THE NEW ARMENIAN MEDICAL JOURNAL
Vol.7 (2013), No 2, p.75-82

THE RESULTS OF EPOXY-TREATED STENTLESS BIOPROSTHESES IMPLANTATION IN AORTIC POSITION

Astapov D.A.[1], Isayan M.V.[2], Demidov D.P.[1], Kapustin B.M.[2]

[1] Academian E.N. Meshalkin Novosibirsk Research Institute of Circulation Pathology, Novosibirsk, Russia
[2] Federal Center for Cardiovascular Surgery, Kaliningrad, Russia

Received 10/6/2012; accepted in final form 4/25/2013

Abstract

Aim: The research objective was to evaluate the long-term results of implanting 3 models of stentless epoxy-treated bioprostheses based on 11-year experience in their clinical application.

Material and Methods: The study involved 106 patients (86% of those discharged in 1999-2011) with stentless bioprostheses "AB-Mono", "AB-Composite", and "AB-Neo" implanted in aortic position.

Results: The survival by the end of 10-year observation in patients with implanted prosthesis "AB-Mono" and "AB-Composite" made 75±15% and 89±5%, appropriately; in 6 year-observation of patients with "AB-Neo" bioprosthesis the survival was 100%. By the 10th year of observation freedom from structural dysfunction in patients below 45 years made 11±10%, in subjects aged 45-59 it was 48±15%, while in those aged 60 and above this parameter amounted 67±27%. The freedom from structural dysfunction and explantation of "AB-Neo" prosthesis to the 6th year was 100%. There was a significant decrease in the "AB-Neo" prosthesis for such parameter as the peak trans-prosthetic pressure gradient: from 19.5±7.0 to 16.0±5.0 mm Hg.

Conclusion: Stentless epoxy-treated bioprostheses demonstrated good clinical and hemodynamic results after implantation in the aortic position of older patients. Changes contributed to the design of "AB-Neo" prosthesis resulted in significant reduction of the peak trans-prosthetic pressure gradient, as well as in reduced risk of adverse outcomes in the late post-surgery period.

Keywords: the aortic valve, implantation, biological prostheses, heart valves.

Introduction

Different types of prostheses are widely represented in modern surgery of aortic root. Mechanical prostheses, as well as skeletal biological xenovalves have common major drawbacks: they create a rigid fixation of the fibrous ring subject to the problem of "patient-prosthesis mismatch". Complete aortic root autoprosthetic, or xenograft, is not always justified in older patients in view of the technical complexity of such operations. From this perspective, stentless bioprostheses occupy an intermediate position: their implantation is less complex than the replacement of the aortic root, these prostheses can be successfully implanted in a "narrow" annulus without the risk of creating a high pressure gradient through the prosthesis and they retain the physiological properties of the aortic root to change its size during the cardiac cycle.

The paper presents long-term results of implanting three models of stentless epoxy-treated bioprostheses, based on 11-year experience in their clinical application. The study included the following models of bioprostheses: "AB-Mono", "AB-Composite" and "AB-Neo" ("Neo-Cor", Russia)(Figure 1). The "AB-Mono" valve is a complex with porcine aortic sinuses saved, which are tailored intraoperatively. "AB-Composite" prosthesis is a leaf pig aortic valve mounted on the xenopericardium. "AB-Neo" model is a modification of "AB-Composite" valve, in which the proximal portion of the cuff is presented by sewn xenopericardium that mimics the contours of the native annulus of the recipient.

Address for Correspondence:
Acad. E.N. Meshalkin Novosibirsk Research Institute of Circulation Pathology
15 Rechkunovskaya Street, 630055, Novosibirsk, Russia,
Tel.: (383) 347-60-66, 8-800-100-07-16.
E-mail: astapovitsch@gmail.com

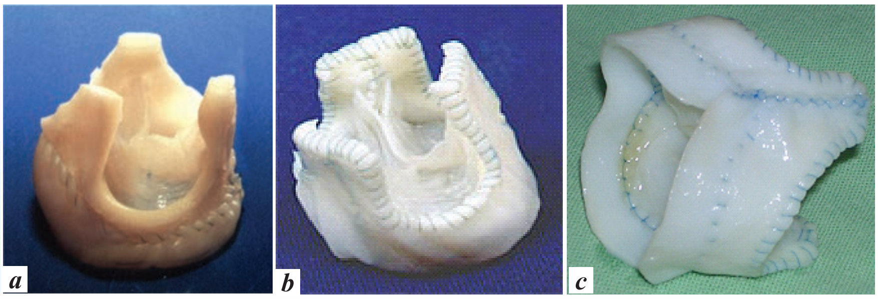

Figure 1.
Epoxy treated biologic prostheses
a *- "AB-Mono" (a),*
b *- "AB-Composite" (b) and*
c *- "AB-Neo"(c).*

MATERIAL AND METHODS

The study is based on survey data of 106 patients, accounting for 86% of those discharged in 1999-2011, who were implanted stentless bioprostheses in the aortic position. Data is available about the fate of 21 (84%) patients with implanted prosthetic device "AB-Mono", 41 (82%) patients with "AB-Composite" and 44 (90%) patients with "AB-Neo" bioprotheses. The mean follow-up in the total group of 52±29 (3-126) months, depending on the model of the implanted prosthesis made 54±30 (11-126), 53±32 (3-126) and 36±16 (6-69) months, respectively. The last stage of gathering information on patients was conducted in July 2011. The smaller mean follow-up of patients with "AB-Neo" prostheses is associated with the later introduction of this model into the clinical practice (in 2005).

The statistical analysis was performed with the help of the program "Statistic 7.0" (Statsoft Inc., USA). We used methods of both parametric and nonparametric statistics. The study was carried out taking into account the "Guidelines for Reporting Morbidity and Mortality after Cardiac Valvular Operations" [*Akins G. et al., 2008*]. In the analysis of long-term results the main methods were as follows: the method of multiplying estimates of Kaplan-Meier, the method of tables and the distribution of lifetimes, as well as regression models.

RESULTS

Data is available on seven deaths in the late post-surgery period. Current survival rates in the total group made 93.4% by the 10th year.

The main cause of patients death in the late period was congestive heart failure (chronic or acute); here belong more than half of the cases.

In two cases, it was not possible to reliably determine the cause of death, but at the time of the last medical examination, no signs of structural failure, prosthetic endocarditis, and other prosthesis-related complications were diagnosed. It can be assumed that the cause of death in those observations was progressive heart failure.

Of the seven deaths, only in one (14%) aortic bioprosthesis dysfunction was the immediate cause, and the consequence was acute myocardial infarction (embolism in the right coronary artery system). At least 43% mortality cases were directly or indirectly related to non-compliance with therapy and inability to timely obtain quality health care.

If we consider the actuarial survival curves for patients with implanted prosthetic devices, "AB-Neo" throughout the observation period (6 years and 9 months) the survival was 100%. Perhaps, this indicator is associated with a lower mean follow-up interval. Figure 2 shows the survival curves of patients with substituted aortic valve prostheses "AB-Mono " and "AB-Composite". By the end of the first-year observation the survival of patients with the implanted prosthesis "AB-Mono" made 95±5% of the observations, by the end of the third year it was 90±7%, by the tenth year – 75±15%; in case of "AB-Composite" bioprosthesis the indices were 98±2%, 89±5% and 89±5%, respectively. There were no significant differences between these two groups (*p*=0.97).

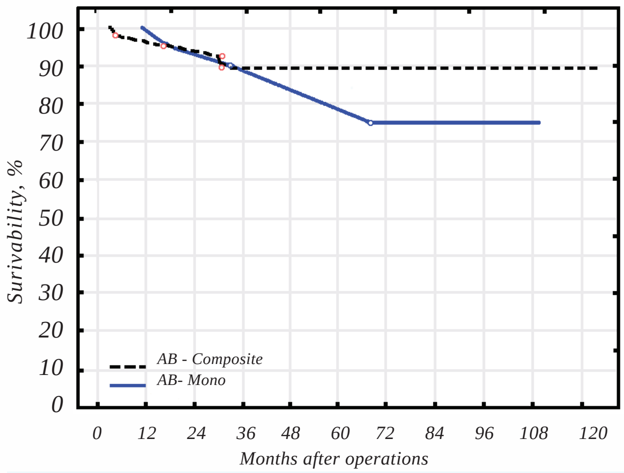

Figure 2. *Survival of patients with implanted prosthetic devices, "AB-Mono" and "AB-Composite".*

TABLE 1.

Peak trans-prosthetic pressure gradient on implanted xenovalves
in post-surgery early and late periods

Parameter	Early post-surgery period			Dynamic observation		
	"AB-Mono"	"AB-Composite"	"AB-Neo"	"AB-Mono"	"AB-Composite"	AB-Neo"
Peak transprosthetic pressure gradient (*mm Hg*)	26.0±8.0	25.5±8.0	19.5±7.0	30.0±9.0*	31.0±8.0*	16.0±6.0*

NOTE: **– p<0.05 compared with preoperative values.*

Thus, patients with implanted stentless prostheses show satisfactory survival rates for 10 years after surgery, and major causes of death are associated with irreversible changes in tissues of the heart and the social status of patients.

In surviving patients we noted the positive dynamics of the physical status, as reflected in the improvement of the functional class (FC) according to NYHA. The average FC in dynamic observation was II (I, II), which was significantly better than before surgery (p<0.001). Major changes occurred in the FC during the first year after surgery remaining virtually unchanged in future.

In 118 months one patient was diagnosed with the expansion of the ascending aorta to 6.5 *cm*, and therefore planned surgery was recommended and performed. In this observation xenovalve dysfunction was not revealed.

Due to syndrome of Frederick development two patients were implanted a permanent pacemaker in the late period.

At ultrasound examination of patients with implanted bioprostheses the dynamics of blood pressure gradient on the stentless prosthesis is of particular interest. The obtained results are presented in Table 1. The analysis involved only patients with aortic stenosis, as the largest group.

The analysis was performed in the time interval of 6 years, taking into account the maximum periods of observation in patients with implanted prosthetic devices "AB-Neo".

By the end of this period a significant increase in peak trans-prosthetic pressure gradient on prostheses "AB-Mono" and "AB-Composite" was marked. To identify factors determining the magnitude of peak trans-prosthetic pressure gradient on these models in the later period, we conducted a multivariate regression analysis and revealed that the greatest (p<0.001) influence to this parameter was produced by the ratio of the diameter of the prosthesis to the diameter of the aortic valve annulus. This dependence is reversed: the larger the ratio, the less peak trans-prosthetic pressure gradient in the late period.

Given the data obtained, prostheses "AB-Neo" were implanted with the selection of size at least 2 *mm* larger than the diameter of the aortic valve annulus. In addition, as shown previously, the existence of sewn cuff in the area of proximal fixation gives an additional mobility of the fibrous annulus, which also reduces the resistance to blood flow, while implantation technique for "free hand" allows to reduce the peak trans-prosthetic pressure gradient already at the hospital stage [*Karaskov A. et al., 2009*]. These factors formed the basis for good performance through a prosthetic blood flow in both early and late post-surgery period. In the first place, it brought forth a significant reduction of peak trans-prosthetic pressure gradient in the follow-up from 19.5±7.0 to 16.0±6.0 *mm Hg*. These rates were significantly lower in comparison with those of "AB-Mono" and "AB-Composite" prostheses both in early and in delayed periods after surgery. The formation of high gradients on the prostheses "AB-Mono" and "AB-Composite", as shown by our experience, was most frequently accompanied by coarse calcification supply of xenoprosthesis with the development of a large prosthetic aortic obstruction holes, sometimes so severe that the output section of the left ventricle was not accessible even to the tip of the little finger.

Table 2 presents the levels of freedom from structural dysfunction in 10-year observation of patients with stentless prostheses of various models.

Certainly, a shorter duration of monitoring on prostheses "AB-Neo " does not allow us to unequivocally state that by the 11th year they will also demonstrate the same dynamics of freedom from structural dysfunction, but data of the five-year period show good performance. In general, data presented

Table 2.

Freedom from structural dysfunction of stentless bioprostheses (%)

Years post surgery	Models of bioprosthesis		
	"AB-Mono"	"AB-Composite"	"AB-Neo"
1 year	100	100	100
3 years	95±5	100	100
5 years	69±13	85±7	100
7 years	55±16	49±11	-
10 years	28±16	30±12	-

in Table 2, in our opinion, reflects the efficiency of changes made to the design of stentless prostheses. It should be noted that no statistically significant differences were obtained between groups of patients with implanted prosthetic devices, "AB-Mono" and "AB-Composite", in the level of freedom from structural dysfunction (p=0.45).

Most of the prostheses during explantation or ultrasound examination carried a few signs of the biological material degeneration. However, only in three cases we observed formation of dysfunction exceptionally due to changes of only one type: in one case there were tears of the valves with no signs of calcification and with good graft endothelialization; in two cases we observed gross calcification of the proximal fixation and a number of commissural grafts with a significant narrowing of the lumen of the valve with intact, well moving cusps. At analysis of the valve breaks localization we did not receive significant difference in the incidence of coronary or non-coronary cusps (p>0.05), which allowed to reject the assumption of excessive load on the non-coronary diastolic leaf as the cause of its insolvency origination in terms of up to 10 years.

Table 3 shows the values of freedom from structural dysfunction of stentless prostheses depending on the patient's age at the time of implantation.

As obvious from Table 3, there is a distinct trend to an increase in duration of the bioprosthesis normal functioning with increasing patient age at surgery. Elderly patients had a minimal risk of dysfunction during the first five years. Two cases of damage to the structure of the valves were observed on the 7th year of the prostheses functioning; in both cases the dysfunction was caused by tears with small calcifications in them without calcification of the prostheses body. It is worth noting that the difference between groups in freedom from structural dysfunction did not reach significant values; however it was close to them (p=0.08). The instantaneous risk of graft dysfunction in young patients (below 45 years of age at the time of surgery) in the first two years amounted to 0.1-0.4% and then began to progressively increase and reached 7.5% by the 10th year. In patients of the average age instantaneous risks in the first two years did not exceed 0.1-0.2% and also began to increase in time up to 3.5% by the end of the observation period. In older patients, the instantaneous risk over 6.5 years of follow-up was maintained at 0.1-0.7% and increased to 3% for the seventh year, while remaining stable further on.

Thus, age has a direct impact on the timing of development and risk of structural dysfunction. This effect, though not statistically significant, turned to be clinically significant allowing us to recommend abandoning implantation of considered stentless bioprostheses to patients of young and middle age, except for situations when implantation of mechanical structures or homografts is not possible or is associated with a high risk of perioperative complications, which exceed the risk of reoperation of aortic valve in a remote period.

Our experience gained in clinical application of artificial prostheses, "AB-Mono" and "AB-Composite", helped us to form tactical and technical views, which have significantly improved the results of implantation of a new generation of "AB-Neo" stentless xenovalves, in particular, to significantly reduce hospital mortality and long-term mortality, to improve clinical and functional parameters (not only due to the upgraded design of this prosthesis, but also because of a more careful

Table 3.

Freedom from structural dysfunction (%) depending on the age of patients at implantation of prosthetic devices "AB-Mono" and "AB-Composite"

Years post surgery	Age (years)		
	below 45	45-59	60 and above
1 year	100	100	100
3 years	96±4	100	100
5 years	73±10	81±10	100
7 years	33±13	61±14	67±27
10 years	11±10	48±15	67±27

approach to the selection of valves in each clinical case), as well as to reduce the risk of structural dysfunction development.

Considering such a prosthesis-related complication as unstructured xenovalve dysfunction, in our study we observed no cases of paraprothetic fistula formation in the long-term period. Several authors described hematomas, which were formed between the casing and the wall of the aortic prosthesis that can lead to a narrowing of the lumen, formation of fistula or aortic root abscess [*Westaby S. et al., 1998; Hubulava G. et al., 2009*]. These situations occur infrequently, and probably in some cases might be related to insufficient fixation of distal or dense number of proximal joints, which leads to their partial eruption; or else it might be associated with the carrying out the operation under conditions of high activity of infective endocarditis. In our study, we detected no similar cases. In all cases of prosthesis explantation (with regard to the structural dysfunction) we observed graft dense structures adjacency to the wall of the ascending aorta; sometimes it was impenetrable that separation represented the most technically difficult stage of the operation. Thus, in numerical terms, the freedom from nonstructural dysfunction for all considered models of stentless bioprostheses was 100% by the end of the observation period.

All operations performed on the valves in the late period were either in connection with structural dysfunction of the aortic xenovalve or without aortic valve replacement solution. Totally, for the reporting period 22 patients had a reintervention on the valves of the heart, thus accounting for 18% of discharged patients. In 13 cases, the solution was performed through aortic valve replacement (in all cases it was in connection with the structural dysfunction); there were 4 cases related to mitral and aortic valves, 4 cases of intervention on only the mitral valve, and in one case the primary mitral valve replacement was done. Altogether we explanted 6 "AB-Mono", 11 – "AB-Composite", 5 – "Kemkor" ("NeoCor", Russia) and 3 "PeriCor" ("NeoCor", Russia) prestheses. In neither case there was a need for "AB-Neo" bioprosthesis explantation (despite the fact that two reoperations on mitral valve were produced in patients with previously implanted "AB-Neo "prostheses in the aortic position).

Thus, freedom from reoperation in the total group of patients by the end of one-year follow-up was 99±1%, by the end of the third year it made 96±2%, by the fifth – 84±5%, by the seventh – 58±9%, by the tenth year – 25±10%. Mostly (n=19) reoperations were done in patients, who at the time of implantation were below 60; this latter proves once again the inexpediency of epoxy-treated xenovalves implantation in the left side of the heart of young and middle age patients without the absolute evidence of medical intervention.

The freedom from explantation of "AB-Neo" prosthesis made 100% throughout the entire period of observation. For "AB-Mono" and "AB-Composite" prostheses this figure was virtually the same throughout the study and did not significantly differ (p=0.78) reaching 26-29% at 126 months.

As mentioned above, we did not observe complications such as abscess and hematoma accompanied by a detachment from the prosthesis or the annulus of the aortic wall. However, in the long-term observation we recorded several cases of prosthetic endocarditis accompanied by the formation of subvalvular abscesses and one case of acute endocarditis proceeding with destruction of the mitral bioprosthesis, but without changes in the stentless aortic valve.

Totally, for the period under review, we recorded 10 cases of prosthetic endocarditis in the late period. In six cases these were patients with prosthetic multivalves, in the other cases – isolated aortic valve prostheses. In seven subjects (14% of discharged patients), "AB-Composite" prosthesis was implanted in the aortic position; in two patients (8% of discharged subjects) the "AB-Mono" prosthesis was implanted. In one case (2% of discharged patients), we observed the development of late prosthetic endocarditis in a patient, who had implanted prosthetic aortic valve prosthesis "AB-Neo" and mitral – "PeriCor" with the formation of the mitral bioprosthesis dysfunction without affecting the aortic xenotissue. A successful mitral valve replacement was performed.

By the end of the first year of observation freedom from prosthetic endocarditis in patients implanted with the prosthesis "AB-Mono" was 100%; by the end of the fifth year – 87±9%, by the tenth year – 87±9%; in patients with the implanted prosthesis "AB-Composite" these indices made 90±4%, 87±5% and 73±10%, respectively, whereas in patients with the implanted prosthesis "AB-Neo" the indices amounted 100%, 94±6% and 94±6%, respectively.

We would emphasize that the groups did not differ significantly on freedom of prosthetic endocarditis in the late period (*p*=0.47); however, more often its development in patients with implanted prosthetic devices "AB-Mono" and "AB-Composite" was more likely caused by an infectious background at the primary operation.

The dynamic observation recorded six episodes of thromboembolism (5% of discharged patients), in particular: 5 cases of acute cerebrovascular accidents and 1 case of thromboembolism in a pool of lower limb arteries. The freedom from thromboembolic complications at the end of the follow-up first year was 97±1%, by the end of the third year − 94±3%, by the tenth year − 87±7%. Two observations of thromboembolic incidents were recorded in patients, who underwent isolated aortic valve prostheses, in the other cases these incidents were registered after multivalve substitution. In this context, it is not necessary to talk about the influence of the implanted prostheses on the risk of thromboembolic complications in the long-term period (*p*=0.52). Two observations of stroke occurred against violations of anticoagulation therapy, and in one case − after the complete withdrawal of anticoagulants and performed haemostatic therapy for gastrointestinal bleeding. In other cases no gross violation of anticoagulant therapy was registered, but patients had risk factors for thrombotic events: atrial fibrillation (n=2), low left ventricular myocardial contractility (n=1), thrombosis of the left atrium in history (n=1). Two observations of thromboembolism occurred against the background of the mitral bioprosthesis structural dysfunction (intact aortic valve), in one case − that of aortic bioprosthesis. In general, the instantaneous risk of thromboembolic complications in the late period of no more than 0.1-1% is considered as a good indicator.

Given the above, we believe the prescription of indirect anticoagulants for up to 6 months after surgery for aortic valve stentless bioprosthesis to be sufficient. Later on, they can be cancelled with no indications for further use without increasing the risk of thromboembolic complications.

Gastrointestinal bleeding due to intake of anticoagulants was recorded in 1 (0.8%) patient. The cause of bleeding was overdose of warfarin with the increased International Normalized Ratio (INR) up to 6.5. Thus, freedom from the "big" anticoagulant-related complications by the end of the observation period (126 months) made 97±3%. The instantaneous risk throughout the remote period ranged from 0.05 to 0.5%.

Regularly occurring and very inconvenient small bleedings were observed in 2 (1.6%) patients. In both cases they were nose bleeds that are difficult to be coped by local haemostatic therapy. One patient did not take anticoagulants, the second had no violations in the mode of anticoagulation therapy (INR in the range of 2-3 in all the period of observation).

DISCUSSION

Numerous studies are devoted to long-term results of aortic valve replacement with different models of stentless biological prostheses [*Westaby S. et al., 1998; Polvani G. et al., 2005; Deleuze P. et al., 2006; David T. et al., 2008; Musci M. et al., 2008*]. Several authors have shown better survival for patients with implanted stentless prostheses compared with the skeletal analogues. This phenomenon is associated with the better physiological characteristics of the stentless devices functioning and a more rapid regression process of the left ventricular hypertrophy [*Tamim M. et al., 2005; Bové T. et al., 2006*]. The randomized study conducted under the direction of S. Lehmann showed that the eight-year survival was significantly better in patients undergoing substitution of the aortic valve with prostheses of "Medtronic Freestyle" ("Medtronic", USA) or "Toronto SPV" ("St. Jude Medical", USA) (78±4%) compared with a group of patients, who had a prosthetic xenovalve carcass "Carpentier-Edwards" ("Edwards Lifesciences", USA) [*Lehmann S. et al., 2007*]. In our study, the actual long-term survival was 93% by the end of 10-year observations, while in patients implanted with the "AB-Neo" model, there was not a single case of death during the 6-year period. The main cause of death likewise the above studies was progression of heart failure. Only in one case death occurred on the background of diagnosed aortic bioprosthesis dysfunction.

An important indicator for estimating long-term results is the freedom from structural dysfunction of the bioprosthesis. Theoretically, the lack of a hard skeleton should lead to a decrease in stress loads on the cusp [*Schoen F. et al., 2005; Zheleznov S. et al., 2011*]. However, empirical research does not support the theory that formation of tears, calcification, or other defects of the valves at implantation of stentless prostheses occurs with almost the same frequency as that of the framed [*Aupart M. et al., 2006; Mohammadi S. et al., 2006*].

Data obtained in our study, on the main, repeat dynamics obtained with imported glutaraldehyde-treated analogues: the freedom from structural dysfunction in elderly and senile patients was 67% by the end of the 10th year of observation. At the same time, dynamic observation revealed a clear dependence of the structural dysfunction risk and the patient's age at the time of implantation: the younger the recipient, the higher the risk of xeno-tissue degeneration in the late period. In one of the few studies on the implantation of stentless prostheses to young patients, M. Vrandecis and co-authors reported on the best long-term results of prosthesis "Biocor Stentless" ("BioCor Ind.", USA) in comparison with its carcass analogue [*Vrandecic M. et al., 2000*]. Currently, we hold the same opinion as the majority of surgeons: implantation of biological prostheses (regardless of the model) can be performed in patients of younger and middle age only in exceptional cases, upon the patient's informed consent and subject to a higher (in comparison with mechanical prostheses) risk of dysfunction in the delayed period.

Development of clear criteria for patient selection and improvement of the implantation technique of stentless prostheses, as well as redesigning incurred by the manufacturer, allowed us to obtain good results for implantation of xenovalve "AB-Neo". We can confidently recommend it to a broad clinical application.

CONCLUSION

Stentless epoxy-treated bioprostheses demonstrated good clinical and hemodynamic results after implantation in the aortic position of the sick elderly and senile patients. In young and middle age patients the risk of structural dysfunction significantly increases during dynamic observation that entails repeated surgery. Changes contributed to the design of "AB-Neo" prosthesis in the form of sewn cuff of xenopericardium, repeating contours of the aortic valve annulus, as well as implantation of prostheses with size of 2-4 *mm* larger than the diameter of the annulus have resulted in significant reduction of the trans-prosthetic gradient in the remote postoperative period and diminished the risk of adverse outcomes.

REFERENCES

1. *Akins G.W, Miller D.C., Turina M.I.* Guidelines for reporting mortality and morbidity after cardiac valve interventions. J. Thorac. and Cardiovasc. Surg. 2008; 135: 732-738.
2. *Aupart M.R., Mirza A., Meurisse Y.A., Sirinelli A.L., Neville P.H., Marchand M.A.* Perimount pericardial bioprosthesis for aortic calcified stenosis: 18-year experience with 1133 patients. J. Heart Valve Dis. 2006; 15: 768-776.
3. *Bové T., Belleghem Y.V., François K., Caes F., Van Overbeke H., Van Nooten G.* Stentless and stented aortic valve replacement in erderly patients: factor affecting midterm clinical and hemodynamical outcome. Eur. J. Cardiothorac. Surg. 2006; 30(5): 706-715.
4. *David T.E., Feindel C.M., Bos J., Ivanov I., Armstrong S.* Aortic valve replacement with Toronto SPV bioprosthesis: optimal patient survival but suboptimal valve durability. J. Thorac. Cardiovasc. Surg. 2008; 135(1): 19-24.
5. *Deleuze P.H., Fromes Y., Khoung W., Maribas P., Lomaire S., Bical O.M.* Eight-year results of Freestyle stentless bioprosthesis in the aortic position: a single-center study of 500 patients. J. Heart Valve Dis. 2006; 15: 247-252.
6. *Hubulava G.G., Shihverdiev N.N., Gavrilenkov V.I., Kucherenko V.S.* [Stentless bioprosthees in surgery of aortic valve defects] [published in Russian]. St. Petersburg. 2009. 187 p.

7. *Karaskov A.M., Barbarash L.S., Semenov I.I., Astapov D.A., Zhelezchikov V.E., Zhuravleva I., Gantimurova I.L., Litasova E.E.* [Tactical and technical aspects of implantation of xeno-aortic stentless bioprosthesis "Kemerovo-AB-Composite Neo"] [Article in Russian]. Pathology of the circulatory and cardiac surgery. 2007; 3: 15-19.

8. *Lehmann S., Walther T., Kempfert J., Leontjev S., Rastan A., Falk V., Mohr F.W.* Stentless versus conventional xenograft aortic valve replacement: midterm results of a prospectively randomized trial. Ann. Thorac. Surg. 2007; 84: 467-472.

9. *Mohammadi S., Baillot R., Voisine P., Mathieu P., Dagenais F.* Structural deterioration of the Freestyle aortic valve: mode of presentation and mechanisms. J. Thorac. Cardiovasc. Surg. 2006; 132: 401-406.

10. *Musci M., Siniawski H., Pasic M., Weng Y., Loforte A., Kosky S., Yankah C., Hetzer R.* Surgical therapy in patients with active infective endocarditis: seven-year single centre experience in a subgroup of 255 patients treated with the Shelhigh stentless bioprosthesis. Eur. J. Cardiothorac. Surg. 2008; 34: 410-417.

11. *Polvani G., Barili F., Dainese L., Muratory M., Porqueddu M., Sala A., Biglioli P.* Long-term results after aortic valve replacement with the Bravo 400 stentless xenograft. Ann. Thorac. Surg. 2005; 80: 495-501.

12. *Schoen F.J., Levy R.J.* Calcification of tissue heart valve substitutes: progress toward understanding and prevention. Ann. Thorac. Surg. 2005; 79: 1072-1080.

13. *Tamim M., Bové T., Van Belleghem Y., François K., Taeymans Y., Van Nooten G.J.* Stentless vs. stented aortic valve replacement: Left verticular mass regression. Asian Cardiovasc. Thorac. Ann. 2005; 13(2): 112-118.

14. *Vrandecic M., Fantini F.A., Filho B.G. de Oliveira O.C., Da Costa I.M., Vrandecic E.* Retrospective clinical analysis of stented vs stentless porcine aortic bioprostheses. Eur. J. Cardiothorac. Surg. 2000; 18: 46-53.

15. *Westaby S., Huysmans H.A., David T.E.* Stentless aortic bioprosthesis. Ann. Thorac. Surg. 1998; 65: 235-240.

16. *Zheleznov S.I., Isayan M.V., Astapov D.A., Sisakyan V.G., Harutyunyan G.G.* Results of aortic valve prosthesis with "Biolab KA/PT" skeletal biological implants in patients above 60. The New Armenian Medical Journal. 2011; 5(2): 44-48.