a cardiac prosthesis under the conditions of a falling non-plunging tornado-like jet. It is well known that in case of the heart and large blood vessels we always deal with the plunging jet. However, when it is considered that, according to the exact solutions, a tornado-like jet stream shows its clear boundaries determined by the respective flow streamline directions, and under due consideration of the fact that the secondary streams, accompanying the evolution of the jet, are also swirled, but in the opposite direction, i.e., the jets in question are physically separated, all this lends credence to our methodology which may be utilized as an assessment technique in evaluating hydrodynamic compatibility of a prosthetic cardiac valve.

3. Chronic experimental prosthetic valve testing

Up to the present, upon an implantation of mechanical cardiac prostheses (especially in aortic position) it has been an imperative to provide a long-life anticoagulation management. Otherwise thrombosis is always initiated because of the presence of some prosthetic valve components washed by the blood flow so that it may lead to thromboembolism of brain and other abdominal organs [11-15]. The aim of the chronic experimental testing is an assessment of the valve performance in vivo, excluding anticoagulation management treatment.

A TCV in the aortic position was implanted in a swine with a weight of 45 kg with artificial blood circulation using cold chemical cardioplegia. The implantation procedure was in full compliance with the generally accepted guidelines on aortic valve prosthetic device implantation. Upon the cardiac surgery, the animal received warfarin dosing to provide INR at a level about 2.5 for 1.5 month that was in conformity with the commonly used clinical practice. Upon expiration of that period of time, warfarin was replaced by aspirin received as dosage of 100 mg/day for one month, whereupon any further medication was stopped. The prosthetic device performance was monitored with echocardiography. Noted was a good functioning of the prosthetic valve; the prosthetic device gradient showed an insignificant increase with the animal body size growth.
Discussion and conclusions

The experience accumulated in engineering and clinical applications of the cardiac prosthetic devices has shown that the replacement of diseased or damaged natural heart valves is an effective and sometimes the only solution to save the patient's life. But at the same time, considering a good progress in cardiac prosthetic device research & development and taking into account a great variety of the prosthetic valve designs available, every cardiac surgery expert is facing now the need to choose the right valve for the right patient to provide the most favorable performance of the valve prosthesis in patients. So far a cardiac surgeon in decision-making has operated with the terms like anatomical, biological compatibility and hemocompatibility of the cardiac prosthetic devices [16]. Hereby we insist on the necessity to introduce a new criterion for this purpose: it is the hydrodynamic compatibility of prostheses functioning in the blood flow.

The existing concepts of blood circulation are not capable of properly considering the blood flow pattern as a criterion in favor of a mechanical cardiac prosthesis type. Therefore, the conventional hydrodynamic studies and tests of the cardiac prosthetic devices are of empirical nature and cannot correlate with real quantitative criteria featuring the blood flow regime in a human body. The factual evidence that the blood flow refers to the class of self-organizing tornado-like flows and may be quantified by the exact solutions to the hydrodynamic non-stationary equations for the said flow class makes it possible to develop an absolutely new design of the cardiac prosthesis avoiding any conflict with the biological blood flow, with lowering risks of activation of the coagulation and triggering action of the other systems connected with the blood flow.

Such approach has allowed us to offer our radically new design of the cardiac prosthesis which has demonstrated its superior performance both in standard hydrodynamic testing in accordance with the applicable standard requirements and specific testing, where an interaction between the new prosthetic valve and the simulated tornado-like jet stream has been evaluated. The factual evidence that the TCV improves the flow regime under the turbulent flow conditions attests that this prosthesis may be applied in those cases, when it is known in advance that we are dealing with a failure of the mechanism of the generation of the tornado-like jet stream within the left ventricular cavity, for instance, in the event of a double-prosthetic repair in a patient. Moreover, the TCV implanted provides a means for administration of a low-level anticoagulation or even full avoidance of a long-life anticoagulation treatment that is inevitable in case of implantation of the conventional mechanical prostheses of other designs and that significantly impairs quality of life in patients upon prosthetic valve replacement.

As a result of our investigations on the hydrodynamic pattern of the blood flow in the left ventricle and the aorta and as a consequence of devising quantitative approaches to analyses of the specific blood flow hydrodynamics, a new design of the mechanical aortic valve prosthesis, which features hydrodynamic compatibility and allows avoiding anticoagulation management therapy, has been offered for application in practice by our R & D team.
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 analyzed the data and contributed to the writing of the manuscript. All authors read the ICMJE criteria for authorship and approved the final manuscript.

References


Linear Eckman friction in the mechanism of the cyclone-anticyclone vortex asymmetry and in a new theory of rotating superfluid

Sergey G. Chefranov1*

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

* Corresponding author e-mail: schefranov@mail.ru

Submitted: 26 February 2014
Accepted: 28 March 2014
Published online: 30 May 2014

Aims
The observed experimental and natural phenomenon of cyclone-anticyclone vortex asymmetry implies that a relatively more stable and showing a longer life, as well as a relatively more intense mode of rotation with an anticyclonic circulation direction (opposite to the direction of rotation of the medium as a whole) is realized as compared with an oppositely directed rotation of the cyclonic vortex mode. Until now, however, it was not a success to identify a universal triggering mechanism responsible for the formation of the corresponding breaking of chiral vortex symmetry.

Materials and methods
In this paper we reveal the said linear universal instability mechanism of breaking of chiral symmetry in the sign of vortex circulation in the rotating medium in the presence of linear Eckman friction.

Results
Obtained is a condition for the linear dissipative - centrifugal instability (DCI), which leads (only when considering the external linear Eckman friction for an above-threshold value of rotation frequency of the underlying boundary surface of fluid) to the breaking of chiral symmetry in the Lagrangian fluid particle dynamics and the corresponding realization of the cyclone-anticyclone vortex asymmetry.

Conclusion
A new non-stationary solution to the problem for the disc which carries out weak axial-torsional oscillations in fluid with the frequency which are superimposed on its rotation with the previously considered frequency $\omega_0$ in connection with the experimental data on the rotating superfluid helium II (see [16, 17]) has been found. It gives the possibility to conclude that the effects of external, linear on velocity, friction forces must be important to include into consideration for the solve of any fundamental problems of hydrodynamics in bounded systems (as for the blood dynamics in cardiovascular system, for example).

Keywords
Dissipative-centrifugal instability • Cyclone - anticyclone vortex asymmetry • Torsional oscillation • Rotating superfluid helium • Viscous incompressible fluid • Surface friction

Imprint
Sergey G. Chefranov. Linear Eckman friction in the mechanism of the cyclone-anticyclone vortex asymmetry and in a new theory of rotating superfluid; Cardiometry; No.4; May 2014; p.46-69; doi: 10.12710/cardio.2014.4.4669. Available from: http://www.cardiometry.net/no4-may-2014/new-theory-of-rotating-superfluid
Introduction

Cyclone-anticyclone asymmetry

In the atmospheres of the fast-rotating planets (Jupiter, Saturn, Earth), in the ocean and also in the laboratory experiments on rotating fluids observed is the so-called cyclone-anticyclone vortex asymmetry that is manifested itself in explicit predominance of the more intense, stable and long-life vortices just with the anticyclonic direction of circulation which is opposite in the direction of the rotation of medium as a whole [1–9]. For example, the Great Red Spot (GRS) of Jupiter has existed for already several hundred years, and it is just the anticyclonic vortex, one of the first nonlinear models of which is presented in [4]. The similar manifestations of a chiral vortex asymmetry breaking are typical also for the observed anticyclonic vortex lenses in ocean [1, 9] and for the vortices created in the rotating vessels containing fluid in the laboratory experiments [2, 3, 7, 8]. In particular, it is noted in [7, 8], that the chiral-symmetric state of vortex dynamics (when identical in intensity and degree of localization vortices with different rotation directions appear in the system), which exists till the beginning of the vessel rotating, is significantly broken when it rotates in a certain finite frequency range. At the same time, in the rotating vessel observed are an acceleration of the rotation velocity of the anticyclonic vortices and a deceleration of the rotation velocity of the cyclonic vortices, which occupy increasingly more area and show a tendency to their merging [7, 8].

Despite the facts that the vortex chiral asymmetry breaking in the rotating medium is already well-investigated, there is still no consensus on understanding of their common trigger mechanism providing an initiation of such an asymmetry breaking and such a realization of the given cyclone-anticyclone vortex asymmetry [6]. In particular, in [6] noted is the failure in the well-known undertaken attempts to obtain a universal conclusion on the relatively greater instability of the vortices with the cyclonic circulation direction, as compared with the anticyclonic vortices, by deriving from the linear theory of hydrodynamic stability [10 – 12]. On the other hand, none of the previously considered various specific non-linear mechanisms of the realization of the given vortex asymmetry in the rotating medium can be accepted as necessary for the realization of this fundamental phenomenon. For example, for a mechanism related to the nonlinear beta effect (when it is possible to obtain a soliton-like solution for anticyclonic structures only [4]) it has become evident after detection of the anticyclonic circulation type dominance even in f-plane approximation [6, 13].

The offered in [7, 8] nonlinear mechanism of the vortex asymmetry initiation related to the nonlinear Eckman friction effects is seemed to be more general. Besides, as well as for the linear Eckman friction, the presence of the circulation in the vertical plane (i.e., the so-called effects of two-dimensional compressibility [13]) must be taken into account. In particular, it is shown in a theory under development in [7, 8] that as the stationary settled cyclonic component of the vortex field approaches the surface of the fluid, it decays faster and makes a lesser contribution to the observed surface stream than it is the case with the anticyclonic component contribution. But in the theory [7, 8], when considering the limit that corresponds to the linear external Eckman friction, even such a weak vortex asymmetry has already not been found (since the very fact of exponential decay upon approaching the fluid surface is realized both for the cyclonic and anticyclonic vortex fields). This weakness of the manifestation of the vortex asymmetry is similar to the observed one in [6] and the
linear theory of stability [12] (where both cyclonic and anticyclonic vortex structures are instable, but in the case the latter has lower values of the exponential rates of growth of the corresponding disturbances). In the nonlinear theory [7, 8] there is no such a possibility of determining the conditions leading to the initial non-stationary stage in the formation of the cyclone-anticyclone vortex asymmetry which can be determined only according to the linear theory of the vortex state chiral symmetry stability. At the same time, a consideration of the combination of the fluid rotation with the Eckman friction (both linear and non-linear), that is corresponding to this rotation, has a universal significance for understanding of the mechanism of the cyclone-anticyclone vortex asymmetry phenomenon observed in the rotating medium only. Besides, it is a success in [7] in achieving an agreement of theory based on the nonlinear Eckman friction with the experimental data obtained in the said research for the range of relatively high fluid rotation frequencies only, which correspond to Rossby numbers less than 1.

In the present paper obtained is the hydrodynamic generalization of conclusion [5] made for the simplest linear mechanic system in the form of two-dimensional linear oscillator that has its own oscillation frequency $\omega$ and is investigated in a coordinate system rotating with the frequency $\omega_0$. In paper [5] shown is a possibility of realization of the linear mechanism of the chiral symmetry breaking due to the linear dissipative - centrifugal instability (DCI) of the zero state of the oscillator which may occur only in case of a sufficiently high coordinate system rotation velocity $\omega_0 > \omega$ and only in the presence of a non-zero linear (in oscillator velocity) friction.

In case of the DCI realization, an index of the exponential growth in time for an amplitude of the disturbance reaches its maximum at a certain finite value of the corresponding linear friction coefficient [5]. The chiral symmetry breaking in the DCI is manifested itself in the fact that it is precisely the anticyclonic rotation direction (which is opposite to the direction of coordinate system rotation with frequency $\omega_0$) of the disturbance trajectory that is realized with a sufficiently large time of evolution regardless of the initial conditions. That is, even if the disturbed direction of the movement of the oscillator leaving its zero position of equilibrium is of the cyclonic nature at the initial moment of time (i.e., it coincides with the coordinate system rotation direction), anyway it is just the anticyclonic resultant rotation direction that is formed with time in the limit of large times in case of the DCI realization. The conclusion from paper [5] on the DCI for the linear oscillator is used to interpret the linear mechanism of the observed cyclone-anticyclone asymmetry initiation for description of the Lagrangian fluid particles motion in case of solid-body rotation of fluid with frequency $\omega$ in the coordinate system rotating with frequency $\omega_0$ taking into account the linear Eckman friction that corresponds to linear oscillator linear on velocity friction force.

The application of the DCI mechanism indicated in [5] is also considered in [14] for describing the first stage of tropical cyclone initiation. The present paper shows that such a hydrodynamic consideration [5, 14] is directly linked with the generalization of the Kármán problem solution in case of taking explicitly into account the external linear (Eckman) friction. Determined is the linear mechanism of the DCI chiral symmetrical vortex state that corresponds to this solution and that leads to the observed cyclone-anticyclone vortex asymmetry phenomenon. It is related to the effect of the linear Eckman friction and can be realized only for an above threshold value of the rotation frequency
of the fluid vessel. At the same time, the conformity to the experiments data [7] on the vortex asymmetry just within the area of relatively low frequencies (for a Rossby number greater than 1, s. Fig.1) has been obtained that supplements the conclusions in [7] made with regard for the nonlinear Eckman friction effect in the rotating fluid.

![Figure 1.](image)

**Linear (Eckman) friction in rotating superfluid helium II**

Nowadays the concept of the L. D. Landau two-fluid model hydrodynamics of superfluid helium II at a finite temperature is used for interpreting the observed effects of interaction between superfluid helium II and bodies moving therein (including cases of the proper helium II rotation in the vessel) [15-17]. The ground for introducing such a concept is the well-known observed properties of helium II showing superfluidity under low temperatures, when, on the one hand, no molecular shear viscosity forces are detected when it flows through narrow slots and capillaries. On the other hand, the measurement of the helium II viscosity by decaying of the torsional oscillations of a solid disc immersed in the superfluid delivers some finite nonzero values of the surface viscous friction force [15]. The latter refers to any examples of the rotation of helium II and bodies immersed therein. P.L. Kapitsa [18] detected in his experiments a sharp decrease in the high-efficient heat transfer along the capillary immediately after the completion of the rotation of a cylindrical bar inserted into the capillary that is typical for helium II.

The investigations on the manifestations of the viscous friction forces in the rotating superfluid helium II show the presence of essential peculiarities in its interaction with the solid disc oscillating therein [16, 17], and it has been considered until now that these peculiarities cannot be manifested themselves in case of interaction of the disc with the normal non superfluid viscous fluid [17, 19]. Mainly this has determined the further formation of the basis of the above macroscopic two-fluid
hydrodynamics for the description of the rotating helium II. The conditional nature of such a concept is particularly emphasized in [15], where it is said “it is possible to speak about the superfluid and normal parts of liquid, but it does not mean at all a possibility of a real separation of the liquid into these two parts” and “as with any description of quantum phenomena in the terms of classical theory, it cannot be quite adequate”. The most significant inconsistence of the Landau two-fluid superfluid theory arise due to the observations by D. V. Osborne [20] on the free surface of helium II in the rotating vessel, where just the entire mass of helium II was found to be involved in the rotating motion as a whole in the contradiction to the two–fluid theory. It should be noted that even before, as noted in [16], such contradictions existed, and they were connected with the necessity of introducing a certain force of friction:”...on the other hand, some experiments seemed to require the existence of yet more frictional forces. And whatever the phenomenological successes of such a friction force, there was no theoretical explanation of its existence” [16].

Richard Feynman offered a solution to this difficult situation related to the contradiction to the two-fluid theory on the zero vortex of superfluid component [21]. His solution is based on the idea about singular vortex filaments that is introduced, however, without taking into account any friction for the rotating helium II in a vessel. It has been used to apply this two-fluid theory to explanation of the observed effects of interaction between helium II and the bodies moving therein despite the contradictions to the Kelvin theorem about circulation conservation and to the impossibility of generation of new vortices in an ideal incompressible fluid of constant mass. About this is also noted in paper [17]: “The question on why are the well-known classical Helmholtz-Thomson-Lagrange theorems disapproving the vortex formation in classical ideal liquid not fulfilled is still open-ended”. However, avoiding this problem, Feynman gave a quantum-mechanical description of a possibility of the singular vortex lines existence in a superfluid liquid [22]. Indeed, the Feynman theory [22] does not consider the mechanism of formation of the singular vortex filaments in helium II, but at the same time it does not offer to disapprove Kelvin theorem for quantum liquid. More over in [22] is giving a quantum-mechanical modification of this classic hydrodynamic theory theorem (for the system of the vortex filaments already existing in helium II) when an invariant quantity of the vortex intensity is supposed to be quantized so that it takes a discrete set of values [16]. The experimental data, on the other hand, explicitly bear witness to the observed evidence of formation of a conventional, but not a singular macroscopic hydrodynamic vortex extending very fast from the surface of the rotating helium II to the vessel bottom [23]. According to the Kelvin theorem, it should indicate a manifestation of a mechanism of friction that takes place between the bottom of the rotating vessel and the helium II contained therein. It is also noted in paper [16] that at a low helium II rotation frequency (with periods of more than one minute) the modified two-fluid model theory based on the Feynman singular vortex concept is not consistent with experimental date. This means that it cannot be identified in principal the threshold value of the rotation frequency for the vortex formation and provide a comprehensive understanding of the corresponding mechanism responsible for the macroscopic vortex formation in the rotating superfluid liquid on the basis of the conventional macroscopic two-fluid model hydrodynamics.

Thereupon, in the second paragraph of the present paper it is offered to take into account the effects of the linear Eckman friction for interpretation of the vortex formation mechanism in the rotating helium II on the basis of the DCI realization, that is considered in [4,14] and the first
paragraph herein in connection with the cyclone-anticyclone asymmetry. At the same time, a consideration of the process of the vortex formation in the rotating helium II, that is an alternative to the two-fluid theory, may be accepted, when it becomes reasonable to take into account even extremely low values of kinematic viscosity coefficient $\nu$ in helium II, the order of magnitude of which is $\nu \cong 10^{-9} \text{cm}^2/\text{sec}$ [18]. The corresponding to such value $\nu$ coefficient of the Eckman external friction force (being linear with respect to fluid velocity) $\alpha = \sqrt{\nu \omega_0 / h}$ (where $\omega_0, h$ are the rotation frequency and the boundary layer thickness, respectively) may be a value of $0.3 \cdot 10^{-4} \text{sec}^{-1}$ for a certain rotation frequency range [24, 25]. It should be also noted that paper [16] also shows the presence of a relationship between an effect of the linear (by a difference in velocities between the normal and the superfluid component) friction and the helium II rotation frequency, where the friction is characterized by a coefficient proportional to the vessel rotation frequency $\omega_0$. Besides, it appears that the measured by disc decay effective value $\nu$ considerably exceeds the value $\nu$ indicated in [18] and is equal to $\nu = \nu_r = (8.5 \pm 1.5) \times 10^{-4} \text{cm}^2/\text{sec}$ [16].

In the present paper the generalization of the theory [19] is obtained, where, as opposed to the theory in paper [19], taken into account are the effects of linear Eckman friction and the possibility of a non-coincidence between the fluid rotation frequency $\omega$ far from the disc and the rotation frequency $\omega_0$ of the disc itself. It allows obtaining a new interpretation of the observed peculiarities of the interaction between the rotating helium II and the solid disc oscillating therein.

**Materials and methods**

**Modification of Kármán problem and DCI**

1. Let us consider the equations of hydrodynamics of viscous incompressible fluid to describe a flow above the solid plane disc, rotating with frequency $\omega_0$, with a sufficiently large radius $R \gg \sqrt{\omega_0 / \nu}$, when the influence of the disc edge may be considered as low [26]. In the rotating with frequency $\omega_0$ coordinate system these equations are as follows (in the cylindrical coordinate system $z, r, \phi$) [26]:

\[
\begin{align*}
\frac{\partial V_r}{\partial t} + V_r \frac{\partial V_r}{\partial r} + V_z \frac{\partial V_r}{\partial z} - \frac{(V_r + r \omega_0)^2}{r} &= - \frac{1}{\rho_0} \frac{\partial p}{\partial r} + \nu (\Delta V_r - \frac{V_r}{r^2}) - 2 \alpha V_r; \\
\frac{\partial V_\phi}{\partial t} + V_r \frac{\partial V_\phi}{\partial r} + V_z \frac{\partial V_\phi}{\partial z} + \frac{V_r V_\phi}{r} + 2V_\phi \omega_0 &= \nu (\Delta V_\phi - \frac{V_\phi}{r^2}) - 2 \alpha V_\phi; \\
\frac{\partial V_z}{\partial t} + V_r \frac{\partial V_z}{\partial r} + V_z \frac{\partial V_z}{\partial z} &= - \frac{1}{\rho_0} \frac{\partial p}{\partial z} + \nu \Delta V_z - g; \\
\frac{\partial V_r}{\partial z} + \frac{1}{r} \frac{\partial r V_r}{\partial r} &= 0
\end{align*}
\]

The system of equations (1) for the velocity and pressure components $V_r, V_\phi, V_z, p$ is derived assuming the axial symmetry of all considered hydrodynamic fields. This means that for all fields in (1) there is no dependence on the angle coordinate $\phi$ and the corresponding derivatives are equal to zero. In (1) $\rho_0$ is a constant density of fluid, and the $z$ axis is directed perpendicularly to the disc plane and coincides with the direction of the rotation axis and the direction of the gravity force.
acceleration g. The forces of the external (Eckman) friction with the coefficient \( \alpha = \sqrt{\nu \omega_0 / h} \), which are linear relatively to the horizontal velocity components, are also additionally taken into consideration in the first two equations of the system (1). This coefficient depends on the disc rotation frequency and the typical vertical scale \( h \), which, in particular, may be determined by thickness of the disc. In the classical Kármán problem formulation, a stationary solution to the system (1) when \( \alpha = 0 \) is to be found, and for the radial and tangential velocity field components accepted is the presence of the linear dependence on the radial coordinate (on condition that the vertical component does not depend on this coordinate) [26].

Let us consider the modified Kármán problem where the effect of linear external friction with non-zero positive coefficient \( \alpha > 0 \) is explicitly taken into account. Let the form of solution (1) be the following:

\[
V_r = rF(z,t); V_\varphi = rG(z,t); V_z = H(z,t) \quad (2)
\]

From the third equation of system (1), after integration by \( z \), the following equation for determination of the pressure field is derived:

\[
p / \rho_0 = -gz + \nu \frac{\partial H}{\partial z} - \frac{H^2}{2} - \frac{1}{\partial t} \int dzH(z,t) + \Phi(r,t) \quad (3)
\]

where \( \Phi \) is an arbitrary function of integration not depending on \( z \). Below its form will be assumed to be in correspondence with the presence of the fluid uniform rotation with a constant frequency far from the disc, when \( \Phi = \frac{\omega_0^2 r^2}{2} \) as it is the case in [26].

As in [26], let us introduce dimensionless functions and variables using the following relations

\[
F = \omega_0 f(\xi, \tau); G = \omega_0 g(\xi, \tau); H = (\nu \omega_0)^{1/2} h(\xi, \tau); \xi = z(\omega_0 / \nu)^{1/2}; \tau = t \omega_0 \quad (4)
\]

If substitute (2), (4) into (1) we obtain (taking into account that the relation \( f = -\frac{1}{2} \frac{\partial h}{\partial \xi} \) is derived from the last equation of the system (1)) the following system of equations from the first two equations of the system (1):

\[
- \frac{1}{2} \frac{\partial^2 h}{\partial \xi^2} + \frac{1}{4} \left( \frac{\partial h}{\partial \xi} \right)^2 - \frac{1}{2} h \frac{\partial^2 h}{\partial \xi^2} - (1 + g)^2 = -\alpha_1 \frac{1}{2} \frac{\partial^2 h}{\partial \xi^2} + \alpha_0 \frac{\partial h}{\partial \xi}, \quad (5)
\]

\[
\frac{\partial g}{\partial \tau} - h \frac{\partial h}{\partial \xi} - \frac{\partial g}{\partial \xi} = \frac{\partial^2 g}{\partial \xi^2} - 2\alpha_1 g, \quad (6)
\]

where \( \alpha_1 = \alpha / \omega_0, \omega_1 = \omega / \omega_0 \).

The system (6) for the case \( \alpha_1 = 0 \) exactly corresponds to the system considered in [8] (however, in [8] this system is considered not in the rotating, but in the fixed laboratory coordinate system) in connection with the cyclone-anticyclone vortex asymmetry problem. So, as opposed to [8], in (6) herein the external (Eckman) friction for \( \alpha_1 > 0 \) has been obviously taken into consideration.
1. Let us find the stationary solution (within the limit of large times, when it is possible to neglect the time derivative terms) to the system (5) and (6) for two unknown functions $h$ and $g$ under the following boundary conditions:

$$
g(\xi = 0) = h(\xi = 0) = \frac{dh(\xi = 0)}{d\xi} = 0;
$$

$$
g(\xi \to \infty) \to g_1 = \text{const}; \frac{dh(\xi \to \infty)}{d\xi} \to h_1 = \text{const}
$$

These boundary conditions on disk surface precisely correspond to those considered by the Kármán problem in [26], if taken into account the fact that we are treating it in the coordinate system referred to the rotating disc. As to the second boundary condition at infinity under finite values of the external (Eckman) friction coefficient, the constants in the right parts of the boundary condition (7) at infinity become dependent on the value $\alpha_i$, and the corresponding important difference from [26] is available.

As in [26], let us consider the derivation of an approximate stationary system (6) solution that is linearized by the amplitudes $g, h$ under the boundary conditions (7) if assume that $|\omega_i^2| \gg 1$. At the same time, (if to take into account the relation $\frac{dh}{d\xi} = -\frac{d^2 g}{d\xi^2} + 2\alpha_i g$), the linearized system (6) comes to a single equation as follows:

$$
\frac{d^4 g}{d\xi^4} - 4\alpha_i \frac{d^2 g}{d\xi^2} + 4g(1 + \alpha_i^2) = 2(\omega_i^2 - 1). \quad (8)
$$

The equation (8) should be solved under the boundary condition which follows from (7) taking into account the above linear relations between the functions $h$ and $g$, when in (7) the constant coefficients are as follows:

$$
g_1 \approx \left(\frac{\omega_i^2 - 1}{2(1 + \alpha_i^2)}\right) \approx \frac{\omega_i^2 - 1}{1 + \alpha_i^2}, h_1 = \frac{\omega_i^2 - 1}{1 + \alpha_i^2} \approx \frac{2\alpha_i(1 - 1) - 1}{1 + \alpha_i^2} \quad (9)
$$

As a result of solving the equation (8) under the boundary conditions (7), with coefficients from (9), we obtain the following relations for the velocity field components of the fixed flow above the rotating disc in the coordinate system connected with the disc:

$$
V_\phi = r \omega_0 g = \frac{r \omega_0 (\omega_i^2 - 1)}{1 + \alpha_i^2} \left[1 - (\alpha_i \sin \xi \bar{\lambda}_2 + \cos \xi \bar{\lambda}_2) \exp(-\xi \bar{\lambda}_1)\right]
$$

$$
V_r = r \omega_0 f = -\frac{r \omega_0 (\omega_i^2 - 1)}{1 + \alpha_i^2} \left[\alpha_i - (\alpha_i \cos \xi \bar{\lambda}_2 - \sin \xi \bar{\lambda}_2) \exp(-\xi \bar{\lambda}_1)\right] \quad (10)
$$

$$
V_\xi = (\nu \omega_0)^{1/2} h = \frac{(\nu \omega_0)^{1/2} (\omega_i^2 - 1)}{1 + \alpha_i^2} \left[A_0 + 2\xi \alpha_i + \frac{(\alpha_i \lambda_1 - \lambda_2) \cos \xi \bar{\lambda}_2 - (\alpha_i \lambda_2 + \lambda_1) \sin \xi \bar{\lambda}_2}{2\alpha_i^2 + 1}\right] \exp(-\xi \bar{\lambda}_1)
$$

In (10) $\bar{\lambda}_1 = \left(\sqrt{\alpha_i^2 + 1} + \alpha_i\right)^{1/2}; \bar{\lambda}_2 = \left(\sqrt{\alpha_i^2 + 1} - \alpha_i\right)^{1/2}$ and $A_0 = \frac{1 - \alpha_i^2 - \alpha_i(2\alpha_i^2 + 1)}{(2\alpha_i^2 + 1)(\sqrt{\alpha_i^2 + 1} + \alpha_i)}$. 

No.4 May 2014
2. When the external Eckman friction coefficient is equal to zero \( \alpha_i = 0 \), the solution (10) precisely coincides with the known Kármán problem solution that is given in [26]. Under the finite values of this coefficient the solution (10) within the limit \( \xi >> 1 \) coincides with the obtained in [14] exact stationary hydrodynamic equation solution (1). This solution corresponds to the solid body rotation with the finite value of helicity (that generalizes the solid body asymptotics of Burgers and Sullivan vortices taking into account the linear external friction) and is considered in [14] in connection with the DCI linear mechanism application for modeling the initial stage of tropical cyclone development. The solution in [14] is obtained for arbitrary values \( \omega_i \), when in (2) the similar system (1) solution representation is used under the condition:

\[
F = F_0 = \text{const}; G = G_0 = \text{const}; H = -2F_0 \xi (11)
\]

It can be shown that Lagrange particles motion (that corresponds to velocity field (2) under the condition (11)) is described in the same way as the two-dimensional oscillator in the rotating coordinate system when friction is linear with respect to velocity (see also [14]). It is just the case that leads to the correspondence between the solution (10) asymptotics and the obtained in [5,14] condition for realization of the DCI of chiral-symmetric state and cyclone-anticyclone vortex asymmetry formation, that, according to (10), is as follows:

\[
|\omega_i| < 1 (12)
\]

Actually, from (10) within the limit of large distances from the disc \( \xi >> 1 \) we obtain an expression for the velocity field that determines the corresponding ordinary differential equations of Lagrange fluid particles dynamics:

\[
V_r = \frac{dr}{dt} = -r \frac{\alpha_i \omega_i (|\omega_i| - 1)}{1 + \alpha_i^2}; \\
V_\phi = r \frac{d\phi}{dt} = r \frac{\omega_i (|\omega_i| - 1)}{1 + \alpha_i^2}; \quad (13) \\
V_z = \frac{dz}{dt} = 2z \frac{\alpha_i \omega_i (|\omega_i| - 1)}{1 + \alpha_i^2}
\]

It follows from the first equation (13) that the equilibrium position of a fluid particle, that is localize at \( r=0 \), is exponentially unstable only when a finite value of the linear Eckman friction coefficient is positive \( \alpha_i > 0 \) and under condition (12), that is at the same time the very condition for the dissipative-centrifugal instability (DCI).

It follows from the second equation in case of the DCI condition realization that the Lagrange particle unstable motion trajectory corresponds to the rotation with a constant negative (when positive disc rotation frequency \( \omega_i > 0 \) ) angular velocity \( \frac{d\phi}{dt} = \frac{\omega_i (|\omega_i| - 1)}{1 + \alpha_i^2} < 0 \), i.e., the trajectory exhibits just the anticyclonic direction. Thus, from the generalization of the Kármán problem, taking into account the linear Eckman friction effects, we obtain the confirmation of the conclusion in papers
3. Let us demonstrate that when considering the system (1) solution in the form of (2) with coefficients (11), a DCI condition can be obtained in the same form as (12), but without supposition that \( \omega_1 - 1 << \omega \). If to substitute the (2) and (11) into the first two equations of system (1), two algebraic equations for two unknown coefficients \( F_0, G_0 \) are obtained:

\[
\begin{align*}
F_0^2 - (G_0 + \omega_0)^2 &= -\omega^2 - 2\alpha F_0; \\
2F_0(G_0 + \omega_0) &= -2\alpha G_0
\end{align*}
\]

From (14) we derive the solution as follows:

\[
F_0 = -\frac{\alpha G_0}{G_0 + \omega_0}, \quad (15)
\]

\[
x = \frac{G_0}{\omega_0} = -1 \pm \frac{1}{\sqrt{2}} \left[ \omega_1^2 - \alpha_1^2 \pm \sqrt{\left( \omega_1^2 - \alpha_1^2 \right)^2 + 4\alpha_0^2} \right]^{1/2} \quad (16)
\]

The condition for linear (exponential) instability of the state when \( r=0 \) is the condition of positivity of the right part of the equation (15), that is observed when \( x+1>0 \) (i.e., when considered is only the solution corresponding to the plus sign in front of the square bracket and in front of the square root sign inside the square bracket) and when \( x<0 \). The DCI criterion follows immediately from the condition \( x<0 \) (12).

For comparing with the paper [7] results, it is possible to use representation (13) for the tangential component of the velocity field (and the corresponding expression for the vertical component of the vortex field \( \omega_c = -\frac{2\omega_0(1-\omega_1)}{1+\alpha_1^2} \)), comparing it with the observation evidence shown in Fig. 1 b in [7].

In paper [7], the laboratory observations of a quasi-two-dimensional vortex flow (that is generated by the system of permanent magnets) were carried out in a rectangular cell that was placed on the rotating platform and filled with a conductive fluid that carried the current of different values. Fig.1 shows the results of the experimental observations which correspond to the different values of the conducted current and are summarized owing to an introduction of a parameter of similarity \( \gamma = (I_0/I)^{2/3} \), where \( I_0 = 50mA \) (in Fig. 1 in paper [7], different current values \( I=30, 40 \) and \( 50mA \) correspond to, respectively, circles, crosses and squares). Besides, in Fig.1, the representation of solution (13) in case of the DCI condition (12) fulfillment corresponds to curve number 2 (on the graph of the vortex field dependence to the third power of the rotation frequency \( 1/T \)), when we obtain the following formula according to (13):

\[
\omega_c^2 = -\frac{64\pi^3(1-\omega_c(1/T))^3}{T^3(1+\alpha_c^2(1/T))^3}; \quad \omega_0 = 2\pi/T \quad \text{when} \quad \alpha_c = 0.2, \omega_c(1/T = 0.05) = 0.3, \omega_c(1/T \geq 0.1) = 0.5.
\]
In Fig. 1, the theory of the nonlinear Eckman friction [7] corresponds to two curves under number 1. The lower index 1 is introduced to designate the rotation frequency $1/T$ and the cube of vortex field $\omega_z^1$, which is used in [7] to display different current modes investigated in the experiment (for example, $1/T_i = \gamma (1/T)$, $\gamma = (I/I_o)^{2/3}$, where $I_o = 50mA$) in the same figure. The conducted in the present paper comparison with paper [7] results actually consists of only one case when $\gamma = 1$, when the lower index of $\omega_z^1 = \omega_z^2$, $1/T = 1/T$ is in Fig. 1. It follows from the shown in Fig. 1 comparison of the developed theory supported by the experiment and theory [7] that in the range of low rotation frequencies curve 2 from (13) fits well with the experimental data. As a result, the conclusions based on the linear external (Eckman) friction exactly in the relatively low-frequency above threshold range of the DCI realization correlate better with the observation evidence than the results of the nonlinear Eckman friction theory [7].

At the same time, for higher frequencies, as it is shown in Fig. 1, the theory [7] appears to be adequate enough to the given experimental data. Thus, the present paper demonstrates that under the DCI condition realization (12), the Lagrange particle radial motion, that is determined by the velocity field (2) with coefficients (11), (15), (16), corresponds to the exponential growth of the radial coordinate only under the synchronous rotation of this particle in anticyclonic direction that is opposite to the disc rotation direction. On the contrary, in case of the realization of the cyclonic direction of Lagrange particle rotation (when inequality (12) is broken), the equilibrium position when $r=0$ for Lagrange particles is already exponentially stable that determines the interconnection between the DCI (12) condition and the mechanism of the observed cyclone-anticyclone vortex asymmetry phenomenon arising in the rotating medium.

Results

Eckman layer on the rotating fluid and DCI boundary

1. In the famous book [26] demonstrated is the coincidence between the obtained approximate Kármán problem solution (in the form of (10), but when $\alpha_i = 0$) and the spiral velocity distribution in the Eckman layer close to the solid boundary above which the rotating fluid flow occurs. It is interesting to derive a generalization of the presented in [26] spiral solution in the Eckman layer (see (4.4.15), (4.4.16) in [26]) taking into account the hydrodynamic equation terms with the linear external (Eckman) friction, and then compare it with the solution (10) when $\alpha_i > 0$.

Let us consider the steady-state fluid motion in the boundary layer when the external friction force with the positive coefficient $\alpha$ are additionally taken into account. In this case, we have the following equation for the steady-state values of the velocity field horizontal components inside the boundary layer:
\[-2V_x \omega_0 = \frac{G_x}{\rho_0} - 2\alpha V_x + \nu \frac{d^2 V_x}{dz^2};\]
\[2V_x \omega_0 = \frac{G_y}{\rho_0} - 2\alpha V_y + \nu \frac{d^2 V_y}{dz^2};\]  
(17)

where \(\omega_0\) is a vertical component of the fluid rotation angular velocity and the steady-state pressure gradient determining the fluid flow is a constant with the components \((-G_x,-G_y)\). These pressure gradient components are expressed by means of the steady-state velocity field horizontal component values \((U_x,U_y)\) in the area above the boundary layer in terms of the following relations:

\[\frac{G_x}{\rho_0} = 2(\alpha U_x - \omega_0 U_y);\]
\[\frac{G_y}{\rho_0} = 2(\alpha U_y + \omega_0 U_x)\]  
(18)

where the effects of the molecular shear viscosity force are not significant, but the manifestation of the external (linear in relation to velocity) friction force remains important. Relations (17) and (18) when \(\alpha = 0, U_y = 0\) precisely coincide with the considered in [26] base equations for describing the fluid that rests relative to the uniformly rotating coordinate axis and is set in motion by a modified pressure uniform horizontal gradient being compensated by the Coriolis force.

The system (17) solution (in case of fulfilling the relations (18)) follows from consideration of zero boundary conditions (on the solid plane \(z=0\) and at infinite large distance from the plane) have the form:

\[V_x = U_x (1 - \cos(\xi \lambda_2) \exp(-\xi \lambda_1)) - U_x \sin(\xi \lambda_2) \exp(-\xi \lambda_1);\]
\[V_y = U_y (1 - \cos(\xi \lambda_2) \exp(-\xi \lambda_1)) + U_y \sin(\xi \lambda_2) \exp(-\xi \lambda_1),\]  
(19)

where the values \(\lambda_1, \lambda_2\) and the variable \(\xi\) precisely coincide with the above determined values of the same quantities which are used in connection with solution (10). When \(\alpha = 0, U_y = 0\), relation (19) precisely coincides with the solution obtained in [26] (see (4.4.15), (4.4.16).

In [26] noted is the applicability of this solution for describing the flow near the Earth surface that is accompanied by formation of a twist similar to the Eckman spiral. At the same time, the horizontal pressure gradients may be actually considered as homogeneous at a distance of many kilometers. Their formation may be determined by large-scale cyclones and anticyclones in atmosphere or temperature changes in the horizontal direction due to nonuniform heating of the atmosphere [26].

The characteristic vertical scale that determines the boundary layer thickness (when \(\xi \equiv \pi\)) for the kinematic viscosity molecular coefficient is equal to only 14 m at the terrestrial Poles while its value observed in the atmosphere is much larger (from 500 to 1000 m). It implies a necessity of considering the \(\nu\) parameter in (17) as a certain effective kinematic viscosity coefficient under conditions of a small-scale turbulent mixing of the fluid horizontal layers [26]. According to [26], the value of this coefficient may be obtained from the data of observation of the velocity field spiral structure in the boundary layer when comparing it with the corresponding theoretical distribution.
2. Using a finite quantity of the external friction coefficient from (19) we can derive the generalization of the known conclusion on turning wind direction by 45 degrees clockwise with elevation referred to the Earth’s surface to the upper boundary of the Eckman boundary layer.

It follows from (19) that the relation between the Lagrange fluid particle motion directions near the Earth’s surface (when \( \xi \to 0 \)) and at the upper part of the boundary layer is as follows

\[
tg \varphi_0 \frac{V_y}{V_x} = \frac{\lambda_1 + \lambda_2}{\lambda_1 - \lambda_2} \cdot tg \varphi_\infty = \frac{U_y}{U_x} \quad (20)
\]

where, as in (10), \( \lambda_1 = (\sqrt{\alpha_i^2 + 1} + \alpha_i)^{1/2} \); \( \lambda_2 = (\sqrt{\alpha_i^2 + 1} - \alpha_i)^{1/2} \). Actually, relation (20) generalizes the above noted conclusion on the wind direction turning with elevations. Thus, when \( \alpha_i = \alpha / \omega_0 = 0 \) (when in (20) \( \lambda_1 = \lambda_2 = 1 \)) and \( U_y = 0 \) we obtain the known result \( tg \varphi_0 = 1 \) from (20), when the derived angle \( \varphi_0 = 45^0 \) does not depend on the rotation frequency \( \omega_0 \) of fluid as a whole [26]. If to choose (as in [26]) the coordinate axis directions so that the wind direction coincides with the x axis direction, from (20) appears the dependence of the angle \( \varphi_0 \) on the rotation frequency \( \omega_0 \), when taking into account the finite value of the linear external (Eckman) friction coefficient \( \alpha_i = \frac{\alpha}{\omega_0} \).

Though the limit (on the upper boundary of the boundary layer) wind direction turning angle for \( \alpha_i > 0 \) in (20) is smaller than \( 45^0 \), but the direction of the turning just clockwise (i.e., in an anticyclonic direction of circulation which is also clockwise) remains the same. For example if \( U_y = 0; \alpha_i = 1 \) from (20) we have \( \varphi_0 = 22.5^0 \).

The correspondence (noted in [26]) between solutions (19) and (10) in the considered case of taking into account the linear external friction effects takes place. Indeed, the expressions for the radial and tangential velocity field component in (10) have the same structure as it is the case with solution (19). Besides, the expression for the tangential velocity field component in (10) precisely coincides with the x component of the velocity field in (19) and the y component (but taken with an opposite sign: the necessity to take an opposite sign in a similar correlation is noted in [26], too).

However, the noted coincidence occurs only in case when the following relations hold

\[
tg \varphi_\infty = U_y / U_x = \alpha_i; U_x = \frac{r \omega_0 \sqrt{(\alpha_i^2 - 1)}}{1 + \alpha_i^2} \quad (21)
\]

Holding of the first equality in (21) leads to a modification of relation (20). At the same time, in (20) the limit value of the wind turning angle, when elevating from the Earth’s surface, depends on only one parameter \( \alpha_i = \alpha / \omega_0 \). For example, within the limit \( \alpha_i \ll 1 \) it follows from (20), (21) that \( \varphi_0 = \pi / 4 + \alpha_i / 2 + O(\alpha_i^2) \) and taking into account a non-zero external friction leads to increasing in an angle of the mean wind turning with elevation if to compare with the \( \varphi_0 = 45^0 \) of classical theory [26]. Within the opposite limit \( \alpha_i \gg 1 \) we obtain from (20), (21) the following expression \( \varphi_0 = \pi / 2 - 1 / \alpha_i + O(1 / \alpha_i^2) \), and as the external friction coefficient increases, the above angle of wind
turning also increases up to the limit value of 90 degrees. When \( \alpha_i = 1 \) from (20) and (21) we have \( \varphi_0 = 67.5^\circ \), which is larger than \( \varphi_0 = 22.5^\circ \)(for \( U_y = 0 \) in (20)) on angle \( 45^\circ \).

If \( \alpha_i = 0 \), the second of the equalities in (21), that is necessary for establishing the precise correspondence between (10) and (19), also coincides with the equality suggested in [26].

The first equality in (21) leads to an important conclusion that, when taking into account the linear external friction, the y velocity field component outside the boundary layer cannot be guessed independent of the x component and eliminated by an appropriate rotation of the coordinate system. This relation between the velocity field components in (21) may be applied to determine the value of the linear external friction coefficient \( \alpha \) on the basis of the angle \( \varphi \) measurement by analogy with the above (and in [26]) method for experimental determination of the kinematic viscosity effective coefficient value.

Actually, subject to the first equality in (21), it follows from (18) that the considered fluid motion is formed exactly by the pressure gradient with the zero component along the x axis (when \( G_x = 0 \) in (18)). Besides, it follows from (18) that

\[
U_x = \frac{G_y}{2\omega_0(1+\alpha_i^2)\rho_0} \quad (22)
\]

On the other hand, it is also possible to consider the condition \( G_x = 0 \), when a single-valued relation between the velocity components \( U_x \) and \( U_y \), coinciding with the first equality in (21), i.e. \( U_y = \alpha_i U_x \), is follow from the hydrodynamic equations in the form of (18). The interrelation between the parameters determining solutions (10) and (19) (when \( \omega > 0 \)) follows from (22) and the second equality in (21) of the form:

\[
\frac{G_y}{\rho_0} = (\omega^2 - \omega_0^2)r \approx 2r\omega_0(\omega - \omega_0) \quad (23)
\]

The dependence on the linear external friction is not present in (23), and the proper expression (23) precisely corresponds to the observed in [26] relation between the modified pressure gradient determining the motion in the Eckman layer and the control parameters in the Kármán problem. At the same time, the condition of pressure gradient value negativity in (23) corresponds to the DCI condition \( \omega_0 > \omega \), which determine the cyclone-anticyclone vortex asymmetry arising.

3. Let us consider the relation between the DCI condition and the condition of flow energy negativity in the rotating coordinate system in case of a sufficiently high super-critical angular velocity of rotation. Indeed, owing to the well-known representation of the energy in the rotating (round the z axis with the angular velocity \( \omega_0 \)) coordinate system \( E = E_0 - M_0z\omega_0 \) by the energy and the angular momentum in the rest (laboratory) system (denoted by zero index herein), the negativity \( E < 0 \) is possible under \( \omega_0 > \omega_{0,th} = E_0 / M_0z \)[27, 28]. In [28] the above condition of the rotation frequency is considered in connection with the determination of the singular vortex filament formation threshold in the rotating vessel containing helium II.
Let us note that for the exact solution to the system of hydrodynamic equations (1) in the form of (2), subject to the equalities (11), (15) and (16), the kinetic energy of the respective flow that is treated in the rotating coordinate system is as follows [14]:

\[
E = \frac{\rho_0}{2} [V_r^2 + V_\varphi^2 + V_z^2 - r^2 \omega_0^2] = \frac{\rho_0 \omega_0^2}{2} \{r^2 a + 4 z^2 b^2 \} \\
a = b^2 + x^2 - 1; b^2 = \alpha_1^2 x^2 / (1 + x)^2
\]

where the x value is determined in (16). As it is shown in [14], a current expression (24) may be transformed (by making it dependent only on the radial coordinate), using an invariance of value \( \Psi = r^2 z = \Psi_0 = const \), that is a stream function for the hydrodynamic equations (1) exact solution in form (2), (11), (15), (16). Besides, it is possible to use the equality \( z = \Psi_0 / r^2 \) in (24) when the expression in square brackets is the function of the radial coordinate only: \( 2E / \rho_0 \omega_0^2 = r^2 a + 4 b^2 \Psi_0^2 / r^4 \). Hence it follows that the necessary condition of the energy negativity \( E < 0 \) is to hold an inequality \( x^2 < 1 \) that provides the DCI realization along with the condition \( x < 0 \) leading to inequality (12). However, it is evident that this condition is not sufficient for holding \( E < 0 \) in (24). Such sufficient condition is holding of the inequality \( a < 0 \) (in case of considering the flow in the plane \( z = 0 \)), which may be expressed as follows:

\[
\alpha_1^2 x^2 < (1 + x)^3 (1 - x)
\]  

Within the limit \( \alpha_1^2 \ll 1 \) it follows from (25) that additionally to the condition \( x < 0 \) (that leads to the inequality \( \omega_1 < 1 \) in (12)) we have an additional inequality \( x > -1 + (\alpha_1^2 / 2)^{1/3} \) that leads to the condition of the energy negativity \( E < 0 \) (which generalizes the DCI condition (12)) of the form:

\[
1 > \omega_1 > (\alpha_1^2 / 2)^{1/3}
\]

In its turn, from (26) it follows that limitations on the rotation frequency \( \omega / (\alpha_1^2 / 2)^{1/3} > \omega_0 > \omega \) both below and above are available. According to experiment [7], the cyclone-anticyclone asymmetry realization is possible not for all rotation frequencies of the vessel containing fluid but have an evident above limitation in this frequency that follows from (26) for the quantity \( \omega_0 \). On the other hand, the below limitations in the rotation frequency were not specified in [7], as the investigations for the rotation periods larger than 20 sec. were not carried out. Therefore, the experiment [7] evidence does not deny the presence of a lower threshold of a rotation frequency specified by the DCI condition in (12) and (26).

The oscillation of the disc in helium II and the DCI

1. In the Introduction we have noted the problem related to a difference by many orders in the helium II viscosity coefficient, when using various methods of its measuring. Indeed, when helium II flows through narrow slots and capillaries (when the flow velocity in the capillary with a diameter \( 10^{-5} \) cm may be approximately several centimeters per second) the measured viscosity value does not exceed \( 10^{-11} \) poise, and when we observe a decay velocity of the torsional axial oscillation of the disc in helium II we obtain the viscosity value variation from \( 2 \times 10^{-5} \) poise (close to \( \lambda \) point when temperature is 2.19 K) to \( 10^{-6} \) poise (when temperature is 1 K) [29]. In the present paper we offer to
take into account the effect of the external (linear on the velocity) friction. The effect depends on the presence or the absence of the fluid rotation relative to the solid surface. If in case of the absence of the rotation, the coefficient of the external (Stokes) linear friction (this coefficient is proportional to the kinematic viscosity coefficient $\nu$) is $\alpha_0 = v/h^2$, and in the presence of the rotation with frequency $\omega$, the coefficient of the external (Eckman) friction is $\alpha = \sqrt{\nu\omega}/h >> \alpha_0$ (see [24, 25]) when the value $v$ is extremely small for helium II.

In paper [19] considered is the issue of low axial and torsional oscillations (with the frequency $\Omega$) of the disc in the viscous incompressible fluid. The disc rotates with this fluid uniformly with the angular velocity $\omega_0$ about the axis coinciding with that axis the disc turns about. This issue is investigated in [19] for interpreting the experimental observation of the same solid disc oscillations in the uniformly rotating helium II in [16,17].

Let us obtain the generalization of the paper [19] conclusions taking into account the linear external (Eckman) friction in the initial hydrodynamic equations (1). At the same time, as in [19], let us consider the system (1) solution linearized representation for low amplitudes of non-stationary disturbances of the velocity and pressure fields caused by low-amplitude disc oscillations in the fluid. As opposed to [19], we use the rotating with frequency $\omega_0$ coordinate system herein, so the disc motion may be expressed as follows: $\varphi = \varphi_0 \exp(i\omega t)$. We consider the case when it is possible to neglect the influence of the disc end surface on the fluid motion as it is the case with the Kármán problem modification in the first paragraph herein. Let the non-stationary solution to the linearized system (1) be similar to (2) when the velocity and pressure fields are as follows:

$$V_z = H(z) \exp(i\Omega t); V_r = rF(z) \exp(i\omega t); V_\varphi = rG(z) \exp(i\omega t)$$

By taking into account up to only linear by $H$, $F$, $G$ terms under $\omega^2 - \omega_0^2 \ll \omega_0^2$, we substitute (27), (28) into (1) and obtain the following system after introduction the functions $U_z = G \pm iF$:

$$\frac{dU_z}{dz} - k^2 U_z = \pm iW; W = \frac{\omega^2 - \omega_0^2}{\nu}; k^2 = \frac{2\alpha + i(\Omega \mu 2\omega_0)}{\nu}$$

System (29), when $W=0$ and $\alpha = 0$, precisely coincides with the considered in [19] system for the fluid motion in the region above the disc. We solve the system (29) under the following boundary conditions:

$$U_z(0) = i\varphi_0 \Omega, z = 0; U_z(\infty) = U_{2\infty} = \mu \frac{iW}{k^2} = \text{const}$$

which follows from the condition of non-slip on the disc boundary when we have the equalities $F=0$ and $G = i\varphi_0 \Omega$ in case when $z=0$. When $z=0$ the boundary condition coincides with the treated in [19] condition, and the boundary condition at infinity on the z axis shows a difference associated with finiteness of the value $W$ only in the right side of the equations (29).
System (29) solution under the boundary conditions (30) is as follows:

\[
U_z = \mu \frac{iW}{k_\mu^2} + A_z \exp(-z k_\mu); A_z = i \varphi_0 \Omega \pm \frac{iW}{k_\mu^2};
\]

\[
k_\mu = \left[ \sqrt{\frac{4 \alpha^2 + (\Omega \mu 2 \omega_0)^2}{4 \nu^2}} + \frac{\alpha}{\nu} \right]^{1/2} \pm \left[ \sqrt{\frac{4 \alpha^2 + (\Omega \mu 2 \omega_0)^2}{4 \nu^2}} - \frac{\alpha}{\nu} \right]^{1/2} (31)
\]

where the sign plus before \( i \) should appear in case when \( \chi = 2 \omega_0 / \Omega < 1 \), and when \( \chi > 1 \) we see the minus sign in the expressions \( k_- \) and \( k_+ \) in (31).

2. Solution (31), as in [19], is used for evaluating the viscous force moment \( M \) that influences on the disc and is determined by the value of the vertical gradient of the velocity field tangential component of the disc surface in the following form [26,19]:

\[
M = 4 \pi \rho_0 \nu \int_0^R \partial_z \left( \frac{V}{\partial z} \right)_{z=0} = -2 \pi \rho_0 \nu \exp(i \Omega t)(A_0 k_- + A_0 k_+ ) (32)
\]

The solution (31) representation and the relation \( G = \frac{1}{2} (U_+ + U_-) \) were used for deriving the (32) formula. When \( \chi = 0; W = 0 \), expression (32) precisely coincides with the representation for \( M \) obtained in [19]. Therefore, for finding the dependence of the disc decay decrement \( \delta \) and its oscillation frequency \( \Omega \) from the fluid rotation frequency \( \omega_0 \), we use the same representations as in [19] (see [17] also) that are expressed by the imaginary and real part of the value \( m = (M / \varphi_0) \exp(-i \Omega t) \) and are as follows:

\[
\delta - \delta_0 ; \Omega_0 = -\pi \text{Im}(m) / \Omega \Omega^2 ; I = \rho_d \pi R^4 h / 2 ;
\]

\[
\Omega_0^2 - \Omega^2 = \text{Re}(m) / I (33)
\]

where the values \( \delta_0 \) and \( \Omega_0 \) correspond to the vacuum values of the decay decrement and the disc oscillation frequency [17]. Besides, in (33) the value \( I \) denotes the moment of inertia of the disc of radius \( R \), thickness \( h \) and density \( \rho_d \). As a result, the following is derived from (32) and (33):

\[
\delta - \delta_0 ; \Omega_0 = \frac{\pi \rho_0}{\rho_d h} \sqrt{v / 2 \Omega \alpha} f_\delta (\beta ; \varepsilon ; \chi),
\]

\[
f_\delta = a_+ + a_- + x \left[ \frac{a_\beta \sqrt{x \pm 1 - x} b_+}{\beta^2 x + (1-x)^2} - \frac{a_\beta \sqrt{x} (1+x) b_+}{\beta^2 x + (1-x)^2} \right],
\]

\[
a_+ = (\sqrt{\beta^2 x + (1 \pm x)^2} + \beta \sqrt{x})^{1/2} ; b_+ = (\sqrt{\beta^2 x + (1 \pm x)^2} - \beta \sqrt{x})^{1/2}, (34)
\]

\[
x = 2 \omega_0 / \Omega ; \beta = \frac{1}{h} \sqrt{2 \nu / \Omega} ; \varepsilon_0 = (\omega_0^2 - x^2) / 4 \varphi_0 = \varepsilon x, \omega_2 - x << x,
\]

\[
\varepsilon = (\omega_2 - x) / 2 \varphi_0 = x (\omega_1 - 1) / 2 \varphi_0 ; \omega_2 = 2 \omega / \Omega = \omega_0 x
\]

In (34) the representation for the external (Eckman) friction coefficient in the form of \( \alpha = \sqrt{\nu \omega_0 / h} \) when \( 2 \alpha / \Omega = \beta \sqrt{x} \) is used. In (34) in the numerator of the first term in the square
bracket we see the plus sign when \( x<1 \) and the minus sign when \( x>1 \). In case when \( \varepsilon = 0, \beta = 0 \), expression (34) precisely coincides with the obtained in [19] formula for the decay decrement.

Similarly, we derive the following representation for the disc oscillation frequency from (32) and the second formula (33):

\[
\Omega_\alpha^2 - \Omega^2 = \frac{\pi \rho \Omega v}{\rho_0 h} \sqrt{\Omega/2v} f_{\Omega};
\]

\[
f_{\Omega} = b_x \pm b_\pm + x\varepsilon \left[ \frac{\pm b_x \beta \sqrt{x - (1-x)a_-}}{\beta^2 x + (1-x)^2} + \frac{(1+x)a_x - b_\pm \beta \sqrt{x}}{\beta^2 x + (1+x)^2} \right] (35)
\]

In (35) as well as in (34), the plus sign (before the second term and in the numerator of the first term in bracket) should appear when \( x<1 \), and the minus sign when \( x>1 \), respectively.

When \( \varepsilon = 0 \) it follows from (35) that the function \( f_{\Omega} > 0 \) is positive for any \( x \) and \( \beta \). At the finite quantity \( \varepsilon \) but this is apparently not the case. For example, when \( \beta << 1; \beta \sqrt{x} << 1 \) we obtain the evaluation \( f_{\Omega} \approx \pm \varepsilon / \beta^{(3/2-1)} \) from (35). Hence it appears a possibility of realization of this function large negative values and the corresponding large value of the disc oscillation frequency under the condition of \( 2/3 < \gamma < 1 \) and also at the DCI condition (12) and \( \varepsilon < 0 \) when the inequality \( x<1 \) holds place. At \( x>1 \), the same conclusion is valid at a positive value \( \varepsilon > 0 \), too, in case when the DCI condition (12) is not fulfilled.

Thus, based on (35), we show a possibility of the realization of a mode where the disc axial-torsional oscillations increase in case when the disc interacts with the conventional rotating fluid owing to the linear (Eckman) friction. It demonstrates that the observed decrease in the oscillation period of the disc (when it have rough surface) in the rotating helium II in [16,17] may be interpreted on the basis of the conventional fluid hydrodynamics even if its viscosity coefficient is as extremely low as \( \nu = 10^{-9} - 10^{-10} \, cm^2 / sec \) [18, 29]. Previously, as well in paper [19] (on the basis of which in [17] excluded was the possibility of using the conventional, not two-fluid model, hydrodynamics for interpreting the observed disc and helium II interaction effects), the possibility of taking into account exactly the external Eckman friction in the helium II experiments was not considered.

In [16] it is noted that the observed increase in the disc oscillation frequency may be related to the superfluid liquid flow realization in antiphase referred to the disc, which the liquid directly interacts with. Such a concept contradicts essentially the two-fluid superfluidity theory and was criticized in [17]. To interpret the observed disc oscillation frequency increase it is utilized in [17] the representation on the necessity of taking into account elastic properties of the singular vortex filaments existing in the rotating helium II in case of an above-critical velocity of this rotation (\( \omega_b > \omega_{exp} \approx 10^{-3} \, sec^{-1} \) for the vessel of 1 cm radius [17, 28]).

At the same time, the concept [16] is concordant with the considered above effect related to the external friction mechanism, and, under the DCI condition, leading to the formation of the solid-body anticyclonic fluid rotation being antiphased referred to the disc. The vortex directed oppositely the fluid rotation is also excited under the DCI. At the same time, not only the frequency but also the
amplitude of the disc vibration may increase when the decay decrement value in (34) is negative near \(x=1\) under a finite value \(\varepsilon < 0\) and a sufficiently small, but not zero value of the parameter \(\beta \ll 1\).

We can also conclude from (34) that, as opposed to [19], the disc oscillation decay decrement value in the conventional fluid may have a local maximum near \(x=1\) under the finite value \(\varepsilon\) and sufficiently small, but not zero values of the linear external Eckman friction coefficient determined in (34) with the parameter \(\beta\). Fig.2, taken from paper [19] (see Fig.5 in [17]), shows the observation data (see the upper curve), the paper [19] result (see the lower curve consisting of the two not connected parts), and also added is the curve from (34) when \(\varepsilon = 1, \beta = 0.1\) (the middle curve having a local maximum). This figure shows that, as opposed to the paper [19] results, the local maximum observed experimentally in superfluid helium II may appear in the conventional normal fluid, too, but only in case of taking into account the linear external Eckman friction and at a finite value of the parameter \(\varepsilon \neq 0\) in (34). The finiteness of the value \(\varepsilon \neq 0\) is determined by the possibility to distinguish the angular rotation frequencies \(\omega_0\) and \(\omega\), for the solid vessel wall and the fluid being far from this solid boundary, respectively.

![Figure 2.](image-url)

Such a finite difference between the fluid angular velocities far from the vessel walls may be observed after establishing the equilibrium distribution at sufficiently large times. Indeed, it is noted in the experiment [23] that for approximately 120 sec. the middle part of the fluid remains flat, though during the process of swirling the vessel containing helium II the peripheral parts of the fluid are rapidly entrained by the vessel walls and move up on the wall surface. In the rotating coordinate system, related to such vessel, the indicated behavior of the fluid middle part fully corresponds to the observation of exactly the anticyclonic rotation of the fluid that is similar to the considered in the first paragraph DCI mechanism conditioned by the effect of the external Eckman friction on the vessel bottom.
Indeed, it is noted in [23] that in case of the maximum rotation velocity of 5 revolutions per second possible in this experiment, a conic depression appears in the center of the steady-state meniscus (that is not observed in the conventional normal fluids including helium II [23]) and have been twice transformed into the vortex extending to the vessel bottom. However, these cases of the macroscopic vortex formation have not been recorded on videotape, and the conditions for such a vortex formation remains unexplored. Nevertheless, the obtained in [23] material allows considering the developed in this paper theory as valid instead of the two-fluid theory of helium II which admits the existence of only the microscopic (having an atomic size nucleus) vortex filaments in helium II.

The same conclusion can be made on the basis of Fig.3 where shown are not only the experimental curve, displayed in Fig.2, but also the theoretical curve 4 corresponding to (34) and the curves 2 and 3 corresponding to the theory [17] that proceeds from the singular microscopic vortices conception. As it is noted in the Introduction herein, the conception of these point (in diameter) vortices was introduced by R. Feynman into the Landau two-fluid theory to eliminate the contradictions upon the results of observation of the meniscus (of a depth not differing from that of a conventional normal fluid meniscus) in the rotating helium II [17]. The developed in the present paper theory of the anticyclonic vortex formation owing to the DCI mechanism does not exclude the possibility of such singular vortex filament excitation and does not contradict with the classical theories of ideal fluid hydrodynamics indicated in the Introduction above.

In Fig.3, that was taken from [17] (see Fig.16 in [17]) the curve 4 derived from (34) and given in Fig.2 is shown. However, we had to compress it on the abscissa. Otherwise, the curve 4 maximum would be located outside Fig.3 when $\omega_0 = 0.29 \text{sec}^{-1}$. The other given in [17] curves in Fig.3 indicate the following: curve 1 describes the experimental evidence (that corresponds to that shown in Fig.2); curve 2 corresponds to the theoretical curve (based on (4.6), (4.21) in [17]) for the rough disc when
nonzero value for the kinematic viscosity coefficient of superfluid component is introduced in [17]; curve 3 corresponds to the same formula [17] calculations but for absolutely smooth disc surface under zero superfluid component viscosity.

It follows from Fig.3 that there is no significant qualitative difference between the conclusions of the theory [17] and the present paper theory. Moreover, the absence of the curve 3 local maximum in case of the disc ideal smooth surface and its presence for curve 2 in case of a finite viscosity exactly of the superfluid component indicate the qualitative conformity to the developed herein conception of the linear external friction against the boundary solid surface that is valid both for the conventional fluid and the helium II.

Thus, the conclusions derived from (34) for the conventional fluid, taking into account the linear external Eckman friction effects, may be a quite sufficient alternative to the two-fluid theory in interpretation of the effects of interaction between a superfluid liquid (helium II) and a solid body moving relative to the fluid.

Conclusions

Taking into account the extremely low kinematic viscosity coefficient values in helium II, the modes with very large Reynolds numbers [18] may be realized even in flow through a thin capillary. Such Reynolds numbers are typical for the flows in geophysical hydrodynamics in the region of planetary boundary layer, i.e., the Eckman layer. Therefore the application of the linear external Eckman friction to the description of the solid disc and helium II interaction seems to be as justified as it is the case with geophysical hydrodynamics [24, 25]. The obtained results indicate the importance of taking into account the linear external friction effects for all physical problems, where treated is the hydrodynamic or gas-dynamic motion of a continuous medium just in case of the presence of any solid or elastic (as in the case of blood dynamic in cardiovascular system) boundaries in this medium.

At the same time, when traditionally introducing viscous effects into hydrodynamics consideration, this is not taken into account, since usually investigated are only volumetric, but not boundary dissipative factors, that are determined by the velocity field space variability, but not by the medium velocity itself at a given point of space [15].

On the other hand, I. Newton [30] empirically introduced exactly the linear in relation to the body velocity friction force (known as Stoke's force [15]) for determination of a force acting on a body moving in fluid, that transforms into the quadratic in relation to the velocity force in case of turbulent flow around a body. However, for determination of the velocity field structure of the fluid flowing around the solid boundary layer no extra force proportional to the fluid velocity and taking into account such solid boundary presence, is introduced into the hydrodynamic equations. Usually considered are only the effects of viscous interaction between different fluid layers determined by the velocity gradient values and the boundary conditions of adhesion to the solid surface confining the fluid.

The present paper demonstrates the necessity for a modification of this traditional approach.
Owing to considerations of the linear external friction in the investigation of the processes of interaction between hydrodynamic flows and solid boundary, both the experimentally observed vortex asymmetry (curve 2 in Fig.1) and the new interpretation of interaction between the rotating superfluid helium II and solid boundary (Fig.2, 3) may be explained. In this case, the traditionally used formal concept of the two-fluid hydrodynamics in helium II is no longer necessary.

Thereupon, it is interesting to obtain the similar generalization of the known exactly solvable problems of hydrodynamics like determination of the Stoke’s force acting on a solid sphere slowly moving in fluid, Hagen-Poiseuille flow in a round tube, etc. where it seems reasonable to take into account the effects of the linear in relation to velocity external friction as it is done in the present paper for the Kármán and Eckman problem and for the description of the interaction between helium II and the solid disc oscillating therein. It may give new view on the many fundamental and apply problems of hydrodynamic (for example to the problem of high energy effectiveness of cardiovascular system job).

It should be separately stressed that the obtained results may be used for solving issues of identification of the cyclonic and anticyclonic vortex activity role in the formation of global climatic disturbances [31, 32]. It is also important to compare the distribution (19) based on the external friction consideration with the conclusion on the Eckman boundary layer spiral structure made in [33], based on the spiral theory of turbulence. Herewith, the distribution derived in [33] may precisely coincide with (19) and give the same distribution of the mean wind with elevation if the relation $\alpha = k_n \omega_0 / k; \nu = (k^2 + k_n^2) / k$ takes place between the friction coefficients introduced above and the semiempirical coefficients of turbulent viscosity $k, k_n$ introduced in [33]. Such relations provide for better understanding of the physical meaning of the turbulent viscosity coefficient.

The conclusions obtained in the present paper are based on the development of the DCI theory offered in [5], where in addition to establishing the proper fact of the DCI existence (that is known for a long time as secular instability specified by the friction forces [34]) for a linear two-dimensional oscillator in the rotating coordinate system, established is also the new fact that the DCI realization is linked with the chiral symmetry breaking. It seems to escape notice in [34] and previous publications.

Let us also note the similarity between the introduction of the linear in relation to velocity Eckman or Newton friction and consideration both of the deterministic [35] and the random non-stationary [36] factors in the hydrodynamic equations when the corresponding linear friction coefficient has the same dimension as some effective frequency of the system.
Acknowledgements
This work was supported by the Program of Presidium of Russian Academy of Science “The Fundamental Sciences to Medicin” 2014.

I would also like to express many thanks to I.I. Mohov and O.G. Chkhetiani for useful discussions as well as to F.A. Pogarsky and A.G. Chefranov for their assistance in figures preparation.

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
18. Kapitza PL. JETP Lett. 1941;11(1).
34. Lyttleton RA. The stability of rotating liquid masses. Cambridge Univ. Press; 1953.
Our book is in Book Citation Index (Web of Science) now

The CARDIOMETRY Editorial Board is glad to inform you that the book “Theoretical Principles of Heart Cycle Phase Analysis” by authors from Russian New University Rudenko M.Y., Zernov V.A., Voronova O.K., et. al. has been approved and included for indexation in one of the largest and most authoritative scholarly Book Citation Index (Web of Science) by Thomson Reuters, the world leader in the field of science analytics. It is a very important step for international recognition and promotion of our scientific achievements.
Occurrence of HLA- and Non-HLA Antibodies after Heart Transplantation are Associated with Cardiac Allograft Vasculopathy

Maja-Theresa Dieterlen¹, Jens Garbade¹, Robert Riede¹, Stefan Dhein¹, Friedrich W. Mohr¹, Hartmuth B. Bittner², Markus J. Barten*²

¹ University of Leipzig, Department of Cardiac Surgery, Heart Center, 04289 Leipzig, Germany
² Florida Hospital Orlando, Department Cardiothoracic Transplantation and Advanced Cardiac Surgery, Orlando, Florida, USA

* Corresponding author phone: +49 (341) 865-14-21, e-mail: markus.barten@herzzentrum-leipzig.de

Submitted: 04 March 2014
Accepted: 14 April 2014
Published online: 30 May 2014

Aims
Cardiac allograft vasculopathy (CAV) accounts for major morbidity and mortality late in the heart transplant (HTx) history. The role of antibodies (Abs) directed against human leukocyte antigens (HLA) and non-HLA antigens in the pathogenesis of CAV are still under investigation.

Materials and methods
Sera of 116 long-term HTx recipients with CAV (n=46) and without CAV (n=70) were analysed by (1) Luminex for Abs against both HLA classes and major histocompatibility complex class I-related chain A (MICA), and by (2) ELISA for Abs against angiotensin-type-1-receptor (AT1R) or endothelin-receptor-A (ETAR). Cellular rejection by endomyocardial biopsies and immunosuppressive drug therapy were analysed, too.

Results
HTx recipients developed higher levels of non-HLA-Abs than of Abs against HLA. CAV appeared more frequently in recipients with non-HLA-Abs (38.3% AT1R; 44.1% ETAR; 13.0% MICA) than in recipients with HLA-Abs (8.7% HLA class I; 8.7% HLA class II). Recipients with non-HLA-Abs developed CAV earlier (73.7±47.4months) than recipients without Abs (85.5±50.6months).

Conclusion
Occurrence of HLA-Abs and non-HLA-Abs contribute to CAV after HTx. Non-HLA-Abs were connected to an earlier and higher incidence of CAV. Recipients with subclinical cellular rejections and AT1R-Abs and ETAR-Abs as well as recipients with certain donor specific-Abs again HLA and MICA specificities are at risk to develop CAV.

Keywords
Heart transplantation • Vasculopathy • HLA antibodies • Non-HLA antibodies

Imprint
Maja-Theresa Dieterlen, Jens Garbade, Robert Riede, Stefan Dhein, Friedrich W. Mohr, Hartmuth B. Bittner, Markus J. Barten. Occurrence of HLA- and Non-HLA Antibodies after Heart Transplantation are Associated with Cardiac Allograft Vasculopathy; Cardiometry; No.4; May 2014; p.71-85; doi: 10.12710/cardiometry.2014.4.7185. Available from: http://www.cardiometry.net/no4-may-2014/cardiac-allograft-vasculopathy
Introduction

Cardiac allograft vasculopathy (CAV) is a major risk factor for morbidity and mortality after heart transplantation (HTx) and occurs in 8-10%, 18-19% and 32-50% within the first, third and fifth year, respectively [1]. As a multifactorial disease CAV is induced by non-immunologic factors, e.g. donor age, hyperlipidemia, hypertension, cytomegalovirus (CMV) infection or donor age, or immunologic risk factors, e.g. cellular and humoral rejection [2].

Acute Cellular Rejection has been proven to be immunologic risk factor for the development of CAV [3]. Whereas humoral immune responses compromise (1) mismatched donor human leukocyte antigen (HLA) [4], (2) post-transplant developing donor-specific antibodies (DSA) [5] and (3) de novo post-transplant not donor specific HLA-Abs [6].

A direct pathogenic effect of Abs against the non-HLA major-histocompatibility complex class I-related chain A (MICA) is currently under discussion as study results show both an effect of cardiac allograft failure or an increased graft survival of MICA-Abs positive patients [7].

More recently, antibodies targeting against other non-HLA antigen like the angiotensin II type 1 receptor (AT1R) and the endothelin receptor A (ETAR), have shown to play a role in several severe alloimmune and autoimmune pathologies ranging from renal allograft rejection [8] to microvasculopathy in systemic sclerosis [9] and in cardiac transplants [10].

In this context we analyzed antibodies directed against HLA-class I and II antigens and directed against non-HLA antigens MICA, AT1R and ETAR in maintenance HTx recipients with CAV in comparison to recipients without CAV. The purpose of this pilot study was to gain further knowledge about the involvement of these antibodies in CAV and, furthermore, to identify recipients at risk for development of CAV after HTx.

Materials and methods

Patient population

Initially, 153 HTx recipients were investigated during their routine follow-up in our department. All recipients with an up-to-date coronary angiogram, known donor-HLA status and performed antibody diagnostic were included in this study (Figure 1). Written informed consent to use serum samples for research purpose was obtained from each patient. The institutional review board of the University hospital Leipzig approved the study.
Coronary angiography

All recipients included in this study underwent coronary angiography after HTx to diagnose epicardial CAV based on ISHLT recommended guidelines and the standardized nomenclature [25]. Coronary angiography is done by protocol in our center starting after one year post-transplant and every other year thereafter if CAV is not detected.

Endomyocardial biopsies

Endomyocardial biopsies were routinely done by protocol six times in the first year post-transplant (day 14 and month 1, 3, 6, 9 and 12) and once per year in the following years out of the right ventricle. Classification of ISHLT working formulations 1990/2004 were used for histological grading of acute cellular rejection [26]. For this study the highest treated BPAR after HTx till study time point was documented.
**Immunosuppressive therapy**

All patients received induction therapy with ATG (1mg/kg body weight on day 0). Initial immunosuppression consisted of a triple drug regimen. Immunosuppression following cardiac transplantation has traditionally comprised a calcineurin inhibitor in combination with mycophenolate mofetil or azathioprine and corticosteroids.

Treatment of BPAR in our center was as follows: BPAR grade 1A (ISHLT 1990) was not treated and all other BPAR grade 1B/1R or higher (ISHLT 1990/2004) were treated with a daily steroid pulse of 500mg methyl-prednisone for 3 days, followed by oral steroid doses of 50mg twice daily tapering down every three days by half of the dose till the standard steroid maintenance therapy is reached (5mg/day). ATG (1mg/kg/body weight for 1 to 3 days) was administered in case of steroid-resistant acute cellular rejection or in case of any cellular rejection with hemodynamic compromise.

**Serologic screening**

Sera were obtained from HTx recipients to determine HLA- and non-HLA-Abs. HLA- and MICA-Abs were screened with LABScreen® Mixed Class I, II and MICA (BMT GmbH, Meerbusch-Osterrath, Germany) according to manufacturers’ instructions. Acquisition and analysis were performed with Luminex® 200™ and HLA Fusion™ Software. Cut-off value for positive results was set to 3.0. For detection of DSA and specific characterization of HLA- and MICA-Abs, positive sera were further analyzed with LABScreen® Single Antigen HLA class I, class II or MICA Detection Tests (BMT GmbH) and a cut-off value for mean fluorescence intensity (MFI) at 500. All sera positive in the first Ab screening and negative in single-antigen tests were consequently termed negative. For determination of DSA the HLA genotype of heart donors was obtained from the German Trust of Organ Transplantation (Deutsche Stiftung für Organtransplantation; DSO). AT1R- and ETAR-Abs were quantified using ELISA employing native receptor conformation immobilized at the solid phase by CellTrend GmbH (Luckenwalde, Germany) as described previously [17,18].

CMV diagnostic was performed by an independent and accredited laboratory with recipients EDTA-plasma samples using the LightCycler® CMV Quant Kit from Roche Diagnostics GmbH (Mannheim, Germany).

**Statistical analysis**

Statistical analysis was performed using SPSS Statistics software 17.0. If not mentioned otherwise, data are displayed as mean±standard deviation. Binominal data (e.g. gender, CAV status, HLA-Ab status) were analyzed using Fisher’s Exact test. P-values of less than 0.05 were considered to indicate statistical significance. The non-parametric Mann-Whitney U test was used to compare differences in the mean or median of continuous variables. Univariate logistic-regression analysis was performed to identify risk factors associated with CAV. Cut-off values were calculated using Receiver Operating Characteristics (ROC) curve analysis. One-way analysis of covariance (ANCOVA) analysis was used to correlate Abs against HLA or non-HLA with CAV and treated BPAR.
Results

Patient characteristics
This study included 116 heart transplant recipients with a mean age of 58.5±12.8 years at time of transplantation. Ninety-one patients (78%) were male and the time from HTx to study begin was 8.5±4.2 years. At time point of transplantation, recipients were between 16.1 and 66.5 years old (50.0±11.5 years). Out of 116 recipients in the post-HTx period were transplanted 1-5 years (n=26), 5-10 years (n=44) and more than 10 years (n=46) ago. Almost 40% of the HTx recipients (39.7%, n=46) developed CAV identified by coronary angiography: 37 patients with CAV1, seven patients with CAV2 and two patients with CAV3. Mean donor age was significantly higher in CAV-positive recipients (45.3±10.9) compared to CAV-negative recipients (37.1±13.9; p=0.003). Gender and recipients’ age had no impact on study results. Detailed demographical and clinical characteristics are given in Table 1.

Non-immunological risk factors for CAV
Diabetes mellitus, hypertension, hyperlipidemia and CMV infection occurred in 27.6% (n=32), 25.9% (n=30), 36.2% (n=42) and 47.1% (n=51) of the HTx recipients, respectively. Diabetes mellitus type I, hypertension and hyperlipidemia could not be associated with increased risk for CAV (Table 1) or positive Ab status. There was no correlation between CMV infection and Ab positivity and CAV. No impact on CAV development was documented for immunosuppressive therapy at time of HTx and at time of study, except for tacrolimus (TAC) treatment at time of HTx. A higher percentage of CAV positive recipients (41.3%) obtained initial TAC treatment after HTx compared to percentage of CAV negative recipients with TAC treatment at time of HTx (14.3%, p=0.02).
Table 1: Demographic and clinical characteristics of the patient population.

<table>
<thead>
<tr>
<th></th>
<th>CAV+ (n=46)</th>
<th>CAV- (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient age at HTx, yrs</td>
<td>49.2±11.4</td>
<td>50.5±11.6</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>39 (85%)</td>
<td>53 (76%)</td>
</tr>
<tr>
<td>Dilated cardiomyopathy, n (%)</td>
<td>29 (63%)</td>
<td>43 (61.4%)</td>
</tr>
<tr>
<td>Ischemic cardiomyopathy, n (%)</td>
<td>13 (28.3%)</td>
<td>20 (28.6%)</td>
</tr>
<tr>
<td>Donor age, yrs</td>
<td>45.3±10.9</td>
<td>37.1±13.9</td>
</tr>
<tr>
<td>Time between HTx and study, yrs</td>
<td>7.9±4.7</td>
<td>8.9±3.7</td>
</tr>
<tr>
<td>Recipient CMV positive, n (%)</td>
<td>18 (39.1%)</td>
<td>23 (32.9%)</td>
</tr>
<tr>
<td>Diabetes mellitus, treated</td>
<td>16 (34.8%)</td>
<td>16 (22.9%)</td>
</tr>
<tr>
<td>Arterial hypertension, treated</td>
<td>12 (26.1%)</td>
<td>18 (25.7%)</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitor</td>
<td>17 (36.9%)</td>
<td>38 (54.3%)</td>
</tr>
<tr>
<td>Angiotensin receptor blockers</td>
<td>18 (39.1%)</td>
<td>23 (32.9%)</td>
</tr>
<tr>
<td>Treated BPAR ISHLT</td>
<td>19 (30.0%)</td>
<td>21 (41.3%)</td>
</tr>
</tbody>
</table>

Immunosuppression at time of HTx

<table>
<thead>
<tr>
<th></th>
<th>CAV+ (n=46)</th>
<th>CAV- (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclosporine A</td>
<td>27 (58.7%)</td>
<td>59 (84.3%)</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>19 (41.3%)</td>
<td>10 (14.3%)</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>31 (67.4%)</td>
<td>41 (58.6%)</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>13 (28.3%)</td>
<td>24 (34.3%)</td>
</tr>
</tbody>
</table>

Data are given as number (n) or mean ± standard deviation of the mean. BPAR, biopsy proven acute rejection; CMV, cytomegalovirus; CAV, cardiac allograft vasculopathy positive (+) or negative (-) at study time; HTx, heart transplantation; ISHLT, International Society of Heart and Lung Transplantation; mo, month; yrs, years.

HLA- and non-HLA-Abs and CAV

At study time twenty-four HTx recipients with CAV (52.2%) and forty-three recipients without CAV (61.4%) had positive Ab status (Table 2). There were no statistically significant differences between CAV positive and CAV negative recipients regarding positivity of transplant relevant Abs. Among CAV positive recipients, 91.7% (n=22) had non-HLA-Abs: 44.1%, 38.2% and 13.0% were positive for ETAR-Abs, AT1R- and MICA-Abs. Whereas 8.7% were positive for either HLA class I or HLA class II-Abs, respectively. Furthermore, there was a trend that recipients with non-HLA-Abs developed CAV earlier (73.7±47.4mo) after HTx than recipients without these Abs (85.5±50.6mo; p=0.113). Recipients with positive Ab status, and especially recipients with HLA-Ab positivity were younger (53.5±14.5yrs and 47.0±17.2yrs respectively) when CAV was diagnosed compared to recipients without these Abs (60.0±7.0yrs; p=0.162 and p=0.104).
Table 2: Detailed antibody status in HTx recipients with and without CAV.

<table>
<thead>
<tr>
<th></th>
<th>CAV+ (n=46)</th>
<th>CAV- (n=70)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibody positivity, n (%)</td>
<td>24 (52.2%)</td>
<td>43 (61.4%)</td>
<td>0.74</td>
</tr>
<tr>
<td>HLA</td>
<td>2 (4.3%)</td>
<td>3 (4.3%)</td>
<td>1</td>
</tr>
<tr>
<td>HLA class I</td>
<td>2 (4.3%)</td>
<td>1 (1.4%)</td>
<td>0.56</td>
</tr>
<tr>
<td>HLA class II</td>
<td>0</td>
<td>1 (1.4%)</td>
<td>1</td>
</tr>
<tr>
<td>HLA class I + II</td>
<td>0</td>
<td>1 (1.4%)</td>
<td>1</td>
</tr>
<tr>
<td>Non-HLA</td>
<td>18 (39.1%)</td>
<td>35 (50.0%)</td>
<td>0.26</td>
</tr>
<tr>
<td>MICA</td>
<td>3 (6.5%)</td>
<td>3 (4.3%)</td>
<td>0.68</td>
</tr>
<tr>
<td>AT1R</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>ETAR</td>
<td>5 (10.9%)</td>
<td>9 (12.9%)</td>
<td>1</td>
</tr>
<tr>
<td>ETAR+MICA</td>
<td>0</td>
<td>1 (1.4%)</td>
<td>1</td>
</tr>
<tr>
<td>ETAR+AT1R</td>
<td>9 (19.6%)</td>
<td>21 (30.0%)</td>
<td>0.28</td>
</tr>
<tr>
<td>ETAR+AT1R+MICA</td>
<td>1 (2.2%)</td>
<td>1 (1.4%)</td>
<td>1</td>
</tr>
<tr>
<td>HLA + non-HLA</td>
<td>4 (8.7%)</td>
<td>5 (7.1%)</td>
<td>0.74</td>
</tr>
<tr>
<td>HLA class I+II+AT1R+ETAR</td>
<td>1 (2.2%)</td>
<td>0</td>
<td>0.40</td>
</tr>
<tr>
<td>HLA class II+AT1R+ETAR</td>
<td>1 (2.2%)</td>
<td>0</td>
<td>0.40</td>
</tr>
<tr>
<td>HLA class II+MICA</td>
<td>1 (2.2%)</td>
<td>0</td>
<td>0.40</td>
</tr>
<tr>
<td>HLA class I+II+MICA+AT1R+ETAR</td>
<td>1 (2.2%)</td>
<td>1 (1.4%)</td>
<td>1</td>
</tr>
<tr>
<td>HLA class I+AT1R+ETAR</td>
<td>0</td>
<td>2 (2.9%)</td>
<td>0.52</td>
</tr>
<tr>
<td>HLA class II+ETAR</td>
<td>0</td>
<td>1 (1.4%)</td>
<td>1</td>
</tr>
<tr>
<td>HLA class II+MICA</td>
<td>0</td>
<td>1 (1.4%)</td>
<td>1</td>
</tr>
</tbody>
</table>

Data are given as number (n); ATR: angiotensin receptor; AT1R: angiotensin-II receptor type 1; CAV, cardiac allograft vasculopathy positive (+) or negative (-) at study time; ETAR: Endothelin subtype A receptor; HLA, human leukocyte antigen; MICA: major histocompatibility complex class I-related chain A.

Calculated cut-off values were for non-HLA-Abs AT1R 8.32 and for ETAR at 8.17. ANCOVA analysis revealed a significant correlation between Ab-positivity and treated BPAR for AT1R-Abs (p=0.001) and ETAR-Abs (p=0.002).

Donor specific antibodies

Three out of eight HTx recipients developed DSA against HLA class I molecules, four recipients against HLA class II molecules and one recipient DSA against both HLA class I and class II antigens, respectively. CAV was diagnosed in four HTx recipients with DSA (50%) compared to 38.9% (n=42) of HTx recipients without DSA.
Mean fluorescence intensity of HLA and MICA specificities

An accumulation of positive tested specificities with MFI of greater than or equal to 5000 was observed for 16 HLA-A specificities, six HLA-B specificities and for one HLA-Cw specificity (Figure 2 A, B and C). Single antigen analysis of HLA class II and MICA showed that five HLA-DP and four HLA-DQ specificities had increased MFIs (Figure 2 D, E and F). Analysis of MICA specificities showed that none of the tested MICA-Abs had increased mean fluorescence intensity.

Some Ab-specificities occurred more frequently after HTx: 66.7% (n=6) and 55.6% (n=5) of recipients with HLA class I-Abs were positive for Abs against HLA-B46 and HLA-B76, respectively. 66.7% (n=6) and 55.6% (n=5) of recipients with HLA class II-Abs had Abs against the specificities HLA-DQ7 and -DQ8. Recipients with Ab-positivity against MICA antigens were frequently positive for MICA1 (61.5%) and MICA19 (53.8%). Fifty percent or more of HTx recipients with positivity for HLA-B46, -B76, -DQ7, -DQ8 and MICA19 developed CAV.
Acute cellular rejection

More treated biopsy proven acute rejection (BPAR) were detected in the CAV negative patient cohort compared to the CAV positive cohort (Table 1). Out of these treated BPAR the highest histological rejection grade post-HTx was 2R for one CAV positive patient and for two CAV negative patients. All three patients were additionally hemodynamically compromised and, therefore, treated with anti-thymocyte globulin (ATG). The other BPARs grade 1R in both study groups were detected during protocol biopsies and not clinical present. No histological evidence of antibody mediated rejection based on the Cd4 criterion was detected in our study cohort.

Table 3: Univariate analysis using logistic regression to determine factors associated with CAV.

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient age / Age at HTx (OR per 1,0yr)</td>
<td>0.994</td>
<td>0.962 - 1.026</td>
<td>0.697</td>
</tr>
<tr>
<td>Male recipient</td>
<td>1.787</td>
<td>0.676 - 4.726</td>
<td>0.242</td>
</tr>
<tr>
<td>Donor age (OR per 1,0 year), 111 rcps</td>
<td>1.055</td>
<td>1.021 - 1.090</td>
<td>0.002</td>
</tr>
<tr>
<td>Diagnosis leading to HTx</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DCM vs. others</td>
<td>0.843</td>
<td>0.209 - 3.407</td>
<td>0.811</td>
</tr>
<tr>
<td>ICM vs. others</td>
<td>0.813</td>
<td>0.183 - 3.600</td>
<td>0.785</td>
</tr>
<tr>
<td>Age at study begin (OR per 1,0 year)</td>
<td>0.987</td>
<td>0.959 - 1.016</td>
<td>0.384</td>
</tr>
<tr>
<td>HLA class I positivity</td>
<td>1.238</td>
<td>0.314 - 4.876</td>
<td>0.760</td>
</tr>
<tr>
<td>HLA class II positivity</td>
<td>1.238</td>
<td>0.314 - 4.876</td>
<td>0.760</td>
</tr>
<tr>
<td>DSA positivity</td>
<td>1.571</td>
<td>0.373 - 6.625</td>
<td>0.538</td>
</tr>
<tr>
<td>MICA positivity</td>
<td>1.350</td>
<td>0.423 - 4.307</td>
<td>0.612</td>
</tr>
<tr>
<td>AT1R level (OR per 1,0 Unit)</td>
<td>0.986</td>
<td>0.948 - 1.025</td>
<td>0.472</td>
</tr>
<tr>
<td>AT1R cut-off 8.325</td>
<td>0.718</td>
<td>0.265 - 1.942</td>
<td>0.513</td>
</tr>
<tr>
<td>ETAR level (OR per 1,0 Unit)</td>
<td>0.981</td>
<td>0.944 - 1.020</td>
<td>0.339</td>
</tr>
<tr>
<td>ETAR cut-off 8.175</td>
<td>0.447</td>
<td>0.150 - 1.330</td>
<td>0.141</td>
</tr>
<tr>
<td>IS regimen at time of HTx</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CsA</td>
<td>0.265</td>
<td>0.111 - 0.633</td>
<td>0.003</td>
</tr>
<tr>
<td>TAC</td>
<td>4.222</td>
<td>1.733 - 10.285</td>
<td>0.002</td>
</tr>
<tr>
<td>MMF</td>
<td>1.462</td>
<td>0.671 - 3.184</td>
<td>0.339</td>
</tr>
<tr>
<td>AZA</td>
<td>0.755</td>
<td>0.336 - 1.697</td>
<td>0.496</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>0.494</td>
<td>0.231 - 1.057</td>
<td>0.069</td>
</tr>
<tr>
<td>AT1R blockers</td>
<td>1.314</td>
<td>0.606 - 2.849</td>
<td>0.490</td>
</tr>
<tr>
<td>Acute rejection treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroid boli</td>
<td>1.642</td>
<td>0.754 - 3.576</td>
<td>0.210</td>
</tr>
<tr>
<td>ATG</td>
<td>1.022</td>
<td>0.979 - 1.067</td>
<td>0.215</td>
</tr>
<tr>
<td>Cellular rejection, ISHLT 1990</td>
<td>1.642</td>
<td>0.754 - 3.576</td>
<td>0.210</td>
</tr>
</tbody>
</table>

ACE: angiotensin converting enzyme; ATG: anti-thymocyte globulin; ATR: angiotensin receptor; AT1R: angiotensin-II receptor type 1; AZA: azathioprine; CI: confidence interval; CMV: cytomegalovirus; CsA: Ciclosporin A; DCM: dilated cardiomyopathy; DSA: donor-specific antibody; ERL: everolimus; ETAR: Endothelin subtype A receptor; HLA: human leukocyte antigen; HTx: heart transplantation; ICM: ischemic cardiomyopathy; IS: immunosuppression; ISHLT, International Society of Heart and Lung Transplantation; MICA: major histocompatibility complex class I-related chain A; MMF: mycophenolate mofetil; OR: odds ratio; rcps.: recipients; TAC: tacrolimus; VAD: ventricular assist device
Discussion and conclusion

The negative impact of HLA-Abs on allograft survival after heart transplantation has been demonstrated in a number of studies so far. The appearance of Abs often results in immunomodulatory effects leading to allograft dysfunction and rejection. As acute and chronic allograft rejection occasionally also occurred in HLA-identical sibling transplants, the search of transplant relevant Abs was extended to non-HLA targets, their antigen specificity and their potential pathogenicity [11].

In this study we showed that HTx recipients developed Abs to a higher degree against the non-HLA antigens AT1R, ETAR and MICA than against HLA antigens. Panigrahi et al. [12] showed in a clinical trial with 185 renal transplanted patients that MICA-positive recipients had significant lower graft survival and a higher number of acute rejection episodes as compared to the non-sensitized group. A correlation between MICA-Abs and an increased risk for acute rejection and vasculopathy has been proved in an earlier study with 159 HTx recipients [13]. These study results including our findings are limited by the fact that only one or two posttransplant serum samples were collected and pretransplant MICA-Ab status is missing. Whereas, Smith et al. [14] measured pre- and several posttransplant serum samples of 491 HTx recipients for MICA-Abs. No negative effect of MICA-specific Abs on cardiac allograft survival, number of acute rejection episodes or CAV has been found in this trial. In contrast, recently it has been demonstrated that posttransplant donor specific antibodies (DSA) MICA antibodies may be associated either alone or in combination with anti-HLA-DSA with antibody mediated rejection (AMR) in some cardiac allografts [15].

Despite MICA-Abs there is a number of non-HLA-Abs, like Abs against AT1R- and ETAR, that are relevant to allograft dysfunction and rejection. AT1R-Abs were studied for the first time in a cohort of 33 kidney-transplant recipients with refractory vascular rejection [16]. It was hypothesized that an AT1R-mediated pathway may contribute to refractory vascular rejection. A following study detected a strong association between the presence of AT1R-Abs and AMR in kidney transplanted recipients whose sera contained no antibody to donor HLA or MICA [8]. A recent pilot study in a small cohort with 30 recipients in the first year after HTx showed a correlation of elevated levels of AT1R-Abs and ETAR-Abs with early onset of microvasculopathy at month 12, and graft loss following HTx, implicating relevant effects on post-transplant morbidity and mortality in that study [10]. Higher levels of AT1R- and ETAR-Abs were observed in patients with acute cellular rejection and antibody-mediated rejection at months 1 and 12 post-HTx [10]. In our large maintenance HTx recipients (n=116) cohort we observed a correlation of AT1R- and ETAR-Abs with subclinical treated BPAR rejection (ISHLT 2004 grade 1R). This finding confirms the results of Raichlin et al. [3] who found a strong influence of recurrent cellular rejections on the incidence of CAV. Thus, it might be explained that cellular rejections trigger an inflammatory process which further stimulates antibody production especially against AT1R- and ETAR resulting in CAV. Moreover, this constellation might accelerate progression of CAV as we observed that recipients with non-HLA-Ab developed CAV earlier than recipients without these antibodies. Thus, it could be speculate that especially HTx recipients with subclinical BPAR and elevated AB-levels of AT1R- and ETAR develop CAV and, therefore, should consequently be treated.
In general, panel reactive Ab (PRA)-screenings are part of pre-HTx monitoring, but single antigen HLA-Ab screenings give more detailed information about the Ab status of a single patient and, therefore about possible clinical complications after HTx. We found that a high percentage of HTx recipients with DSA developed CAV. Our study confirmed the necessity for HLA-Abs monitoring after transplantation in order to detect the appearance of DSA and the risks involved in CAV development. A regular monitoring of post-transplant DSA for identification of recipients at risk of allograft failure was recommended earlier. For example, a large retrospective study about 250 HTx recipients that were screened pre- and post-HTx for HLA-Abs and DSA showed that de novo-production of DSA after transplantation is associated with poor graft survival [17]. A strong correlation between the development of DSA and adverse outcome after HTx in a study including over 200 recipients [18], but results are limited by the fact that sera were tested only once after HTx by ELISA detection.

Furthermore, we identified HLA- and MICA-Abs specificities, whose appearance was accompanied with an increased risk for development of CAV. Our study is the first that identified and described high MFI and frequently occurring Ab specificities that may be involved in CAV progression and development in a larger study cohort. Studies including single antigen analysis of HLA- and MICA-Abs are rare to our knowledge, possibly caused by the lack of a standardized MFI analysis. The MFI has been suggested to be a determinative factor but the MFI determining the border between positive and negative reactions differs between centers and amongst studies [19]. PRA-screenings of HTx recipients alone are not conclusive enough to identify recipients with increased risk for graft rejection or developing CAV. Thus, it is necessary to monitor Abs-specificities of sensitized patients in further studies to clarify the role and influence of single Ab specificities on CAV development.

Despite immunological events, there are a number of non-immunological factors that have been implicated in the pathogenesis of CAV such as donor factors, viral infection, immunosuppressive drugs and metabolic risk factors [20]. Among these factors donor’s age was identified as risk factor for CAV. This result is in accordance with a retrospective analysis of almost 40,000 patients comprising study of the United Network for Organ Sharing heart transplant database that assessed the association between donor variables and the onset of CAV for adult recipients and found that older donors conferred a higher risk of developing CAV [21]. But not only donor age has an influence on CAV development, younger recipient’s age in combination with positive Ab status could be associated with CAV in our study, most notably when HLA-Ab status was positive.

CMV infection is believed to play a key role in CAV progression, possibly through its complex interaction with the host immune system and immunomodulatory effects [20,22]. In our study CMV seropositivity was not associated with CAV and did not correlate with an increase of Ab status. For diabetes mellitus type I, hypertension or hyperlipidemia no correlation with CAV or Ab positivity was found in our study. We analyzed the impact of immunosuppressive drugs on CAV at time of HTx and found, that initial treatment with TAC after HTx seems to be involved in CAV progression. A more pronounced progression of CAV in TAC treated HTx recipients compared to CsA treated recipients was also obtained in a prospective study by detecting CAV with intra-vascular ultrasound (IVUS) in the first year post-transplant [23].

The concomitant statistical significance for an initial treatment with cyclosporine A (CsA) can be attributed to the fact, that initial immunosuppressive regimen after HTx consist administration of
either CsA or TAC. It is standard in our center to convert immunosuppression of patients with CAV to the mTOR-inhibitor everolimus to prevent or retard the development of CAV and to improve long-term survival as already recommended by other groups [3,24].

In summary, this study identified a number of factors that are linked to CAV after HTx, and consequently gave rise to reduced graft and patient survival. Despite donor and recipient age, the presence of non-HLA-Abs after transplantation, DSA to mismatched HLA and initial immunosuppressive therapy with TAC after HTx were identified as risk factors for cardiac allograft survival in our study. We could show for the first time that non-HLA-Abs against AT1R and ETAR are connected to the development of CAV and subclinical acute rejection after cardiac transplantation and may therefore serve as markers to identify patients with increased risk for allograft failure in consequence of CAV.

A comprehensive monitoring of transplant-relevant Abs before and after HTx may help to evaluate the individual risk for CAV. Thus, we suggest a comprehensive monitoring should comprise analysis of sera before transplantation, in the first year after HTx and continuously at least once annually. The screening should involve quantification of AT1R- and ETAR-Abs, detection of DSA and MFI analysis of HLA- and MICA-Ab specificities. Furthermore, a functional testing for HLA-Abs, like analysis of C1q-binding Abs will further help to identify complement fixing DSA. Prospective clinical studies with well-defined cohorts and careful analysis to different immunosuppressive protocols as well as to BPAR may help to elucidate the complex correlations of immunological and non-immunological risk factors for CAV.

**Abbreviations**

Abs antibodies  
ACE angiotensin converting enzyme  
ATG anti-thymocyte globulin  
AT1R angiotensin II type 1 receptor  
AZA azathioprine  
BPAR biopsy proven acute rejection  
CAV cardiac allograft vasculopathy  
CI confidence interval  
CMV cytomegalovirus  
CsA cyclosporine A  
DCM dilated cardiomyopathy  
DSA donor-specific antibody  
ELISA enzyme-linked immunosorbent assay  
ERL everolimus  
ETAR endothelin-1 type A receptor
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.

Authors contributions
M. T. D. participated in research design, the writing of the paper, the performance of the research and in data analysis.
J. G. participated in research design, the writing of the paper and in data analysis.
R.D. participated in the writing of the paper, the performance of the research and in data analysis.
S.D. participated in the writing of the paper.
F.W.M. participated in the writing of the paper.
H.B.B. participated in the writing of the paper.
M.J.B. participated in research design, the writing of the paper, the performance of the research and in data analysis.
References


Familial arrhythmogenic right ventricular dysplasia in afrocaribbeans: treadmill stress test the key to early diagnosis

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

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

* Corresponding author phone: +1876 881-7844, e-mail: sandrap@cwjamaica.com

Submitted: 22 March 2014
Accepted: 30 April 2014
Published online: 30 May 2014

Abstract
Arrhythmogenic right ventricular dysplasia is a rare entity and a significant cause of sudden death especially in the Italian population and athletes. The familial form is uncommon especially in the Afro-Caribbean population. This Index family represents an Autosomal Dominant form in a maternal parent who had sudden death at 39 years of age. The Index case was diagnosed at 18 years with increasing palpitations since 8 years of age, becoming symptomatic two decades younger than her mother. This was confirmed using the Treadmill Stress test. This is the 1st Case of Familial Arrhythmogenic right ventricular dysplasia documented in an Afro-Caribbean family.

Learning objective
Familial Arrhythmogenic right ventricular dysplasia is a rare entity and a significant cause of sudden death especially in the Italian population and athletes. This the first case of Autosomal Dominant type of ARVD with variable penetrance, documented in an Afro-Caribbean family where diagnosis was aided by Ventricular Tachycardia occurring during a Treadmill Stress Test.

Keywords
Arrhythmogenic right ventricular dysplasia • Ventricular tachycardia • Familial • Gene

Imprint
Sandra Williams-Phillips. Familial arrhythmogenic right ventricular dysplasia in afrocaribbeans: treadmill stress test the key to early diagnosis; Cardiometry; No.4; May 2014; p.86-93; doi: 10.12710/cardiometry.2014.4.8693. Available from: http://www.cardiometry.net/no4-may-2014/arrhythmogenic-right-ventricular-dysplasia

Introduction
Arrhythmogenic right ventricular dysplasia (ARVD) is a rare structural cardiac anomaly characterized by predominantly right ventricular free wall myocardial atrophy with fibro fatty replacement leading to ventricular arrhythmias and Sudden Death. First described by Giovanni Maria Lancisi (1736) who published in his book “De Hereditaria ad Cordis Aneurysmata Constitutione: De Cordis Prolapsu”, the occurrence in four (4) generations of an Italian family, the classical symptoms and signs of palpitations, aneurysmal formation in dilated right ventricle, congestive cardiac failure and sudden death [1]. Sergio Dalla Volta (1961) published cases which had ventricular arrhythmias which occurred in right ventricles, which were ineffective in systole as there was “auricularization”
of the right ventricular pressure, where blood was transmitted to the pulmonary artery by atrial systole [2].

Over two and half centuries after the first description, Frank et al (1978) described the Electrocardiogram (ECG) findings in four (4) cases of right ventricular dysplasia with the first description of the Epsilon Wave after the QRS complex, seen in only 8% of confirmed ARVD. [1]. Marcus et al (1982) in 24 post mortem cases documented the worst end of the spectrum of Arrhythmogenic Right Ventricular Dysplasia and described the pathognomonic “Triangle of Dysplasia” in the inflow, apex and outflow of the right ventricle.

The early pathology can start in any part of the right ventricle and interventricular septum, which can explain the clinical, ECG and diagnostic phenotypic heterogeneity, which may not have all the classical findings of ARVD. These clinical, ECG and diagnostic findings may be difficult to ascertain in the attempt of early diagnosis of Familial ARVD, without using histology from an invasive cardiac muscle biopsy, with the attendant risk of perforation, before Sudden Death occurs and becomes the presenting feature [3]. Cardiac Magnetic Resonance Imaging (MRI) would not be cost effective, nor recommended, for repeated use in pre-pubertal or adolescent patients.

Prevalence of ARVD varies from 1:5000 in USA to 20:5000 in Italy and Germany and constitute up to 25%, of the main causes of Sudden Death in Italy amongst athletes under 35 years of age [4]. The familial occurrence has been substantiated by the detection of 12 gene abnormalities with over 800 pathogenetic mutations. The genes encode for five (5) desmosomal proteins and seven (7) non-desmosomal proteins, the most common of which was the ARVD (type 9) seen in up to 40% of cases, caused by mutations in PKP2 gene which encode plakophilin-2 protein. Desmosomal genes are protein parts of the cell membrane which facilitates the function and structural integrity of the cell. The ARVD gene type 1 has been found on chromosome 14q23-q24 with marked phenotypic heterogeneity. More than 50 % of cases of the genes identified with ARVD are familial, Autosomal Dominant with variable penetrance and phenotypic expression as in the Index case. Cutaneous-Cardiac phenotypes which are Autosomal recessive forms are associated with Naxos Disease and Carvajal Syndromes [5].

Case report

The Index case is an 18 years old Afro-Caribbean female at a tertiary level institution with a 10 year history of intermittent palpitations with increasing frequency, associated with dizziness and 9 years of retrosternal or praecordial “sharp sticking” chest pain not associated with palpitations. She functions at NYHA11 but becomes NYHA 111 on exertion. There was no history of syncope, seizure or deafness.

There was also no history of caffeine ingestion, energy drinks, high dose steroids, stimulants or illicit drugs.

The Index cases mother developed palpitations in her twenties and developed Complete Heart Block. She died at 39 years of age from Ventricular arrhythmias secondary to diagnosis of ARVD, when the index case was eight years old. The Index case was her only child.
On examination her weight was 49 kg and Height 174 cms with BMI of 16, and BSA 1.55m2. Cardiovascular examination revealed heart rate of 80/minute with normal volume and rhythm. Her Apex beat was at the 5th left intercostal space in the mid-clavicular line, normal in character. First and second heart sounds were normal; a grade 1/6 systolic murmur was noted in lower left sternal border. There were no signs of cardiac failure or pulmonary hypertension.

Investigations revealed Haemoglobin of 12.8 g/dl and packed cell volume of 38.2%. There were normal thyroid function tests.

The Chest-X Ray had normal cardiothoracic ratio with no filling of the anterior space, normal lung fields, normal ratio right and left bronchi and normal position of abdominal viscera ruling out Isomerism.

Transthoracic Echocardiogram showed RVAWd 0.5 cm, RVIDd 0.6 cm, IVSd 1.1 cm, LVIDd 3.9 cm, LVPWd 1.6 cm, IVSs 1.3 cm, LVIDs 2.4 cm and LVPWs 2.0 cm. Normal IVS/LVPW ratio, Normal LA-AO ratio, Normal Fractional shortening of 38% and Ejection Fraction of 70%. Right ventricular wall was non-homogenous. There was mild Tricuspid regurgitation and normal pulmonary artery pressures. Cardiac MRI, Cardiac CT and Gene studies are not available in the Index country.

The resting Electrocardiogram (ECG) showed heart rate of 71bpm, Sinus arrhythmia, and normal QRS duration of 90 msein, Normal Qtc of 0.398 ms and QRS axis of 89. P axis was -22 and T axis was 62. T wave was inverted in V1 only. There was early repolarization in V2 and V3. A small variant of an Epsilon (ie., Postsilon) wave in V3, V4, V5 and V6 was noted (Fig.1). These atypical Epsilon waves were not seen on other resting ECG’s nor during the treadmill stress test. There were no Epsilon waves, or variants thereof, in V1 and V2.

Figure 1. Variant Epsilon (Postsilon) Wave V3 - V6.
Bruce Protocol Treadmill Stress Test showed on ECG monitor, within 30 seconds of Stage 1, Atrial Flutter, Atrial Fibrillation and Isolated (premature ventricular contractions (PVC)) (Fig. 2). Within two minutes there were more frequent isolated 2 to 1 wide QRS complex PVC (Fig.3) Within 3 minutes there were bizarre wide QRS complex Ventricular Tachycardia (VT) (Fig.4). Whilst the ECG abnormalities were noted, the Index case did not feel or complain of palpitations and fatigue in the first 3 minutes, which is an ominous sign, as this could be occurring without the patient’s knowledge. The Index case complained of palpitations when VT commenced and continued to complain until 30 seconds after cessation of treadmill test. During the recovery period there was Atrial Flutter and Atrial Fibrillation intermittently up to 5 minutes, when the normal pre-test resting ECG occurred (Fig.5). The ECG abnormalities noted in Figures displayed, occurred in all leads simultaneously recorded, ruling out the possibility of artifact as a cause of abnormalities noted.

Figure 2. Atrial Dysrhythmias with Isolated PVC.

Figure 3. Isolated 2 to 1 Wide QRS Complex.
Medications initially started were cost effective anti-arrhythmic Digoxin and beta-blocker Atenolol. A Dual chambered implantable cardio vertex defibrillator was inserted. Index case is now maintained on beta-blocker only.

There continues to be recommended exercise restrictions, with no competitive sports or sustained exertion in Index case.

Discussion

The diagnosis of ARVD was based on a criteria first developed by McKenna et al (1994) which has been revised by the International Task Force in 2009. ARVD diagnosis needs 2 Major criteria or 1 major and 2 Minor criteria or 4 Minor criteria based on Family history of Sudden Death, and ARVD, ECG abnormalities, right ventricular arrhythmias, right ventricular structural or functional abnormalities with myocardial atrophy and fibro-fatty replacement. The 2009 diagnostic criteria included additional magnetic resonance imaging of the heart, genetic testing and new ECG abnormalities including LBBB morphology in ventricular arrhythmias. A new ECG criterion has also been developed as only 8% of ARVD cases have the classical Epsilon wave, which makes it more difficult to diagnose. Epsilon waves in ARVD are usually in V1- V3, but it would be possible to
understand that the ECG abnormality would be a direct reflection of the part of the ventricle involved in the early pathology, which can start in any part of the right ventricle and interventricular septum.

Basso et al noted that the most common ECG abnormality in 79% of cases is inverted precordial T wave especially in right precordial leads, as noted in VI of the Index case. Involvement of the interventricular septum occurs in 20% and left ventricle at autopsy in 47% of cases at the severe end of the spectrum of the disease [3, 6]. The Index case had 2 major and one minor criterion, Epsilon wave noted on one ECG, family history of death from ARVD and Ventricular Tachycardia during Treadmill Stress Test. The Ventricular Tachycardia was confirmed only during the Treadmill stress Test and hence helped to confirm the diagnosis of ARVD using the revised McKenna criteria.

There has been a diagnostic dilemma in determining what investigation or clinical assessment is needed to determine which family members would phenotypically inherit ARVD, prior to the occurrence of Sudden Death. There is no direct correlation noted between the genotype and when the phenotypic expression would occur. Sudden Death may be the presenting phenotypic expression. This anecdotal case suggests that Treadmill Stress tests, elucidating the Ventricular Arrhythmia in a controlled environment, could be the answer to early diagnosis of ARVD. Treadmill Stress Tests using the Modified Bruce Protocol annually after 10 years of age, or before the earliest age of Sudden Death in the Family with ARVD, could be the key to early detection and hence early treatment. Further large scale multicenter trials in descendants of ARVD, would be needed to elucidate if this method of assessment, starting in late childhood would be helpful in early diagnosis, leading to enhanced monitoring, treatment and prophylactic care.

The Epsilon waves in this Index Case are atypical of ARVD, in its appearance on the ECG and were not consistently seen in all ECG’s completed within the year preceding the diagnosis. This confirms the finding of some authors who indicate also absence of Epsilon wave on some ECG’s in the same patient but also beat to beat variability. There were no Epsilon waves (or variants thereof), ever seen in V1 and V2. Atypical variants of the Epsilon waves were only seen in V3, V4, V5 and V6 (Fig.1). The classical ARVD usually have Epsilon waves in V1 to V3. It is noted by some authors that there can be progression of Epsilon waves from V1 to V3 to all other leads with progression of the disease and that involvement of the myocardium may be non-homogenous, postulating that this could lead to variability in types of Epsilon waves and ECG leads that they are seen in. The new criterion for diagnosis is made easier without histology and or biopsy when not readily available. [1-3, 6]. The ECG abnormalities noted during the Treadmill test were initially not noticeable to the Index case indicating that Arrhythmias can be occurring without the patients awareness of Palpitations, leading to Syncope, Cardiac Arrest or even Sudden Death, without forewarning.

The etiological-pathological cause has been identified to be secondary to programmed “Apoptosis” of myocardial cells, metabolic degenerative with loss of myocardium, inflammatory with an inflammatory necrosis as seen in mice after coxsackie virus infection and sympathetic nerve disruption analogous to amine depletion. These theories and confirmed disease processes have not yet translated into curative therapy which at this time is purely symptomatic with increased survival with predominantly defibrillators and improved drug therapy [7]. Some patients may present with Sudden Death and the new criteria is hoped to be helpful with early diagnosis of familial
asymptomatic cases, who can have palpitations without cognizance of family history of ARVD or occurrence of a new mutation of ARVD [4-7].

The literature is replete with studies in Italians, Greeks, Germans and Caucasians. The International Registry in 2006 in Europe and North America was beneficial in providing additional genetic evaluation with 5 new genes identified. This registry should now be extended to other countries where the ARVD diagnosis is made [1-7].

Thiene and Basso et al in his analysis of 38 families with detection of desmosomal genes DSP, PKP2, DGS2 and MM found increased left ventricular involvement and larger right ventricles in PKP2 and MM groups but there was no difference in long term morbidity or mortality between the groups confirming phenotypic heterogeneity. The Index family would benefit from Genetic testing to determine if the gene responsible belong to any of the 12 genes identified thus far, or if there is a different gene in the Afro-Caribbean population [1-8].

An index family that has an Autosomal Dominant Familial Arrhythmogenic right ventricular dysplasia displaying variable penetrance and phenotypic heterogeneity, confirmed with Ventricular Tachycardia during Treadmill Stress test, documented for the first time in an Afro-Caribbean family, in the English Medical Literature.

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


Phase characteristics of rheograms. Original classification of phase-related changes of Rheos

Mikhail Y. Rudenko

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

Submitted: 25 March 2014
Accepted: 20 April 2014
Published online: 30 May 2014

Abstract

The phase characteristics of a rheogram are described in literature in general only. The existing theory of impedance rheography is based on an analysis of the form of rheogram envelopes, but not on the phase-related processes and their interpretation according to the applicable laws of physics. The aim of the present paper is to describe the phase-related characteristics of a rheogram of the ascending aorta. The method of the heart cycle phase analysis has been used for this purpose. By synchronizing an ECG of the aorta and a rheogram, an analysis of specific changes in the aorta blood filling in each phase is provided. As a result, the phase changes of a rheogram associated with the ECG phase structure are described and tabulated for first time. The author hereof offers his own original classification of the phase-related changes of rheograms.

Keywords

Impedance cardiography • Rheogram • Classification • Phase-related changes • Heart cycle phase analysis • ECG • Ascending aorta

Imprint

Mikhail Y. Rudenko. Phase characteristics of rheograms. Original classification of phase-related changes of Rheos; Cardiometry; No.4; May 2014; p.94-96; doi:10.12710/cardiometry.2014.4.9496. Available from: http://www.cardiometry.net/no4-may-2014/phase-characteristics-of-rheograms

Introduction

Despite the fact that diagnostic capabilities of rheograms have been investigating for a long time, nowadays the heart cycle phase analysis is ignored by every method of the Rheo interpretation in general [1-4]. In its turn, the phase analysis is the basis for understanding the biophysical processes occurring in the cardiovascular system. Therefore, all the existing methods of the Rheo interpretation, including the pulse contour analysis, have not found their wide application. CARDIOMETRY considers a rheogram from the point of view of hemodynamic phase-related processes and offers a new approach to the cardiovascular system diagnostics [6-9].
Materials and methods

The experience accumulated when using the Cardiocode device allows describing the phase structure of a rheogram and creating a fundamentally new classification of the Rheo phase-related changes [6-8]. This original classification of the phase-related changes in rheograms is presented in Fig.1 below. The rheogram curve changes are classified by considering 6 phases in total. These changes characterize the energetic capabilities of the heart and the influence of the systemic and pulmonary circulation vessel resistance on hemodynamics.

![PHASE-RELATED CHANGES OF RHEOGRAM (RHEO) OF ASCENDING AORTA](image)

**Figure 1. Original classification of phase-related changes of rheograms.**

Conclusions

The above classification is successfully used in practice. In combination with the heart cycle phase analysis and the synchronously recorded ECG of the aorta it is possible to make diagnostics in the most accurate way and identify primary causes of the changes [6-10].
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


CARDIOCODE is Device & Technology No.1 in noninvasive measuring of hemodynamic parameters. Designed for automatic measuring & assessment of 7 blood volume parameters + qualitative evaluation of 12 cardiovascular system functions.

CARDIOCODE

A new paradigm in cardiovascular diagnostics: enjoy it!
International Scientific Symposium CRO-e-CARDIOLOGY 2014: 
Russian New University’s Co-Organizer mission successfully accomplished.

CARDIOMETRY as a new scientific field in cardiology and the innovative device CARDIOCODE developed by R & D team at Russian New University, Moscow, Russia have been the focus of attention of the Symposium.

In April, 2014, the Russian innovative device CARDIOCODE was presented at the international scientific symposium CRO-e-CARDIOLOGY 2014 organized by the Croatian Cardiac Society (Croatia), Association of Cardiologists of Bosnia & Herzegovina (Bosnia & Herzegovina) and Russian New University RosNOU (Russian Federation).

The symposium covered the most interesting areas of information technologies applied in various fields of cardiology. Cardiologists, general practitioners, anaesthesiologists, medical equipment developers, medical physicists and other experts from Germany, Croatia, Italy, Bosnia & Herzegovina, Russia and the Netherlands took part in the event held on April, 4, 2014 in Zagreb, Croatia.

CARDIOMETRY as an innovative theory of heart cycle analysis developed by the R&D team at Russian New University was among the key topics of the Symposium. Prof. Mikhail Rudenko, one of the advocates of the CARDIOMETRY philosophy, reported on the basic concepts of the theory and the hemodynamic analyzer CARDIOCODE based thereon. CARDIOCODE is capable of efficient identifying, monitoring and predicting various processes of the human cardiovascular system in their progression. The application of the device in practice permits to reduce mortality rate by 40%. Such results were obtained by Dr. V.V. Chepenko due to the application of the CARDIOCODE device in one of the hospitals in Vladimir region, Russia.

“I am glad to state that an interest to cardiometry and the readiness to apply the theory in medical practice worldwide are significantly increasing”, said Mikhail Rudenko.

At the symposium it was arranged to organize a centralized training in CARDIOMETRY and practical application of the CARDIOCODE device for medical staff from different countries of the world. The device was submitted to the Institute for Cardiovascular Diseases and Rehabilitation, Zagreb, Croatia. A good chance is given Croatian practitioners to save many patients’ lives and increase the efficiency of diagnostics of different heart and blood vessel diseases with the use of the CARDIOCODE device.

We are happy to present to you our video materials covering Mr. Rudenko’s report at the Symposium CRO-e-CARDIOLOGY 2014 that is available at [http://www.cardiometry.net/about/new-research-field](http://www.cardiometry.net/about/new-research-field) (English & Russian).
Exercise testing to stratify risk in asymptomatic moderate and severe aortic stenosis

Zumreta Kušljugić¹*, Fahir Baraković¹, Larisa Dizdarević-Hudić¹, Mirza Dilić², Elnur Smajić¹, Melika Avdagić¹, Katarina Kovačević-Divković¹, Amira Bijedić¹

¹ University Clinical Center Tuzla, Tuzla, Bosnia and Herzegovina
² Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina

* Corresponding author phone: +387 (35) 303-500, e-mail: zumreta.kusljugic@ukctuzla.ba

Introduction
The literature contains various data regarding the value of the exercise testing in patients with asymptomatic aortic stenosis (AS). The aim: To determine the importance of exercise testing in cardiovascular risk stratification in patients with moderate severe to severe aortic stenosis.

Methods and results
Out of a total 33 patients with moderate severe to severe asymptomatic aortic stenosis (mean aortic area EOA 0.9±0.34 cm²) we followed up 31 patients (two were excluded) during the 12 months‘ period by clinical, transthoracic echocardiogram and treadmill stress testing. 18 (58%) patients discontinued the test due to limiting symptoms, and had severe aortic stenosis (EOA ≤0.8 cm²).

During the follow-up, 11 patients spontaneously developed severe symptoms within 12 months‘ period, of whom 8 underwent aortic valve replacement, one patient died (sudden cardiac death), and two patients had a stroke. A total of 20 patients remained free of any symptoms. The highest predictive value is EOA ≤0.8 cm² for the provoked symptom test and it is 85%. ST depression had the highest negative predictive value.

Conclusion
Only limiting symptoms with critical aortic area (EOA ≤0.8 cm²) have a positive predictive value.

Keywords
Asymptomatic aortic stenosis • Treadmill stress • Testing • Prognosis
Cardiometry as a new fundamental scientific field in cardiology

Mikhail Y. Rudenko1*, Vladimir A. Zernov1, Olga K. Voronova1

1Russian New University, Moscow, Russian Federation

* Corresponding author phone: +7 (495) 925-03-83, e-mail: cardiocode.rudenko@gmail.com

Abstract

Our fundamental research in hemodynamics allows us to develop a new mathematical model of blood flow in the cardiovascular system which is in line with actual data in practice. It provides us some new data on the performance of various cardiovascular system segments responsible for the circulation maintenance. Our research has resulted in the development of an innovative technology and a device for accurate non-invasive measuring of hemodynamic parameters which was not possible earlier. The use of the device helps us obtain some new information that is the basis for a radically new ECG and Rheo classification. It is based on the cardiac cycle phase analysis. It is precisely the methodology that is capable of revealing the heart performance mechanism, which could not be explored earlier, and investigating progression of various pathological processes.

Mechanisms of sudden cardiac death and those of energetic resources responsible for maintaining the normal hemodynamics have been detected by our R & D team. The method for non-invasive assessment of cardiac muscle metabolic processes has been developed. The core principles which constitute the basis of cardiometry as a new scientific field have been defined in our research.

Keywords

Cardiometry • ECG • Rheo • Hemodynamics • Mathematical model of blood flow

Literature


The theory of chaos suggests that all events in nature are chaotic and unpredictable and that physical laws can only operate within the confined boundaries, giving space for creativity and spontaneity. Cause and consequence are reversed, since the fractal as a cause attracts consequential effects. Chaos means a kind of temporal behavior in which the difference between the two states initially grows exponentially with time. Chaotic system is extremely sensitive to the initial state and unpredictable in the long time scale, where the initial state is rarely known with absolute precision [2]. The systems we find in nature exhibit the characteristics of nonlinear and chaotic behavior. We can attempt to show all systems as linear, near-equilibrium systems. However, if a continuous “flow” of energy is sufficient to arouse the system sufficiently, it will become nonlinear or even chaotic. Chaos can be more easily understood when compared with the other two forms of behavior by a random, uncontrolled system and system of periodicity. Random behavior is never repeated in the same form and it is unpredictable and disorganized. A typical example is normal sinus rhythm recorded by ECG. If we know the amplitude, frequency and phase of the sine wave, we can at any time predict the incidence and amplitude of the sine wave [3]. Chaos is different from the behavior of periodicity and randomness, but it also includes the features of the both systems at the same time. Although chaotic behavior seems to be disorganized, random behavior, it is actually a deterministic, periodic behavior. The most important criteria of chaotic behavior are: Chaos can be deterministic and aperiodic. Unlike the Newton’s laws of physics, the chaotic behavior is never exactly repeated. There are no visible cycles that circulate at regular time intervals. Chaotic systems are very dependent on the initial conditions [4]. This means that very small changes in the initial condition can result in large differences at a later time period. Even chaotic behavior is limited. As the system is becoming controlled, behavior is becoming limited and predictability grows and eventually every chaotic behavior has an ultimate form [5].
Chaotic behavior in general has a definite form, while parts of a pattern have a similar form [6]. Thus, the theory of chaos shows that our universe is in no way deterministic, but it is creative and eternally evolving [7]. In an attempt to unify Einstein’s theory of relativity and that of quantum physics, and in accordance with the mainstream physics, the Holy Grail of contemporary physics would be the theory of string. The theory of string should allow the Einstein’s unification theory that would connect the four existing force fields (strong and weak nuclear forces, electromagnetic forces and forces of gravity) in a unified theory of everything (theory of everything; T.O.E.) [8].

In theory, string is the building block of a matter, a vibrating variable, which can have loose ends or is one-dimensional closed loop. Depending on a variety of spins and frequencies of vibrating string, various subatomic particles are reflected. In theory of string, there is only one fundamental cause, vibration of the string, but the note played on the string is actually accountable for a different type of a particle. The string itself is so small that it is impossible to imagine its existence. The string is hypothetically said to be as big as an atom, if the atom is as big as the Earth. This means that the string is incredibly small. Should the theory ever be effective, the basic inquiry will be whether scientists will be able to prove the existence of strings in their laboratories. The theory of string predicts the existence of at least 10 or more dimensions. Physicists around the world today still agree that such physical dimensions themselves still cannot explain our physical reality. The problem of the theory of string is also the existence of several theories of string in order to obtain a more efficient model and those theories of string are so complex that their complete understanding and explanation is still eagerly expected. In fact, we are going to face an interesting future!

---

**Keywords**

Theory of chaos • Fractal • Theory of string

---

**Literature**


Extended abstract

Cardiovascular implantable electronic devices and electromagnetic interference

Hrvoje Vražić¹,²*, Christof Kolb²

¹ University Hospital Dubrava, Zagreb, Croatia
² German Heart Centre of the State of Bavaria and the Technical University Munich, Munich, Germany

* Corresponding author phone: +385 (1) 290-24-44, e-mail: vrazic@gmail.com

Introduction

Most frequently used cardiovascular implantable electronic devices for the treatment of arrhythmias are pacemakers and implantable cardioverter defibrillators (ICDs). It has been shown that the function of these cardiac rhythm devices can be impaired by electromagnetic interference from the devices and systems emitting magnetic fields, causing either temporary or permanent system malfunction.

Methods

Literature review [1-3] and own results [4] from the studies examining the potential electromagnetic interference of hand metal detectors among the patients with implanted cardiovascular implantable electronic devices performed in Deutsches Herzzentrum Munich will be used.

Results

Sources of electromagnetic interference are frequently encountered in daily life, emanating from cellular phones, anti-theft devices, metal detectors, various remote controls, improperly wired/grounded appliances coming into the contact with the body, MP3 players, induction ovens and many other devices [1-3] Increasing global efforts to intensify security screening measures in the past decade have also brought into focus the use of metal detectors (which create a magnetic field that might interfere with the function of cardiovascular implantable electronic devices); they are nowadays routinely used in many settings to detect ferrous and other dangerous items. Patients with pacemakers and implantable cardioverter defibrillators are often advised to avoid screening with metal detectors because of the risk for electromagnetic interference. Another important group of sources of electromagnetic interference is that which is encountered in workplace and/or industrial environments, such as high voltage power lines, transformers, welders, electric motors, and many others. Last, but not least, are those sources found in the medical environment: magnetic resonance image scanners, electrosurgery, defibrillation, neurostimulators, TENS devices, radiofrequency catheter ablation, and therapeutic diathermy.

Conclusions

Altough the majority of data available is based on case reports, there are a few studies examining effects of electromagnetic interference on cardiovascular implantable electronic devices. Majority of problems that occur are transient in nature, and, more important, easily avoidable. Physicians should be aware of and familiarized with the most common interactions of electromagnetic interference and cardiovascular implantable electronic devices.

Keywords

Cardiovascular implantable electronic device • Pacemaker • Implantable cardioverter defibrillator • Electromagnetic interference
Literature


Extended abstract

Single versus dual chamber implantable cardioverter defibrillator for the avoidance of inappropriate shocks - results from the OPTION trial

Christof Kolb1*

1 German Heart Centre of the State of Bavaria and the Technical University Munich, Munich, Germany
* Corresponding author phone: +49 (89) 1218-2020, e-mail: kolb@dhm.mhn.de

Introduction

Implantable Cardioverter Defibrillators (ICD) are considered to be the treatment of choice for primary and secondary prevention of sudden cardiac death. However, the therapy is burdened by inappropriate ICD shocks (for example for supraventricular tachyarrhythmias) which reduce patient’s quality of life and acceptance of the device, although dual chamber (DC) ICD have access to atrial and ventricular information for tachyarrhythmia discrimination. Recent studies have failed to show a clear benefit in reducing inappropriate shocks by these devices [1-3]. But adequately powered trials with a long-term follow-up are scarce.

Methods

Patients (pts) were recruited in 54 international centres and supplied with a DC ICD. A total of 453 pts were randomised to receive either standard SC programming or optimised DC programming [4]. Optimised DC programming was defined by the activation of the discrimination algorithm (PARAD+) and a mode (SafeR) to minimise ventricular pacing (Vp). ICD indications were primary (75%) or secondary (25%) prevention of sudden cardiac death; pts were aged 63±11 years (86% males). For the both groups, zones of arrhythmia detection were set with the following inferior cutoffs: VF 240; Fast VT 200; VT 170; slow VT 120 bpm. ATP and/or shock therapies were recommended to be activated in all these zones. Pts’ outcome measures were the occurrence of inappropriate shocks, all-cause mortality and cardiovascular morbidity.

Results

During an average follow-up (FU) of 23±8 months, DC ICD-therapy, as compared to SC ICD-therapy, was associated with significantly fewer pts experiencing inappropriate shocks (10/230 pts=4.3% vs. 23/223 pts=10.3%; p=0.0146) and longer time to first occurrence of inappropriate shock (p=0.0122 in Kaplan Meier analysis). Comparing DC and SC ICD-therapy referring to mortality or cardiovascular events statistical equivalence was reached (p=0.0001), with similar rates in the sub-items of all cause deaths (21/230 pts=9 % vs. 18/223 pts=8%) and cardiovascular events (33/230 pts=14% vs. 40/223 pts=18%).

Conclusions

DC-therapy with optimized arrhythmia discrimination and minimised Vp, as compared to standard SC therapy, was associated with a significantly lower occurrence of inappropriate shocks over the 2 years follow up. This benefit was reached with an equivalent rate of all-cause mortality and cardiovascular events.

Keywords

Arrhythmia discrimination • Inappropriate shocks • Implantable cardioverter defibrillator • Pacing • Shock • Survival • Tachyarrhythmias.


Extended abstract

Identifying post-myocardial infarction patients at risk by imaging techniques

Nico Bruining¹*

¹ Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands

* Corresponding author phone: +31 (10) 703-39-34, e-mail: n.bruining@erasusmc.nl

Abstract

Most myocardial infarction patients will undergo emergency percutaneous intervention (PCI) today. However, most of these patients will have diffuse cardiovascular disease and will often show more disease than a single culprit lesion. It is important to identify those patients at risk after a myocardial infarction (MI). The current guidelines suggest that the resting left ventricular (LV) function must be assessed as part of the risk stratification by both the ESC (ESC ST-elevation myocardial infarction (STEMI) in 2012) [1] as well by the ACCF/AHA (2013) [2]. The guidelines suggest that patients with an LV ejection fraction (LVEF) <30-40% and New York Heart Association (NYHA) functional class I or II should receive an implantable cardioverter-defibrillator (ICD) treatment.

However, there are two major concerns to this classification and those are: 1) Are the current imaging methods accurate enough to measure this threshold in LVEF? And 2) the great majority of patients with a sudden cardiac death (SCD) have an LVEF > 30% [3]. So the major question is how we can identify the patient at risk and wheter we any other possibilities to identify them by imaging [4]?

There are currently many additional imaging methods available who aimed at identifying vulnerable coronary lesions [5], such as: intravascular ultrasound (IVUS), optical coherence tomography (OCT) and near infrared spectroscopy (NIRS), to name a few. Some of these imaging methods can be used for in-depth analysis of plaque components as by example IVUS-Virtual Histology. Most of these intracoronary imaging techniques are used to identify the so-called thin-cap fibroatheroma’s (TCFA’s) [6, 7]. Also functional measurements of coronary blood flow, e.g. fractional flow reserve (FFR) [8] or even virtual FFR by multi-slice computed tomography (MSCT) [9].

However, not a single imaging method could identify these vulnerable plaques at itself, the results up until now are somewhat disappointing. We expect that combination of the results of the individual methods by multi-modality imaging, might improve this [10]. The ultimate multi-modality assessment of the LV and the heart might be "electro-mechanical imaging" [11].

Identifying the vulnerable patient at risk after MI is a difficult task3. Although the imaging guidelines today recommend to measuring the LVEF at rest to identify patients at risk and who might benefit from additional treatment, there is still a large scientific debate if this is appropriate enough. More recent imaging methods are necessary and perhaps multimodality imaging could provide better insight into the very important topic of identifying patients at risk.

Keywords

Myocardial infarction • Risk stratification • Imaging • Left ventricular function
Literature


Magnetic resonance imaging of the heart: more than the morphological analysis

Viktor Peršić

Thalassotherapija Opatija, Opatija, Croatia

Corresponding author phone: +385 (51) 202-724, e-mail: viktor.persic@ri.t-com.hr

Abstract

Magnetic resonance imaging (MRI) of the heart is one of the key non-invasive techniques in modern cardiology. In the last period it developed from the useful research method into a clinically evidence-based, safe and comprehensive diagnostic test. The development of the technology has resulted in its wider application in various fields of cardiology, in evaluation of regional and global systolic function of the heart, perfusion and tissue characterization of the heart muscle, evaluation of pericardial disease, heart tumor and follow-up of patients with congenital heart disease and diseases of the aorta. In ischemic heart disease there are great possibilities for identifying segmental contractility failures after administration of dobutamine, or applying vasodilatating tests such as adenosine, with a satisfactory safety profile and a good degree of diagnostic accuracy. The principle of gadolinium-based imaging is based on a lower speed of wash out of gadolinium from myocardium replaced by fibrosis or scar. On these grounds, a delayed imaging 5 to 20 minutes after injection of contrast agent will clearly show a fibrosis or a scar and thus also give an answer to the question as to the benefits of further revascularization procedures.

The main advantages of cardiac MRI versus other non invasive imaging methods are high spatial resolution, excellent reproducibility (suitable for monitoring patients), non-ionizing radiation, high intrinsic contrast, numerous techniques within one method and 3D reconstruction.

Keywords

Magnetic resonance imaging • Perfusion • Tissue characterization

Literature


Abstract

Coronary Computed Tomography Angiography (CCTA) is now the fastest and only growing application for computed tomography in the United States, with approximately 500,000 Americans undergoing CCTA each year [1]. On the other hand, this has stimulated professional and public concern about appropriateness of its widespread use.

AHA/ACC Appropriate Use Criteria (AUC) for CCTA from 2006 defined 37 clinical situations where this method was considered appropriate, whereas in 2010 this has extended to 93, demonstrating and obvious growth.

However, although recommendations for CCTA still remain cautious, on the other hand, diagnostic Invasive Coronary Angiography (ICA) is now recommended only if the results of non-invasive testing suggest high likelihood of significant 3-vessel disease, or left main affection, and also if the patient is willing to accept the possibility of immediate revascularization [2]. In general, therefore, the AHA/ACC guideline update was less prescriptive than the earlier NICE guideline, perhaps partly because it put less emphasis on the cost efficiency of its recommendations. Although the indications might vary among different institutions, ICA and CCTA are now being commonly, and widely, used by clinicians to assess anatomic disease burden in patients with coronary artery disease (CAD), while other noninvasive imaging techniques are primarily used to ascertain ischemic burden.

Beside a recent analysis has de facto called into question the rationale for many of the revascularization procedures performed until recently, at least in patients with stable CAD [3]. In the meta-analysis including more than 5,000 patients, PCI seemed to be no better than medical therapy alone, patients with documented ischemia on stress testing or fractional flow reserve (FFR).

As a curiosity in this respect, when George W. Bush was stented in August 2013 a fierce dispute arose whether this intervention was really necessary or if he would have fared better off with only medical therapy. Also possibly interesting, the primary diagnostic work-up used in his case was CCTA, not ICA.

Luckily, we believe, this dispute was settled after the COURAGE-trial systematically showed that patients with stable angina fare as well with optimal medical therapy alone, as they do with angioplasty/stenting, or by-pass.

In our own series of roughly 800 patients, we also tried to evaluate how CCTA influenced the management and treatment of patients with CAD, where we showed
that CCTA can reliably replace diagnostic ICA in majority of stable patients, no regardless of the pre-test risk stratification [4]. In this respect, we would like to present a case "To stent or not to stent” our own debate (Figure 1 and 2).

Figure 1. Coronary computed tomography angiography and invasive coronary angiography. Borderline distal right coronary artery stenosis, on coronary computed tomography angiography and invasive coronary angiography.

Figure 2. Cardiac computed tomography (CCT) and fractional flow reserve. Contrast-enhancement deficit on inferior left ventricular wall (under 10%) on CCT in the same patient, and hemodynamically non-significant stenosis on invasive coronary angiography-fractional flow reserve, which was not regarded to require stenting.

Having in mind the most recent evidence-based data that suggests that revascularization (coronary stenting, as well as by-pass) should probably be reserved only for patients with non-stable CAD, while patients with stable CAD should be treated conservatively, we think that also diagnostic work-up for these patients should be kept as non-invasive as possible, as the majority of the patients can be adequately managed in this way alone.

To conclude, based upon this data and our clinical experience, we believe that CCTA can provide reliable diagnostic and prognostic information for adequate clinical decisionmaking and treatment of the majority of patients with stable CAD.

The still ongoing 8,000-patient ISCHEMIA and other trials, will hopefully yield some more insights in this respect.
Keywords
Coronary artery disease • Coronary computed tomography angiography • Invasive coronary angiography

Literature


Extended abstract

Quantitative spatial cardiac localization of premature ventricular contractions using the cardiac isochrone positioning system

Peter van Dam¹*

¹ University of Nijmegen, Nijmegen, The Netherlands
* Corresponding author phone: +31 (62) 219-83-96, e-mail: peter.van.dam@peacs.nl

Introduction

The precise localization of the site of origin of a premature ventricular contraction (PVC) or ventricular tachycardia (VT) prior to ablation would facilitate the planning and execution of the electrophysiological procedure [1]. Current electrocardiographic imaging (ECGI) techniques uses body surface mapping that is costly, complex, and requires as many as 256 leads to localize the PVC origin. We have developed and tested the novel cardiac isochrone positioning system (CIPS) utilizing the readily available 12 lead ECG to localize the PVC origin.

Methods

The myocardial activation based ECGI requires a patient specific model of the heart and thorax. For the PVC or VT origin localization, the fastest route algorithm [2, 3] is used on patient specific models created by the newly developed morphing software [4].

For this study population the electrodes were not recorded accurately. The influence of electrode misplacement was Consequently we developed and tested new Kinect camera software to document and determine the ECG electrode locations on the chest wall5. This software fuses the recorded tested on one of the cases by moving the precordial electrodes up and down. The amount of electrode misplacement alters significantly the PVC location determined by CIPS, shown with white dotes. An electrode misplacement of 5 mm resulted in a range of 0-22 mm PVC location.

3D Kinect camera image with the MRI derived thorax model [4].
Ten patients that underwent electrophysiological mapping and ablation of PVCs were studied. The PVCs origins were localized on the endocardium of the mid left ventricular wall, the anterior right ventricular outflow tract (RVOT), the left ventricular superior septum, septal RVOT and mid wall of the RVOT. In one patient the PVC origin was located on the epicardial RVOT. PVC localization by the 12-lead ECGI was correlated to the site of successful ablation. All patients (10/10) had accurate prediction of the PVC origin. However, in two patients without patient specific models the localization was reversed between the RV free wall and septum of the RVOT. With patient specific models and accurately reconstructed electrode positions, these latter two cases would likely be localized correctly.

This feasibility study of CIPS shows its ability to localize the PVC origin based on only the standard 12 lead ECG. This ECGI method yields activation estimates of isochrones on both ventricles from which the PVC origin location is derived. This new ECGI technique can localize the PVC from any part of the ventricular endocardium, intramyocardium or epicardium. Accurate localization of the precordial ECG electrodes, however, is still required. The Kinect camera offers the functionality to quickly and reliably localize these electrodes on the chest wall, potentially increasing the accuracy of CIPS. We are currently in the process of designing a prospective study using CIPS with the Kinect camera to localize PVCs and VT origins.

Cardiac isochrone positioning system • Inverse problem • Kinect • Non-invasive premature ventricular contraction localization


4. van Dam PM, van Der Graaf AWM, Gotte MJW, editors. A new 3D patient specific morphing tool enabling clinical application of non-invasive cardiac activation imaging. ESC; 2012; Munich.

Extended abstract

Using electronic health records in clinical research

Enno T. van der Velde 1*

1 Leiden University Medical Center, Leiden, The Netherlands
*
Corresponding author phone: +31 (71) 526-17-95, e-mail: ETvanderVelde@lumc.nl

Background

Information technology has transformed the way healthcare is carried out and documented. Presently, the practice of healthcare generates, exchanges and stores huge amounts of patient-specific information. In addition to the traditional clinical narrative information, databases in modern health centres automatically capture structured data relating to all aspects of care, including: diagnosis, medication, laboratory test results, imaging data and many other.

Electronic health record (EHR) data comprise various data types, structured data as well as unstructured data, and can be exploited for care, statistics and research.

Despite the great potential, researchers who wish to analyse large amounts of patient data are still faced with technical challenges of integrating scattered, heterogeneous data, in addition to ethical and legal obstacles that limit the access to the data.

In short, the use of data from EHR systems is still hampered by the lack (or lack of implementation of) standards for interoperability and schemes for privacy and consent.

Interoperability

When an EHR system is implemented, it is often customized for the users. This means that even EHR’s developed by the same vendor could collect the same information in different ways for different institutions. Without the use of common vocabularies, it is impossible for a given hospital’s computer to understand a patient record from another hospital, but also for researchers to compare data across organizations. Therefore, the use of common vocabularies should be implemented as much as possible in each EHR.

There are many interoperability domains: Organizational interoperability (who does what when), semantic interoperability (meaning of the data), syntax interoperability (structure of the data), and technical interoperability (connecting computers on a technical level).

To solve these interoperability issues, many healthcare IT standards have been developed; some of them are overlapping. There are standards on medical/clinical content (e.g. CDA, HL7), and standards on structure & implementation (CCR, DCM) [1].

Privacy

Privacy legislation in many countries has traditionally placed a great weight on personal autonomy, and has required informed consent for accessing personal health data for research. A legitimate public concern related to the use of personal health data is the risk of privacy breaches. A technical solution is to de-identify research data according to the specifications in the Health Insurance Portability and Accountability Act privacy rule.

De-identification (anonymization) allows researchers to circumvent costly and timely consent procedures, but the lack of identifiers makes the inclusion of follow-up data difficult. In practice, the following measures are taken to overcome this problem:
attributes with identifying information such as ‘name’, ‘phone number’, ‘SSN’ will be omitted. Necessary fields for later linkage such as PatientID will be encrypted, with the decryption codes only accessible for certain people [2, 3].

Conclusion

The present widespread use of electronic health record systems holds great promise for the use of this data for clinical research. Despite the great potential, researchers who wish to analyse large amounts of patient data are still faced with technical challenges of integrating scattered, heterogeneous data, in addition to ethical and legal obstacles that limit access to the data. However, it is to be expected that large-scale adoption of health information technology infrastructure in the form of EHRs and standards for interoperability and schemes for privacy and consent will allow to fully exploit EHR data in clinical research.

However, it is difficult to predict when a major shift in availability of EHR data may take place. EHR’s and EHR related data mining can further improve the quality of care and also reduce overall cost of healthcare in the long-term.

Keywords

Electronic health record systems • Clinical research • Data standardization • Privacy

Literature


Intelligent data analysis (IDA) is an important tool for data based medical research. It is often combined with statistical techniques. The primary goal of IDA is data understanding and hypothesis creation while statistics is used for hypotheses validation. Aim: Presentation of novel approaches for pattern recognition, example clustering, and data understanding tasks in cardiological applications.

A new generation of machine learning algorithms, like Random Forest [1] and Random Rules, is based on efficient and systematic construction of many independent classifiers. Besides increased predictive quality, the algorithms have some distinguished properties like inherent estimation of the probability of correct classification for each example and estimation of the similarity of pairs of examples. The probability of correct classification is measured by the difference in the number of votes for different classes while similarity of examples is measured by the percentage of classifiers that correctly predict both examples. These new options are potentially very useful for pattern recognition and example clustering results that may be applied for the predictive and descriptive analysis of medical data.

The problem of fetal heart rate (FHR) monitoring is known as an important and difficult problem [2]. Typically it is solved by sophisticated signal processing techniques. We demonstrate how it may be solved by transforming the four simultaneous noninvasive fetal ECG signals into a single probability sequence. From such probability sequence it is much easier to identify positions of actual fetal QRS complexes. A model based on many independent classifiers is used for this transformation. The starting point for constructing the model is a few ECG sequences on which medical experts have already identified the positions of fetal QRS complexes.

The second application is clustering of coronary heart disease (CHD) patients. The experiments start from a set of 238 patients. A classification problem is formed so that the original set of examples is used as positive examples while negative examples are obtained by randomized shuffling of attribute values of the original set. The goal of constructing a predictive model for discriminating original from randomized data is to obtain a similarity table for original examples. In the second step clusters of examples are iteratively constructed by minimization of the internal variance of the similarity table for all 238 examples. The main result is identification of relevant subgroups of CHD patients, description of properties of these subgroups, and detection of outlying examples.
Conclusion

The presented methodology and its appropriate applications enable novel approaches to data analysis in cardiology. The applications that are discussed in this work are only an illustration of its potentials. A long term goal is better understanding of the methodology and its comparative evaluation with standard techniques.

Keywords

Pattern recognition • Clustering of examples • Data understanding • Random forest algorithm • Example similarity table

Literature


Extended abstract

The process of collecting data for the Acute Myocardial Infarction / Acute Coronary Syndrome Register for the City of Zagreb

Inge Heim

1 Institute for Cardiovascular Prevention and Rehabilitation, Zagreb, Croatia

* Corresponding author phone: +385 (1) 461-23-08, e-mail: inge.heim@srcana.hr

Introduction

The Acute Myocardial Infarction Register for the City of Zagreb was established in 1979 in the Institute for Cardiovascular Prevention and Rehabilitation as a population-based register including all cases among Zagreb residents. It contained mostly epidemiological data. As time passed and diagnostic procedures and therapy in cardiology advanced, cardiologists were interested to get more clinical information. In 2003 we established the Acute Coronary Syndrome Register for the City of Zagreb containing a series of clinical data. All age groups are covered. Sources of information are: mortality data and hospital discharge of consecutive patients admitted to all Zagreb hospitals with Acute Cardiology Units. Main inclusion criteria: suspected or confirmed acute coronary syndrome (ACS); those who died outside hospital with ACS as the main cause of death (confirmed or not confirmed by autopsy); sudden cardiac death (in- and out-of-hospital).

Methods

Physicians regularly visit all Zagreb hospitals which have Acute Cardiology Units. In the hospital admission list they look for Zagreb residents who were discharged with a diagnosis of ACS. Data collection method is cold pursuit.

They fill in a questionnaire with the following data: history data (risk factors, previous percutaneous coronary interventions or coronary artery bypass graft surgery), exact date and time of the onset of symptoms, date and time of admission, time of entering coronary care unit, 12-lead ECG on admission, markers of necrosis (CK-MB, troponin), PCI or PTCA, working diagnosis from the emergency clinic, diagnostic procedures during hospitalization, laboratory findings (TC, HDL, LDL, triglycerides), therapy in the first 24 hours, complications, final diagnosis, groups of drugs taken in the last 3 months prior to arrival at the hospital and medications recommended at discharge, date and place of death (hospital death occurring within 28 days) and whether autopsy was performed. In fatal cases, autopsy report is checked and if it is proven that the cause of death is not an ACS, the patient is not entered in the Register.
Results

The comparison between in-hospital and out-of-hospital death from ACS by gender shows great differences. Out-of-hospital death in men is much higher than in-hospital death and the both show a declining trend seen from 2007 to 2011 (Figure 1). In women we see the opposite (Figure 2). In-hospital death is much higher than out-of-hospital death. There is no change in out-of-hospital death but the in-hospital death shows a declining trend. Each year only about 10% of the patients included in the ACS Register join the outpatient cardiac rehabilitation program in Zagreb.
Discussion

Advantages of the Register - It is intended for health professionals and policy makers and gives the information on the characteristics, the burden and consequences of ACS in the City of Zagreb. It provides a more precise and valid monitoring of ACS. Continuing hospital computerization and personal identification number should allow record linkage and better data quality. Data is published in the Croatian Health Service Yearbook. Limitations: Financial problems, lack of data collection staff, unrecognized value of such population-based registers among health professionals, lack of validation of discharge diagnoses. One of the problems is, also, that we no longer have the possibility to check the diagnosis on the death certificate at the Hospital Department of Pathology because the Central Bureau of Statistics refuses to give us the names of deceased patients due to data protection.

Conclusion

Out-of-hospital mortality has declined in the last few decades, but it still remains high representing great concern in men. From the epidemiological point of view emphasis should be placed on CV prevention, population education and better out-of-hospital emergency care. The use of a reliable information system has enabled the development of such a register and contributed to a relatively simple data processing. Medical professionals and patients should be better informed on the advantages of the cardiac rehabilitation program.

Keywords

Acute coronary syndrome • Population-based register • Epidemiology • Mortality • Outpatient cardiac rehabilitation program

Literature


Heart disease is the leading cause of death in the modern world. Cardiac image processing is now routinely applied for detecting, classification and diagnosis of heart diseases. One of the most common uses of processing methods that are now widely applied are cardiac segmentation [1] and registration methods [2], that are used in order to extract the detailed anatomy and function of the heart.

Automatic segmentation plays a central role when inspecting reconstructed 3D cardiac images from CT or MR scanners. An accurate classification of the different cardiac regions is usually the first step of tasks like: cardiac visualization, coronary artery inspection, measurement of the ejection fraction for the left and right ventricles and wall motion analysis.

In a clinical context, physicians often mentally integrate image information from different modalities. Automatic registration, based on computer programs, might, however, offer better accuracy and repeatability and save time [3]. Cardiac image registration remains a challenge because of the numerous specific problems mainly related to the different motion sources (patient, respiration, heart) and to the specificity of each imaging modality. Up to now, no general method could automatically register any modality with any other modality so far.

This paper presents a survey of shape modeling applications to cardiac image analysis from MRI, CT, echocardiography, PET, and SPECT and aims to introduce new methodologies in this field, classify major contributions in image-based cardiac modeling, provide a tutorial to beginners to initiate their own studies, and introduce the major challenges of registration and segmentation and provide practical examples.

Image-driven processing methods, such as thresholding, region-based or edge-based techniques, or else pixel classification [4-6], provide a limited framework for further medical image analysis. They can include geometrical information, as well as high level information, in the so-called shape prior based segmentation framework, or through active shape models and active appearance models. At last, atlas guided segmentation also make use of a set of manually segmented images.

By using different analysis software of cardiac images, CAD prototypes can be used in clinical routines in order to provide a computer output as a second reader to assist physicians in the detection of abnormalities, quantification of disease progression and differential diagnosis of lesions [7]. Computerized analysis of cardiac images in combination with artificial intelligence can be used in clinical practice and may contribute to more efficient diagnosis.

**Keywords**

Cardiac image processing • Analysis • Artificial intelligence
Literature


mHealth in cardiology

Mario Ivanuša1*

1 Institute for Cardiovascular Prevention and Rehabilitation, Zagreb, Croatia
* Corresponding author phone: +385 (1) 461-23-46, e-mail: mivanusa@gmail.com

Abstract

The development of mobile telecommunications and multimedia technologies has resulted in providing one segment of medical services when a patient and a physician are at remote locations. Mobile health (mHealth) is a system of remote monitoring the health status during the 24/7 and is primarily designed for patients with chronic diseases, but also those who are at home care after acute events and/or emergency medical intervention, patients involved in programs for the improvement of health status or for clinical trials.

The basis of the mHealth is supported by enthusiasm of a growing use of technologies in the community that keeps up with the 21st century developments and medical equipment that gathers information from the body (the sensor for a patient, communication device, medical application), and accessories. Blood pressure, heart rate, electrocardiogram, blood glucose, oxygen saturation and other variables are collected by sensors and can be simultaneously or in a certain period of time transmitted to the server, enabling the option of integration with electronic medical record and signaling in case of any disorders.

In addition to the unequal development of broadband communication networks, the main problems of mHealth are:

• Lack of technical skills of medical professionals, particularly middle-aged and elderly ones;
• Technical problem of sensors — devices dependent on the size, design and battery life;
• The need for interoperability — linking diverse technologies for the purpose of exchanging and using information (from textual to complex multimedia messages), technology (WLAN, Bluetooth, satellite communications, etc.) and connectivity (wireless, wired, PC, PDA devices);
• Necessity of certifying the devices — the credibility of procedure (information of mobile monitoring are credible medical information or additional indicators), data protection, lack of standards and unclear legislation;
• Lack of financial incentives for the application of mHealth technology.
Telecardiology and mHealth principles and technology in cardiac rehabilitation can be used as a tool for promoting ever greater involvement of patients with coronary heart disease, which, in addition to the availability and price is the global problem for the mentioned cardiovasculae activity. Mobile technology has proved to be potentially useful in intervention programs that detect and modify risk factors in psychosocial support, physical activity programs and therapeutic education. Time will show whether this mHealth potential will increase availability, participation and outcomes of patients with coronary heart disease.

Keywords mHealth • Telecardiology • Coronary heart disease

Literature


Extended abstract

Design and implementation of health information systems in cardiology

Elnur Smajić1*, Nihad Mešanović1

1 University Clinical Center Tuzla, Tuzla, Bosnia and Herzegovina
* Corresponding author phone: +387 (35) 303-500, e-mail: Nihad.Mesanovic@ukctuzla.ba

Abstract

The practice of collecting and maintaining information on health is as old as the history of medicine itself. Since the earliest times, those who were engaged in the art of healing found it necessary to record various outcomes in relation to the number of patients attended. At the beginning, health information systems were oriented to collect information on diseases and on health service outputs. In the meantime, there has been a tremendous progress in medicine as well as in informatics. In contemporary times, health information systems were transcended to the domain of modern health practices, and they hold great significance in the planning and decision-making of health delivery services [1-3].

Health information systems are there to bridge the gap between disease occurrence and the response of health professionals to fight diseases. The drive for the reform of health information systems coincided with a revolution in information and communication technology, as a result the computer has made its entry, but many of the resulting computerized systems are suffering from the lack of appropriately trained staff, thereby also facing hardware and software maintenance problems.

However, it is important to make sure that, computerization of health information systems does not dominate the health information system reform improvement process [4]. The problems of implementation of information systems are well known and invariably they concern the interplay of human, organisational, and technical factors, which cannot be easily separated. It is important especially in field of cardiology. The heart is a specific organ, besides morphologic characteristics, the functional status is very important and the relationship between heart and blood vessels, well known as arterioventricular coupling.

We can describe this complex interlinking by conceptualizing computer-based information systems as social systems in which technology is only one of the elements [5]. Information systems are much more than computers and telecommunications equipment, as they also involve people and their actions in the organizational settings in which they work. One of the good and in developing health information systems is provided in University Clinical Center Tuzla at Tuzla county in Bosnia and Herzegovina [6,7].

Keywords

Health information system • Computer • Cardiology
Literature


Extended abstract

Internet-based interventions for cardiovascular prevention: focus on overweight and obesity

Alen Ružić

University Hospital Centre Rijeka, Rijeka, Croatia

Corresponding author phone: +385 (51) 407-149, e-mail: alen.ruzic1@rit-com.hr

Abstract

At a time when the Internet has become an inseparable part of the everyday lives in the population of developed countries, the awareness of the need for its use in health promotion and disease prevention is continuously increasing. Although there are numerous studies in this field that are still in progress, at the time being we have more open questions than safe answers. Health issues are on the internet dominated largely by unfounded commercial promotions and sales campaigns, while professional content tends to be limited to the official web site of professional societies. Promotion health campaigns that are based on proven and effective — evidence based platforms are still sporadic. Because of its specificity and longevity, the prevention and treatment of obesity is area of a special interest. It seems that the Internet-based education, practical materials, web — medical and psychological counseling, and controlled support groups within social networks represent the next major step in the development of effective therapeutic strategies for obesity.

Keywords

Internet • Obesity • Cardiovascular disease • eHealth • Home-based • Self-delivered

Literature


Radiation exposure in interventional cardiology

Robert Steiner*1

1 University Hospital Centre Osijek, Osijek, Croatia
* Corresponding author phone: +385 (31) 511-511, e-mail: steiner_robert5@hotmail.com

Abstract

Radiation exposure rises with growing number of computed tomography, nuclear cardiological exams, coronary angiography and fluoroscopy leading to a higher risk of patient overexposure to radiation. It is estimated that 40% of radiation exposure is due to cardiological procedures. Interventional cardiologists and cardiac electrophysiologists are two to three times more exposed to radiation than diagnostic radiologists. In high volume cath labs the most experienced interventional cardiologists have annual exposure about 5mSv and lifetime exposure increases cancer risk by 1%. There are two main biological effects of radiation: tissue reaction (deterministic effects) that becomes evident days or months after exposure and include skin injuries and cataract, and stochastic effect which is related with potential and future harm damaging DNA or indirectly (free radicals and reactive oxygen species) leading to cancer manifestation after many years. Increased cancer risk is for doses more than 50mSv. Risk is 3-4 times higher in children than in adults, 38% higher in females than in males, 50% lower in octogenarians than in 50 year-old old patients. Some tissues are more sensitive than others. Highest radiosensitivity organs are breast, colon, lung and stomach.

Patients and doctors protection can reduce the radiation exposure by 90%. Radiation doses in cath lab depend on operator experience, arterial approach, distance of image intensifier from patient, cine-duration, performing ventriculography or not, projection, magnified views and also some patient characteristics: BMI, coronary lesion type and sort of arrhythmia to be ablated as maintained and quality controlled technology.

In our investigation we compared doses of exposure to patients and operators in 2007 compared with 2009 and found that as we had more experience and awareness of harmful effect of radiation, doses were lower and 2.7% of patients had exposure more than 2Gy and they are included in the follow up. Doses were similar to other cath labs.

We need more epidemiological, and biodosymetry data on radiological protection in patients (children and adults), interventional cardiologists and staff (including genetic studies), non-cancer effects, innovative devices and procedures.
### Table 1. Standard reference doses for common cardiological examinations

<table>
<thead>
<tr>
<th>Diagnostic procedure</th>
<th>Effective dose (mSv)</th>
<th>Equivalent number of PA chest radiography each (0.02mSv)</th>
<th>Approximate equivalent period of natural background radiation (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest X-ray</td>
<td>0.02</td>
<td>1</td>
<td>0.008</td>
</tr>
<tr>
<td>Coronary angiography</td>
<td>7 (2-16)</td>
<td>350 (100-800)</td>
<td>2.9</td>
</tr>
<tr>
<td>Percutaneous coronary intervention</td>
<td>15 (7-57)</td>
<td>750 (350-2800)</td>
<td>6.3</td>
</tr>
<tr>
<td>Radiofrequency ablation</td>
<td>15 (7-57)</td>
<td>750 (350-2800)</td>
<td>6.3</td>
</tr>
<tr>
<td>Dilatation chronic coronary occlusion</td>
<td>81 (17-149)</td>
<td>4050 (850-9600)</td>
<td>33.7</td>
</tr>
<tr>
<td>Aortic valvuloplasty</td>
<td>39</td>
<td>1950</td>
<td>16.2</td>
</tr>
<tr>
<td>Endovascular thoraco-abdominal aneurism repair</td>
<td>76-119</td>
<td>3800-5950</td>
<td>31.6-49.5</td>
</tr>
<tr>
<td>64-slice coronary CT</td>
<td>15 (3-32)</td>
<td>750 (150-1600)</td>
<td>6.3</td>
</tr>
<tr>
<td>Coronary calcium CT</td>
<td>3 (1-12)</td>
<td>150 (50-600)</td>
<td>1.2</td>
</tr>
<tr>
<td>Sestamibi stress test (1 day)</td>
<td>9</td>
<td>450</td>
<td>3.7</td>
</tr>
</tbody>
</table>

**Keywords**  
Interventional cardiology • Risk • Radiological protection • Radiation • Imaging

**Literature**


Extended abstract

Interventional cardiology in acute coronary syndrome — what is next to do?

Jure Mirat¹*

¹ Polyclinic Kardioton, Zagreb, Croatia
* Corresponding author phone: +385 (1) 580-27-36, e-mail: jure_mirat@yahoo.com

Abstract

A change of the paradigm in the treatment of some diseases rarely changed so radically as the strategy for the treatment of acute myocardial infarction (AMI) has changed over the last few decades. A long period with a completely passive and expectative attitude was followed by two radical revolutions. The first occurred in the eighties by introducing fibrinolytic therapy, while the other was even more spectacular, when primary percutaneous coronary interventions (PCI) were introduced, being accompanied by a significant decrease in mortality. The second wave affected us in Croatia 10 years ago, whereas intervention skills, technology and enthusiasm were the trias in the genesis of success. If we drew a cross-section today, we can ask ourselves — What is next to do? Have we reached the maximum which is followed by the plateau or is there still room for upward curve of success? This second variant seems to be more realistic. The reasons for this can be found primarily in spreading PCI to non-ST segment elevation myocardial infarction (NSTEMI), that are subject to less invasive strategy or strategy of longer waiting for PCI, significantly longer in practice than what is prescribed in the guidelines, which can explain epidemiological data of the difference in mortality between STsegment elevation myocardial infarction (STEMI) and NSTEMI in some follow-ups. Another moment is the limitations of electrocardiographic methods in the classification of AMI, which determines the treatment strategy. The differences reflected by the electrocardiographic method are not always an expression of real pathophysiological events, so the treatment strategy should not be different. In addition to the methods of unmasking false NSTEMI and real STEMI showing terminology inadequacy of the existing names, we should take into account the technological advance in the diagnostics of AMI, as a potential moment for further jump. Imaging methods in cardiology have not yet, at least in our regions, taken their full advantage and we can expect that diagnostic hodograms will change when they become available. To conclude, we can say that there is still a lot of work to do for us to optimize the approach to the treatment of acute coronary syndrome.

Keywords

Acute coronary syndromes • Primary percutaneous coronary interventions • Ischaemic heart disease
Literature


Extended abstract

Why transradial instead of transfemoral approach for the percutaneous coronary intervention

Hrvoje Pintarić1*

1 University Hospital Centre Sestre milosrdnice, Zagreb, Croatia
* Corresponding author e-mail: hrvojepintaric@yahoo.com

Abstract

Despite the fact that transradial approach (TRA) requires a longer learning curve than transfemoral approach (TFA), the transradial challenges are usually overcome with experience. Nowadays, in view of its benefits, there is no longer any justification for ignoring the transradial approach [1]. Multiple randomized clinical trials and reports consistently demonstrate benefits to the patient and improved outcomes from TRA [2]. TRA is particularly appealing in patients with coagulopathy, elevated international normalized ratio due to warfarin, or morbid obesity [3]. A recent meta-analysis of nine studies involving 2,977 patients with ST elevation myocardial infarction (STEMI) demonstrated an impressive nearly 50% reduction in mortality for the TR approach [4].

TR percutaneous coronary intervention (PCI) can be performed by low-to-intermediate volume operators with standard equipment with a low failure rate [5]. Age over 75 years, prior coronary artery bypass graft surgery, and short stature are independent predictors of TR-PCI failure [6]. Appropriate patient selection and careful risk assessment are needed to maximize benefits offered by TR-PCI.

In the Sestre milosrdnice University Hospital Centre, Zagreb, Croatia, seven interventional cardiologists perform almost 900 coronary percutaneous coronary interventions a year (40% pPCI). Our Cath Lab is one of the largest highvolume interventional cardiology centers in Croatia. In the last few years, our center has become dedicated to the radial approach with nearly 90% of PCI performed with either left or right radial access route. In time radial approach has become the first choice even in patients with STEMI. At the 2nd Advanced International Masterclass, September 2013 in New York we have had the opportunity to present our results dedicated to TR approach. In patients with STEMI undergoing primary PCI in our, radial dedicated center, there is no difference in effectiveness, safety, and blood loss between radial and femoral approach. Also there is no significant difference in either left or right radial access type [7]. There are situations when radial arterial approach is not possible (e.g. congenital anomalies, tortuous configurations, radioulnar loop, weak or absent radial pulse secondary to previous puncture or catheterization). In such situations, a common second-line approach is used (femoral or ulnar). Many clinicians considered transbrachial (TB) angiography as a high-risk and obsolete procedure. However, our overall success rate was 95.5% (21/22). There were no major complications and we noticed only two minor complications (9%), both hematomas.
According to our results TB approach, when used by dedicated transradialists, seems to be easily feasible, safe, and effective. Local vascular complications could be avoided by cautious and sensitive puncture technique. Other important factors are using 6 Fr catheters, defensive anticoagulation, and careful observation by the nursing team after sheath withdrawal. TB approach has all advantages of the arm approach over the femoral (early ambulation, patient preference, suitable for patients with severe occlusive aortoiliac disease and for patients with difficulty in lying down) [8].

Radial access use has been growing steadily but, despite encouraging results, still varies greatly among operators, hospitals, countries and continents. Twenty years after its introduction, it was felt that the time had come to develop a common evidence-based view on the technical, clinical and organisational implications of using the radial approach for coronary angiography interventions [9].

Keywords
Transradial approach • Percutaneous coronary intervention • Learning curve

Literature


Cardiometry: new options in cardiology

Mikhail Y. Rudenko1*, Vladimir A. Zernov1, Olga K. Voronova1

1 Russian New University, Moscow, Russian Federation

* Corresponding author phone: +7 (495) 925-03-83, e-mail: cardiocode.rudenko@gmail.com

Abstract

Cardiometry as a new fundamental field of cardiology is described in the paper. The laws of cardiometry are identified herein. Cardiometry is based on an adequate mathematical model of hemodynamics that is described by the Poyedintsev-Voronova equations. The mode of elevated blood fluidity was first described by the mathematics. This allows both to properly interpret the mechanism of the heart performance and to calculate phase-related volumes of blood in each cardiac cycle. The new interpretation of the SA and AV nodes functioning as baroreceptors is provided by the authors.

A new classification for all of the varieties of ECG curve shapes has been proposed [1 - 13]. Clearly identified boundaries in each phase are provided according to the new theory of hemodynamics, and some new symbols for newly defined ECG points has been proposed. Point L which denotes the beginning of the rapid ejection phase has been introduced. The exact location of point j that is the end of the rapid ejection phase has been given by the authors [5, 13-16].

The existing ECG recording methods has been revised, and an original single-lead ECG of the ascending aorta has been developed. A rheogram is recorded in synchronism with obtaining the original single-lead ECG. Phase synchronization of the ECG and Rheo curves supplies us with a new source of data on all phase-related changes in arterial pressure. A new diagnostic device CARDIOCODE has been developed on the basis of the new theoretical basis. CARDIOCODE delivers non-invasively data on 7 phase-related volumes of blood in every cardiac cycle that was absolutely incredible in the past [1 - 11].

Keywords

Cardiometry • ECG • Rheo • Hemodynamics • Baroreceptors

Literature


3. Rudenko M, Zernov V, Voronova O. Fundamental research on the mechanism of cardiovascular system hemodynamics self-regulation and determination of the norm-pathology boundary for the basic


Relevance of heart rate variability in assessment of autonomic nervous system function in subjects in perioperative period

Meldijana Omerbegović1*, Jasminka Džemidžić1

1 University Clinical Centre Sarajevo, Sarajevo, Bosnia and Herzegovina
* Corresponding author phone: +387 (33) 297-000, e-mail: meldi@bih.net.ba

Abstract

Assessment of the autonomic nervous system function could be of great importance in evaluation of the risk factors of the patients in perioperative period. Surgery and anaesthesia as integral medical procedures aimed as restoring and improving different disorders of homoestasis and physical conditions of subjects with different ailments and functional cardiac reserves have strong influence on haemodynamic function in perioperative period and it is of a great importance to clearly define if an individual patient is at a great risk of autonomic dysfunction in addition to the underlying morbidity, which increase the risk of morbidity and mortality in the perioperative period.

Clinical tests for evaluation of autonomic nervous dysfunction have not become widely used by clinicians for several reasons. Some of the clinical tests are quite demanding what makes them less possible for performing in patients with poor reserve and more comorbidities and there are also difficulties in interpretation of subjective findings. Monitoring of heart rate variability as a parameter of autonomic nervous system activity has been clearly advocated in the risk assessment and follow up of the patients who develop diabetes mellitus and patients with coronary syndrome [1].

In subjects with diabetes mellitus who could have cardiac autonomic diabetic neuropathy, the quite serious condition of haemodynamic instability could increase the risk of aggravation and complications of the general condition in perioperative period [2]. On the other hand, most subjects with different stages of coronary syndrome have been shown to have different alterations of heart rate variability, and monitoring of heart rate variability in perioperative period could be a part of predicting tools of risk factors for surgery and anaesthesia [3]. The aim of this paper to give a review of the importance of assessment of heart rate variability in relatively healthy subjects and subjects with different comorbid states, focusing on presenting of different findings of linear measures of the analysis of parameter by means of two different softwares.

Keywords

Heart rate variability • Autonomic nervous system • Perioperative period
Literature


Contributing factors in heart failure development-results from CRO-HF Registry

Duška Glavaš1*, Davor Miličić2, Stojan Polić1, Branka Jurčević Zidar3, Katarina Novak1

1 University Hospital Centre Split, Split, Croatia
2 University Hospital Centre Zagreb, Zagreb, Croatia
3 Public Health Institute of Split and Dalmatian County, Split, Croatia

* Corresponding author phone: +385 (21) 556-111, e-mail: duskag@net.hr

Introduction
There are many causes of heart failure (HF), and these vary in different populations. The aim of the study was to analyse the contributing factors in heart failure development.

Methods
We analyzed the results from CRO-HF Registry [1,2]. This on-line registry was established in 2005.

Results
A total of 2203 in-hospital HF patients from CROHF Registry were analyzed: 1,028 (46.7%) females (F) and 1,175 (53.3%) males (M); median age was 76 years. Preserved left ventricular systolic function (LVEF 50%) was recorded in 37.8% patients.

History of arterial hypertension was recorded in 67.5% patients, diabetes mellitus in 34.4%, myocardial infarction in 22.7%, renal insufficiency in 19.2%, chronic obstructive pulmonary disease (COPD) in 17.3%, and cerebrovascular disease in 16.5% patients. Atrial fibrillation or undulation was noted in 53.7% patients. Active smoking habit was recorded in 11.1% patients and 15.6% patients were former smokers. Overweight was recorded in 46.3% patients and obesity in 25%.

The frequent precipitating factors of HF were arterial hypertension (55.5% patients), arrhythmias (51.3%), valvular heart disease (32.8%), acute coronary syndrome (19.7%), and infections (19.6%).

Lower levels of haemoglobin was recorded in 51.9% patients, higher levels of creatinine in 46.8%, ALT in 29.8%, cholesterol in 32.7%, triglycerides in 31.9%, uric acid in 79.3% and hyperglycaemia in 99.8% patients. Females had higher values of ALT (F-33%, M-27%, P=0.012), cholesterol (F-36.8%, M-29.1%, P=0.009), triglycerides (F-36.1%, M-28.3%, P=0.014), and uric acid (F-82.9%, M-76.4%, P=0.007). Opposite to expectation, males had lower haemoglobin levels (M-58%, F-44.8%, P 0.001).

In-hospital mortality rate was 13.8%.

Conclusion
The considerable underlying diseases of HF were hypertension, diabetes mellitus, myocardial infarction, renal insufficiency and COPD. One-third of HF patients were smokers (active or former) and two-third of them were overweight or obese. Hypertension was the most important “trigger” of our HF patients, close to arrhythmia, ACS, and infections.
Literature


Machine learning approach for fetal QRS complexes detection

Dragan Gamberger¹*, Goran Krstačić²

¹ Rudjer Bošković Institute, Zagreb, Croatia
² Institute for Cardiovascular Diseases and Rehabilitation, Zagreb, Croatia

* Corresponding author phone: +385 (1) 456-11-11, e-mail: dragan.gamberger@irb.hr

Aims
The study presents a novel methodology for the detection of QRS events from four simultaneous noninvasive fetal ECG signals.

Methods
We have developed a three step procedure consisting of: A) transformation of ECG signals into a set of instances with 5 msec distance, so that each instance is defined by 93 features that describe characteristics of signals in the concrete time slot, B) evaluation of a multi-rule model on the set of instances so that a value in the range -200 to +200 is generated which is proportional to the probability that the instance is a fetal QRS event, C) transformation of a string of generated values into a string of QRS events taking into account that typical distance between fetal QRS is 250-600 msec. The central part of the approach is the preparation of the multi-rule model that consists of about 70,000 rules that vote either yes or no for fetal QRS [1]. Probability of fetal QRS is proportional to the difference between yes and no votes. The model is constructed by a machine learning approach from a set of 10,000 examples described by the same set of features. Positive examples are coming from time slots with known fetal QRS events, while negative examples are from time slots that are 50 msec far from the positive examples.

Results
For the Physionet Challenge in the year 2013 [2] the methodology enabled reasonable quality of QRS detection. For Task 4 the error in respect of the square of beats per minute has been 244.13 (best score 18.08) while for Task 5 mean squared error in milliseconds has been 11.72 (best score 4.34).

Conclusion
The achieved result demonstrates that the implemented approach is already able to recognize fetal QRS events with a reasonable quality, especially in respect of the precise position of the peaks. The further work is expected to result in an improvement of the quality of all three steps A-C. The main problem is very high time complexity of step b in which multi-rule model with many rules has to be evaluated on many instances.

Keywords
ECG signals • Fetal QRS • Random rules algorithm • Pattern recognition

Literature


Corticosteroids and heart rate variability in spinal cord injury

Antonija Krstačić1*, Goran Krstačić2

1 University Hospital Centre Sestre milosrdnice, Zagreb, Croatia
2 Institute of Cardiovascular Disease and Rehabilitation, Zagreb, Croatia
* Corresponding author phone: +385 (1) 469-70-00, e-mail: akrstacic@gmail.com

Introduction
Spinal cord injury (SCI) is an insult to the spinal cord resulting in a change, either temporary or permanent, in the cord’s normal motor, sensory, or autonomic function. SCI may cause loss of cardiovascular reflexes mediated by sympathetic drive due to interruption supraspinal control of spinal sympathetic motoneurons. Aim: The purpose of this study was to analyze sympathovagal balance after acute spinal cord injury demonstrated by the linear measures in time and frequent domain of heart rate variability (HRV) and effect of corticosteroids on the HRV parameters.

Methods
We have analyzed a sample of 40 tetraplegic patients after acute spinal cord injury and 40 healthy persons of the controls. In the group with cervical spine injury 29 patients received a corticosteroid therapy, and 11 did not. Cardiac autonomic balance was evaluated by analysis of HRV in time and frequents domain.

Results
The ratio of low and high frequencies (LF/HF) was significantly reduced in the groups of patients with acute trauma with and without corticosteroid therapy, as compared to controls. However there was no statistically significant difference in the two SCI groups. [(1.74 (0524) with corticosteroids therapy and 1.75 (0534) without)].

This study establishes analyzing of the heart rate variability (HRV) by linear methods as objective measures of normal and abnormal function of autonomic nervous system.

Conclusion
This study shows that sympathovagal balance is altered in quadriplegic patients in acute phase of cervical spinal cord trauma. SCI causes dysfunction of the autonomic cardiovascular regulation demonstrated by the spectral measures of heart rate variability and leads to disturbances of modulatory sympathetic activity on cardiovascular system. Finally, the effect of corticosteroids on the parameters of HRV in SCI patients was not found.

Keywords
Cervical spinal cord injury • Corticosteroid therapy • Heart rate variability • Sympathovagal balance
Extended abstract

**CroDiab NET as a powerful tool for tracking cardiovascular risk factors in diabetic patients: data from Bjelovar-Bilogora County collected during the period from 2001 to 2012**

Saša Magaš

1 Bjelovar General Hospital, Bjelovar, Croatia

* Corresponding author e-mail: sasa.magas@zg.t-com.hr

**Abstract**

Diabetes mellitus (DM) and its chronic complications are the major world health problem having an upward trend in the whole world. It is believed that currently 366 millions of people suffer from DM worldwide, and by the year 2030 the number of diabetics will increase to 552 million. The number of patients with DM rises in all countries, and 80% of the world’s population suffering from diabetes live in developing countries or newly industrialized countries [1].

The Republic of Croatia and the Bjelovar-Bilogora County are not exempt from this trend and the prevalence of DM in Croatia is 6.1% [2]. The influx of patients in the Center for Diabetes of the Bjelovar-Bilogora County is rising. The values of body mass index (BMI), Hba1c levels and the incidence of hypertension and dyslipidemia are worrisome. Therefore the incidence of modifiable cardiovascular risk factors increases too. Cardiovascular complications are the leading cause of morbidity and mortality among patients with DM, and the risk of coronary artery disease is 2-4 times higher than in the general population [3].

This study has involved 4,408 outpatients whose e-records are maintained by the national register of diabetic persons. CroDiab NET, a computer software designed on the basis of world quality indicators, integrates electronic patient records and generates discharge summaries parallel to collecting data for the national diabetes registry [4]. Type 2 diabetes was recorded in 93% of patients, while type 1 diabetes was recorded in only 3% of patients. Hypertension was present in 51% of patients with upward trend in the last three years. The highest rate of dyslipidemia was 39% in 2004, with downward trend at about 25% in the last 3 years. The frequency of patients with myocardial infarction was stable at around 10%, with the lowest value of 7.4% in 2010. The prevalence of patients with stroke also showed a downward trend from 14.9% to 7.4%. Only 10% of patients had BMI <25 kg/m2, while 32% of them were overweight persons with BMI from 25 to 30 kg/m2, and 50% were obese persons with BMI >30 kg/m2. Good disease control was achieved by only 18% of patients, a further 18% of them had borderline disease control.

The level of regulation of diabetes, BMI, as well as other observed modifiable cardiovascular disease risk factors (arterial hypertension, dyslipidemia) is not satisfactory. Therefore further efforts for better glycemic control, control of hypertension, and dyslipidaemia are needed. CroDiab NET is a powerful tool for tracking cardiovascular risk factors in diabetic patients.

**Keywords**

Diabetes mellitus • Cardiovascular risk factors • Cardiovascular complications • Body mass index • Glycated hemoglobin • Hypertension
Literature


Introduction

Information System Irata© was implemented at Institute for Cardiovascular Prevention and Rehabilitation, Zagreb, Croatia in 1995 as a DOS application, and since 2010 as a NET application which is aimed to facilitate the daily workup of patients and improve the quality of services rendered. Every workplace, at both institution locations is linked in a Novell 6 network [1,2]. The aim of this study was to determine the satisfaction of employees with the existing IT system.

Methods

The study was conducted on a sample of 29 medical professionals with secondary school qualification and higher expertise education (Bachelor of Science) by using the method of a structured questionnaire, which was anonymous. In addition to demographic data, the questions were aimed to find out the length of work experience, professional qualification and satisfaction and benefit of using the existing information program.

Results

83% of employees were surveyed. Only one respondent was male, while the remaining respondents were women. A total 17/29 (58%) of respondents have the higher expertise education and 12/29 (41%) have the secondary school qualification. Most of the respondents (19/29; 66%) have more than 20 years of experience and are over 40 years of age. The majority of the respondents (20/29; 69%) have attended some IT course, and the majority (25/29; 86%) have a computer at home, which they commonly use for emailing (26/29; 98%), listening to music (24/29; 83%), education in medical contents (23/29; 79%), browsing the Internet and reading news (21/29; 72%), watching movies (20/29; 69%), and for browsing professional medical journals, preparation of articles and lectures (11/29; 40%). The existing information system is used by almost all respondents when entering patients data for examinations and cardiovascular diagnostics. Nurses and physical therapists rarely browse patients' findings (10/29; 35%), and use the IT system to write medical records very rarely (5/29; 17%). Only a quarter of respondents (7/29; 24%) considers the existing information system adapted to their daily work. A large number of respondents (23/29; 79%) find additional IT training and information system training necessary.
Conclusion

Today, the information system has entered into all spheres of our life, and so the most of the respondents have and use a computer at home for emailing, browsing the Internet, watching movies, etc. The information system should facilitate the work of medical professionals and thus shorten the time of admittance which would free up the time for work with patients and enable certain type of triage. The obtained results similar to the results of some other authors [3-5] indicate the need for additional IT training and additional training in using the information system.

Keywords

Information system • Satisfaction • Evaluation

Literature


Short report

Cardiometry: pioneering experience in assessment of the heart performance and evaluation of fatal arrhythmia risks in intensive care unit patients

Vladimir V. Chepenko1,2*

1 Vladimir State University, Faculty of Applied Mathematics and Physics, 600026, Russia, Vladimir, Stroiteley av. 3/7
2 Central Regional Hospital, Intensive Care Unit, 601143, Russia, Vladimir region, Petushki, Moskovskaya str., 3

* Corresponding author phone: +7 (49243) 220-11, e-mail: chepenko.vladimir.49@mail.ru

Submitted: 25 April 2014
Accepted: 15 May 2014
Published online: 30 May 2014

Abstract

In the paper presented is an application study of the heart performance phase mechanism with the use of the Cardiocode analyzer based on principles of cardiometry for evaluating iatrogenic complications caused by antiarrhythmic therapy and monitoring the quality of treatment of hemodynamic disorders in in-hospital intensive care units. The aim of the study is a thorough estimation of the diagnostic and functional quality of the performance of the Cardiocode device and developing a new methodology of its application under the conditions of the intensive care units, when predicting fatal arrhythmia progression. 50 patients with true cardiogenic shock of different degrees of severity have been examined with Cardiocode. As a result, it is established that the application of the heart cycle phase analysis in diagnostics, hemodynamics evaluation and management with the medication and infusion therapy supported by the Cardiocode device allows reducing the mortality rate by 32 ± 3.4 %.

Keywords

Iatrogenic complications • Antiarrhythmic • Treatment quality • Cardiogenic shock • Mortality • Heart cycle phase analysis • Cardiocode • Cardiometry

Imprint

Vladimir V. Chepenko. Cardiometry: pioneering experience in assessment of the heart performance and evaluation of fatal arrhythmia risks in intensive care unit patients; Cardiometry; No.4; May 2014; p.151-155; doi:10.12710/cardiometry.2014.4.151155. Available from: http://www.cardiometry.net/no4-may-2014/fatal-arrhythmia-risks

Introduction

In the Russian Federation, the mortality rate caused by cardiovascular system is one of the most critical in the world and reaches 1462 deaths per 100,000 people a year. Besides the primary and secondary myocardial fibrillation amount to 86% of cardiac arrests, and the causative agents of the genesis of fibrillation are varied. The main cardiovascular system death causes are as follows: progression of chronic heart failure (nearly half of all lethal outcomes) and sudden cardiac death (SCD) (the other half of the lethal outcomes). According to the statistics, every year 200,000-250,000 people suddenly die of cardiac diseases in Russia. Actually, the problem of SCD is extremely urgent
for the Russian National Health Service. A great interest to the problem is also determined by the fact that the SCD rate is increasing. Nevertheless it is obvious that there is a possibility to use effective preventive measures for improving the existing situation [1, 2].

The main cause of the death is progression of fatal rhythm disorders, but the arrhythmias are connected not only with electrical activity disorders, but also with the contraction function disorder, and it follows that the cause of arrhythmia is a disorder in a synchronous interaction between the electrical and mechanical processes in myocardium [3]. The iatrogenic cases which are very often associated with an application of the 1st class antiarrhythmic medication, digitalis and some pharmaceutical like tricyclic antidepressants and phenothiazides, which extend the QT interval, are widely represented in literature. It was shown long ago that the 1st class antiarrhythmic drugs have a paradox pro-arrhythmic activity effect in case of heart pathology. To regret, this phenomenon has been confirmed by the recent CAST program investigations where it has been shown that the cases of SCD are more frequent in the group of asymptomatic post MI patients with ventricle ectopia treated with flekainid and encainid than it is the case in the group of patients who did not receive the treatment.

Materials and methods

The PC-assisted hemodynamic analyzer Cardiocode is designed for the electrocardiogram (ECG) recording in one lead with the synchronous rheogram (Rheo) recording and automatic calculation of the cardiovascular system hemodynamic parameters using phase durations and qualitative evaluation of the given parameters [4-8]. The severity of a patient state is evaluated according to the NIH scale, and the prognosis is assessed according to the GRASE scale.

Examined was a group of 50 patients with true cardiogenic shock of different degrees of severity with a composition as follows: 49 cases with acute myocardium infarction, 1 case with aneurism rupture of Valsalva sinus. 48 males and 2 females were in the group.

13 patients had a repeated myocardial infarction, and 2 patients had a recurrent one. Considering the group, 29 patients had transmural myocardial infarction, 12 patients had large-focal myocardial infarction and 8 patients had a small-focal one.

All the patients were divided into 2 subgroups. The first subgroup consisted of 30 patients that died during different time periods after their admission to hospital. 14 of them died during the first 6 hours after the admission. Their middle age was 72±2,3 years. The III degree cardiogenic shock was observed in all patients. 7 patients died during the first 24 hours after their admission. Their middle age was 74,5±1,8 years. The III degree cardiogenic shock was observed in 5 patients, and the II degree cardiogenic shock was reported in 2 patients. 9 patients died on day 3 after their admission. Their middle age was 80,5±1,2 years. The III degree cardiogenic shock was recorded in 4 patients and the II degree cardiogenic shock was reported in 5 patients.

The second subgroup consisted of 20 patients with favorable outcome of the disease. Their middle age was 64±1,4 years. The III degree cardiogenic shock was observed in 1 patient, the II degree cardiogenic shock was reported in 16 patients, and the I degree cardiogenic shock was recorded in 3 patients. The systemic thrombolysis within intensive care system was received by 13
patients (9 patients with favorable outcome and 4 patients with lethal outcome). The rest of the patients did not receive thrombolysis due to their late admission or because of the presence of explicit contraindications. The examinations were carried out on days 1, 3, and 5 after admission and also under postmortem conditions immediately upon the death, considering the conducted medication therapy.

The results of the study show that, when considering an individual heart cycle, in case of a deviation or failure in a cardiac cycle phase, the next phase undertakes a compensation to improve or eliminate the deviation or the failure in the most adequate way. Such an interrelation between the phases determines the compensation mechanism of the phase performance of the heart and the blood vessels [9]. The phases responsible for the heart blood filling influence on the phases responsible for building up of the initial minimum and maximum arterial pressure, and vice versa. When identifying pathology it is important to detect the phase with the primary cause that leads to deviations in the other phases. 6-8 hours before the fatal arrhythmia, the following changes are observed: loss of the contractility function of the interventricular septum. The minimum R wave amplitude indicates it.

The S wave expansion is a marker of the compensatory function. As the myocardium muscle undertakes an increased contractility load, it expands in volume. An elevation of the S-L wave on ECG is found in case of an increase in arterial pressure. In this case it is a marker of a constant myocardium tension, since the S-L phase amplitude is located above the isoelectric line in each cardiac cycle.

Thus, the main mechanism of the heart performance control is the respective level of blood pressure in each phase of a cardiac cycle. The levels are interrelated with the respective phase volumes of blood, and their serious changes cause fatal disturbances in rhythmogenesis and trigger progression of fatal arrhythmias.

**Results and conclusions**

The investigations of the cardiac phase mechanism are being continued. The application of the system hemodynamic evaluation and the medication and infusion therapy supported by monitoring with the Cardiocode device allows reducing the mortality rate by $32 \pm 3.4\%$. Survival rate analysis by the Kaplan-Meier method is shown in Fig.1 below [10].
Figure 1. Survival rate analysis by Kaplan-Meier.

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


Join the ESC Working group e-Cardiology

The ESC Working Group e-Cardiology covers multidisciplinary areas of electronic and information technology applications in cardiovascular practice and research. These include signal analysis, cardiovascular image processing, computer simulation of physiological processes, databases and statistical modelling, clinical information systems, and structures and standards of data exchange. The Working Group develops or contributes to standards in these areas and aims at providing a professional communication platform between clinicians, engineers and information technology specialists.

The Working Group welcomes suggestions for support and scientific endorsement of consensus documents, standardization reviews, focused seminars and meetings, and professional collaboration and exchange programmes.

Prof. Marek Malik, FESC
Chairperson 2012-2014