UDK: 615.461:616.12-098.843

BIOMATERIALS IN CARDIAC SURGERY (TERMINOLOGY, PROCESSING, MODELING IMPLANTS, EXPERIMENTAL RESEARCH, CLINICAL USE, APPLICATION PROSPECTS)

V. N. Khrapunov, A. G. Goryachev, A. A. Pishchurin, M. Atamanyuk, M. F. Zinkovsky

National M.M. Amosov institute of cardiovascular surgery of NAMS of Ukraine

Our experience and analysis of different types of biomaterials use in in cardiac surgery is presented in the article. Legitimacy of using xeno - and gomomaterials in experiments and in clinical practice is substantiated. The role of chemical sterilization of biotransplantants for long term storage and use in operation proved. The need for a variety of biological materials in reconstructive surgery of acquired and congenital heart lesions and the prospect of this trend in cardiovascular surgery is demonstrated.

Key words: *cardiovascular surgery, biological materials, prosthetic heart valves, conduits*

The problem of development and application of biological substitutes in cardiovascular surgery has more than half a century the fundamental story. Following the global trends in our institution since the 70s to create and apply the whole range of biomaterials to replace damaged elements of the cardiovascular system. Used different bioimplantanty, which included both xeno - and gomomaterial .According to the terminology transplant in my practice, we used the following concepts , namely anatomical materials - organs , tissue, anatomical structures , human or animal cells; bioimplantanty - medical applications , made of materials anatomical dead people; homografts - human anatomical materials intended for transplantation; xenografts - anatomical animal material intended for transplantation; autograft - transplanting a person to take his body material. Also used different types of conduits. " Conduit " (from the English . Conduit - pipe) - a prosthesis that connects one of the chambers of the heart with one of the main arteries or its branches and performing , so the function of ventricular outflow tract of the heart. Similarly, the concept of " conduit " there is the notion of "graft" (from the English . Graft - sprout, transplant surgery) - a prosthesis that replaces a missing piece of tissue. Drew strength and ductility of the material, and finished natural structures such as valves ksenoaortalnye notable for their high physiologic and hemodynamic efficiency. The main advantages of biological valves over mechanical prostheses clearly occurred: physiology, hemodynamic efficiency, minimal risk of venous thromboembolism, no need for lifelong use of anticoagulants (contraindicated in patients with blood diseases, gastrointestinal tract, pregnant, etc.), there is no acute dysfunction of the prosthesis, the minimum risk of endokarditis, the availability of different sizes [7]. However, many questions about the art of the fence, biocompatibility, decalcification, conservation methods, sterilization techniques to create new durable structures are still not fully resolved. At the turn of the 60s and 70s, thanks to Alan Carpentier fundamental research on biomaterials chemical preservation method was proposed for conditioning, is to combine the use of sodium metaperiodate and glutaraldehyde (GA) [5]. Through active NH- groups GA crosslinking was performed (cross- link) structures of collagen- elastin skeleton biomaterial. Besides destroying metaperiodate cell nuclei was achieved biological inertness, biomaterial was converted to polymer. This method is superior to all of the proposed early on antigenodepressivnomu, sterilizing and crosslinking effects. However, these bioprosthetic 2-3 years exposed massive calcification. It turned out that sodium metaperiodate enhances the ability of collagen to calcium phosphate crystallization. Then Warren Hancock removed from flowsheet sodium metaperiodate, and later created the first flexible support frame for bioprosthesis .

It has been proven that the frame and reduces the voltage stress on the damping unit casement, which reduces fatigue and increases its fabric durability. In the mid-'80s, it was found that the structure occupies a major share of complications calcification and degeneration of the material [6, 11]. After 10-12 years after the implantation there are dysfunctions of the second type . They are caused by fatigue deformation chemically crosslinked collagen dead. Electron microscopy revealed the disintegration and fragmentation of collagen fibers, disorganization phenomena [4]. Due to the high incidence of dysfunction of bioprostheses interest in them declined sharply. Today implanted patients older than 70 years (reduced risk of calcification in this group due to low levels of calcitonin), patients with contraindications to anticoagulation . In addition, regardless of the age of the patient in the position recommended bioprosthetic tricuspid and pulmonary valves in connection with the hemodynamic features of these valves. In congenital surgery ksenomaterial seek autoperikard or replace well-established synthetic material - polytetrafluoroethylene (Gore - Tex) [8]. Even with these limitations, the global demand in the bioprosthetic valve is now about 50,000 units per year. Therefore, finding ways to overcome the main limiting complications - calcification - being very intense and in recent years has achieved great success [10]. Lifespan biovalves increased to 20 years, but at the same time increased and their cost. We also have experience in experimental and clinical use of biomaterials in cardiac surgery .The purpose of this communication - to provide the expertise and the results of the use of biological materials in cardiac surgery.

Material and methods. In addition to ready-made designs of natural animal and human drew our attention calf pericardium (TA) as a raw material to create a valve and vascular prostheses and as a plastic material in reconstructive surgery for congenital heart defects. But apart from their vicarious functions implantable material had to answer to the main principles of transplantation availability, biological stability, sterility, strength, stability and durability. These requirements depend primarily on the method of sterilization and preservation.So, as base material we chose TP - it is plastic, it is easy to work and , by virtue of its size , you can create designs used for individual use. Veal ksenoperikard 6-8 months of age climbed in non-sterile conditions at the factory. Mechanically removes excess tissue, fat, and then washed in running water pericardium - thereby removed water-soluble proteins, small particles of fat and scraps of fabric. Then the cascade was carried out in the solution treatment of the material, representing increasing concentrations of alcohol, namely: - 40 °, 60 °, and 80 ° - day in each of the solutions. We applied this technique, modernized classic - alcohol free. The reasons for the change were the reports of phospholipids and triglycerides contained in the biomaterial - these compounds serve as templates for the deposition of calcium and phosphorus. Further, our experimental studies have shown the expediency of just such a procedure [3]. After three days of alcohol treatment, TC was placed in a container of 0.625 % solution of HA (buffer phosphates potassium, pH 7.4) . At the same time slices used pericardium went on microbiological research that showed that 3% of the samples were inoculated yeast, which forced us to apply additional processing fabrics 4% formaldehyde solution, sodium acetate buffer at pH 5.6%. After double fabric treatment were completely sterile and ready for use. While working with TA we conducted laboratory studies of native and processed in the laboratory ksenoperikarda Polytechnic University tensile machine «VIRKERS». The results showed that the elastic properties of TP saved and strength increases by 30% - Specific tensile stress increased from 183 kg/cm² to 218 kg/cm². The next stages of our work were experiments on rats. Purpose of which was to study the morphological changes in the TP -treated by the standard method and the modified double cascade- alcoholic. Laboratory rats - 10 individuals - subfascially implanted pieces of TP; 8 months later the animals were sacrificed and examined histologically material. It should be noted that the 8- month life rats correlated with 20-25 years of life. Histological studies showed that 40% of the samples treated with the standard method revealed a proliferation of connective tissue calcification clumps, while the samples treated according to the method of alcohol- HA changes are detected. Thus, the application of our proposed TA processing techniques allows to hope for increase in terms of the functioning of bioprosthesis by 50-60%.The object of our research were also turkey trachea, which are structurally represent an ideal vascular prosthesis is provided with annular frame. Trachea turkey processed by the above procedure, then subjected to mechanical studies on a specially designed machine in the form of pulse duplicator allows you to create different modes of pressure and volume loads. During the experiment, we achieved volume measures 900 cm^3 at a pressure of 217 mm Hg. In this case the trachea maintained its integrity. In experiments on dogs (7 dogs) tracheal samples as abdominal aortic anastomoses showed their kompententnost and reliability in places anastomoses noted increase neonitimy deep trachea to 1 cm. Pioneer in the use of biomaterials in cardiac surgery is a professor Zinkovskiy MF, which from the beginning of the 70s began to actively introduce biomaterials in clinical practice - mainly in reconstructive surgery of complex congenital heart disease [1, 2]. Used as auto- and ksenoperikad, ksenoaortalnye, xenopericardial and valves. For the reconstruction of outflow tract of the right ventricle were used different materials and designed various constructions - patch monoflap with biological valves, synthetic and biological conduits. TP was also used as a plastic material for closing intracardiac defects, plastic aorta and pulmonary artery .Particularly worth mentioning is the use of cryopreserved and treated in nutrient - antibiotic medium ("fresh") homografts prepared by the method of D. Ross [9]. This biomaterial is a very valuable (and sometimes indispensable) for the correction of defects associated with hypoplasia (atresia) and other complex congenital heart defects. In clinical practice, we have used both types of 51 homografts (16 pulmonary and 35 aortic) for correction of congenital with good immediate hemodynamic effects. In the laboratory we have bioprosthesis valve prostheses made of treated TA mounted on rigid titanium frames - PBA (aortic) and MSDS (mitral). In the aortic position 49 implanted prostheses, in mitral - 28. Additionally, the mitral position, we applied 25 prostheses " DOLLAR -M" domestic production. Total Used 102 bioprosthesis with good clinical effect - closing function bioprosthesis competent and gradient on the aortic prostheses ranged from 5 to 15 mm. Hg, for mitral - from 0 to 4 mm.

Hg. Also used in our clinical practice and ksenoaortalnye prostheses imported - "Hanckok" - I, "Hanckok" - II (Medtronic) "Edwards", "St. Jude" etc. Their number is small - 15-20 per year, which is associated with a higher cost compared to mechanical , as well as restrictions on their use in younger patients.

Results. All surviving patients (n=46) with homograft (90,2 %) achieved a positive effect of the operation to the pressure gradient in Conduit 9,91 ± 2,26. Long-term results were studied in 85,3% of the number of patients discharged. Actuarial survival of patients undergoing implantation of the conduit, excluding hospital mortality after 5 years was 97,1 %, 10 – 74,6 %, and depend on the type of conduit and on the nature of the vice. In the late period (10,5 ± 0,46 years) good functional usefulness of low systolic pressure gradient between the right ventricle and the pulmonary arteries preserved pulmonary homografts (30,5 ± 2,65 mm Hg). Calcination and stenoses are most susceptible to aortic homografts (72,16 ± 6,02 mmHg). For 10 years we have been able to trace more than 30% of patients with ksenovalves, so the correlation function parameters - time can not be considered reliable. Within this group the survival rate was - 78 %. Among the subjects in the three cases were identified dysfunction of the prosthesis - two due to recurrence bakendokarditis, leading to fibrosis and calcification of bioprostheses partial, they have been successfully reimplantirovany in one - we spotted a gap on the wing valve commissure . Given this, we have proposed to strengthen commissure strip of Dacron, which falls and commissural seam. In the study of tensile strength properties of the modified car suture was found that tensile stress on the traditional seam was 140 kg/cm^3, on modified - 528 kg/cm^3. Most time functioning bioprosthesis - PBM we recorded in 19 years - the patient died because of severe tricuspid insufficiency, progressive liver cirrhosis, while the autopsy showed himself as a bioprosthesis in the mitral position was intact with a good closing function.

Conclusions. Thus we improved methodological concept two - preservation and sterilization ksenoperikarda proved its competency, developed time and temperature treatment regimens. Created the original tools and accessories for the manufacture of bioprostheses and a special surgical instrument for implanting bioprostheses. The ingenious laboratory facility for the study of the hydrodynamic properties of a pulsating flow. Studied mechanical properties of native and "stabilized" TP, justified the use of treated ksenoperikarda eligibility for bioprostheses. An original design methodology bioprosthesis, commissural suture technique. Xenopericardial successfully applied patches, multiple conduits , prostheses turkey tracheal surgery for congenital heart defects . Introduced into clinical practice methods of sterilization and preservation of bioprostheses, including homografts . The technique of using various operations bioprosthesis and conduits, as well as a system of indications and contraindications to their use in surgery of acquired and congenital heart defects.

Literature

1. *Зиньковский М. Ф., Бондаренко Н. Д.* Бычий перикард как ксеноматериал для протезирования крупных сосудов сердца / М. Ф. Зиньковский, Н. Д. Бондаренко // IX Всесоюзная конференция по пересадке органов и тканей. – Тбилиси, 1982. – С. 160–161.
2. *Зиньковский М. Ф., Бондаренко Н. Д., Андриенко Т. В.* Биологический протез лёгочного ствола и его структурные преобразования после имплантации / М. Ф. Зиньковский, Н. Д. Бондаренко, Т. В. Андриенко // Клиническая хирургия. – 1985. – № 10. – С. 17-19.
3. *Храпунов В. Н., Захарова В. П., Пищурин А. А., Горячев А. Г. и др.* Структуральные изменения ксеноперикарда в зависимости от метода обработки (эксперимент *in vivo* с последующим патоморфологическим исследованием / В. Н. Храпунов, В. П. Захарова, А. А. Пищурин, А. Г. Горячев и др. // Щорічник наукових праць асоціації серцево-судинних хірургів України. – К., 2010. – Випуск 18. – С. 668–671.
4. *Bortolotti U., Milano A., Thiene G., et al.* Long-term durability of the Hancock porcine bioprosthesis following combined mitral and aortic valve

replacement: an 11 year experience / U. Bortolotti, A. Milano, G. Thiene [et al.] // Ann. Thorac. Surg. –1987. – Vol. 44. – P. 139–144.

5. *Carpentier A., Lemaigre G., Robert L.* Biological factors affecting long-term result of heterografts / A. Carpentier, G. Lemaigre, L. Robert // J. Thorac. Cardiovasc. Surg. – 1969. – Vol. 58, № 3.–- P. 467–472.

6. *Edwards W. D., Agarwal K. C., Feldt R. H.* Surgical pathology of obstructed right-sided porcine-valve extracardiac conduits / W. D. Edwards, K. C. Agarwal, R. H. Feldt // Arch. Pathol. Lab. Med. – 1983. – Vol. 107, № 4. – P. 400–405.

7. *Holper K., Wottke M., Lewe T., et al*. Bioprosthetic and mechanical valves in the elderly: benefits and risks / K. Holper, M. Wottke, T. Lewe [et al.] // Ann Thorac Surg 60 (Suppl.). – 1995. – P. 443–446.

8. *Molina J.* Use of Polytetrafluoroethylene (GORE-TEX®) grafts for the construction of right ventricle-pulmonary-artery conduits / J. Molina // Ann. Thorac. Surg. – 1985. – Vol. 40. – P. 405–407.

9. *Ross D*. Homograft replacement of aortic valve / D. Ross // Lancet. – 1962. – Vol. 2. – P. 487.

10. *Hazekamp M*. Stentless biovalve prostheses / M. Hazekamp // Leiden: Met lit. opg., 1996. – 152 p.

11. *Thandroyen F., Whitton I., Pirie D*. Severe calcification of glutaraldehyde-preserved porcine xenografts in children / F. Thandroyen, I. Whitton, D. Pirie // Amer. J. Cardiol. – 1980. – Vol. 45, № 2. – P. 690–696.

БІОМАТЕРІАЛИ В КАРДІОХІРУРГІЇ

(термінологія, обробка, моделювання імплантів, експериментальне дослідження, клінічне використання, перспективи застосування)

Храпунов В.М., Горячев А.Г.,

Піщурін О.А., Атаманюк М.Ю., Зіньковський М.Ф.

В роботі представлено наш досвід і аналіз застосування різних видів біоматеріалів у кардіохірургії. Обґрунтовано правомочність використання ксено- і гомоматеріалів в експериментах та клінічній практиці. Доведено роль хімічної стерилізації для тривалого зберігання і функціонування *біотрансплантатів. Продемонстровано необхідність використання різних біологічних матеріалів і конструкцій у реконструктивній хірургії набутих і вроджених вад серця та перспективу цього напряму в серцево-судинній хірургії.*

Ключові слова: *серцево-судинна хірургія, біологічні матеріали, протези клапанів серця, кондуїти.*

БИОМАТЕРИАЛЫ В КАРДИОХИРУРГИИ

(терминология, обработка, моделирование имплантов, экспериментальное исследование, клиническое использование, перспективы применения)

Храпунов В.Н., Горячев А.Г., Пищурин А.А., Атаманюк М.Ю., Зиньковский М.Ф.

В работе представлен наш опыт и анализ применения различных видов биоматериалов в кардиохирургии. Обоснована правомочность использования ксено- и гомоматериалов в экспериментах и клинической практике. Доказана роль химической стерилизации для длительного хранения и функционирования биотрансплантатов. Продемонстрирована необходимость использования различных биологических материалов и конструкций в реконструктивной хирургии приобретенных и врожденных пороков сердца и перспектива этого направления в сердечно-сосудистой хирургии.

Ключевые слова: *сердечно-сосудистая хирургия, биологические материалы, протезы клапанов сердца, кондуиты.*