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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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"EX VIVO" MACHINE PRESERVATION OF THE ABDOMINAL ORGANS OF A PIG

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Abstract.

Aim: The aim of the study is to test the developed perfusion machine for long-term preservation of the liver, to evaluate the perfusion scheme that provides two different (arterial and venous) flows, and to evaluate hemodynamic of parallel perfusion of the liver together with the kidney.

Material and methods: We have developed a perfusion machine to enable simultaneous perfusion of the liver and kidney, based on clinically proven constant flow blood pump. In the developed device, constant blood flow is converted into pulsed blood flow using a device of its own design - a pulsator. The device was tested on 6 pigs, whose liver and kidney were explanted for preservation. Organs were explanted along with the aorta and caudal vena cava on a common vascular pedicle and perfused through the aorta and portal vein. With a constant flow pump, part of the blood was directed through a heat exchanger, an oxygenator, and a pulsator and delivered to the organs through the aorta. The other part was sent to the upper reservoir, from which the blood gravitationally entered the portal vein. The organs were irrigated with warm saline. Blood flows were regulated by gas composition, temperature, blood flow volume and pressure.

Results: One experiment was put to an end due to technical problems. In 5 experiments, during the 6-hour perfusion, all physiological parameters remained within the normal range. During the conservation process, slight, correctable changes in gas exchange parameters affecting pH stability were noted. The production of bile and urine was noted.

Conclusion: Results of the experiments with the achievement of a stable 6-hour perfusion preservation with confirmed physiological activity of the liver and kidney, make it possible to consider the design capabilities of the applied device with pulsating blood flow. It is possible to assess the original perfusion scheme, which provides two different flows, by one blood pump. The possibility of increasing the duration of liver preservation with further improvement of the perfusion machine and methodological support was noted.

Key words. Isolated organs, organ perfusion, machine preservation.

Introduction.

The ever-growing demand for donor organs is forcing transplant surgeons to look for alternative ways to meet the needs of recipients who are in the terminal stages of disease. It is known that not all obtained organs are used for transplantation due to their unfavorable condition [1]. Efforts are being made to improve the quality of rejected organs [2-6]. The key role in improving of the quality of transplant organs is assigned to the "ex vivo" machine perfusion method. Recently, there has been a tendency to bring the conditions of conservation as close to physiological norms as possible. This gives a rise to the need to create artificial conditions as close as possible to natural ones [7-9]. It should also be noted here that effective conditioning of a marginal transplant can be achieved by long-term (many hours, many days) perfusion. This was made possible by constant technological improvement of artificial analogues of the heart, lungs, blood vessels, etc. During "ex vivo" machine perfusion for the purpose of long-term preservation of the liver, a number of technical and methodological issues arise [8,10]. Among them, the management of hemodynamic parameters of perfusion (the nature of the pulse wave, minute volume of blood flow, pressure in the hepatic artery and portal vein) is important. Equally important is the monitoring and management of the biochemical composition of the perfusate/blood (correction of urea, uric acid, creatinine, proteins, glucose, cholic acid, bile acids, etc.) [11-13]. As for "ex vivo" preservation, some of the listed agents are produced by the liver itself, they enter the blood, and a number of metabolic products are subject to elimination.

In modern perfusion machines, non-pulsating roller and centrifugal pumps provide blood circulation. However, non-pulsatile flow is characterized by a number of known disadvantages that affect hemodynamics and homeostasis [7,14-16]. On the other hand, for the maximum physiological hemodynamics of artificial perfusion during liver preservation, the device must provide both venous - non-pulsating, and arterial - pulsating blood flow. As a perfusate, most authors use whole blood or erythrocyte mass in dilution, hypo-, subnormal- or normothermic temperature. The biochemical composition of the perfusate is corrected by incorporating various filters, dialyzers, artificial kidney analogues in the perfusion scheme [17]. All this complicates the perfusion scheme, apparatus control, and increases the cost of the procedure. But yet, the costs are justified by the end goal, since to some extent it increases the likelihood of using organs rejected for transplantation, taken from marginal donors.

The aim of the study is preliminary experimental testing of the developed new perfusion apparatus for long-term preservation of the liver, evaluation of the perfusion scheme in which two different (arterial and venous) flows are provided for the liver by one pump, as well as the assessment of the results of parallel perfusion of the kidney on a common vascular pedicle with the liver.

Materials and Methods.

An apparatus of our own design was used for "ex vivo" machine preservation of the abdominal organs. In this device the circulation of the perfusate was provided by a centrifugal pump (Sarns). After lengthy bench tests, the device was tested

in preliminary adjustment experiments on animals.

The apparatus for preservation and static scheme of organ perfusion. For the preservation of the hepatic-renal complex, we tested a perfusion apparatus of our own design, which is assembled on a movable cart and is a portable device with a size of 60 x 50 x 50 cm. The main part of the apparatus is a centrifugal (or roller) blood pump. It is equipped with an electronically controlled pulsator of its own design. The pulsator is a device of small dimensions (6 x 8 x 9 cm) and is fixed on the arterial tube of the circulation circuit. It converts the constant flow of the pump by pinching the arterial tube and creates a pulse wave that is as close to natural as possible. The device also includes accessories for a pediatric cardiopulmonary bypass kit. One of the accessories is a common venous sump with a volume of up to 1 liter. It was placed 40-50 cm below the liver. The second reservoir up to 500 ml for "splanchnic" blood was placed 50-60 cm above the liver on a vertically movable holder. The perfusion apparatus also included a heat exchanger, venous and arterial filters, an organ reservoir, a portable oxygen cylinder, a set of silicone and PVC blood tubes with dosing taps and dispensers. The overall control of the apparatus was carried out by a digital control unit, which combines the control of the operation parameters of the pump, heat exchanger, and the flow distribution system within the circulation circuit of the apparatus. The arterial tube after the pump was divided into two branches. One branch was sent to the upper reservoir, and the second branch was sent to the oxygenator. The tube after the oxygenator was again bifurcated. One branch was connected to the tube leading to the upper reservoir, and the second (arterial) branch was directed through a pulsator to the arteries of the organs (Figure 1).

Dynamic scheme "ex vivo" of machine organ preservation. All accessories of the device were assembled in accordance with the scheme shown in figure 1 (details indicated in the diagram by numbers in the text are given in parentheses). A distinctive detail of this scheme is the usage of only one pump (18), but two different flows for the liver are achieved at the same time. Namely, arterial pulsating blood flow enters the liver (2) from the abdominal aorta (9) through the vascular pedicle (8, 7), and mixed (venous with a high oxygen content) blood from the upper venous reservoir (24) enters the portal vein (6) in a gravitational, non-pulsating flow. In addition, the right kidney (10) receives oxygenated normothermic blood from the aorta (through the vascular pedicle 11) in a pulsating flow. It is shown in the diagram, that all hemocirculation tubes are equipped with dosing taps (28), which makes it possible to create the required blood flow in their lumen and regulate both pressure and volumetric blood flow. Thus, a stable blood level is maintained

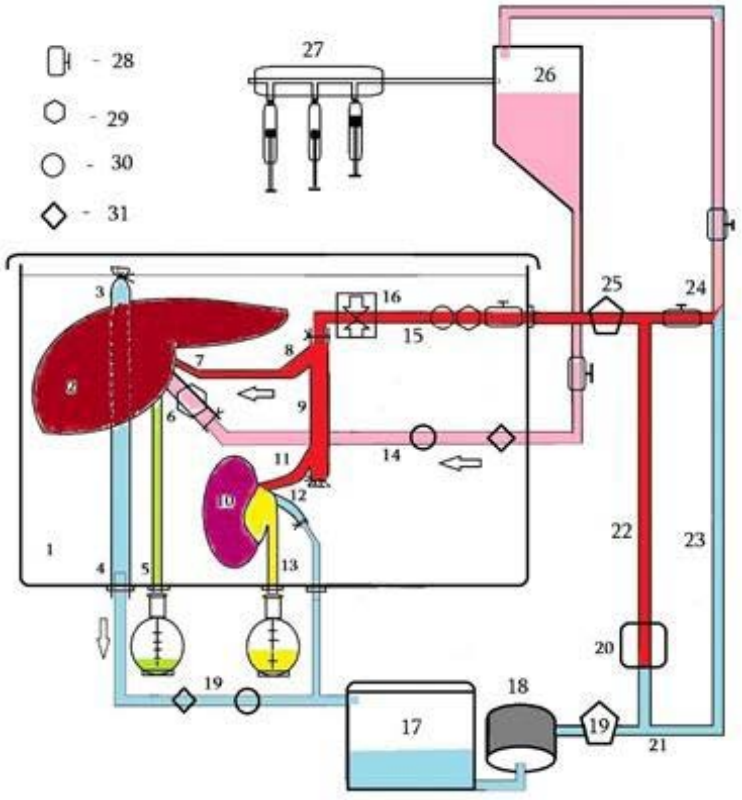

Figure 1. *Scheme of simultaneous preservation of the liver and right kidney on a common vascular pedicle.*

1.Reservoir for organs; 2.Liver; 3. Ligated suprahepatic part of the caudal vena cava; 4. Infrahepatic (cannulated) part of the caudal vena cava; 5. Cannulated common bile duct; 6. Cannulated portal vein; 7. Hepatic artery; 8. Celiac trunk; 9. Abdominal aorta; 10. Right kidney; 11. Renal artery; 12. Renal vein; 13. Cannulated ureter; 14. Tube from the upper tank with mixed blood; 15. Arterial cannula; 16. Pulsator on the arterial tube; 17. Lower reservoir with total venous blood; 18. Blool pump; 19. Venous filter; 20. Oxygenator with heat exchanger; 21. T-tube with venous blood; 22. Common arterial tube under pressure;23. Venous tube under pressure; 24. Tube with mixed venous blood; 25. Arterial filter; 26.Upper venous reservoir; 27. Infusomat with nutritional components; 28. Dosing taps; 29. Sensors of volumetric blood flow; 30. Pressure sensors; 31. Temperature sensors.

in both reservoirs and the required oxygen saturation of the venous blood in the upper reservoir (26) is maintained as well. On the perfusion scheme, sensors for volumetric blood flow (29), pressure (30) and temperature (31) are located in different areas.

Figure 2 shows one of the options for assembling the perfusion apparatus during the experiment.

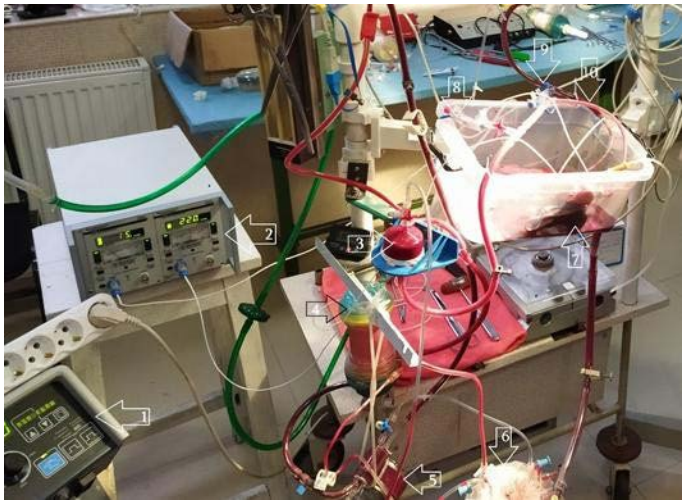

Figure 2. *General view of the perfusion apparatus during the preservation of the hepatic- renal complex.*

1. Centrifugal pump control module; 2. Two-channel flowmeter; 3. Arterial filter; 4. Oxygenator; 5. Heat exchanger; 6. Lower venous reservoir; 7. Reservoir for organs; 8. Blood pressure sensor; 9. Pressure sensor in the portal vein; 10. Aortic and venous cannula.

Explantation of organs on a common vascular pedicle: The experiments strictly adhered to international requirements for the use and euthanasia of animals in biomedical research [18,19]. Organs were obtained from 6 pigs of both sexes weighing up to 20 kg. As for anesthesia, endotracheal anesthesia (halothane 0,1 ml/kg, propofol 0,15 ml/kg, ketonal 0,05 ml/kg) with artificial lung ventilation was used. After laparotomy, drainage tubes were placed in the interintestinal pockets to ensure maximum intraoperative blood drainage. The ligaments of the liver were isolated and transected. The vessels of the liver and right kidney, as well as the common bile duct and ureter were mobilized. The suprahepatic and subhepatic parts of the caudal vena cava and the portal vein were isolated. Initial pressure was measured in the portal vein, caudal vena cava and celiac trunk (Monitor Mindray T 5). Volumetric blood flow velocity was measured in the same vessels (Transit Time Flowmeter TTFM-2). The subphrenic part of the abdominal aorta was isolated with ligation and cutting off the vessels of the left kidney. The aorta was skeletonized in the retroperitoneal space. After a transverse transection of the aorta distal to the origin of the renal arteries, the blood that had flowed into the abdominal cavity was drained into the lower venous reservoir (17) of the perfusion machine (Figure 2). The liver with the caudal vena cava was dissected as a single block, crossing it after ligation in the suprahepatic part (3). The subhepatic part of the vena cava was cut off distally to the confluence of the right renal vein, and the portal vein was cut off along the length towards the spleen. The aorta was transected proximally to the origin of the celiac trunk under the diaphragm. All vessels extending from the celiac trunk were ligated and cut off, except for the common hepatic artery, which was also skeletonized. The right renal artery was preserved distally (11). The right ureter (13) was cut off also along the length of the organ. The organovascular block, consisting of the liver with the caudal vena cava and the right kidney, together with a section of the aorta, was removed from the abdominal cavity of the animal and transferred to the perfusion reservoir (1). The caudal end of the vena cava (4) was cannulated and drained into the lower reservoir. The aorta was cannulated (18 Fr) and connected to the arterial tube of the apparatus (15). The free end of the portal vein was cannulated (20 Fr) and the cannula (14) was connected to the upper reservoir. The right renal vein (12), which flows into the caudal vena cava, was cut off and the outflow from the kidney was carried out into the lower venous reservoir through the cannula. Catheters were inserted into the common bile duct and ureter (5, 13) and connected to graduated tubes.

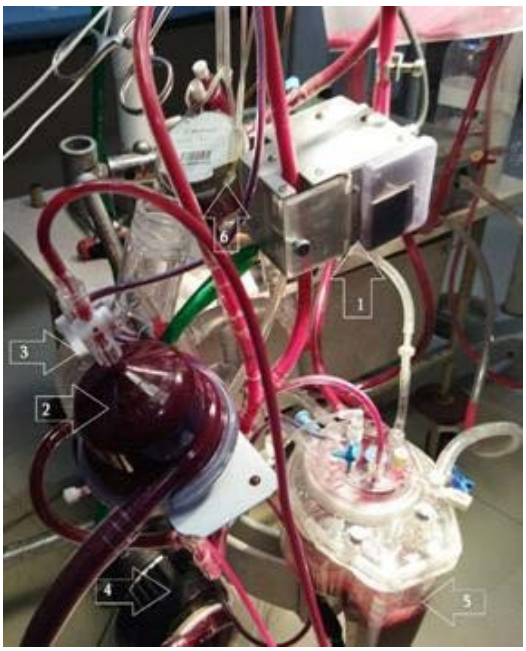

Figure 3. *Section of the perfusion device with a pulsator.*

1. Converter of a laminar blood flow into a pulsating (pulsator); 2. Venous filter;3. Pediatric oxygenator; 4. Blood pump; 5. Lower venous reservoir; 6. Heat exchanger.

Perfusion technique: In the organ reservoir, the liver and the right kidney were placed on a self- designed pneumomattress, which served as a shock absorber and imitated diaphragm movements at a frequency of 20 strokes/min. In addition, the organs were drip-irrigated with normothermic saline in the recirculation mode. The perfusion apparatus was preliminarily filled with blood drained from the abdominal cavity. Recirculation was initiated, the temperature of native blood was set at (37-37.5°C), air bubbles were eliminated, and perfusion commenced. In the aorta and, accordingly, in the hepatic and

renal arteries, a pulsating blood flow was reproduced by means of a pulsator, at a frequency of 70 beats/min (Figure 3). The pulsator converted the constant flow of a centrifugal pump into a pulse, with a characteristic pressure curve inherent in organ arteries. Oxygenated blood passed through the heat exchanger and oxygenator into the aorta. In the portal vein, mixed blood under the control of the volumetric blood flow velocity and pressure was supplied by gravity from the upper reservoir. The percentage of mixing of arterial and venous blood was regulated by dosing taps (28) on the respective tubes. The upper reservoir was filled from the lower reservoir with a blood pump that supplied two different streams of blood to it. Venous blood that was warmed in a heat exchanger and arterial blood (through tube 22), which passed through a heat exchanger and an oxygenator were mixed in the upper reservoir (through tube 23). Venous blood from the liver and right kidney was drained into the lower reservoir and after the blood pump it flew through the venous filter, and then was distributed into the two aforementioned streams (22, 23). Figure 4 shows the reservoir for organs at the time of preservation of the hepatic-renal complex on a common vascular pedicle.

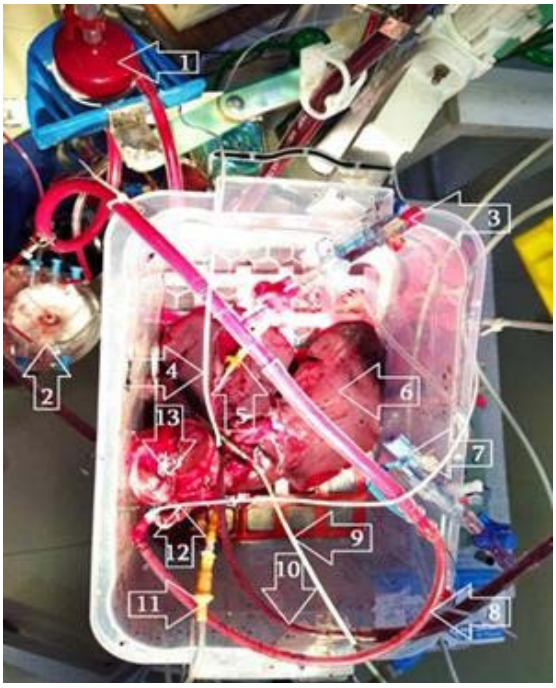

Figure 4. *Location of cannulas and probes in the organ reservoir. 1. arterial filter; 2. venous reservoir (lower); 3. pressure sensor on the arterial tube; 4. flow meter sensor on the portal vein; 5. catheter in the ureter; 6. liver; 7. pressure sensor in the portal vein; 8. aortic cannula; 9. temperature sensor; 10. cannula in the portal vein; 11. catheter in the bile duct; 12. flow meter sensor on the aorta; 13. right kidney.*

Results and Discussion.

In order to comparatively assess the obtained results, at the beginning of each experiment, the initial indicators of pressure and volumetric blood flow in the organ arteries and in the portal, vein were measured after laparotomy. To control the quality of the preservation, hematological, biochemical, coagulation and other indicators of homeostasis were initially determined, which were subjects to dynamic monitoring and correction. Many of them were recorded at the beginning of the surgical intervention and evaluated as baseline indicators. Subsequently, these indicators were again controlled every 2 hours of conservation (see table 1). Of the 6 experiments in one, thrombosis of the oxygenator occurred due to a violation of blood clotting at the 3rd hour of perfusion and the experiment was interrupted. Therefore, only 5 stable, 6-hour perfusions were evaluated. The table shows the average indicators of some of the studied parameters that were obtained during experiments.

The table shows that the initial temperature slightly decreased by the end of perfusion, but by the 5th hour of perfusion, the blood oxygen saturation indicators remained within the physiological limits. The pH was maintained by permanent correction of gas metabolism. Indicators of hepatic metabolism increased slightly only by the end of the 5th hour, while bile formation decreased. With stable adequate perfusion of the kidney, urine formation was not disturbed.

The indicators, of course, largely depended on the perfusion parameters, which were maintained within the initial range, noted before organ explantation. Table 2 shows the main hemodynamic parameters within a biotechnical system created by connecting a perfusion machine to a two-organ complex. The beginning of perfusion included a gradual increase of blood flow from half of the initial norm to normal values in the period of 15-30 minutes. From that moment on, the overall performance of the blood pump did not lessen until the end of the experiment. The redistribution of flows by volume was carried out by dosing taps. The main hemodynamic criterion for the sufficiency of tissue microcirculation was the blood flow through the portal vein. Table 2 shows the average hemodynamic parameters maintained in various parts of the bio-technical complex.

The first experiments involving simultaneous preservation of the liver and kidney as a complex on a common vascular pedicle, using a perfusion device of our own design, showed the validity of both the developed preservation method as a whole and the encouraging technical capabilities of the perfusion device itself. The developed design of the device differs from standard perfusion machines, which are described in the literature [20]. It allows to provide the required flow of perfusate even during a longer preservation, as it is based on the resource capabilities of the main, clinically proven pump and a simple pulsator. This is confirmed by the fact that the level of pressure in the aorta throughout the entire perfusion was maintained as close to the initial values as possible. The pulsator controlled both the pulse rate and the systolic-diastolic gradient. Arterial flow to the organs was reproduced using the main pump and pulsator. The venous flow to the liver came gravitationally from the upper reservoir (26). Therefore, the required pressure at the entrance of the portal vein was set by changing the gradient between the organ and the upper reservoir. The perfusion scheme tested in the experiments provided two hemodynamically and metabolically different blood flows by one pump. The perfusion scheme also made it possible to control and maintain various oxygen saturations of both arterial blood supplying the hepatic artery and venous blood supplying the portal vein. When

Table 1. *Monitoring of some of the indicators of liver homeostasis during machine perfusion preservation.*

#	Indicator	Initial values	Preservation					
			1 hour		3 hours		6 hours	
			Organ	Perfusate	Organ	Perfusate	Organ	Perfusate
1	t° C	37.0	36.2	36,4	36.2	36,4	36,1	36,2
2	pH	7,5	7,4		7,6		7,5	
3	PO2	58,6	48,4		50,3		42,0	
4	pCO2	17,3	19,9		19.0		14,2	
5	Ht	≤15	≤15		≤15		≤15	
6	AST	131	260		360		248	
7	ALT	32	31		32		59	
8	Glucose (mg/dl)	110	122		240		156	
9	ACT (min)	5	4		10		12	
10	Urea (mmol/l)	4,2	5,2		7,0		8,1	
11	Creatinine (μmol/l)	86,6	86, 8		88,4		116,5	
12	Bile (ml)	-	5		14		3	
13	Urine (ml)	10	10		8		12	

Table 2. *The main hemodynamic parameters recorded during conservation.*

#	Hemodynamic index	Initial	1 hour	3 hour	6 hour
1	Total volumetric blood flow of the blood pump (ml/min)	-	600	600	600
2	Volumetric blood flow in the aorta (ml/min)	1400	100	95	100
3	Volumetric blood flow in the portal vein (ml/min)	370-400	400	390	400
4	Volumetric blood flow in the caudal vena cava (ml/min)	110	500	500	490
5	Mean aortic pressure (mm Hg)	95	90	90	80
6	Portal vein pressure (mm Hg)	30	40	34	32

assessing the method of preservation, which was developed in the presented experiments, the significance and the originality of the simultaneous preservation of the liver along with one of the kidneys, which is combined with the main organ by a common vascular pedicle is noteworthy [11,21]. In principle, this approach has been tested for the purpose of its application in long-term, multi-day perfusions to study the possibility of elimination of hepatic metabolites by a native organ instead of a complex and expensive hemodialysis system, which is included in the perfusion scheme by experimenters. In addition, the kidney, constantly monitored and evaluated during perfusion, is in itself an adequate graft and can be used for transplantation. Thus, the experiments carried out revealed the capabilities of the perfusion machine and the developed method of preserving the liver for 6 hours. The results obtained allow us to plan further studies that will be aimed at increasing the duration of liver preservation up to several days, with confirmation of the quality of the procedure through subsequent transplantation.

Conclusion.

In a liver and kidney perfusion machine, a roller or centrifuge pump can be used along with a pulsator that converts part of the constant flow into a pulsating one. The pulsator developed by us is structurally simple. It is cheap and easy to manage. In accordance with the scheme developed by us, it is sufficient to use only one pumping device and two venous (upper and lower) reservoirs to achieve two blood flows that are different in terms of hemodynamic parameters. The first results of experiments on animals, that showcased the achievement of a stable 6-hour duration of preservation with confirmed physiological activity of the isolated liver and kidney, allow us to consider the possibility of increasing the duration of preservation (for many hours) by the future improvement of both the perfusion machine and methodological support.

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РЕЗЮМЕ

“EX VIVO” МАШИННАЯ ПРЕЗЕРВАЦИЯ БРЮШНЫХ ОРГАНОВ СВИНЬИ

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Целью исследования является апробация разработанного перфузионного аппарата для длительной консервации печени, оценка перфузионной схемы, обеспечивающей два различных (артериальный и венозный) потока и гемодинамическая оценка параллельной перфузии печени вместе с почкой.

Материал и методы. Мы разработали перфузионный аппарат для одновременной перфузии печени и почки на базе насосов крови постоянного потока. В разработанном аппарате постоянный кровоток преобразуется в пульсовой устройством собственной конструкции – пульсатором. Аппарат апробировали на 6 свиньях. Эксплантированные органы извлекали вместе с аортой и каудальной полой веной на общей сосудистой ножке и перфузировали через аорту и воротную вену. Насосом постоянного потока часть крови направляли через теплообменник, оксигенатор, пульсатор и подавали органам через аорту. Другую часть направляли в верхний резервуар, из которого кровь гравитационно поступала в воротную вену. Органы орошали теплым физиологическим раствором. Потоки крови регулировали по составу газов, температуре, объему кровотока и давлению.

Результаты. 1 эксперимент был прерван из-за технических проблем. В 5 экспериментах к концу 6-го часа префузии все физиологические показатели оставались в пределах нормы. В процессе презервации отмечались незначительные, поддающиеся коррекции изменения показателей газообмена, влияющих на pH. Отмечалась продукция желчи и мочи.

Заключение. Результаты экспериментов, с достижением стабильной, 6-часовой презервации, с подтвержденной физиологической активностью печени и почки позволяют судить о конструктивных возможностях примененного аппарата с пульсирующим кровотоком. Отмечена возможность увеличения продолжительности презервации печени при дальнейшем усовершенствовании перфузионной машины и методологического обеспечения.

Ключевые слова: изолированные органы, перфузия органов, машинная презервация.

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ღორის მუცლის ღრუს ორგანოების " X VIV " მანქანური პრეზერვაცია

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ა შრომი შესრულებულია შოთა რუსთაველის საქართველოს ეროვნული სამეცნიერო ფონდის მხარდაჭერით (გრანტი ღ-19-7543)

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