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IMMEDIATE CLINICAL RESULTS OF THE NEW BIOLOGICAL SUPPORT RING FOR CORRECTION OF MITRAL INSUFFICIENCY

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Highlights

• Clinical first experience application of a new biological closed semi-rigid ring for mitral valve annuloplasty "NEORING" (Closed Joint-Stock Company "NeoKor", Kemerovo) was evaluated.

• Intracardiac hemodynamics after the mitral valve annuloplasty with a biological semi-rigid ring "NEORING" was analyzed.

Aim	To make the first clinical experience evaluation of the new biological closed support ring for mitral valve.
Methods	26 patients (16 men, 10 women, mean age 55 [49; 62] years) with dysplastic mitral insufficiency were implanted "NEORING" biological ring for the first time from March 2020 to June 2021. The etiological factor of the defect formation in all cases was the connective tissue dysplasia. The mean functional class of heart failure before surgery was 2 [2; 3] according to NYHA, the effective regurgitant orifice (ERO) was 0.4 [0.3; 0.5], vena contracta was 0.7 [0.6; 0.8]. Ten patients received rings of 28 mm diameter, ten patients – 30 mm, six patients – 32 mm.
Results	No significant adverse events such as death from any causes, strokes, myocardial infarction, cardiac complications, bleeding, and return of regurgitation or failure of plastic surgery requiring reoperation, infective endocarditis after the intervention were observed. In two cases a permanent pacemaker was implanted due to sinus node dysfunction. At discharge all patients had no regurgitation (ERO 0), medium transvalvular gradient was 4.0 [3.0; 5.3] mm Hg. All the patients were assigned to NYHA functional class I heart failure after the surgery.
Conclusion	New biological support ring "NEORING" ("NeoKor", Kemerovo) use in the middle age group of patients showed high hemodynamic efficiency, the absence of specific complications in the early stages after the surgery. It is planned to expand the clinical material on the use of the biological ring, as well as to evaluate the long-term results in the format of a prospective, randomized trial and compare the new device with the existing ones.

Keywords Mitral valve • Support ring • Annuloplasty • Connective tissue dysplasia

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Список сокращений

MV – mitral valve FC – functional class

Introduction

Mitral valve insufficiency (MV) is the second most common acquired heart defect after aortic stenosis [1]. Surgical treatment significantly improves the prognosis of such patients' survival and the probability of valve preservation reaches 90–100% if degenerative and secondary forms of insufficiency are involved. A. Carpentier was the first to develop a valve-saving technology using a support ring in 1969 [2] since then the technique has been constantly improving. The remodeling of the valve fibrous ring with special devices, support rings, is the essential component of annuloplasty.

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Nowadays cardiac surgeons have got a wide range of mitral valve plastic support rings which differ in such key characteristics as rigidity, shape and materials. The common feature in the majority of models is the use of synthetic materials as a cuff [3, 4]. However, the abundance of support ring made of synthetic materials indicates the absence of an ideal option. Moreover, according to the results of some studies in case of infectious endocarditis the use of such rings is contraindicated due to a high risk of relapse of the disease unlike xenopericardial cuffs which do not increase the relapse risk [5]. Scientists of Federal State Budgetary Scientific Institution "Research Institute for Complex Issues of Cardiovascular Diseases" in collaboration with Closed Corporation "NeoKor" (Kemerovo) specialists have developed a new biological support ring for mitral annuloplasty "NEORING". The ring has got no analogues in the world yet and it ensures the preservation of MV natural fibrous ring shape and physiology with its unique biomechanics. The frame is made of superelastic nitinol with shape memory effect as well as high radiopacity. The product has MV natural saddle-shaped fibrous ring and is made of xenopericardium stabilized with ethylene glycol diglycidyl ether with an antithrombotic coating (Fig. 1).

The aim of the study is to make the first clinical experience evaluation of the new biological closed support ring for mitral valve.

Materials and Methods

26 patients with dysplastic mitral insufficiency were implanted "NEORING" support rings for the first time from March 2020 to June 2021 and a prospective analysis of the surgical treatment immediate results was carried out using a continuous sampling method. The clinical characteristics of the patients are given in Table 1.

The patients mean age was 55 [49; 62]. 8 patients suffered from MV insufficiency combined with ischemic heart disease but it was not its manifestation. Hemodynamically insignificant coronary artery stenoses were detected in all examined patients according to angiography. The connective tissue dysplasia was the etiological factor of the defect formation in all cases. The average functional class (FC) of heart failure before surgery was 2 [2; 3] according to the NYHA classification, the effective regurgitation orifice (ERO) was 0.4 [0.3; 0.5] cm^2, vena contracta was 0.7 [0.6; 0.8] cm.

Figure 1. Biological closed support saddle ring "NEORING"
Note: *the images of the biological support ring for mitral valve annuloplasty are published with the written permission of "NeoKor".*

Table 1. General characteristics of patients, Me [Q1; Q3]

Index	Value
Age, years	55 [49; 62]
Male/Female, n	16/10
Body surface area, m^2	1,95 [1.81; 2.16]
FC NYHA of heart failure	2 [2; 3]
MV Regurgitation	4 [3; 4]
Concomitant disease, n:	
ischemic heart disease	8
multifocal atherosclerosis	4
chronic obstructive pulmonary disease	3
diabetes mellitus	2
atrial fibrillation	5
GFR MDRD, ml/min/m^2	91 [83; 111]

Note: *FC – functional class; GFR – glomerular filtration rate; MDRD – Modification of diet in renal disease; MV – mitral valve; NYHA – New York Heart Association. Me – median; Q1 – lower quartile; Q3 – upper quartile.*

All interventions were performed under conditions of artificial blood circulation, CO2 was insufflated into the wound for the prevention of embolic complications, and myocardium was protected with "Custodiol" (Kohler Chemie, Germany) solution.

After the revision of the valves and the subclavian apparatus of the MV the following reconstruction methods were used: chord prosthetics in 2 cases, second-order chord translocation in 14 cases, resection techniques were applied in 16 cases, a combination of several reconstruction techniques was accomplished in 6 patients. In all cases the mitral valve plasty (MVP) was completed by the implantation of a biological support ring with U-shaped seams on the gaskets.

The first stage was the stitching of the MV fibrous ring in the hinge zone with U-shaped seams on Teflon gaskets. The second stage was to stitch the biological support ring once with one needle through the xenopericardial cuff with the circumference of the nitinol frame from the inside and the second needle – through the xenopericardial cuff

from the outside of the nitinol frame. The threads were held opposite each other which contributed to a closer fit of the frame to the MV fibrous ring and leveling the risk of suture penetration through the xenopericardial cuff of the biological support ring (Fig. 2).

Ten patients were implanted with 28 mm diameter rings. Ten more patients got 30 mm diameter rings and 32 diameter rings were used for six patients. The ring sizes correlated with the body surface area of the patients. The individual selection size technology of the support ring was not different from the generally accepted one. The reconstructive procedure consistency was monitored using intraoperative transesophageal echocardiography. Radiofrequency biatrial ablation of MAZE IV for atrial fibrillation was performed simultaneously with MV intervention in five cases, and correction of secondary tricuspid insufficiency with a biological tricuspid support ring was performed in two cases.

The study was approved by the local Ethics Committee of the *Research Institute for Complex Issues of Cardiovascular Diseases*. All patients signed an informed voluntary consent to participate in the study.

Statistical Analysis

The distribution type was checked using the Kolmogorov-Smirnov criterion. The distribution type is abnormal. Nonparametric statistics methods were used. The dependent variables analysis was performed with the Wilcoxon test. The data are presented in the form of median (Me) and interquartile range [Q1; Q3]. The error probability of the first kind is assumed to be 5% (0.05).

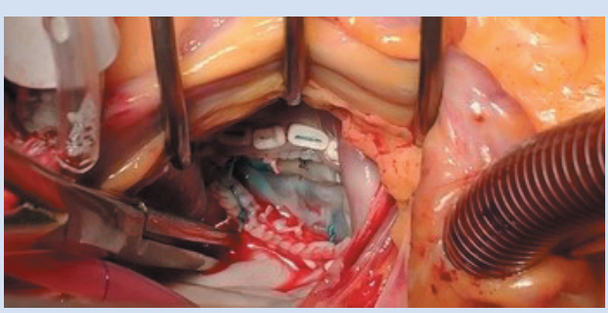

Figure 2. The view of the biological support ring after implantation

Results

Death, stroke, myocardial infarction, cardiac complications, bleeding, regurgitation return or failure of the plastic surgery requiring re-operation, infectious endocarditis after intervention were not observed in any cases. Two patients were implanted with pacemakers due to the initial sinus node weakness syndrome. The time of artificial blood circulation (114 [98; 128] min) and cardiac anoxia (75 [68; 93] min) were different depending on the volume of intervention (Table 2).

The average time of artificial lung ventilation was 7 [7; 8] hours. The next day after the surgery the patients were moved from the intensive care unit. The number of bed days from the surgery until the discharge from hospital was 10 [9; 13]. By the time of discharge all patients had significantly decreased the phenomena of circulatory insufficiency and increased exercise tolerance. After the surgery the patients were classified FC I of heart failure according to the NYHA classification judging by the results of the six-minute walk test. Moreover, all the examined patients had no regurgitation (ERO 0). The average transvalvular gradient was 4.0 [3.0; 5.3] mmHg. The positive dynamics of heart chamber remodeling and the pressure decrease in the small circle of blood circulation were revealed (Table 3).

Table 2. Characteristics of the hospital period, Me [Q1; Q3]

Index	Value
Time AC, min	114 [98; 128]
Aortic occlusion time, min	75 [68; 93]
Ring size, n (%): 28 мм / mm 30 мм / mm 32 мм / mm	 10 (38) 10 (38) 6 (23)
Duration AVL, h	7 [7; 8]
Inotropic support, n (%): mono double	 8 (61.5) 2 (15.4)
Inotropic support duration, h	12 [7; 18]
Bed-days in intensive care	1 [1; 1]
Bed-days from the moment of surgery to discharge	10 [9; 13]

Note: *AVL – artificial ventilation of the lungs; AC – artificial circulation; Me – median; Q1 – lower quartile; Q3 – upper quartile.*

Discussion

Mitral regurgitation is the second most frequently diagnosed heart valve defect after aortic valve stenosis and is most often found in the general population [6]. In developed countries the most common cause of mitral regurgitation is degenerative changes in the MV. Two leading types of connective tissue degeneration, Barlow's disease and fibroelastic deficiency, are associated with types I and II of mitral insufficiency according to A. Carpentier classification [1, 7].

The prognosis of severe dysplastic mitral insufficiency is unfavorable. After an initial long asymptomatic period severe mitral insufficiency passes into a symptomatic phase accompanied by dilation of the left ventricle and is followed by left ventricular failure, dilation of the left atrium, high pulmonary hypertension. The timely correction of mitral insufficiency contributes

to the life expectancy which is about the one of the healthy population [8]. A number of highly effective technologies of MV reconstruction have been developed now: French correction (A. Carpentier, 1983 [9]), Respect Rather Than Resect (P. Perrier, 2008 [10]) and the American Correction (M. Lowry, 2009 [11]). One of the most important and mandatory stages of these technologies is the fixation of the mitral valve compromised native fibrous ring by a special anatomically verified design which is called the annuloplasty support ring. The use of support rings should pursue two main goals: resizing (restoring the size of the fibrous ring) and reshaping (giving the deformed fibrous ring a physiological shape), however, not all rings are able to restore the unique 3D configuration of the mitral valve fibrous ring.

R. Masaaki and the co-authors [3] demonstrated the effectiveness of restoring the mitral valve physiological three-dimensional saddle shape after annuloplasty with semi-rigid (Carpentier-Edwards Physio II ring) and rigid (St. Jude Medical Rigid Saddle Ring) closed support rings but with the loss of the valve morphometry dynamics in different cardiac cycle phases. The high efficiency of Memo 3D semi-rigid support rings has been demonstrated in preserving the physiological dynamics of the fibrous ring and the flap apparatus of the MV but with no possibility of forming an anatomical saddle shape.

In A.V. Afanasyev's study [12], based on the results of a semi-rigid closed support D ring (Closed Corporation "MedInzh", Penza, Russia) and a flexible semi-ring (band) C flex (Closed Corporation "MedInzh", Penza, Russia) comparison for the correction of dysplastic mitral insufficiency, it was demonstrated that the use of one or another type of support ring does not affect the survival of patients and the functional class of heart failure during the long-term follow-up period.

Despite a significant number of clinical studies conducted on the use of different types of support rings for the dysplastic mitral insufficiency correction, recommendations about the choice of a support ring for various mitral insufficiency etiologies have not yet been presented due to the lack of proper evidence base.

Having studied the evolution of the support rings design, two main directions can be traced which are the restoration of the original spatial configuration of the MV fibrous ring and the preservation of its physiological mobility during the cardiac cycle.

These trends are classically manifested both in the device of rigid saddle rings by the example of Rigid Saddle Ring (St. Jude Medical) in the formation of the MV anatomical configuration and semi-rigid support rings Memo 3D (LivaNova, Sorin Group) in achieving dynamic adaptation of the mitral papillary continuum to different phases of the cardiac cycle. Thus, the problem of creating a device that combines all of the above properties remained unresolved.

This study presents the immediate clinical results of a new support ring "NeoRing" use, combining such qualities as: a closed support part that allows to accurately fix the fibrous ring in a certain diameter without the risk of its further dilation; a frame made of X-ray contrast titanium nickelide with shape memory; anatomical saddle-shaped support ring which is able to adapt to different phases of the cardiac cycle does not interfere with physiological three-dimensional deformation and thereby leveling the effect on transmittal flows due to the absence of excessive reduction of the mitral-aortic angle and reduction of left atrium afterload; xenopericardial braid, preserved with ethylene glycol diglycidyl ether with antithrombotic coating, contributing to faster endothelization in the recipient's body and reducing the risk of thromboembolic events in the early postoperative period. According to the results of the study, the positive dynamics of the heart chambers remodeling at the early postoperative period and the absence of specific postoperative complications, including MV annuloplasty were observed.

Table 3. Indicators of EchoCG, Me [Q1; Q3]

Index	Before surgery	At discharge	p
EDD, cm	6.2 [5.8; 6.5]	5.6 [5.0; 6.0]	0.003
ESD, cm	4.0 [3.5; 4.6]	3.9 [3.4; 4.3]	0.086
EDV, cm	194 [167; 216]	142 [116; 177]	0.003
ESV, cm	70 [51; 97]	58 [47; 83]	0.086
LV EF, %	64 [61; 69]	53 [52; 61]	0.050
LA, cm	5.0 [4.8; 6.0]	4.6 [4.2; 5]	0.004
RA, cm	5.0 [4.5; 5.3]	4.6 [4.1; 4.8]	0.086
SPPA, mm Hg	40 [33; 50]	27 [23; 36]	0.116
IVS, cm	1.0 [1.0; 1.0]	1.0 [1.0; 1.0]	0.655
PWLV, cm	1.0 [1.0; 1.0]	1.0 [1.0; 1.0]	0.655
ERO, cm	0.4 [0.3; 0.5]	–	–
Vena cotracta, cm	0.7 [0.6; 0.8]	–	–
Regurgitation MV	4 [3; 4]	Not identified	–
Vmean, cm/s	–	97 [71; 105]	–
Pmean, mm Hg	–	4.0 [3.0; 5.3]	–

Note: *PWLV – posterior wall of the left ventricle; EDV – end-diastolic volume; EDD – end-diastolic dimension; ESV – end-systolic volume; ESD – end-systolic dimension; LA – left atrium; IVS – interventricular septum; MV – mitral valve; RA – right atrium; SPPA – systolic pressure of the pulmonary artery; LV EF – left ventricular ejection fraction; ERO – effective area of the regurgitant orifice; Me – median; Q1 – lower quartile; Q3 – upper quartile.*

According to L. Eric's and his colleagues work [13], which shows cyclic deformation of the MV subjected to annuloplasty by a support ring with fixation by the classical method with separate seams without gaskets, cyclic changes in the shape of the fibrous ring along the anterior leaf, saddle–shaped valve, filling of the aorta and displacement of the fibrous triangle are factors that lead to increased stress pressure on the seams in the mitral-aortic contact zone, which, in turn, contributes to the rupture of the thread itself due to its high strength, and the penetration of the seam through the fabric of the MV hinge zone. Taking into account these data, we preferred to use U-shaped seams on Teflon gaskets to prevent the separation of the support ring; in addition, the adaptive structure of the ring distributes the load on the seams evenly.

Conclusion

The use of the biological support ring "NEORING" (Closed Corporation "NeoKor", Kemerovo) in patients with dysplastic mitral insufficiency showed high hemodynamic efficiency and the absence of specific complications in the early stages after the surgery. We plan to expand the use of a biological ring for getting more clinical material in the future and evaluate long-term results in the format of a prospective randomized study, and also compare the product with the existing models.

Conflict of Interest

I.V. Dvadtsatov declares no conflict of interest. A.V. Yevtushenko declares no conflict of interest. A.N. Stasev declares no conflict of interest. A.V. Sotnikov declares no conflict of interest. R.N. Komarov declares no conflict of interest. L.S. Barbarash - chief editor, the journal "Complex Issues of Cardiovascular Diseases".

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Author Contribution Statement

DIV – data analysis and interpretation, editing, approval of the final version, fully responsible for the content

EAV – data collection and interpretation, editing, approval of the final version, fully responsible for the content

SAN – data collection and interpretation, editing, approval of the final version, fully responsible for the content

SAV – data interpretation, editing, approval of the final version, fully responsible for the content

KRN – data interpretation, editing, approval of the final version, fully responsible for the content

BLS – data interpretation, editing, approval of the final version, fully responsible for the content

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