

Selected aspects of the application of the hybrid circulatory system in the analysis of heart insufficiency

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Purpose: There are many causes of heart failure, one of them being valvular heart disease. In this case, the stage and type of the disease can significantly affect the hemodynamic parameters of the left ventricle of the heart. In turn, these parameters can significantly influence the mode, type and strategy of clinical treatment. The aim of the study was to analyze and map the hydrodynamic conditions of the heart using a hybrid-digital model of the circulatory system. **Methods:** The tests performed using the circulatory system model allowed for the simulation of the failure of both heart's left ventricle and a set of arteries in the systemic circulation. Furthermore, the changes in hemodynamic parameters for valvular anomalies at various heartbeats were obtained. **Results:** The results suggested that a higher heartbeat should be sustained in such cases of complex mitral-aortic anomalies in the clinical practice. When observing low aortic pressures, heartbeat should be increased to compensate for the valvular insufficiencies. **Conclusions:** Extending the already conducted research could result in constituting a wide database for clinicians who are treating the insufficiency of the left ventricle of the heart. Moreover, the information included in this paper may be used for a comparison of the clinical anomalies, which facilitates a correct diagnosis. The test-stand used in the research can be applied to predict the anomalies of the circulation system for a quick and precise analysis of a clinical anomaly of a patient without physical presence.

Key words: hybrid-digital model of the circulatory system, heart insufficiency, heart valves defects

1. Introduction

Heart failure may be defined as a set of hemodynamic and clinical symptoms caused by the heart working insufficiently as a suction and force pump. The failure usually leads to the damage of the tissue blood flow in relevance to the metabolic tissue requirement [9], [16], [22]. There are three main causes of heart failure: direct cardiac muscle damage, which can be further subdivided into: cardiac infarction [3], [15], cardiomyopathies [13], [16], heart muscle inflammation [4], [5], [10], drug-induced and toxic damage [19], [36] and systemic diseases [30]; mechanical dysfunctions, which result in blood pressure, cardiac overload

(arterial hypertension [31], pulmonary artery valve or aortic valve stenosis and pulmonary hypertension [1], [7]), volume overload due to valvular insufficiency and leakage between cardiac chambers [11] or aneurysms [17], [20], [21]; impairment of filling the heart with blood (pericardium diseases, ventricle hypertrophy, mitral valve or tricuspid stenosis) [6], [14], [39].

In the case of valvular heart disease, we are faced with simple, combined and complex anomalies. The stage and the type of valvular heart disease can significantly influence the basic hemodynamic parameters of the left ventricle of the heart. These parameters can significantly influence the mode, type and strategy of treatment. The analysis of the condition of the valves and the heartbeat frequency can have a great

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importance in the pharmacological procedure that is chosen to be followed in order to correct the level of the heart insufficiency.

1.1. Modelling the circulatory system

The circulatory system of the human body is a complex structure, which encompasses multiple organs through a network blood vessels. Due to the complexity and its dynamic nature, the system can be difficult to model. Nevertheless, in the literature, many approaches to this problem can be found. The models of the circulatory system, or some of its parts, can be divided into two major groups: numerical and hybrid.

The numerical models vary in terms of their complexity and the numerical frameworks to solve them [8], [12], [18], [26], [32]. In most cases, lumped parameters are employed [2], [23]. Nevertheless, multi-physics and multi-scale models are also applied [2]. These models have been applied for modeling the left ventricle [2], to model enhanced external counterpulsation [23], to describe the human foetal circulatory system [25].

The second major group consists of hybrid models, often referred to as mock circulatory systems. These structures are of various complexity and feature a hardware implementation of some of the elements of the circulatory system, such as the heart and the vessels, which are controlled with a software side to ensure that the structure as a whole mimics the behavior of the actual cardiovascular system of the human body [24], [27], [28], [33], [38], [40]. The main advantage of the hybrid systems is that they can be used to test and assess cardiovascular implants, support and assist devices [27], [29], [34], [35]. As the hybrid systems can simulate various conditions, they can also be employed for clinical training [37].

1.2. The aim of the paper

The aim of the work was to map the hydrodynamic conditions with the use of a hybrid-digital model of the circulatory system. The tests were performed to simulate the failure both heart's left ventricle and of a set of arteries in the systemic circulation. Furthermore, the simulation allowed us to observe changes in hemodynamic parameters for individual valvular anomalies at various frequencies of heart work. The obtained results can be used in clinical practice for the evaluation of the effectiveness of future pharmacological treatment.

2. Materials and methods

In chronic illnesses of the circulatory system, there is a variety of pathologic combinations of pressures, flows and resistances. In this paper, we decided to simulate the changes of the quantities of the flows through the mitral and aortic valves, and to simulate the changes of pressure in the left ventricle and the arteries of the systemic circulation taking the resistance parameters of these valves and the simultaneous change of the heartbeat frequency into account. The tests were performed using a hybrid-digital model of the circulatory system, previously proposed in [33] (Fig. 1).

The model contained an electro-mechanical block composed of four chambers and a control system based on a real-time operating system. Its main feature was in a custom bio-pump, which allowed for accurate representation of the heart hemodynamics. The model was validated based on clinical data, which proved that it was capable of reproducing soft and medium valvular stenosis.



Fig. 1. The hybrid-digital model of the circulatory system

During the tests, the heartbeat was modified in a range from 55 to 110 bpm (in the first two groups, the tests were conducted at the most frequent heartbeat, i.e., from 70 to 90 bpm). The resistance of the valves was changed in the following ways:

- $20 \text{ [g}\cdot\text{s/cm}^4]$ (about $0.015 \text{ [mmHg/ml/s]}$): a regular and mild degree of valvular stenosis,
- $30 \text{ [g}\cdot\text{s/cm}^4]$ (about $0.023 \text{ [mmHg/ml/s]}$): a moderate degree of valvular stenosis,
- $40 \text{ [g}\cdot\text{s/cm}^4]$ (about $0.030 \text{ [mmHg/ml/s]}$): a high degree of valvular stenosis.

Four pathologies that refer to valvular anomalies and which are present in clinical conditions were analyzed on the test-stand. The circulatory system model

used in this study allowed for monitoring and modifying of a wide range of parameters describing the flow characteristics in the heart. In this study, the following parameters were employed:

- Plv – the pressure in the left heart ventricle,
- $Pcas$ – the pressure in the arteries of the systemic circulation,
- Qli – the flow to the left heart ventricle through the mitral valve,
- Qlo – the flow from the left ventricle to the aorta through the aortic valve,
- Rli – the resistance in the mitral valve,
- Rlo – the resistance in the aortic valve.

In order to simplify the analysis of the results, the performed tests were subdivided into the following three groups:

- Group I: time characteristics Plv and $Pcas$ were measured for a range of values for Rli and Rlo with the number of the heartbeats per minute set to 75 and 85 bpm.

- Group II: time characteristics Qli and Qlo were measured for a range of values for Rli and Rlo with the number of the heartbeats per minute set to 75 and 85 bpm.
- Group III: time characteristics Plv , $Pcas$, Qli and Qlo were measured at the equally increasing Rli and Rlo for with the number of the heartbeats per minute set from 55 bpm (pathology: bradycardia) to 110 bpm (pathology: tachycardia).

3. Results

The results obtained from the presented system were in the form of graphs of pressure and flow with regards to time. The graphs obtained for mild valvular pathologies are presented in Figs. 2 and 3. It is worth noting that the pathological state significantly affected the values of the $Pcas$ pressure and the flow Qlo .

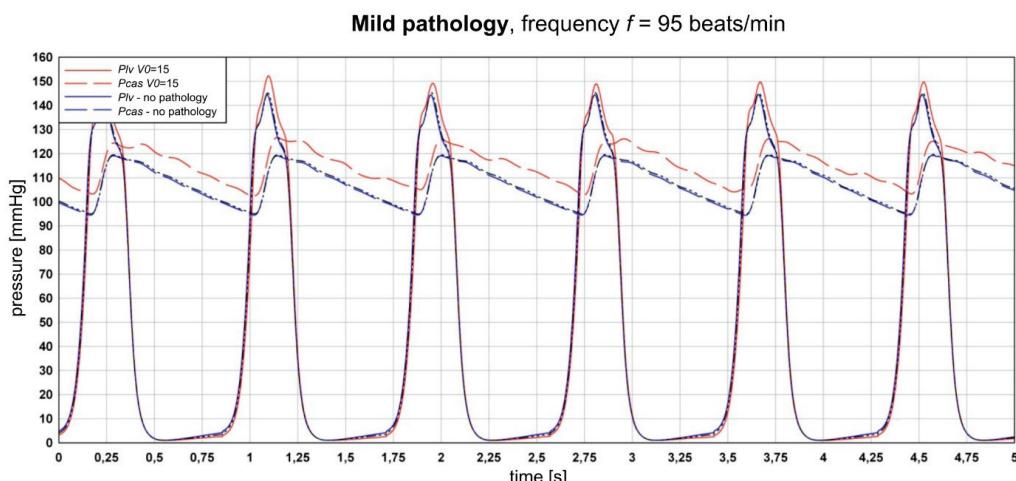


Fig. 2. The time characteristics of pressures Plv and $Pcas$ in a healthy system and under mild valvular pathologies

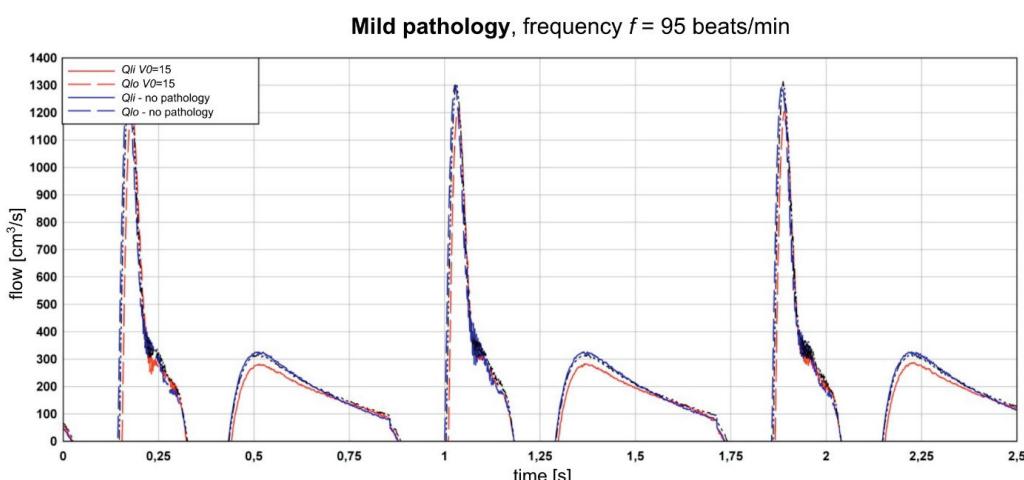


Fig. 3. The time characteristics of flows Qli and Qlo in a healthy system and under mild valvular pathologies

These results were in line with some of the previous flow characteristics obtained in [33]. In order to increase the clarity of the results, the remaining experiments were summarized in histograms.

The initial values of the pressure in the left ventricle (Plv), the pressure in the arteries of the systemic circulation ($Pcas$), the flow through the mitral valve (Qli) and the aortic valve (Qlo) are presented in Table 1, with the initial resistance of the mitral valve (Rli) and the aortic valve (Rlo) set to $20 \text{ [g}\cdot\text{s}/\text{cm}^4]$ (a regular and mild degree of stenosis).

Table 1. The initial values for pressure and flow, depending on the number of beats per minute with normal and mild degree of the stenosis (low resistance) of the mitral and aortic valve

Frequency [bpm]	Plv [mmHg]	$Pcas$ [mmHg]	Qli [cm^3/s]	Qlo [cm^3/s]
55	33.0	24.7	261	535
75	38.2	27.7	271	849
85	38.5	28.0	273	955
110	36.7	27.2	289	1079

The analysis of the initial hydrodynamic parameters obtained during the tests shows that the lowest values of the parameters occur at 55 bpm – a pathologic heartbeat called bradycardia. For the subsequent heart-

beat frequencies (75, 85, 110), the pressures in the left ventricle (Plv) and the pressures in the arteries of the systemic circulation ($Pcas$) are practically at the same level (a minute decrease for 110 bpm) but the flow through the mitral valve (Qli) for 110 bpm (pathologic heartbeat called tachycardia) shows a slight increase. However, the most conspicuous results are seen in the changes of the flow through the aortic valve (Qlo) where the value at the highest heartbeat frequency is twice the size of the value at the lowest heartbeat frequency.

The results from group I are shown in Fig. 4. The graphs represented the changes of Plv and $Pcas$ with Rlo increasing when compared to Rli , and under increasing heartbeat frequency. The figure also contained a reversed situation – for an increasing Rli with reference to Rlo , also under increasing heartbeat frequency.

In group II, the experiments focused on measuring the flows Qli and Qlo . The conditions of the system were the same as in the experiments carried out in the group I. The results were shown in Fig. 5.

In the first part of group III, the changes in the pressure in the left ventricle (Plv) and the pressure in the arteries of the systemic circulation ($Pcas$) with the uniformly increasing mitral resistance (Rli) and aortic resistance (Rlo) together with the increase in the heartbeat frequency were measured (Fig. 6).

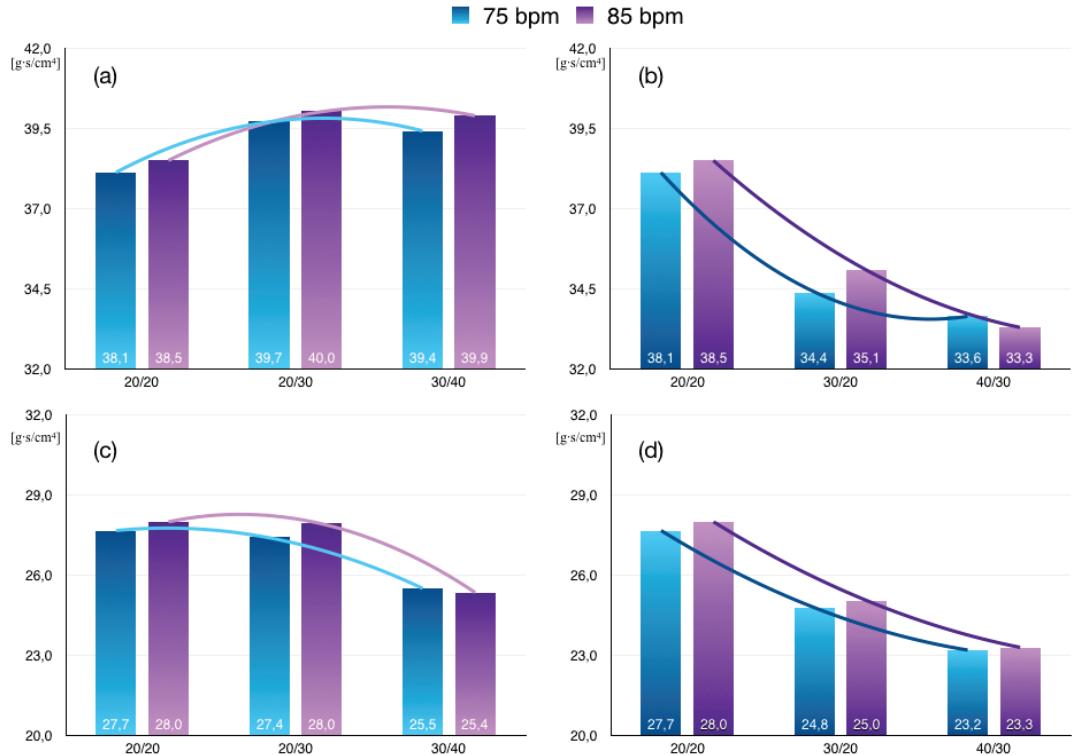


Fig. 4. The change of pressures Plv (a), (b) [mmHg] and $Pcas$ (c), (d) [mmHg] at high stenosis of the atrial valve (a), (c) [$\text{g}\cdot\text{s}/\text{cm}^4$] and at a reverse clinical situation – an increase in mitral valve resistance (b), (d) [$\text{g}\cdot\text{s}/\text{cm}^4$]

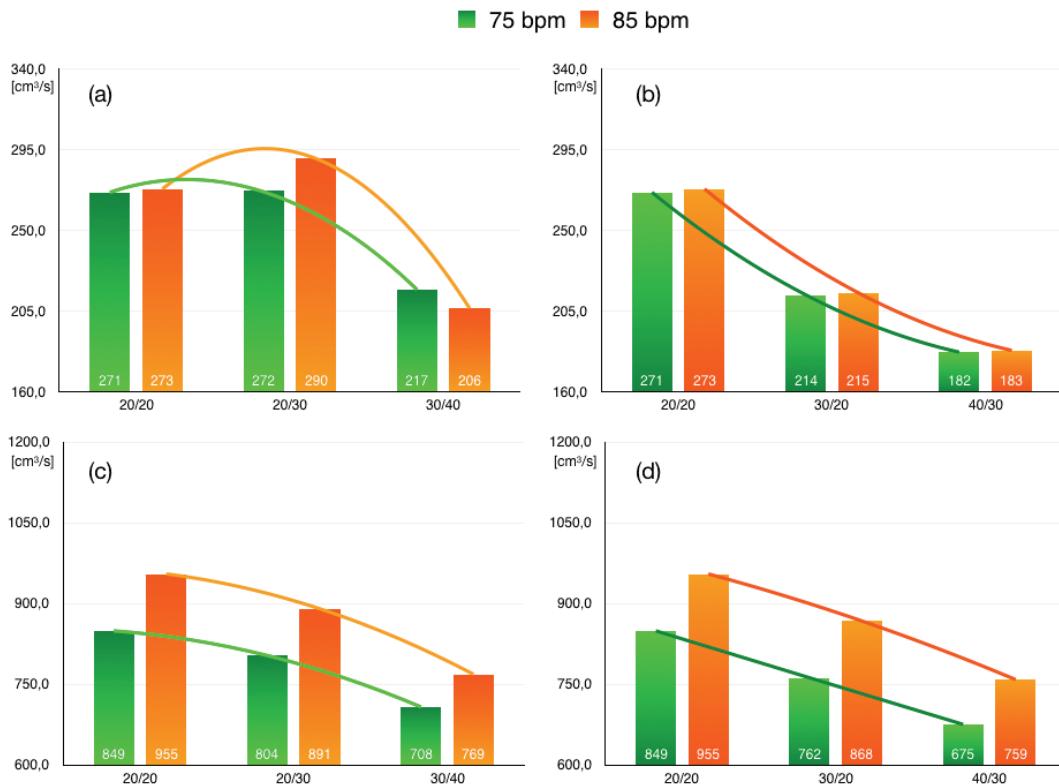


Fig. 5. The change of flows Qli (a), (b) [cm³/s] and Qlo (c), (d) [cm³/s] at high stenosis of the atrial valve (a), (c) [g·s/cm⁴] and at a reverse clinical situation – an increase in mitral valve resistance (b), (d) [g·s/cm⁴]

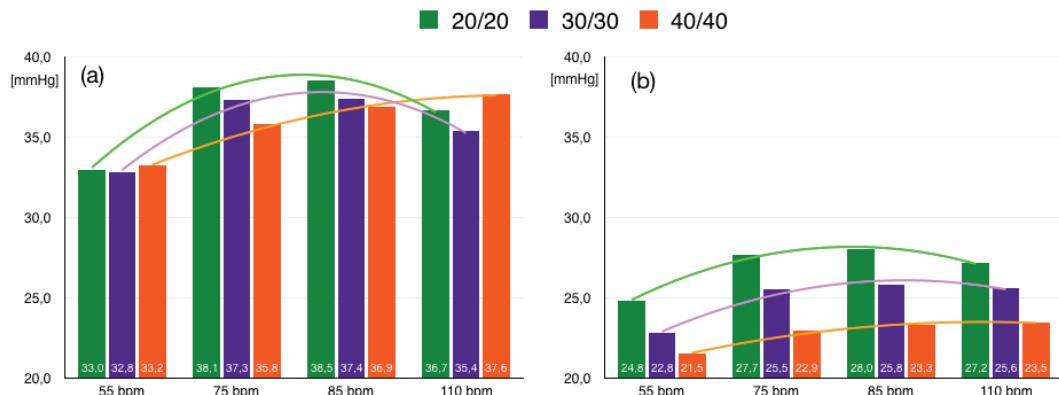


Fig. 6. The change of pressures P_{hv} (a) [mmHg] and P_{cas} (b) [mmHg] at the same level of stenosis of the atrial and mitral valves [g·s/cm⁴]

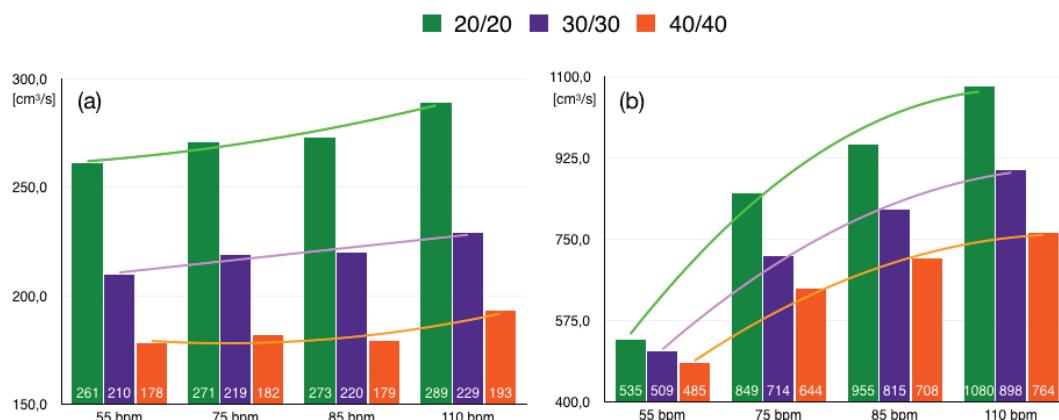


Fig. 7. The change of flows Qli (a) [cm³/s] and Qlo (b) [cm³/s] at the same level of stenosis of the atrial and mitral valves [g·s/cm⁴]

In the second part of group III, changes in the flow through the mitral valve (Rli) and the aortic valve (Rlo) with the uniformly increasing mitral resistance (Rli) and aortic resistance, and together with the increase in the heartbeat frequency were measured (Fig. 7).

4. Discussion

In the case of little or moderate degree of the stenosis areas of the outlets of both valves, the flow through the aortic valve is a hemodynamic parameter which is most sensitive to changes. The flow increased twice in the examined frequency range. In the case of the remaining hemodynamic parameters: the flow through the mitral valve (Qli), the pressure in the left ventricle (Plv) and the pressure in the arteries of the systemic circulation ($Pcas$), the changes are insignificant (Table 1).

In the case of the increase in the aortic valve resistance with respect to the mitral valve, it can be observed that the pressure in the left ventricle (Plv) slightly increases. However, in the arteries of the systemic circulation ($Pcas$), for the regular and mild degree of mitral valve stenosis ($20 [g\cdot s/cm^4]$) and the moderate degree of aortic valve stenosis (resistance $30 [g\cdot s/cm^4]$), the left ventricle compensated for the aortic valve insufficiency.

An approximate 10% drop in the pressure in the arteries of the systemic circulation ($Pcas$) occurred at the moderate degree of mitral valve stenosis (resistance $30 [g\cdot s/cm^4]$) and a high degree of aortic valve stenosis (resistance $40 [g\cdot s/cm^4]$). In the case of flows, we observed that at the moderate degree of aortic valve stenosis (resistance $30 [g\cdot s/cm^4]$) the flow through the mitral valve (Qli) remained unchanged. It decreased significantly only for the moderate degree of mitral valve stenosis (resistance $30 [g\cdot s/cm^4]$) and a high degree of aortic valve stenosis (resistance $40 [g\cdot s/cm^4]$) by about 20% for 75 bpm, and about 30% for 85 bpm. In the aortic valve (Qlo), the flow decreased together with the increase in the resistance of the aortic valve. However, it was still bigger by about 10% for the frequency 85 bpm.

In the case of the increase in the mitral valve resistance with respect to the aortic valve, it can be observed that the pressure in the left ventricle (Plv) and in the arteries of the systemic circulation ($Pcas$) continuously decreased. At the same time it was slightly higher for the frequency of 85 bpm. In the case of flows through both the mitral valve (Qli) and the aortic valve (Qlo), we also observed a constant decrease

together with the increase in resistances in the mitral valve. However, it is bigger by about 12% for the frequency of 85 bpm.

For the same changes of the valve resistances, in the regular and mild stenosis in both valves (the resistance reaches the increase in pressure in the left ventricle (Plv) in the range 55 to 75 bpm, together with a further increase in frequency (from 85 to 110 bpm), a pressure drop in the left ventricle takes place. In the case of moderate resistance in both valves (resistance $30 [g\cdot s/cm^4]$), we observed a similar tendency within the range of pressures in the left ventricle. However, in the case of a big degree of stenosis in both valves (resistance $40 [g\cdot s/cm^4]$), we observe a constant tendency of the pressure in the left ventricle to increase for the whole range of frequencies from 55 to 110 bpm. A constant little increase in pressure in the arteries of the systemic circulation ($Pcas$) occurs for all the degrees of resistance growth in both valves (mitral and aortic). There is also a tendency to stabilize and decrease the pressure at the frequency of 110 bpm.

A constant slight increase in flow through the mitral valve (Qli) was also observed for all the degrees of resistance growth in both valves (from 20 to $40 [g\cdot s/cm^4]$). However, very large drops in the flows between the individual increases in resistances in both valves can be seen. The drops were from about 20% for the moderate resistance in both valves to above 30% when there was a high degree of stenosis in both valves. The same dependency occurs for the flow through the aortic valve (Qlo). There is a constant growth for the whole range of frequencies from 55 to 110 bpm. However, significantly smaller flows at increasing resistances in both valves are noticed (respectively, about 15% for the moderate resistance in both valves, and about 25% for a high degree of stenosis in both valves).

5. Conclusions

The analysis of the selected hydrodynamic parameters enables to evaluate the clinical anomalies of the most important element of the circulation system, i.e., the heart. In the case of the combined aortic-mitral anomalies, resulting in various degrees of stenosis, mutual reactions that result from resistance of the valves and the heartbeat, significantly affect hemodynamic parameters.

The results suggest that a higher heartbeat frequency should be sustained in the cases of a complex mitral-aortic anomaly in the clinical practice. How-

ever, for regular (average) pressures in the aorta, there is a possibility of obtaining a lower overload of the left heart ventricle at a lower heartbeat. In the case of low pressure, the heartbeat should be increased.

Extending the already conducted research could result in constituting a wide database for clinicians who are treating the insufficiency of the left ventricle of the heart. Moreover, the information included in this paper may be used for a comparison of the clinical anomalies, which facilitates a correct diagnosis. The test-stand used in the research can be applied to predict the anomalies of the circulation system for a quick and precise analysis of a clinical anomaly of a patient without physical presence. It can be supposed that the pharmacological support leading to the normal rhythm and heart rate will reduce the number of thrombotic accidents on the heart's valves and chambers.

References

- [1] ABRAHAM W.T., ADAMSON P.B., BOURGE R.C., AARON M.F., COSTANZO M.R., STEVENSON L.W., STRICKLAND W., NEELAGARU S., RAVAL N., KRUEGER S., WEINER S., SHAVELLE D., JEFFRIES B., YADAV J.S., *Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial*, Lancet, 2011, 377 (9766), 658–666, DOI: 10.1016/S0140-6736(11)60101-3.
- [2] BHATTACHARYA-GHOSH B., SCHIEVANO S., DÍAZ-ZUCCARINI V., *A multi-physics and multi-scale lumped parameter model of cardiac contraction of the left ventricle: A conceptual model from the protein to the organ scale*, Comput. Biol. Med., 2012, 42 (10), 982–992, DOI: 10.1016/j.combiomed.2012.07.010.
- [3] BONOW R.O., CASTELVECCHIO S., PANZA J.A., BERMAN D.S., VELAZQUEZ E.J., MICHLER R.E., SHE L., HOLLY T.A., DESVIGNE-NICKENS P., KOSEVIC D., RAJDA M., CHRZANOWSKI L., DEJA M., LEE K.L., WHITE H., OH J.K., DOENST T., HILL J.A., ROULEAU J.L., MENICANTI L., *Severity of Remodeling, Myocardial Viability, and Survival in Ischemic LV Dysfunction After Surgical Revascularization*, JACC Cardiovasc. Imaging, 2015, 8 (10), 1121–1129, DOI: 10.1016/J.JCMG.2015.03.013.
- [4] CAFORIO A.L.P., CALABRESE F., ANGELINI A., TONA F., VINCI A., BOTTARO S., RAMONDO A., CARTURAN E., ILICETO S., THIENE G., DALIENTO L., *A prospective study of biopsy-proven myocarditis: prognostic relevance of clinical and aetiopathogenetic features at diagnosis*, Eur. Heart J., 2007, 28 (11), 1326–1333, DOI: 10.1093/EURHEARTJ/EHM076.
- [5] COOPER L.T., BAUGHMAN K.L., FELDMAN A.M., FRUSTACI A., JESSUP M., KUHL U., LEVINE G.N., NARULA J., STARLING R.C., TOWBIN J., VIRMANI R., *The role of endomyocardial biopsy in the management of cardiovascular disease: a scientific statement from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology. Endorsed by the Heart Failure Society of America and the Heart Failure Association of the European Society of Cardiology*, J. Am. Coll. Cardiol., 2007, 50 (19), 1914–1931, DOI: 10.1016/J.JACC.2007.09.008.
- [6] CORRÀ U., PIEPOLI M.F., ADAMPOULOS S., AGOSTONI P., COATS A.J.S., CONRAADS V., LAMBRINOU E., PIESKE B., PIOTROWICZ E., SCHMID J.P., SEFEROVIC P.M., ANKER S.D., FILIPPATOS G., PONIKOWSKI P.P., *Cardiopulmonary exercise testing in systolic heart failure in 2014: the evolving prognostic role: a position paper from the committee on exercise physiology and training of the heart failure association of the ESC*, Eur. J. Heart Fail., 2014, 16 (9), 929–941, DOI: 10.1002/EJHF.156.
- [7] DONAL E., LUND L.H., OGER E., REYNAUD A., SCHNELL F., PERSSON H., DROUET E., LINDE C., DAUBERT C., *Value of exercise echocardiography in heart failure with preserved ejection fraction: a substudy from the KaRen study*, Eur. Hear Journal Cardiovasc Imaging, 2016, 17 (1), 106–113, DOI: 10.1093/EHJCI/JEV144.
- [8] FERNANDEZ DE CANETE J., SAZ-OROZCO P. DEL, MORENO-BOZA D., DURAN-VENEGAS E., *Object-oriented modeling and simulation of the closed loop cardiovascular system by using SIMSCAPE*, Comput. Biol. Med., 2013, 43 (4), 323–333, DOI: 10.1016/j.combiomed.2013.01.007.
- [9] FILIPPATOS G., KHAN S.S., AMBROSY A.P., CLELAND J.G.F., COLLINS S.P., LAM C.S.P., ANGERMANN C.E., ERTL G., DAHLSTRÖM U., HU D., DICKSTEIN K., PERRONE S. V., GHADANFAR M., BERMANN G., NOE A., SCHWEIZER A., MAIER T., GHEORGHIADE M., *International REgistry to assess medical Practice with lOnitudinal obseRvation for Treatment of Heart Failure (REPORT-HF): Rationale for and design of a global registry*, Eur. J. Heart Fail., 2015, 17 (5), 527–533, DOI: 10.1002/ejhf.262.
- [10] FRIEDRICH M.G., SECHTEM U., SCHULZ-MENGER J., HOLMVANG G., ALAKIJA P., COOPER L.T., WHITE J.A., ABDEL-ATY H., GUTBERLET M., PRASAD S., ALETRAS A., LAISSY J.P., PATERSON I., FILIPCHUK N.G., KUMAR A., PAUSCHINGER M., LIU P., *Cardiovascular magnetic resonance in myocarditis: A JACC White Paper*, J. Am. Coll. Cardiol., 2009, 53 (17), 1475–1487, DOI: 10.1016/J.JACC.2009.02.007.
- [11] FUKUTA H., GOTO T., WAKAMI K., OHTE N., *Effects of drug and exercise intervention on functional capacity and quality of life in heart failure with preserved ejection fraction: A meta-analysis of randomized controlled trials*, Eur. J. Prev. Cardiol., 2016, 23 (1), 78–85, DOI: 10.1177/2047487314564729.
- [12] GABRYŚ E., RYBACZUK M., KĘDZIA A., *Blood flow simulation through fractal models of circulatory system*, Chaos, Solitons and Fractals, 2006, 27 (1), 1–7, DOI: 10.1016/j.chaos.2005.02.009.
- [13] GARBI M., McDONAGH T., COSYNS B., BUCCIARELLI-DUCCI C., EDWARDSEN T., KITSIOU A., NIEMAN K., LANCELOTTE P., *Appropriateness criteria for cardiovascular imaging use in heart failure: report of literature review*, Eur. Hear Journal Cardiovasc Imaging, 2015, 16 (2), 147–153, DOI: 10.1093/EHJCI/JEU299.
- [14] GARNIER F., EICHER J.C., JAZAYERI S., BERTAUX G., BOUCHOT O., AHO L.S., WOLF J.E., LAURENT G., *Usefulness and limitations of contractile reserve evaluation in patients with low-flow, low-gradient aortic stenosis eligible for cardiac resynchronization therapy*, Eur. J. Heart Fail., 2014, 16 (6), 648–654, DOI: 10.1002/EJHF.78.
- [15] JOLICŒUR E.M., DUNNING A., CASTELVECCHIO S., DABROWSKI R., WACLAWIW M.A., PETRIE M.C., STEWART R., JHUND P.S., DESVIGNE-NICKENS P., PANZA J.A., BONOW R.O., SUN B., SAN T.R., AL-KHALIDI H.R., ROULEAU J.L., VELAZQUEZ E.J., CLELAND J.G.F., *Importance of angina in patients with coronary disease, heart failure, and left ven-*

- tricular systolic dysfunction: insights from STICH*, J. Am. Coll. Cardiol., 2015, 66 (19), 2092–2100, DOI: 10.1016/J.JACC.2015.08.882.
- [16] KELLY J.P., MENTZ R.J., MEBAZAA A., VOORS A.A., BUTLER J., ROESSIG L., FIUZAT M., ZANNAD F., PITI B., O'CONNOR C.M., LAM C.S.P., *Patient selection in heart failure with preserved ejection fraction clinical trials*, J. Am. Coll. Cardiol., 2015, 65 (16), 1668–1682, DOI: 10.1016/j.jacc.2015.03.043.
- [17] KOBIELARZ M., *Effect of collagen fibre and elastic lamella content on the mechanical behaviour of abdominal aortic aneurysms*, Acta Bioeng. Biomech., 2020, 22 (3), 1–21, DOI: 10.37190/ABB-01580-2020-02.
- [18] KOPERNIK M., DYRDA K., KURTYKA P., MAJOR R., *Discrete phase model of blood flow in a roughness microchannel simulating the formation of pseudointima*, Acta Bioeng. Biomech., 2022, 24 (1), DOI: 10.37190/ABB-01989-2021-02.
- [19] KOTECHA D., HOLMES J., KRUM H., ALTMAN D.G., MANZANO L., CLELAND J.G.F., LIP G.Y.H., COATS A.J.S., ANDERSSON B., KIRCHHOF P., VON LUEDER T.G., WEDEL H., ROSANO G., SHIBATA M.C., RIGBY A., FLATHER M.D., *Efficacy of β blockers in patients with heart failure plus atrial fibrillation: an individual-patient data meta-analysis*, Lancet (London, England), 2014, 384 (9961), 2235–2243, DOI: 10.1016/S0140-6736(14)61373-8.
- [20] KOZUŃ M., KACZROWSKI M., HALOŃ A., *The Layer-specific Biomechanical Properties of Dissecting Ascending Aortic Aneurysm (Stanford type A of dissection)*, Acta Bioeng. Biomech., 2022, 24 (2), DOI: 10.37190/ABB-02020-2022-01.
- [21] KOZUŃ M., PŁONEK T., JASIŃSKI M., FILIPIAK J., *Effect of dissection on the mechanical properties of human ascending aorta and human ascending aorta aneurysm*, Acta Bioeng. Biomech., 2019, 21 (2), 127–134, DOI: 10.5277/ABB-01376-2019-01.
- [22] LANG R.M., BADANO L.P., MOR-AVI V., AFILALO J., ARMSTRONG A., ERNANDE L., FLACHSKAMPF F.A., FOSTER E., GOLDSTEIN S.A., KUZNETSOVAT T., LANCELLOTTI P., MURARUD., PICARD M.H., RIETZSCHEL E.R., RUDSKI L., SPENCER K.T., TSANG W., VOIGT J.U., *Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American society of echocardiography and the European association of cardiovascular imaging*, Eur. Heart J. Cardiovasc. Imaging, 2015, 16 (3), 233–271, DOI: 10.1093/eihci/jev014.
- [23] LI B., WANG H., LI G., LIU J., ZHANG Z., GU K., YANG H., QIAO A., DU J., LIU Y., *A patient-specific modelling method of blood circulatory system for the numerical simulation of enhanced external counterpulsation*, J. Biomech., 2020, 111, 110002, DOI: 10.1016/j.jbiomech.2020.110002.
- [24] MISGELD B.J.E., RÜSCHEN D., SCHWANDTNER S., HEINKE S., WALTER M., LEONHARDT S., *Robust decentralised control of a hydrodynamic human circulatory system simulator*, Biomed. Signal Process Control, 2015, 20, 35–44, DOI: 10.1016/j.bspc.2015.04.004.
- [25] MYERS L.J., CAPPER W.L., *A transmission line model of the human foetal circulatory system*, Med. Eng. Phys., 2002, 24 (4), 285–294, DOI: 10.1016/S1350-4533(02)00019-X.
- [26] NG B.C., SALAMONSEN R.F., GREGORY S.D., STEVENS M.C., WU Y., MANSOURI M., LOVELL N.H., LIM E., *Application of multiobjective neural predictive control to biventricular assistance using dual rotary blood pumps*, Biomed. Signal Process Control, 2018, 39, 81–93, DOI: 10.1016/j.bspc.2017.07.028.
- [27] PETROU A., GRANECKER M., MEBOLDT M., DANERS M.S., *A versatile hybrid mock circulation for hydraulic investigations of active and passive cardiovascular implants*, ASAIO J, 2019, 65 (5), 495–502, DOI: 10.1097/MAT.0000000000000851.
- [28] PORPHIRIEV A.O., PUGOVKIN A.A., SELISHCHEV S.V., TELYSHEV D.V., *Development of artificial ventricles for modeling the cardiovascular system*, Biomed. Eng. (NY), 2016, 49 (6), 331–334, DOI: 10.1007/s10527-016-9560-z.
- [29] PUGOVKIN A.A., MARKOV A.G., SELISHCHEV S.V., KORN L., WALTER M., LEONHARDT S., BOCKERIA L.A., BOCKERIA O.L., TELYSHEV D.V., *Advances in Hemodynamic Analysis in Cardiovascular Diseases Investigation of Energetic Characteristics of Adult and Pediatric Sputnik Left Ventricular Assist Devices during Mock Circulation Support*, Cardiol. Res. Pract., 2019, 4593174, DOI: 10.1155/2019/4593174.
- [30] RAHIMI K., BENNETT D., CONRAD N., WILLIAMS T.M., BASU J., DWIGHT J., WOODWARD M., PATEL A., McMURRAY J., MACMAHON S., *Risk prediction in patients with heart failure: a systematic review and analysis*, JACC Heart Fail., 2014, 2 (5), 440–446, DOI: 10.1016/J.JCHF.2014.04.008.
- [31] VAN RIET E.E.S., HOES A.W., WAGENAAR K.P., LIMBURG A., LANDMAN M.A.J., RUTTEN F.H., *Epidemiology of heart failure: the prevalence of heart failure and ventricular dysfunction in older adults over time. A systematic review*, Eur. J. Heart Fail., 2016, 18 (3), 242–252, DOI: 10.1002/EJHF.483.
- [32] RUAN W., CLARK M.E., ZHAO M., CURCIO A., *Global solution to a hyperbolic problem arising in the modeling of blood flow in circulatory systems*, J. Math. Anal. Appl., 2007, 331 (2), 1068–1092, DOI: 10.1016/j.jmaa.2006.09.034.
- [33] RUMIAN S., MILEWSKI G., KOPACZ M., ZAMARLIK S., *The possibility of the hydrodynamic evaluation of bio-pumps with the use of a hybrid-digital model of the circulatory system*, Meas. J. Int. Meas. Confed., 2016, 80, 281–287, DOI: 10.1016/j.measurement.2015.11.038.
- [34] RÜSCHEN D., RIMKE M., GESENHUES J., LEONHARDT S., WALTER M., *Online cardiac output estimation during transvalvular left ventricular assistance*, Comput. Methods Programs Biomed., 2019, 171, 87–97, DOI: 10.1016/j.cmpb.2016.08.020.
- [35] SIMAKOV S., TIMOFEEV A., GAMIROV T., KOPYLOV P., TELYSHEV D., VASSILEVSKI Y., *Analysis of operating modes for left ventricle assist devices via integrated models of blood circulation*, Mathematics, 2020, 8 (8), 1–18, DOI: 10.3390/MATH8081331.
- [36] SWEDBERG K., KOMAJDA M., BÖHM M., BORER J., ROBERTSON M., TAVAZZI L., FORD I., *Effects on outcomes of heart rate reduction by ivabradine in patients with congestive heart failure: is there an influence of beta-blocker dose?: findings from the SHIFT (Systolic Heart failure treatment with the I(f) inhibitor ivabradine Trial) study*, J. Am. Coll. Cardiol., 2012, 59 (22), 1938–1945, DOI: 10.1016/J.JACC.2012.01.020.
- [37] TELYSHEV D., PUGOVKIN A., SELISHCHEV S., RUSCHEN D., LEONHARDT S., *Hybrid mock circulatory loop for training and study purposes*, Proc. – 2018 Ural Symp. Biomed. Eng. Radioelectron Inf. Technol. USBEREIT, 2018, 29–32, DOI: 10.1109/USBEREIT.2018.8384542.
- [38] TOMASZEWSKI M., SYBILSKI K., MAŁACHOWSKI J., WOLAŃSKI W., BUSZMAN P.P., *Numerical and experimental analysis of balloon angioplasty impact on flow hemodynamics improvement*, Acta Bioeng. Biomech., 2020, 22 (3), 169–183, DOI: 10.37190/ABB-01660-2020-03.
- [39] ZAMORANO J.L., ANASTASAKIS A., BORGER M.A., BORGGREVE M., CECCHI F., CHARRON P., HAGEGE A.A., LAFONT A., LIMONGELLI G., MAHRHOLDT H., MCKENNA W.J., MOGENSEN J., NIHOYANNOPOULOS P., NISTRI S., PIEPE P.G., PIESKE B., RAPEZZI C., RUTTEN F.H., TILLMANNS C., WATKINS H., O'MAHONY C., ACHENBACH S., BAUMGARTNER H., BAX J.J., BUENO H., DEAN V., DEATON C., EROL Ç., FAGARD R.,

FERRARI R., HASDAI D., HOES A.W., KIRCHHOF P., KNUUTI J., KOLH P., LANCELLOTTI P., LINHART A., PIEPOLI M.F., PONIKOWSKI P., SIRNES P.A., TAMARGO J.L., TENDERAS M., TORBICKI A., WIJNS W., WINDECKER S., ALFONSO F., BASSO C., CARDIM N.M., GIMENO J.R., HEYMANS S., HOLM P.J., KEREN A., LIONIS C., MUNERETTO C., PRIORI S., SALVADOR M.J., WOLPERT C., 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task

Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC), Eur. Heart J., 2014, 35 (39), 2733–2779, DOI: 10.1093/EURHEARTJ/EHU284.

- [40] ZIELIŃSKI K., DAROWSKI M., KOZARSKI M., FERRARI G., *The need for hybrid modeling in analysis of cardiovascular and respiratory support*, Int. J. Artif. Organs, 2016, 39 (6), 265–271, DOI: 10.5301/ijao.5000513.