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# RESULTS OF CORRECTION OF AORTIC VALVE DEFECTS USING SMALL-DIAMETER "BioLAB" XENOPERICARDIAL PROSTHESIS IN OLD PATIENTS

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A prosthesis-patient mismatch (PPM) describes a state in which the valve prosthesis implanted during surgery is too small in relation to the patient's body size. This leads to high transvalvular pressure gradients. We investigate direct results and dependence of transvalvular pressure gradients on body mass index and surface area in patients after correction of aortic valve defects using small-diameter BioLAB prosthesis. **Material and methods.** From January 2011 to August 2018, 65 small-diameter (18, 20) BioLAB scaffold xenopericardial prostheses were implanted in aortic position at the Department of Emergency Surgery for Acquired Heart Defects, Bakulev National Medical Research Center of Cardiovascular Surgery. The average age of the patients was 75.4 ± 4.1 (65–86 years). The average patient body mass index was 25.74 ± 5.11 kg/m$^2$ (19.57–39.54). The average body surface area was 1.79 ± 0.15 (1.54–2.18). **Results.** Isolated aortic valve replacement was performed in 38 (58%) patients, the rest of the surgeries were combined with other techniques. There were no reoperations due to early prosthetic endocarditis or prosthetic dysfunction in hospital. Hospital mortality was 6% (4 patients). Correlation dependence of peak pressure prosthesis gradient on body surface area and body mass index was 10% and 8%, respectively. **Conclusions.** This study confirmed the safety and effectiveness of using small-diameter BioLAB scaffold xenopericardial prostheses in aortic valve position.

*Keywords: aortic valve replacement; bioprosthetic replacement; prosthesis-patient mismatch.*

Over the past decades, as a result of aging population in general, an increasing number of elderly patients are referred to aortic valve replacement surgery. Biological prostheses are strongly recommended for this cohort, since they provide freedom from lifelong administration of indirect anticoagulants and potential durability, which provides better survival without valve-dependent complications compared to mechanical prostheses [4].

In 2004, the Bakulev National Medical Research Center of Cardiovascular Surgery (Moscow, Russian Federation) was the first in Russia to create a low-profile xenopericardial prosthesis on a rigid frame for an aortic position of 18, 20, 22 and 24 mm. The first experience with prosthesis implantation showed good immediate results and excellent hemodynamic parameters in the early postoperative period [1]. Early results showed significant regression of left ventricular myocardial mass in patients with critical aortic valve stenosis and severe left ventricular hypertrophy [2].

Our report analyzes the experience of using the small size BioLAB scaffold xenopericardial prosthesis in elderly patients, considering the peculiarities and risks of the hospital period, the occurrence of structural valvular degeneration, non-structural dysfunctions and endocarditis after surgery.

## MATERIALS AND METHODS

January 2011 to August 2018, the emergency surgery department of acquired heart defects implanted 65 BioLAB frame xenopericardial prostheses of small [18, 20] size into the position of the aortic valve; one patient received a size 20 prosthesis twice, the second time due to late prosthetic endocarditis. The average age of patients was 75.4 ± 4.1 (65–86). Of 64 patients, there were 53 (85%) women, 10 (15%) men. In addition to general clinical examination methods, all patients underwent coronarography before surgery. According to the study results, the problem of the need for coronary artery bypass grafting was resolved. Operational mortality was defined as the death of patients during hospitalization. Postoperative serious complications worsening the prognosis of the course of the underlying disease were considered mediastinitis, prolonged ventilation, pneumonia, and rethoracotomy. BSA and BMI were measured in all the patients. Weight was considered insufficient with the BMI less than 20 kg/m$^2$, normal BMI from 20.0 to 24.9 kg/m$^2$, and excessive with BMI from 25.0 to 29.9 kg/m$^2$, obesity was stated with BMI of 30.0 to 34.9 kg/m$^2$ and morbid obesity with BMI of over 35 kg/m$^2$.

Transthoracic echocardiography was performed on all patients before surgery and in the early postoperative pe-

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riod (10–30 days after surgery). To calculate the average and peak systolic gradients on the aortic valve, a modified Bernoulli formula was used. In the postoperative period, in addition to gradients on the aortic prosthesis, the effective area of the hole, the indexed area of the hole, the mass of the left ventricular myocardium and the indexed mass of the left ventricular were measured. All measurements of peak and systolic gradients on the aortic prosthesis were performed at blood pressure indices of 110–130/70–90 mmHg and HR of 60–90 bpm. The studies were performed on SiemensAcuson and HewlettPackard Sonos-2500 devices with sector phase-electronic sensors with 2.5 and 3.6 MHz frequencies.

## Statistical analysis

The statistical analysis was carried out with standard procedures (Student t-test, Mann–Whitney U-test, Chi-square test); for quantitative indicators, the mean value (M), standard deviation (SD), maximum and minimum values, median, and IQR were defined.

## RESULTS

The characteristics of all operated patients are presented in Table 1. The average BMI was 25.74 ± 5.11 kg/m$^2$ (19.57–39.54). According to our classification used by us, 19 patients were overweight, 12 obese (BMI over 30 kg/m$^2$) and 8 had morbid obesity with BMI more than 35 kg/m$^2$. All operations were performed under cardiopulmonary bypass and pharmaco-hypothermic cardioplegia. The main access used was median sternotomy, six patients (9%) underwent a ministernotomy (j-shape). The indications for access were obesity in three patients (BMI 35.43; 39.54 and 33.79), obstructive pulmonary disease with decrease to 47% and osteoporosis. The patients were aged 70, 78, 79 (two patients), and 86 (two patients). All patients underwent an isolated aortic valve replacement. In three patients, the sternotomy was repeated due to previously performed interventions (aortic valve mechanical prosthesis, aortic valve BioLAB scaffold xenopericardial prosthesis, and bypass (anterior interventricular). One patient was previously implanted with the prosthesis in the aortic position endovascularly, regrafted as the result of prosthesis degeneration after four years (Table 2). 4 prostheses of size 18 and 61 of size 20 were implanted.

There were no reoperations associated with early prosthetic endocarditis or dysfunction at the hospital stage. One patient was reoperated 15 months after surgery due to late prosthetic endocarditis; she was implanted with a size 20 "BioLAB" frame xenopericardial prosthesis. The operation went as planned, without postoperative AEs, and the patient was discharged from the department on the 10$^{th}$ day in a satisfactory condition.

The average resuscitation time spent in the ICU was 48.1 ± 38.7 h (19 to 521 h).

Table 1

**Demographic indicators and risk factors (n = 65)**

| Parameter | Abs. (%) |
|---|---|
| Mean age | 75.4 ± 4.1 (65–86) |
| Over 75 | 39 (60%) |
| Gender, f/m | 55(85%) / 10 (15%) |
| BMI (kg/m$^2$) | 25.74 ± 5.11 (19.57–39.54) |
| BSA (m$^2$) | 1.79 ± 0.15 (1.54–2.18) |
| Arterial hypertension | 28 (44) |
| Diabetes melitis | 13 (30) |
| CVA in history | 3 (5) |
| COPD | 11 (17) |
| LVEF (%) | 61.96 ± 5.9 (40–80) |
| FC III–IV NYHA | 65 (100) |

Table 2

**Surgical interventions and intraoperative parameters (n = 65)**

| Intervention | Abs. (%) |
|---|---|
| Aortic valve replacement (AVR) | 38 (58%) |
| AVR + mitral valve plasty | 9 |
| AVR + tricuspid valve plasty | 6 |
| AVR (ministernotomy) | 6 (9%) |
| AVR + myectomy | 3 |
| AVR + CABG | 14 (22%) |
| Regrafting (+ after TAVI) | 3 |
| *CPB (min) | 120 (41) |
| *Aortic compression time (min) | 76 (12) |

*Note.* * – median (IQR).

Table 3

**Hemodynamic parameters of the early postoperative period (n = 61)**

| Parameter | Mean (range) |
|---|---|
| ESV | 34.5 ± 12.0 |
| EDV | 99.8 ± 28.4 |
| LVEF | 61.54 ± 8.53 |
| Peak, mmHg | 16.6 ± 5.7 (6–27) |
| Mean, mmHg | 8/6 ± 3.4 (2.8–17) |

The analysis of hemodynamic parameters showed that the maximum gradient on the size 20 prosthesis was 27 mm Hg (peak) and 17 mm Hg (mean systolic) in one patient with the BSA of 1.83 and BMI of 24.51 kg/m$^2$. We studied the effect of BSA and BMI on the peak gradient of the aortic prosthesis in the early postoperative period (Table 3). The correlation dependence turned out to be very low and reached 10% and 8%, respectively (Fig. 1, 2).

At the hospital stage, there were 4 (6%) lethal casts with the ages of 71, 75, 77 and 86. The causes were not related to the prosthesis type. One of the patients who died, aged 77, had the BMI of 19.57 and was the only one with cachexia. She endured the operating period

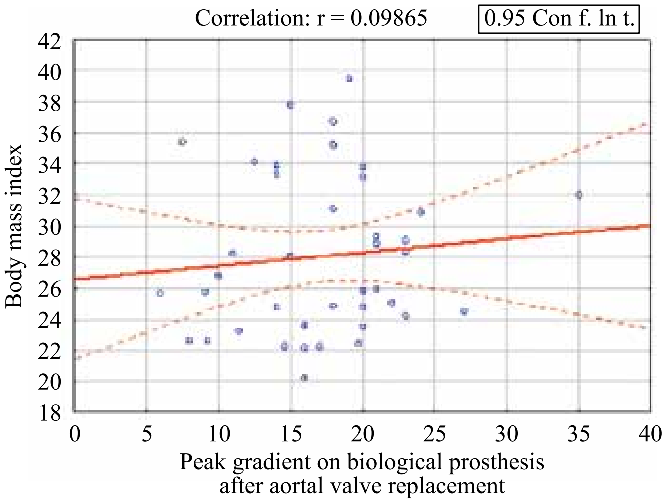


Fig. 1. Dependence of the peak gradient of the aortic prosthesis on the patient's BMI (correlation dependence 10%)

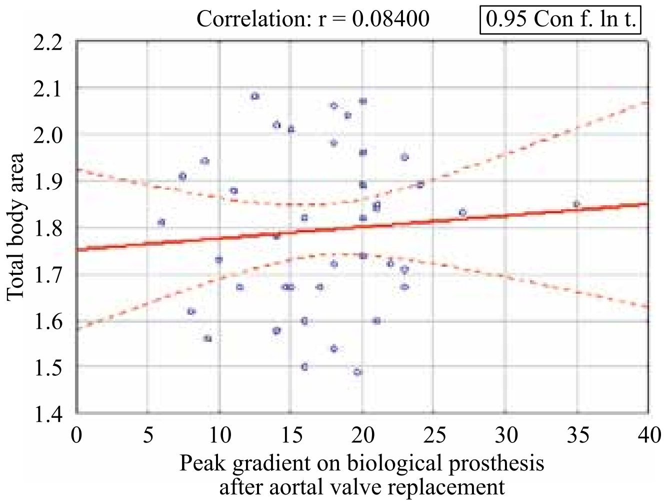


Fig. 2. Dependence of the peak gradient of the aortic prosthesis on the patient's BSA (correlation dependence 8%)

well, was transferred to the ward on the 2nd day, however, physical activity was restoring extremely slowly, and on the 9th day of being in the ward, her condition worsened, pneumonia was diagnosed, and the patient was transferred to the ICU with respiratory failure. Further, heart and multiple organ failure progressed. One patient, operated at the age of 86, with the BMI of 21.26, also went through a smooth postoperative period, was transferred to the ward, but at night of the 7th day there was a sudden cardiac arrest followed by resuscitation which was complicated by multiple organ failure. Another 75-year-old patient at the stitching stage of the sternum experienced massive bleeding (1.5 L) from the aortotomy incision, the sternum was reconstituted, artificial circulation was connected, and the aortotomy defect was sutured. However, due to prolonged aorta clamping and time of cardiopulmonary bypass, multiple organ failure progressed, and the patient died. Another patient, 71 years old, died of multiple organ failure; she was operated for post-radiation heart damage (aortic stenosis and coronary heart disease), a long and traumatic operation was the result of the initial severity, a large amount of surgery, a long period of aorta clamping and cardiopulmonary bypass.

## DISCUSSION

In Europe, the prevalence of aortic stenosis is 3–8% among people over 75. It is known that in the absence of treatment in 90% of patients with severe aortic stenosis, the expected life expectancy does exceed 10 years, and 50% of patients die within 2 to 3 years after the onset of the disease symptoms [11]. Calcined aortic stenosis, i.e. the formation of fibro-calcium nodules on valve structures, has a prevalence of 0.4% in the general population and 1.7% in the population of people over 65 [12]. The degenerative disease has become the most common cause of aortic valve disease in developed countries. These changes are no longer considered a benign consequence of aging, valve calcification is the result of an active process, which, like atherosclerotic vascular disease, caused by destruction of the base membrane between the endothelium and connective tissue of the leaflet, inflammatory cell infiltration, and lipid deposition. Diabetes, hypercholesterolemia, hypertension, and smoking [13] are still the risk factors.

Aortic valve replacement in the treatment of aortic stenosis is one of the most common heart valve operations performed in current cardiac surgery. Typically, mechanical valves, which are more thrombogenic but also more durable, are implanted in patients under 65, while biological valves are mainly used in older people. The problem of tissue valves is well known, it is their tendency to degenerate [14]. However, more than half of the valves used in the world to replace the aortic valve are bioprostheses, as a result of the patients' preference and an increase in the number of long-living persons in the general population, especially after the the TAVI technique was introduced in 2007. Predictors of bioprosthesis tissue degeneration include patient-related factors (younger age, higher body mass index), cardiovascular and related factors (smoking, diabetes, dyslipidemia, renal failure, left ventricular hypertrophy, and small prosthesis size). An analysis of the long-term results of implantation of 12,569 Carpentier-Edwards scaffold xenopericardial prostheses showed that for patients under 60, the reoperation risk associated with degeneration in 10, 15 and 20 years was 5.6% (95% confidence interval [CI], 4.7–6.8), 20% (95% CI, 17–23) and 45% (95% CI, 39–52), for patients of 60 to 80 – 1.5% (95% CI, 1.3 to 1.7), 5.1% (95% CI, 4.4 to 5.8) and 8.1% (95% CI, 6.7 to 9.7), respectively, and for patients over 80 – 0% (for the entire observation period). Earlier, we reported that the indication for implanting a biological prosthesis in the aortic position is the age over 65 [3]. However, now we consider the indication for implantation of a bioprosthesis into the aortic position to be over 70, therefore in this study the average age of patients is 75.4 ± 4.1 years, and 60% of them are over 75.

Many researchers believe that the small size of the prosthesis is not directly tied to the risk of degeneration and explantation of the bioprosthesis in the long term, but a problem that must be considered when implanting the small size of the prosthesis in the aortic position is the probability of a mismatch between the prosthesis and the patient (PPM), which was first described in 1978 by Rahimtoola [9]. Douglas R. Johnston et al. investigated the effect of the peak gradient on the prosthesis in the early postoperative period on long-term results and, in particular, the relationship of indicators with the prosthesis degeneration. It turned out that high peak gradient values affected bioprosthesis degeneration to a greater extent in young patients and were not associated with biological tissue degeneration in patients over 80. An increase in the peak gradient by more than 10 mmHg from the normal value in the early postoperative period in young patients was associated with a more than twofold-increased risk of explantation associated with degeneration of biological tissue 20 years after surgery [14]. In the present study, despite the use of only small sizes of frame xenopericardial prostheses, including patients with obesity and a large BSA, the average peak gradient was 16.6 ± 5.7 (6–27) mm Hg and the average systolic gradient of 8.6 ± 3.4 (2.8–17) mm Hg, We investigated the dependence of the peak gradient on the patient's myocardial mass index and on the surface area in the early postoperative period. It turned out that the correlation dependence is extremely low: 10% and 8%, respectively. Zheleznev S.I. et al. [4] analyzed the results of implantation of 52 BioLAB prostheses of 20 sizes for old and greater age patients. In this group, average BMI was 28.1 ± 5.5 kg/m$^2$, i.e. slightly more than in the present study (25.74 ± 5.11 kg/m$^2$) and the average BSA was 1.6 ± 0.1. A study by the authors of trans-prosthetic gradients in the early postoperative period showed: peak gradient 23 ± 6 mm Hg, average systolic 12 ± 4 mm Hg, effective area 2.4 ± 0.2 sq.cm and indexed area of the hole 1.5 ± 0.2, which corresponds to good performance. Zheleznev S.I. et al. [4] conclude that the technical simplicity of implantation, the formation of a sufficiently large passage opening, and blood flows characterized by laminarity, predict the stability of the results in the early postoperative period.

The literature reports discuss the effect of the prosthesis size and the indexed area of the hole on the regression of left ventricular myocardial mass, which largely determines the quality of life in the long term and overall survival of patients. However, Rajappan et al. demonstrated that the degree of disturbance of the reserve of coronary blood flow measured by positron emission tomography was associated with the severity of valve stenosis before surgery, not with the mass of the left ventricle. Changes in coronary blood flow after aortic valve replacement were not directly related to regression of left ventricular myocardial mass, but were more dependent on the magnitude of the change in the indexed area of the valve opening as a result of aortic valve prosthetics [6, 7]. Garcia et al. [8] reported that if the index of the indexed area of the opening on the aortic valve exceeds 0.8–0.9 cm$^2$/m$^2$, then the reserve of coronary blood flow is practically unchanged but decreases sharply when the indexed area of the opening is below this threshold, and it becomes almost completely exhausted when the indexed area of the hole is less than 0.5 cm$^2$/m$^2$.

Basically, all the presented results of aortic valve replacement in elderly patients necessarily include a subgroup with coronary heart disease and coronary artery bypass grafting. The subgroup analysis shows differences in the results of aortic valve replacement with or without coronary artery bypass grafting, but these differences are not statistically significant [10]. In the present study, at the hospital stage, one patient died after correction of the combined pathology; however, it was a patient with post-radiation damage to the heart and coronary arteries. It is known that this pathology is associated with pathological malignant calcification of the base of the heart and coronary arteries, which can lead to a more traumatic surgical process. In general, the treatment of concomitant pathology did not affect the length of hospital stay.

An important question remains open: the impact of BMI on the results of surgical treatment, both at the early stage and in the distant postoperative periods. In the present study, the average BMI was 25.7, which, according to the classification we used, should be classified as overweight. Many studies on patients with congestive heart failure have shown a remarkable association between patients losing weight before surgery and high mortality [16]. The mechanical weight loss associated with heart failure is explained as part of metabolic disorders, namely insulin resistance and excessive catabolic activity due to the release of catecholamines. As a result, the metabolic phenotype of heart failure is characterized by depletion of body tissues, including muscles, fat, and bones, leading to significant weight loss and, ultimately, to cachexia development. Therefore, a favorable prognosis for patients with obesity and heart failure suggests that they have higher metabolic reserves which allow them to better tolerate catabolic stress compared to patients without excess weight [17]. One of the 77 patients who died in our study had a BMI of 19.57 and was the only one with cachexia. She smoothly passed the operating period, but recovery of physical activity was extremely slow, respiratory failure due to muscular-respiratory dysfunction persisted, she felt worse on day 9, pneumonia was diagnosed, and the patient was transferred to the ICU. Further, heart and multiple organ failure progressed. In the present study, a J-shaped ministernotomy was performed for three obese patients in order to avoid the development of respiratory failure and wound complications in the postoperative period. It is known that ministernotomy with isolated aortic valve replacement is a safe procedure, it reduces the risk of blood loss, reduces postoperative hospital bed/day, patients suffer less from pain in the early postoperative period [18, 19]. Nobuyuki Furukawa et al. consider that the main advantages of the ministernotomy should be the reduction in postoperative pain, improved respiratory function, as well as an earlier return to daily activities which is significantly more important for elderly patients than the cosmetic effect of the procedure [20].

We believe that the present study has important clinical significance, as it supplements the accumulated experience and confirms the safety and efficacy of implementing small sizes of BioLAB frame xenopericardial biological prostheses in the aortic position. Based on this analysis, we can say that it is not necessary to resort to methods of expanding the fibrous ring in elderly patients with a narrow aortic root, as the desire to expand the fibrous ring to implant a larger prosthesis lengthens the perfusion time and may put patients at unreasonable risk.

*The authors declare no conflict of interest.*

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