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Hydrodynamic performance of a composite heart valve prosthesis

Klyshnikov K.Yu., Kostyunin A.E., Onishchenko P.S., Glushkova T.V., Akentyeva T.N., Borisova N.N., Kutikhin A.G., Ovcharenko E.A.

Research Institute for Complex Issues of Cardiovascular Diseases (RICICD)
6 Sosnoviy Blvd., 650002 Kemerovo, Russian Federation

ABSTRACT

The aim of the study was to conduct a hydrodynamic assessment of the efficiency of heart valve prostheses made of xenopericardium protected by polyvinyl alcohol.

Materials and methods. Experimental prostheses based on the UniLine bioprosthesis model were manufactured for the study. The xenopericardium used for the valve cusps was modified with polyvinyl alcohol to improve its resistance to biological and mechanical effects. Hydrodynamic tests were performed on a Pulse Duplicator system, which simulates the function of the "left heart". The key parameters of the prosthesis operation were estimated including average transprosthetic gradient, effective orifice area, locking volume, and regurgitant volume. Unmodified prostheses of similar size were used as a control.

Results. Hydrodynamic tests showed that the experimental prostheses demonstrate an increase in the average transprosthetic gradient to 6.59 mm Hg (compared to 5.29 mm Hg in the control group) and a decrease in the effective orifice area to 1.52 cm² (1.69 cm² in the control group). The regurgitant volume also increased to 23.3 ml per cycle, which is higher than the control value of 12.2 ml per cycle. Despite this, all indicators remain within the permissible values established by the state standard (GOST).

Conclusion. The use of polyvinyl alcohol to protect the xenopericardium demonstrates potential advantages such as increased resistance of the material to biological effects, but is accompanied by some decrease in the hydrodynamics of the prosthesis. Nevertheless, the efficiency indicators remain within the standards, which opens up opportunities for further improvement of the technology. It is necessary to continue research in order to optimize the material and design to improve both the biocompatibility and functional characteristics of the prosthesis.

Keywords: hydrodynamic testing, prosthetic heart valve, transprosthetic gradient, effective orifice area, regurgitation

Conflict of interest. The authors declare the absence of obvious or potential conflicts of interest related to the publication of this article.

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✉ *Akentyeva Tatiana N.,* akentn@kemcardio.ru

Гидродинамическая эффективность композитного протеза клапана сердца

Клышников К.Ю., Костюнин А.Е., Онищенко П.С., Глушкова Т.В., Акентьева Т.Н., Борисова Н.Н., Кутихин А.Г., Овчаренко Е.А.

Научно-исследовательский институт комплексных проблем сердечно-сосудистых заболеваний (НИИ КПССЗ) Россия, 650002, г. Кемерово, б-р имени академика Л.С. Барбараша, 6

РЕЗЮМЕ

Целью исследования стала гидродинамическая оценка эффективности работы протезов клапанов сердца, изготовленных из ксеноперикарда, защищенного поливиниловым спиртом.

Материалы и методы. Для исследования были изготовлены экспериментальные протезы на основе модели биопротеза «ЮниЛайн». Ксеноперикард, использованный для створок, был модифицирован поливиниловым спиртом для улучшения его стойкости к биологическим и механическим воздействиям. Гидродинамические испытания проводили на стенде Pulse Duplicator, который моделирует функцию «левого сердца». Оценивали ключевые параметры работы протеза: средний транспротезный градиент, эффективная площадь отверстия, запирающий объем и объем регургитации. В качестве контроля использовали немодифицированные протезы аналогичного размера.

Результаты. Гидродинамические испытания показали, что экспериментальные протезы демонстрируют увеличение среднего транспротезного градиента до 6,59 мм рт. ст. (по сравнению с 5,29 мм рт. ст. у контрольной группы) и уменьшение эффективной площади отверстия до 1,52 см² (в контрольной группе – 1,69 см²). Объем регургитации также увеличился до 23,3 мл/цикл, что выше показателя контроля в 12,2 мл/цикл. Несмотря на это, все показатели остаются в пределах допустимых значений, установленных ГОСТом.

Заключение. Использование поливинилового спирта для защиты ксеноперикарда демонстрирует потенциальные преимущества в повышении стойкости материала к биологическим воздействиям, однако сопровождается некоторым ухудшением гидродинамических характеристик протеза. Тем не менее показатели эффективности остаются в пределах нормативов, что открывает возможности для дальнейшего совершенствования технологии. Дальнейшая трансляция технологии в клиническую практику требует корректировки характеристик материала для улучшения функциональных показателей протеза.

Ключевые слова: гидродинамические испытания, протез клапана сердца, транспротезный градиент, эффективная площадь отверстия, регургитация

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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INTRODUCTION

Cardiovascular diseases remain the leading causes of death worldwide and a significant burden on the healthcare system [1]. Surgical (SAVR) and transcatheter aortic valve replacement (TAVR) are becoming common treatment modalities, providing patients with the opportunity to prolong their lifespan and improve quality of life.

Thus, 2,526 SAVR (according to data for 2022) [2] and 1,467 TAVR (according to data for 2021) [3] procedures took place in the Russian Federation. Bioprosthetic heart valves used for these interventions are made using bovine or porcine xenopericardium stabilized with preservatives such as glutaraldehyde or ethylene glycol diglycidyl ether [4, 5]. These materials have good bio- and hemocompatibility properties and are used worldwide in manufacturing of

bioprostheses [6]. However, failure of such prostheses observed in clinical practice due to calcification of the xenopericardium, structural degeneration due to prolonged function in the bloodstream, exposure to immune cells and blood proteinases, prevent specialists from referring to this material as "ideal" [7]. Therefore, the field of materials science for implantable medical devices puts emphasis on the complete or partial replacement of xenopericardium with a synthetic polymer material that is more resistant to mechanical and biological influences during functioning and can withstand aggressive environment of the recipient`s body [8–10].

A number of authors propose the development of a fully polymeric heart valve, demonstrating successful *in vitro*, preclinical *in vivo*, and human trial results [8, 11–13]. Other authors modify xenopericardium with additional agents that reduce the immunogenicity of the material or the tendency toward calcification [14, 15]. Our team has developed the concept of a "protected" material, it is centered around the idea of insulating the pericardium with layers of polymer – polyvinyl alcohol (PVA) [16]. The polymer covers and impregnates the pericardial base, thus preventing proteolytic blood enzymes, immune cells, albumin, and other factors from penetrating into the tissue and inducing calcification. Thus, PVA creates a protective layer.

However, the introduction of a new component into xenopericardial material will affect the bio- and hemocompatibility of the device and mechanical properties of the cusps, and, consequently, the function of the bioprosthesis as a whole. The key indicators of the reliability and effectiveness of a heart valve prosthesis can be evaluated using hydrodynamic tests. Hydrodynamic tests performed with high-precision systems are highly informative due to qualitative and quantitative assessment of the key performance indicators of the prosthesis at all phases of its function – opening and closing [17]. The more accurately the system simulates the function of the heart, the more reliable the results of the study of the prosthesis will be.

The aim of this study was to conduct a hydrodynamic assessment of the function of a novel heart valve prosthesis made of a polyvinyl alcohol-protected xenopericardial tissue using a hydrodynamic tester system.

MATERIAL AND METHODS

Prosthetic Heart Valves

Experimental prostheses were made on the basis of the UniLine heart valve bioprosthesis for tricuspid heart valves replacement (NeoCor, Russia), which proved itself as an effective medical device for the treatment of acquired heart valve defects [18, 19]. The prosthesis consists of three cusps made from bovine xenopericardium stabilized with ethylene glycol diglycidyl ether. The cusps are mounted on a three-pronged polypropylene support frame, covered inside and outside with synthetic woven lining. The sewing ring is located at the base of the prosthesis (Fig. 1). The device is designed for open implantation in the tricuspid position and suture fixation.

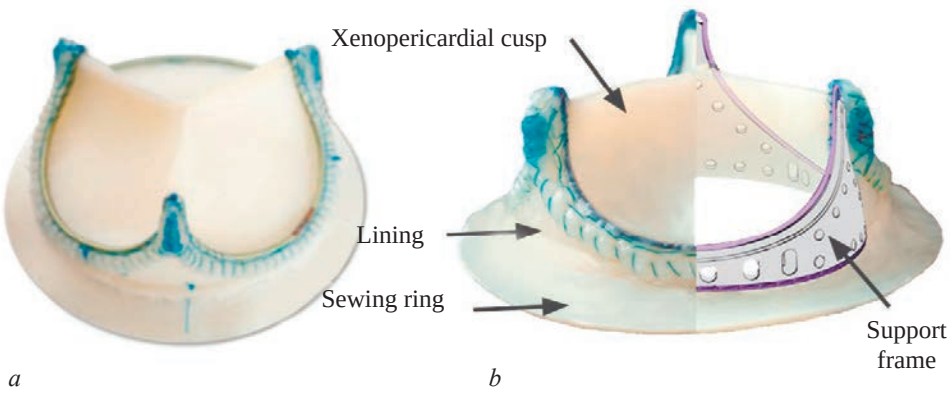

Fig. 1. The UniLine bioprosthesis, standard 26 mm in size, and its main components: *a* – isometric view, *b* – side view

To improve the stability of the biomaterial of this prosthesis, we have proposed an additional polymer modification of the xenopericardial tissue that is used to cut out and manufacture cusps. It is an experimental technology that has been described earlier [16]. For the modification we used a 15% modification solution of PVA, prepared by dissolving this polymer (Mw = 89,000–98,000 99+% hydrolyzed, Sigma-Aldrich, USA) in deionized water at 100° °C for 2.5 hours and constantly stirred. After dissolution, the solution

was cooled to room temperature, and xenopericardial patches were immersed in this solution for 24 hours. Then, the samples were removed from the solution and placed between two glasses, the gap between which was fixed with metal plates. Next, the samples were subjected to three cryostructuring cycles, consisting of the following successive steps: the samples were kept at –40° C for 24 hours, then at –2° C for 12 hours, and finally at +8° C for 12 hours. After cryostructuring, the samples were washed in water for 24 hours to remove unbound PVA, the water was changed regularly.

After that, NeoCor manufactured a series of prototype prostheses using this protected material (n = 5), which we assessed *in vitro*. All devices in this study were of standard 26-mm size.

Hydrodynamic Tests

The functional properties of experimental protected prostheses were evaluated using the Pulse Duplicator hydrodynamic testing system (Vivitro Labs, Canada). The system is a model of the "left heart", simulating the work of the ventricle and atrium (Fig. 2).

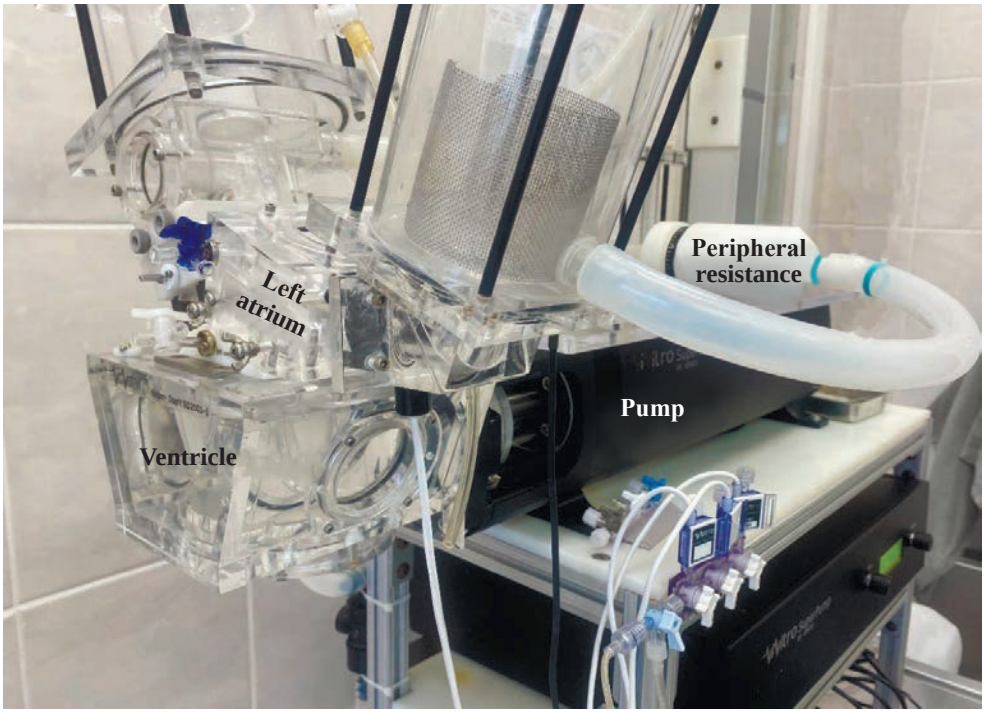

Fig. 2. Pulse Duplicator system and its main components

The study was carried out by reproducing the physiological function of the "heart" as defined by state standards (GOST 31618.1-2012): stroke volume – 70 ml; minute volume – 5 l/min; heart rate – 70 beats/min; the mean back pressure on the prosthesis – 120 mm Hg. Saline solution was used as the test medium. During the study, the following parameters were quantified: mean transprosthetic gradient, effective orifice area, locking volume, and regurgitant volume. All parameters were evaluated during 10 steady "cardiac" cycles for each prosthesis. Moreover, these cardiac cycles were recorded using a FastVideo-250 video camera (NPO ASTEK, Russia).

Unmodified UniLine bioprostheses (n = 5) of the same standard size (26 mm) for the implantation in tricuspid position were used as controls. All tests on controls were carried out under the same conditions.

Statistical data processing was performed using the Statistica 10.0 program (StatSoft, Russia). Given the small sample size, the presence of statistically significant differences in quantitative hydrodynamic parameters between the groups was assessed using the Mann–Whitney U-test, a nonparametric criterion for independent samples. The data are presented as the median and the interquartile range Me (Q_1–Q_3). The differences between the groups were considered statistically significant at $p < 0.05$.

RESULTS

The results of comparison of prosthesis quantitative characteristics are presented in Table 1. There was no statistically significant decrease in the parameters, however, the experimental samples tended to function less efficiently compared to controls. Their performance

worsened as the effective orifice area decreased while the mean transprosthetic gradient increased. The analysis of the video recordings confirmed these conclusions – the experimental samples opened with a small geometric orifice area, thus showing higher transprosthetic gradients and smaller effective orifice area (Fig. 3).

Table 1

Hydrodynamic Performance of Experimental and Control Prostheses, *Me* (Q_1–Q_3)			
Parameter	Experimental samples	Controls	*p*
Mean transprosthetic gradient, mm Hg	6.59 [6.10–7.22]	5.29 [5.19–6.13]	0.143
Effective orifice area, cm^2	1.52 [1.51–1.61]	1.69 [1.60–1.76]	0.296
Locking volume, ml/cycle	1.12 [1.22–1.055]	1.77 [1.405–1.92]	0.094
Regurgitant volume, ml/cycle	2.33 [1.93–2.465]	1.22 [1.115–1.45]	0.296

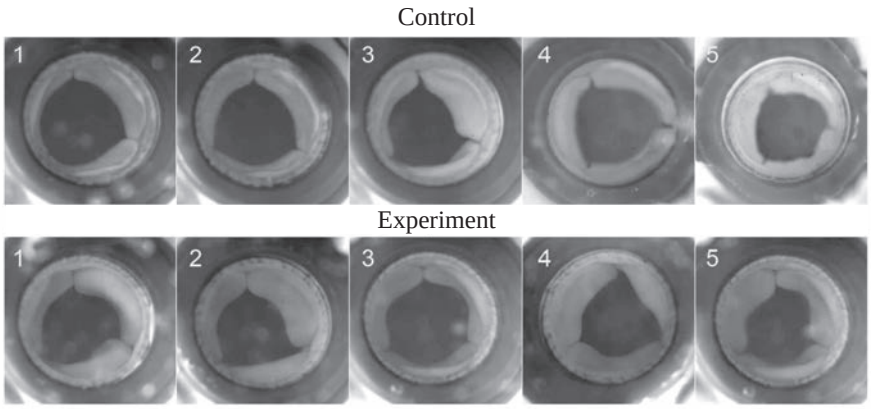

Fig. 3. Pairwise comparison of experimental and control prostheses in sped up video recording at maximum opening (several selected samples)

Regurgitant volume increased as well, however, it remained within the limits allowed by state standards (GOST 31618), there were no significant differences compared to controls.

DISCUSSION

Bioprosthetic heart valve dysfunction is a significant challenge for engineers and researchers developing these medical devices. The need to create an optimal geometry of cusps and support frame is complicated by the aggressive operating conditions of the device such as exposure to blood components (proteolytic enzymes and immune cells) and extremely long duration of loading (tens of years, 200–400–600 million cycles). Therefore, the research and implementation of new materials resistant to such impacts are important aspects of the development of future bioprosthetic heart valve designs.

Modern promising materials in this field are likely to be synthetic polymer and/or composite. The present study demonstrates the latter using a unique concept – a xenopericardial patch commonly used to create cusps for prostheses protected from the factors and blood cells by a biocompatible polymer material [16]. Such a concept can improve the biocompatibility and stability of prostheses, increase their durability, i.e. delay the onset of dysfunction and, as a result, the need for repeated surgical intervention.

It is worth noting that the introduction of PVA into the composition of the material also affects the biomechanics of the final product in close-to-real conditions. This effect is expected, but its severity and potential significance should be carefully evaluated for further adjustment of the prosthesis design and balancing between the protective properties of PVA and efficiency, primarily in terms of hydrodynamic parameters. This effect was fully demonstrated in our study.

To form the protective layer, we selected a standard 0.5 ± 0.01-mm-thick pericardial patch used in the actual manufacturing of bioprostheses. Modification with PVA changed its the physical and mechanical characteristics – increased the thickness. Despite the fact that PVA itself had an extremely low modulus of elasticity (less than 0.1 MPa) [20], even such small addition to the “xenopericardium + PVA” composite material negatively affected its hydrodynamic characteristics compared to unmodified xenopericardium. It is worth mentioning that any prosthetic heart valves based on biological materials have some variability in their parameters, since the animal tissues themselves are variable. However,

we have noted a clear trend (albeit not statistically significant) towards a decrease in the effectiveness of experimental protected prostheses *in vitro*, which means that it was the introduction of PVA that affected the parameters, not the random variability.

Given the negative experience with PVA-protected xenopericardium, the positive results of such modification. Firstly, despite the worse performance of the prosthesis, its parameters remain within acceptable limits allowed by state standards (GOST 31618.1-2012 "Prosthetic heart valves. Part 1"). Thus, the effective orifice area for this standard size should not be less than 1.4 cm^2, and the regurgitant volume should be 10 ml/cycle, i.e. experimental protected prostheses have an acceptable performance.

Secondly, to make cusps based on such composite material, one can use a thinner xenopericardial patch. In this study, the baseline material had a thickness of 0.5 ± 0.01 mm, which increased to 0.55 ± 0.01 mm after the modification with PVA, i.e. it thickened and changed the biomechanics of the device as a whole (its hydrodynamics). The use of a 0.45–0.475-mm-thick xenopericardial material, taking into account the subsequent modification with PVA, should result in better physical and mechanical properties of the composite, similar to the unmodified material used in the prosthesis. It will be difficult to find a thin xenopericardial material since the manufacturing process at NeoCor is already established. However, taking into account the advantages provided by the PVA protection like increased durability and reliability of the prosthesis, it is possible to justify the amendments to technical regulations and selection of new materials (thinner xenopericardium), including the costs.

CONCLUSION

In conclusion, the use of the PVA-protected xenopericardium opens up new opportunities for the development of a new generation of prosthetic heart valves with longer lifespan and protection from aggressive factors of recipient`s body. The first experience of creating the material and a prosthetic heart valve based on it demonstrate the high potential of the technology, which, however, already requires prototyping adjustments. Further research in this area with a larger scope of tests is needed to assess the long-term effectiveness, safety, and duration of new designs.

In general, the relevance of developing a new prosthetic heart valve based on PVA-protected xenopericardium is scientifically and practically justified. The successful implementation of this type of prosthesis in clinical practice can change the treatment of cardiovascular diseases, improving the quality of life of patients and reducing the financial costs of treatment.

REFERENCES

1. Virani S.S., Alonso A., Benjamin E.J., Bittencourt M.S., Callaway C.W., Carson A.P. et al. Heart Disease and stroke statistics-2020 update: a report from the American Heart Association. *Circulation*. 2020;141(9):e139–e596. DOI: 10.1161/CIR.0000000000000757.
2. Bockeria L.A., Milievskaya E.B., Pryanishnikov V.V., Yurlov I.A. Cardiovascular Surgery - 2022. Diseases and Congenital Anomalies of the Circulatory System. A.N. Bakulev Centre for Cardiovascular Surgery, 2023. (In Russ.).
3. Alekyan B.G., Grigoryan A.M., Staferov A.V., Karapetyan N.G. X-ray Endovascular Diagnostics and Treatment of Diseases of the Heart and Blood Vessels in the Russian Federation - 2021. *Russian Journal of Endovascular Surgery*. 2022;9:1–254. (In Russ.). DOI: 10.24183/2409-4080-2022-9S.
4. Oveissi F., Naficy S., Lee A., Winlaw D.S., Dehghani F. Materials and manufacturing perspectives in engineering heart valves: a review. *Mater. Today Bio*. 2020;5:100038. DOI: 10.1016/j.mtbio.2019.100038.
5. Mohammadi H., Mequanint K. Prosthetic aortic heart valves: Modeling and design. *Med. Eng. Phys*. 2011;33(2):131–147. DOI: 10.1016/j.medengphy.2010.09.017.
6. Barbarash L.S., Zhuravleva I.Yu. Bioprosthetic Heart Valve Evolution: Two Decades of Advances and Challenges. *Complex Issues of Cardiovascular Diseases*. 2012;1:4–11. (In Russ.).
7. Glushkova T.V., Kostyunin A.E. Calcification of Bioprosthetic Heart Valves Treated with Ethylene Glycol Diglycidyl Ether. *Complex Issues of Cardiovascular Diseases*. 2021;10(2):16–24. (In Russ.). DOI: 10.17802/2306-1278-2021-10-2-16-24.
8. Rotman O.M., Kovarovic B., Chiu W.-C., Bianchi M., Marom G., Slepian M.J. et al. Novel Polymeric Valve for Transcatheter Aortic Valve Replacement Applications: *In Vitro* Hemodynamic Study. *Ann. Biomed. Eng*. 2019;47(1):113–125. DOI: 10.1007/s10439-018-02119-7.
9. Motta S.E., Falk V., Hoerstrup S.P., Emmert M.Y. Polymeric valves appearing on the transcatheter horizon. *Eur. J. Cardio-Thoracic Surg*. 2021;59(5):1057–1058. DOI: 10.1093/ejcts/ezab089.
10. Singh S.K., Kachel M., Castillero E., Xue Y., Kalfa D., Ferrari G. et al. Polymeric prosthetic heart valves: A review of current technologies and future directions. *Front. Cardiovasc. Med*. 2023;10. DOI: 10.3389/fcvm.2023.1137827.
11. Claiborne T.E., Xenos M., Sheriff J., Chiu W.-C., Soares J., Alemu Y. et al. Toward optimization of a novel trileaflet polymeric prosthetic heart valve via device thrombogenicity emulation. *ASAIO J*. 2013;59(3):275–283. DOI: 10.1097/MAT.0b013e31828e4d80.
12. De Gaetano F., Bagnoli P., Zaffora A., Pandolfi A., Serrani M., Bruberrt J. et al. A newly developed tri-leaflet polymeric heart

valve prosthesis. *J. Mech. Med. Biol*. 2015;15(02):1540009. DOI: 10.1142/S0219519415400096.
13. Stasiak J.R., Serrani M., Biral E., Taylor J.V., Zaman A.G., Jones S. et al. Design, development, testing at ISO standards and: In vivo feasibility study of a novel polymeric heart valve prosthesis. *Biomater. Sci*. 2020;8(16):4467–4480. DOI: 10.1039/d0bm00412j.
14. Bondarenko N.A., Surovtseva M.A., Lykov A.P., Kim I.I., Zhuravleva I.Yu., Poveshchenko O.V. Cytotoxicity of Xenogeneic Pericardium Preserved with Epoxy Compounds as Cross-Linking Agents. *Modern Technologies in Medicine.* 2021;13(4):27. (In Russ.). DOI: 10.17691/stm2021.13.4.03.
15. Timchenko T.P. Bisphosphonates as Potential Inhibitors of Calcification in Bioprosthetic Heart Valves (Review). *Modern Technologies in Medicine*. 2022;14(2):68–79. (In Russ.). DOI: 10.17691/stm2022.14.2.07.
16. Ovcharenko E.A., Glushkova T.V., Shishkova D.K., Rezvova M.A., Velikanova E.A., Klyshnikov K.Y. et al. Anti-adhesive properties of epoxy-treated xenopericardium modified with polyvinyl alcohol: in vitro study of leukocyte adhesion in the pulsatile flow model. *Sovrem. Tehnol. Med*. 2024;16(2):40–46. DOI: 10.17691/stm2024.16.2.04.
17. Susin F.M., Bagno A., Gerosa G. Hydrodynamic performance of heart valve prostheses: Open discussion on European Committee for Standardization International Organization for Standardization standard 5840. *J. Thorac. Cardiovasc. Surg*. 2010;139(5):1356–1357. DOI: 10.1016/j.jtcvs.2010.01.025.
18. Kozlov B.N., Petlin K.A., Pryakhin A.S., Seredkina E.B., Panfilov D.S., Shipulin V.M. Immediate and Remote Results of the Use of Bioprostheses UniLine in the Aortic Position. *Clinical and Experimental Surgery. Petrovsky Jounral.* 2017;5(4(18)):37–42. (In Russ.).
19. Karaskov A.M., Zheleznev S.I., Rogulina N.V., Sapegin A.V., Odarenko Yu.N., Levadin Yu.V. et al. Next Generation Russian Biological Prosthesis “Unilin” for Mitral Valve Replacement: First Experience. *Grudnaya i Serdechno-Sosudistaya Khirurgiya.* 2017;59(2):98–104. (In Russ.). DOI: 10.24022/0236-2791-2017-59-2-98-104.
20. Studenikina L.N., Domareva S.Y., Golenskikh Y.E., Matveeva A.V., Melnikov A.A. Increasing the Strength and Water Resistance of Materials Based on Polyvinyl Alcohol with Boric Acid. *Proceedings of the Voronezh State University of Engineering Technologies*. 2022;2(92):249–255. (In Russ.). DOI: 10.20914/2310-1202-2022-2-249-255.

Author Contribution

Klyshnikov K.Yu., Kostyunin A.E., Onishchenko P.S., Glushkova T.V., Akentyeva T.N., Borisova N.N., Kutikhin A.G. – data collection and interpretation, drafting and editing of the manuscript, full responsibility for the manuscript. Ovcharenko E.A. – data collection and interpretation, drafting and editing of the manuscript, approving the final version of the manuscript for publication, full responsibility for the manuscript.

Author Information

Klyshnikov Kirill Yu. – Cand. Sci. (Med.), Senior Researcher, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, klyshku@kemcardio.ru, https://orcid.org/0000-0003-3211-1250

Kostyunin Aleksandr E. – Cand. Sci. (Biology), Senior Researcher, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, kostae@kemcardio.ru, https://orcid.org/0000-0001-6099-0315

Onishchenko Pavel S. – Junior Researcher, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, onisps@kemcardio.ru, https://orcid.org/0000-0003-2404-2873

Glushkova Tatiana V. – Cand. Sci. (Biology), Senior Researcher, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, glushtv@kemcardio.ru, https://orcid.org/0000-0003-4890-0393

Akentyeva Tatiana N. – Junior Researcher, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, akentn@kemcardio.ru, https://orcid.org/0000-0002-0033-9376

Borisova Natalya N. – Junior Researcher, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, borinn@kemcardio.ru, https://orcid.org/0009-0004-1138-9653

Kutikhin Anton G. – Dr. Sci. (Med.), Department Head, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, kytiag@kemcardio.ru, https://orcid.org/0000-0001-8679-4857

Ovcharenko Evgeny A. – Cand. Sic. (Tech.), Laboratory Head, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, ovchea@kemcardio.ru, https://orcid.org/0000-0001-7477-3979

(✉) **Akentyeva Tatiana N.,** akentn@kemcardio.ru

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