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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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INFLUENCE OF VASCULAR STENT SURFACE TREATMENT WITH AN ADAPTIVE COMPOSITION (ADC) FOR IMPROVING ITS BIOCOMPATIBILITY AND RESTENOSIS PREVENTION

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Abstract.

Aim: The article describes a method of implant surface treatment that reduces the risk of an inflammatory reaction to vascular implants.

Materials and methods: The research was conducted on 34 male rabbits of the "Flemish Giant" breed weighing 2.5-3.0 kg, following the standards of bioethical principles. The blood vessels of the experimental animals were previously provoked by the administration of endogenous pyrogenic solution according to a predetermined protocol. Under general anesthesia, the animals were endovascularly (via femoral access into the abdominal aorta) implanted with standard Z-shaped stents made of 316L stainless steel. To obtain indicative results, 10 rabbits were implanted with non-treated stents, while another 12 rabbits had stents pre-treated with the adapting composition (AdC) implanted. After 8 weeks, the animals were withdrawn from the experiment.

Results and discussion: Vessel wall morphometry revealed that the treatment of stents with AdC before their placement into the vessel resulted in a reduction of vessel wall thickness at the site of their implantation.

Conclusions: The clinical application of AdC aimed at improving the biocompatibility properties of implants with respect to the recipient's body is characterized by a 100% (95% CI 78.2% - 100%) likelihood of absence of complications.

Key words. Endovascular stenting, restenosis, implants, rejection, biocompatible materials, adaptive composition, aorta.

Introduction.

Every year, surgeries for the installation of various implants are performed worldwide. In 25-30% of cases, implants are not accepted by the recipient's body [1-4].

In cardiovascular and interventional radiology surgery, implants in the form of stent grafts or stents are used to treat stenotic and occlusive lesions of the arterial lumen due to atherosclerosis and/or diabetes. One of the reasons for restenosis or reocclusions is the body's reaction to the implantation of stents.

The basis of the foreign material rejection reaction is aseptic inflammation, which results from the immune response of the body to the surface of implants. Specific "binding sites" called epitopes exist on the surface of implants, which are recognized by the recipient's immune system's protective elements, immunoglobulin class G (IgG), as foreign. Therefore, upon initial contact of the body's tissues with the implant, the epitopes on its surface are recognized by IgG, a component of the recipient's humoral immune system. The strength of the binding between IgG and the surface is directly proportional to the quantity of epitopes on it that are "sensitive" to a specific pool of IgG. The formation of an affinity bond between the surface of the prosthesis and IgG leads to the activation of the recipient's cellular immune response. This results in the formation of an isolating capsule, the thickness of which is directly proportional to the degree of inflammation. The adhesion of IgG to the epitopes on the surface of the implant itself is accompanied by the generation of peroxide radicals, which play a leading role in the degradation of the prosthesis surface [5-7].

The presence of such rejection reactions to stent placement necessitates the search for ways to solve the problem of these reactions in order to increase the patency of the angioplasty zone with stenting and reduce the number of re-interventions.

One of the options for reducing reactions to implants is the search for and use of more biocompatible materials with the recipient's organism [8]. In the search for effective methods of preventing restenosis at stent implantation sites, the use of special coatings on the surface of the implant, such as stents coated with "Paclitaxel" (a mitotic inhibitor used in cancer chemotherapy), is also being explored. However, according to the meta-analysis of randomized controlled trials, despite the reduction in the inflammatory response to the stent and, as a result, the increase in primary patency of the stenting area, there is data on an increased risk of mortality from the use of such coating methods [9,10]. These studies have become the second reason for seeking alternative methods aimed at preventing restenosis at stent implantation sites.

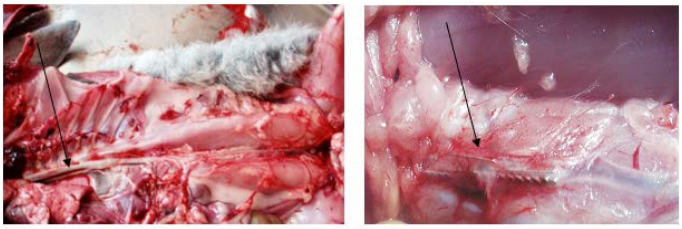
Several studies have demonstrated that the introduction of patient serum albumin solution modifies the surface of implants, reducing the frequency of side effects.

Albumin solution has also been successfully used to block epitopes that did not react during ELISA analysis [11-13].

The aim of this study was to develop a method of coating the surface of vascular implants (stents) to reduce the risk of inflammation reaction (rejection), enhance their biocompatibility, and prevent restenosis.

Materials and Methods.

The experiments were conducted in accordance with the Law of Ukraine "On the Protection of Animals from Cruel Treatment" (No. 3447–IV dated February 21, 2006) and adhered to the requirements of the European Parliament and Council (2010). The research was carried out on 34 male rabbits of the "Flemish Giant" breed with a weight of 2.5–3.0 kg. The animal experiments were performed in the vivarium of the Department of Surgery and Transplantology named after O.O. Shalimov of the National Academy of Medical Sciences of Ukraine, following the standards of bioethical principles [14,15].



A B

Figure 1A, B. *Z-shaped stents in the abdominal aorta of rabbits.*

Under general anesthesia, rabbits were subjected to endovascular procedures via femoral access to the abdominal aorta. Standard Z-shaped stents made of 316L stainless steel (Figure 1) were implanted using a 4F catheter. To ensure reliable results, a control group of 10 rabbits received non-coated stents, while an experimental group of 12 rabbits received stents pre-coated with AdC.

To create an atherogenic model according to the developed methodology, rabbits were intramuscularly injected with a solution of Pyrogenal at a dose of 1.25 mg every other day for 2 weeks. Then, in the postoperative period, a dose of 1.25 mg was administered once a week for 8 weeks. The inflammation model was chosen for the experiment based on the works of Aleksyeyeva T.A., Lazarenko O.N., et al. [16,17].

The technology for preparing AdC and the method of implant surface treatment to enhance their biocompatibility are described in the European patent and the methodological recommendations titled "Clinical Application of Implant Surface Treatment with an Adaptation Composition to Improve their Biocompatibility in Reconstructive and Restorative Surgery" 58.16/140.16 [13,17].

The main processing stages included the following procedures. Blood was collected from the experimental animals through a vein using a vacuum container. After clot formation for 10-16 minutes, it was centrifuged using an NF 200 centrifuge (Nuve, Turkey) for 7 minutes at 500g. Then, 2 ml of the obtained serum, which had been pre-filtered through a membrane filter with pore sizes of 0.22 μm (Minisart, Sartoriusstedium, Biotech corp.), was mixed in a sterile container with 18 ml of sterile physiological solution (0.9% NaCl).

In molar terms, the concentration of albumin in the resulting serum is an order of magnitude higher than that of immunoglobulins. The adsorption kinetics of albumin to the surface is also higher than that of immunoglobulins. Therefore, during the preparation of AdC, it is not necessary to get rid of serum immunoglobulins, which simplifies the process of its preparation.

After the AdC is prepared, it is poured into a sterile container (cuvette, tray, denture packaging container, etc.) suitable for immersion of the prosthesis and kept in it for 5 minutes, after which it is implanted.

The vessel or container for immersing the prosthesis should have a volume sufficient for complete immersion of the prosthesis. A packaging container for a voluminous prosthesis is an optimal solution for its immersion in AdC, as it requires minimal quantity for immersion.

The immunohistochemical and histomorphological examination was performed 8 weeks after implantation.

The composition of the proposed AdC is presented in Table 1.

For statistical data analysis, the software packages MedCalc v.17.2 (MedCalc Software Inc, Broekstraat, Belgium, 2017) and MedStat (Lyakh Yu.Ye., Guryanov V.G., 2004–2011) were used. The impact of risk factors was evaluated using the indicator of Absolute Risk Reduction (ARR) and by constructing and analyzing logistic regression models. The quality of the models was assessed by constructing Receiver Operating Characteristic (ROC) curves and calculating the Area Under the Curve (AUC), as well as the Positive and Negative Predictive Values. The corresponding 95% Confidence Intervals (95% CI) were also calculated.

Results and Discussion.

The results of vascular wall morphometry revealed that stents pre-treated with AdC led to a reduction in vessel wall thickness at their placement site. The data are presented in Table 2.

The results of the research have demonstrated that the proposed method, which involves the prior treatment of stents with AdC, leads to a reduction in the reaction of surrounding tissues by modifying the surface of the implants. This also decreases the thickness of neointimal growth, indicating the absence of inflammation processes and the formation of fibrous tissue around the implant (Figures 2 and 3).

On the Figure 4., Immunohistochemical staining illustrating the native (healthy) rabbit tissue (A), tissue around the AdC-treated implant (B), and tissue around the implant without AdC treatment (C).

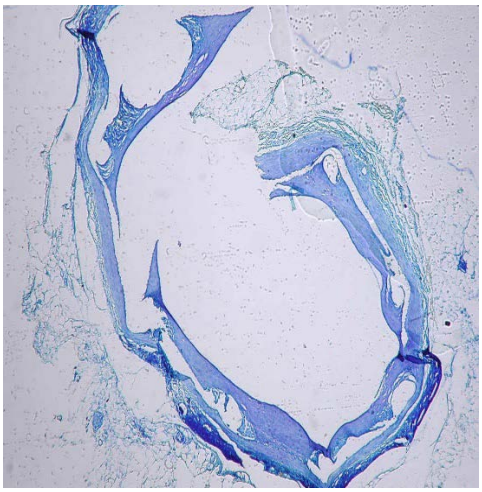


Figure 2. *Rabbit aortic wall. Stent not treated prior to implantation. Hematoxylin-eosin staining. Magnification approximately 10x, field of view 20x.*

Table 1. *The composition of the proposed AdC.*

Protein fractions of the recipient's serum:	**The absolute amount of proteins in 20 ml of AdC is grams per 20 ml (± grams per 20 ml).**	**The ratio of protein components, % (± %)**
albumins	0,94 ± 0,26	61,1 ± 16,7
α1-globulins	0,04 ± 0,002	2,4 ± 0,12
α2-globulins	0,14 ± 0,02	9,6 ± 1,3
β-globulins	0,18 ± 0,015	11,5 ± 1,0
γ-globulins	0,24 ± 0,06	15,4 ± 3,9

Table 2. *Changes in rabbit aortic wall thickness depending on the type of stent treatment.*

Groups (N = 34)	The wall thickness of the aorta (μm)
Control (N = 12)	124 ± 32
Untreated (N = 10)	305± 82
AdC Treatment (N = 12)	140 ± 28

N - Number of animals in the group (p≤0.005)

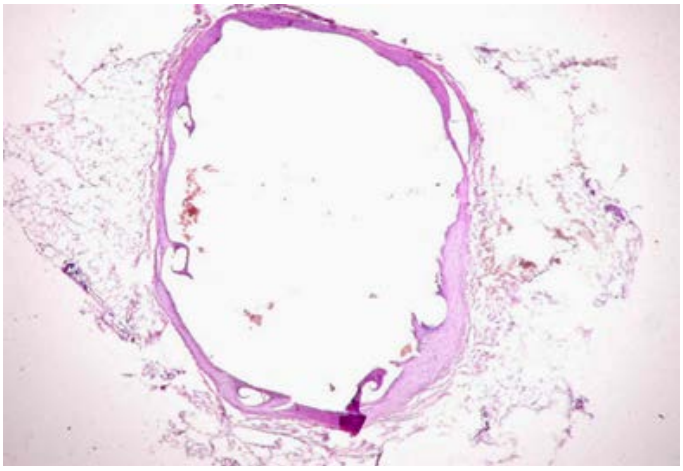


Figure 3. *Rabbit aortic wall. Stent pre-treated with AdC prior to implantation. Hematoxylin-eosin staining. Magnification approximately 20x, field of view 20x.*

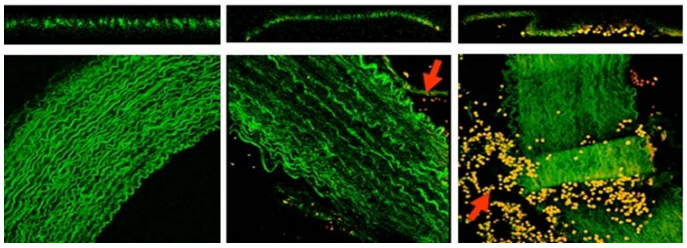


Figure 4. *Immunohistochemical staining of tissues near the implant site after 8 weeks of stent placement: A - collagen fibers; B - slight accumulation of lymphocytes; C - intense lymphocytic infiltration.*

The tissue of a healthy experimental animal, depicted in Figure 4 (A), is uniformly stained with clear visualization of collagen fibers. In Figure 4 (B), a slight accumulation of lymphocytes is observed in the area of the implant element, while in Figure 4 (C), there is intense lymphocytic infiltration.

We suggest that the albumin layer on the surface of implants can lead to the shielding of binding sites with IgG and block the initial stage of the immune response. As a result, the immune system doesn't "react" to the implant as a foreign object. Therefore, the processing of implants with recipient serum prior to implantation using the proposed technology reduces (p=0.04) the level of local inflammation, thus decreasing the frequency of intra- and post-operative complications when using AdC. The Absolute Risk Reduction (ARR) is 35.7% (6.8% – 61.2%) compared to untreated implants.

Thus, no animals exhibited pathological histomorphological changes associated with AdC stent processing. The results of immunohistochemical and histomorphological examinations of the tissues around the implant showed that the application of the proposed AdC stent processing method reduces the level of pro-inflammatory changes. There is a significant decrease in the vessel wall thickness at the site of implantation after AdC stent processing ($p<0.05$) compared to untreated implants.

A number of researches have shown the benefits of in vitro treatment of artificial surfaces and the advantages of in vitro treatment of artificial surfaces in contact with blood using autologous endothelial cells have been demonstrated. This was exemplified by Zilla et al. over 20 years ago when they successfully reduced the occurrence of stenosis and reocclusions after femoropopliteal polytetrafluoroethylene grafting [18-22].

However, the clinical application of this strategy was complicated by the challenges of obtaining endothelial cells through additional invasive procedures, such as harvesting from healthy native vessels. Other approaches to cell isolation included extracting endothelial progenitor cells (EPCs) from bone marrow, which required invasive and painful bone marrow aspiration [23], as well as cultivating microvascular endothelial cells from dermal tissue. The latter also remained problematic due to difficulties in obtaining a pure cell population without fibroblast contamination, low yield of endothelial cells, and the short lifespan of isolated cells [24]. Due to the fact that peripheral blood is readily available, the creation of AdCs is a relatively simple procedure that can provide results in preventing vascular and tissue reactions to foreign material. There have also been studies aimed at improving the neoendothelialization of arterial grafts, such as the application of a proactive VEGF (vascular endothelial growth factor) design on the surface of PTFE (polytetrafluoroethylene) grafts [25]. However, these results have not been widely implemented in clinical practice. On the other hand, the results of our research clearly demonstrate the advantages of using AdC-treated vascular stents and hypothetically stent grafts. In the case of stent graft implantation into the aorta for aneurysms, there is an oversized contact area with the aorto-iliac segment, which may trigger reactions to foreign agents.

The probability of the absence of complications associated with vascular implant rejection after AdC treatment in our study reaches 100% over 12 months (95% CI 78.2% – 100%), and the overall clinical effectiveness of the proposed technology achieves a moderate level (AUC = 0.69; $p<0.001$). These research findings correlate with the results of Chen Z's study [26], in which the immobilization of serum albumin and peptide aptamer for EPC on a polydopamine-coated titanium surface was investigated for enhanced in situ endothelialization.

Therefore, based on the experimental data, it can be concluded that the surface treatment of various types of vascular implants with AdC to enhance their biocompatibility with the recipient's organism is justified.

Conclusion.

The research has confirmed that the implantation of any exogenous material is a trigger for the activation of the immune response by the recipient's body. This is due to the presence of epitopes on the surface of implants - antigenic determinants that recognize the recipient's IgG, leading to the activation of his or her humoral and cellular immunity.

Treating the implant with the recipient's blood serum solution right before the surgery effectively blocks active sites on its

surface, preventing adhesion of recipient's immunoglobulins and the activation of the immune response. The outcome of using this proposed technique is a significant reduction in the recipient's body reaction to foreign material.

The clinical application of the adapting composition (AdC) for implant adaptation to enhance their biocompatibility with the recipient's body is characterized by a 100% (95% CI 78.2% - 100%) likelihood of complication-free outcomes.

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Authors' contributions. According to the order of the Authorship

Conflicts of interest. The Authors declare no conflict of interest.

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ВПЛИВ ОБРОБКИ ПОВЕРХНІ СУДИННИХ СТЕНТІВ АДАПТУЮЧОЮ КОМПОЗИЦІЄЮ (AdC) ДЛЯ ПОЛІПШЕННЯ ЇЇ БІОСУМІСНОСТІ ТА ПРОФІЛАКТИКИ РЕСТЕНОЗУ
(експериментальне дослідження)

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Резюме. В роботі висвітлюється метод обробки поверхні імплантатів, що знижує ризик виникнення реакції запалення на судинні імплантати. **Матеріали і методи.** Дослідження проводили на 34 кролях, самцях, породи «сірий велетень» масою 2,5-3,0 кг у відповідності до стандартів біоетичних принципів. Судини експериментальних тварин були попередньо спровоковані введенням ендогенно розчину пірогеналу по загально визначеній схемі. Тваринам під загальною анестезією були ендоваскулярно (через стегновий доступ у абдомінальну аорту) встановлені стандартні Z-подібні стенти із нержавіючої сталі 316L. Для отримання показових результатів 10 кролям встановлені не оброблені стенти, іншим 12 кролям були встановлені стенти попередньо оброблені адаптуючою композицією (AdC). Через 8 тижнів тварин виводили з експерименту. **Результати та їх обговорення.** Морфометрія стінки судини показала, що обробка стентів AdC перед встановленням їх до судини призводить до зменшення товщини судини у місці їх встановлення. **Висновки.** Клінічне застосування AdC з метою поліпшення біосумісних властивостей імплантатів по відношенню до організму реципієнта характеризується 100% (95% BI 78,2%-100%) вірогідністю відсутності ускладнень.

Ключові слова: ендоваскулярне стентування, рестеноз, імплантати, реакція відторгнення, біосумісні матеріали, адаптуюча композиція, аорта.