Chapter

Clinical Implication of Cardiac Valve Allografts in Rare Surgical Circumstances

Roman Komarov, Mikhail Nuzhdin, Alisher Ismailbaev and Nikita Bashmakov

Abstract

The unique clinical and surgical experience with cardiac valve allografts is presented in the study. Cutting-edge approach with regard to clinical course of the disease, particular diagnostic findings, patient's preference, and allograft accessibility is highlighted in case series. State-of-the-art techniques, initial and mid-term results are summarized with a specific focus on allograft tissue application in cardiovascular surgery. Four patients underwent surgery during the period between February 2020 and February 2023 with inferior vena cava tumor involvement, destructive double valve endocarditis, rheumatic aortic and mitral insufficiency, and severe tricuspid regurgitation in patients with large ostium secundum and atrial fibrillation. All patients demonstrated an uneventful postoperative course.

Keywords: allograft, inferior vena cava, endocarditis, rheumatic heart disease, tricuspid replacement

1. Introduction

Cardiac valve allografts have been utilized since the late 1960s predominantly for surgical treatment of single valve infective endocarditis, rheumatic heart disease, and congenital valve anomalies [1–4]. The absence of strict indication, challenging surgical technique, along with allograft shortage used to prevent them from being widely acceptable in everyday clinical practice. Due to recent scientific advances in cardiac valve anatomy and physiology, development in surgical and preservation techniques, cardiac valve allografts have demonstrated their feasibility in those clinical scenarios where common valve substitutes have not shown significant clinical superiority [5]. Moreover, in some rare clinical circumstances, the choice between different valve prostheses might be a rather tough decision-making process regarding immediate and long-term results. In our study, we tried to summarize our experience with cardiac valve allografts in unusual clinical situations. The pulmonary artery trunk allograft in the surgical treatment of inferior vena cava tumor involvement, monoblock aorta-mitral homograft for destructive double valve endocarditis, mitral valve allograft in Bekhterev's disease, and mitral allograft (MA) for tricuspid replacement in a patient with large ostium secundum are consequently presented in our study. All four patients successfully underwent surgical repair in two departments with an uneventful postoperative course.

2. Case series description

2.1 Patient's population

During the period between February 2020 and February 2023, four patients underwent surgery due to different cardiac pathology at the two institutions ("Sechenov University" and "Chelyabinsk Regional Clinical Hospital"). All patients, their clinical course, and surgical interventions were considered exclusive regarding technique and cardiac valve allografts implanted. This study was approved by the Regional Ethics Committee of each hospital, and all patients signed their informed consent. The overall patient characteristic is depicted in **Table 1**.

2.2 Inferior vena cava replacement with pulmonary homograft

A 60-year-old woman with a clinical picture of dyspnea, weakness, and discomfort on moderate physical exertion was admitted to the Clinic of Faculty Surgery No. 1 of "Sechenov University". From the previous medical history, there was evidence of a left-sided hemicolectomy performed in 2017 for splenic flexure transverse colon cancer pT4AN2AM0 (TNM 8, histologically moderately differentiated adenocarcinoma). The patient was further operated on twice for liver metastases in 2018 (liver segments 2, 3, and 4A were resected) and in 2019 (liver segmentectomy IV b (the number of segment) was performed). The patient received a total of 8 courses of poly-chemotherapy. Initial investigation showed subtotal thrombosis of the right atrium due to tumor involvement of the vena cava and atrium wall. Contrast-enhanced computed tomography (CT) revealed a hepatic segment I metastasis with inferior vena cava thrombosis, spreading into the right atrial cavity. Thrombotic masses in the right atrial lumen were confirmed by transesophageal echocardiography (TEE).

The patient was scheduled for median sternotomy and upper median laparotomy approach that was performed on February 5, 2020. The stage of mobilization and removal of the first segment of the liver was performed before cardiopulmonary bypass. Standard ascending aorta, superior vena cava, and inferior vena cava in the infrahepatic segment bypass were initiated. After adhesiolysis, the superior vena cava and inferior vena cava (IVC) were snared, and a longitudinal cavatomy was performed. Invasion of the inferior vena cava wall into the tumorous process was revealed. Thrombotic masses were visualized that spread into the right atrium and were fixed to its wall; the tricuspid valve was intact. Radical excision of the tumor masses entailed resectioning the right atrium and inferior vena cava area with subsequent replacement of the part of inferior vena cava and right atrium wall with a cryopreserved pulmonary homograft (28 mm in diameter). The cardiopulmonary bypass time was 67 minutes. The resected tumor, inferior vena cava, and the final view after reconstruction are shown in **Figures 1** and **2**.

In the 3-year follow-up period, transthoracic echocardiography and contrast-enhanced CT depicted no evidence of tumor recurrence.

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	Age (year)/ sex	Primary pathology	Homograft type utilized	Cardiac structure replaced	30-Day mortality	Complication	Follow-up period, month	Mid-term survival
Patient 1	60/F	Metastatic liver cancer	Pulmonary trunk	Inferior vena cava and right atrium	—	—	36	Survived
Patient 2	56/M	Double valve infective endocarditis	Aortomitral block	Aortic root and mitral valve	—	—	6	Survived
Patient 3	52/F	Bekhterev's disease	Mitral valve	Mitral valve	—	—	12	Survived
Patient 4	44/F	Large secondary ASD and severe tricuspid regurgitation	Mitral homograft	Tricuspid valve	—	—	4	Survived

Table 1.
The overall patient's characteristic.

Figure 1.
Intraoperative view. Tumor mass deleted from the inferior vena cava.

2.3 Double valve destructive infective endocarditis treatment with monoblock aortomitral homograft implantation

A 56-year-old male patient with subacute infective endocarditis (presumably from September 2021) with aortic (severe failure) and mitral (severe failure) valve involvement and aortic root abscess was operated on in June 2022. The patient had a commonplace clinical course of infective endocarditis that had been confirmed under current guidelines before admission. Considering the limited but promising world experience with monobloc aorta-mitral homografts, we assumed that monobloc aortomitral homograft implantation could be an alternative to the "standard" Commando procedure. The median sternotomy approach and standard cardiopulmonary bypass with bicaval cannulation and cold cardioplegia. This technique used in our clinic entailed several steps described below.

2.3.1 Technique of aortomitral homograft implantation

1. After the transverse aortotomy, the inspection of aortic valve revealed total leaflet destruction, vegetation, and abscess cavity on the level of aortic annulus. The valve was excised, and total root debridement was performed in order to get rid of infected and necrotic masses. Then deep mobilization of the aortic root, excision of valsalva sinus, and coronary arteries mobilization. From the middle of the noncoronary sinus, an incision was made down to the anterior mitral valve leaflet. The left atrial roof was opened. For better exposure of the mitral

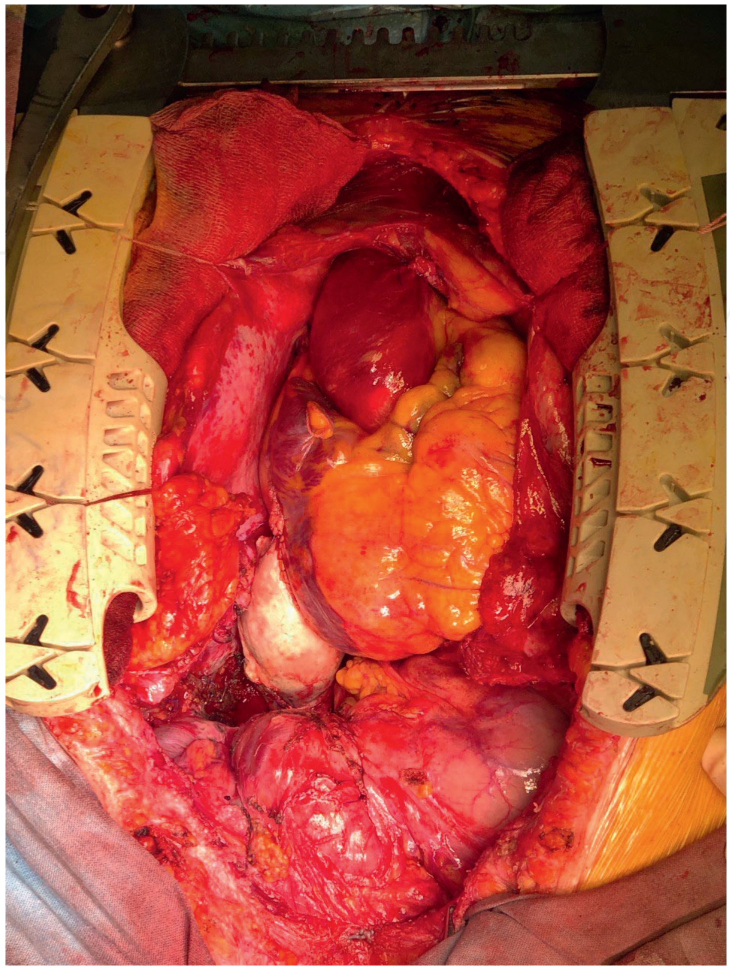

Figure 2.
The final view. Inferior vena cava replaced by pulmonary allograft.

valve, the incision of the left atrium can be extended by dissecting the interatrial septum and the right atrium (**Figure 3**).

2. Having the mitral valve excised, the aortomitral homograft was fixed in the mitral position. The homograft was sewn first along the posterior annulus, then along the anterior one. In the area of the aortomitral junction, homograft sutures were placed oriented to the fibrous triangles, and one suture was placed to capture the aortic fibrous ring tissue, in order to close it (**Figure 4**).

3. The papillary muscles of the homograft were anastomosed side-by-side to corresponding papillary muscles with four interrupted stitches using "Ethibond" 3-0 sutures. The aortic part of the homograft was inserted into the left ventricle (LV cavity and was sewn into the aortic root position afterward (**Figure 5**).

4. The aortic homograft is everted from the LV; the coronary artery mouths are implanted into the homograft. Posterior partial ring mitral homograft annuloplasty is performed (**Figure 6**).

Cardiopulmonary bypass time was 235 minutes; myocardial ischemia time was 210 minutes. The patient was in the intensive care unit for 3 days and in the hospital

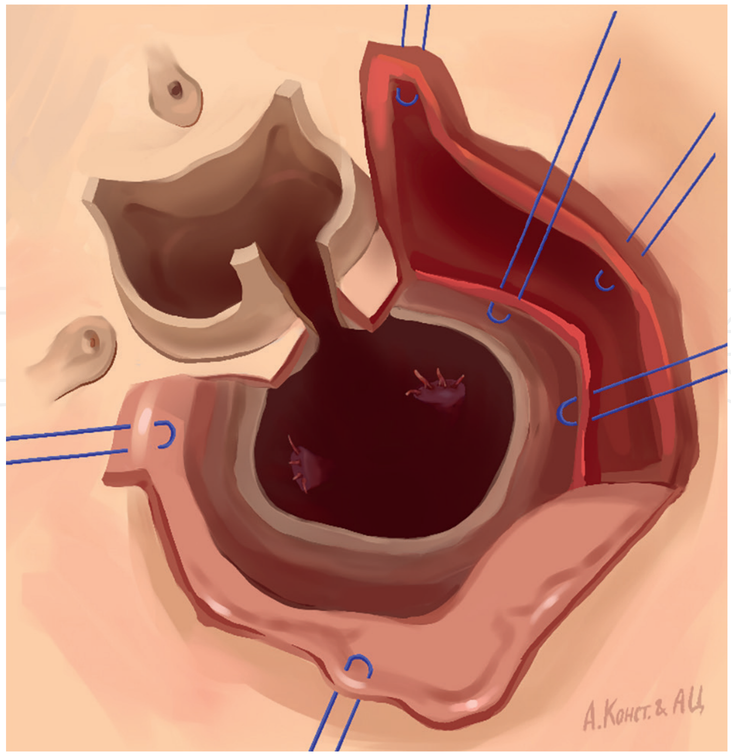

Figure 3.
Aortic and mitral valve are excised. The incision of the left atrium is extended by dissecting the interatrial septum and the right atrium.

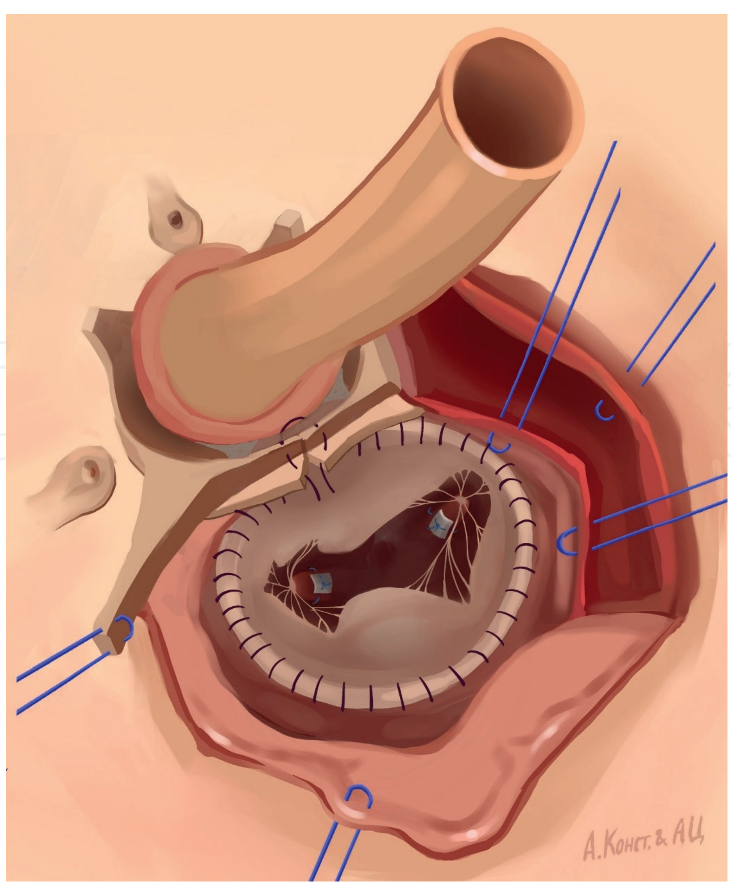

Figure 4.
The aortomitral homograft is fixed in the mitral position.

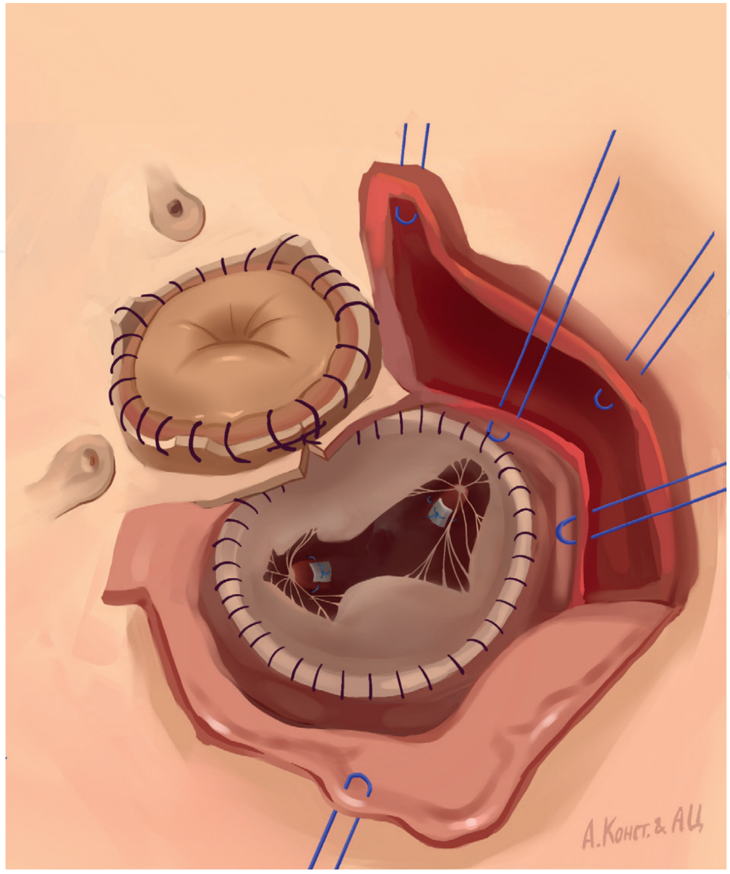

Figure 5.
The aortic part of the homograft is inserted into the left ventricle (LV cavity) and is sewn into the aortic root position.

for 12 days. In the postoperative period, the patient underwent echocardiography assessment and was discharged from the hospital with excellent homograft function.

2.4 Concomitant homograft mitral valve replacement and aortic autopericardial neo-cuspidalization in patient with Bekhterev's disease

A 52-year-old woman with Bekhterev's disease was admitted to the Department of Cardiac Surgery ("Sechenov University") for elective aortic and mitral valve surgery. On admission, the patient's clinical status was presented with pronounced dyspnea at rest, cough, increased fatigue, and moderate pain in the heart area. From the past medical history, we found out that the first manifestation of Bekhterev's disease occurred at the age of 25 with iridocyclitis, which at that time was regarded as a manifestation of herpes-virus infection. At age 42, the presence of the HLA B-27 gene was laboratory confirmed. Back in those days, mild-to-moderate mitral regurgitation was revealed. Four years later, at the age of 46, transthoracic echocardiography showed mild aortic regurgitation. Sulfasalazine was first prescribed in a dosage of 1 g two times a day. In 2022, at the age of 52, after a coronavirus infection, patient's condition went to decline with increased dyspnea and swelling of the lower extremities. Heart auscultation revealed a diastolic murmur, mainly in the area of the aorta, and a systolic noise irradiating to the left axillary region. Spinal mobility was limited due to stiffness in the lower back and in the cervical region. Transthoracic echocardiogram showed enlarged LV (LV end-diastolic diameter 57 mm, end-diastolic volume 190 ml), LV EF at rest 58%,

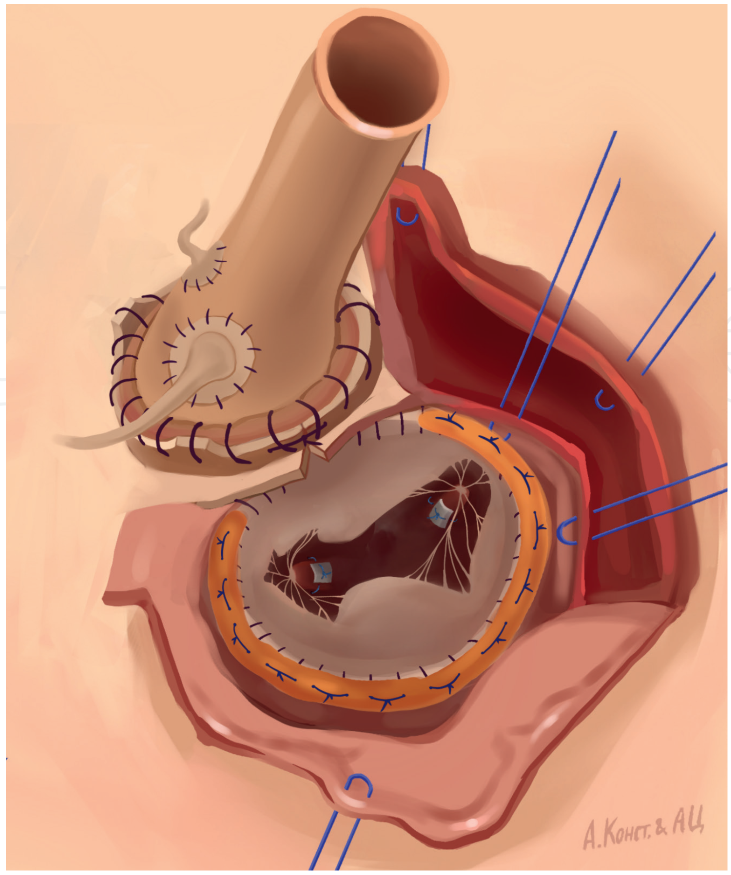

Figure 6.
Posterior partial ring mitral homograft annuloplasty is performed. Final view.

thickened aortic root wall, marginal fibrosis of aortic valve cusps, right coronary cusp thickened, central coaptation defect, and restricted leaflet motion. The mitral valve leaflets were thickened with restricted motion as well. The doppler-echocardiography confirmed severe central aortic regurgitation and severe mitral insufficiency.

2.4.1 Surgical homograft mitral valve replacement and aortic autopericardial neo-cuspidalization

Instead of the mechanical double valve replacement, the autopericardial neocuspidization was opted for aortic valve procedure, while MA was chosen for mitral valve replacement. After the median sternotomy a pericardial flap was harvested with its subsequent preservation in 0.6% glutaraldehyde. Standard cardiopulmonary bypass and cold cardioplegia were applied. Intraoperative assessment revealed bicuspid aortic valve pathology with leaflet fibrosis. Mitral valve leaflets were also significantly thickened and were not considered for mitral repair. Three semilunar cusps of the same size were dissected from the pericardial flap. The aortic valve neocuspidization with autologous pericardium leaflets was performed. The autopericardium valve was formed (**Figure 7a**). The next step was mitral homograft implantation in the mitral position (**Figure 7b**). The mitral homograft papillary muscles were fixed to the LV papillary muscles with four U-shaped sutures using 4-0 sutures. The mitral homograft was placed into the LV cavity, then mitral homograft was fixed to the mitral annulus with continuous 5-0 polypropylene sutures (**Figure 7c**). The posterior mitral annulus was reinforced with soft band (**Figure 7d**). TEE and postoperative

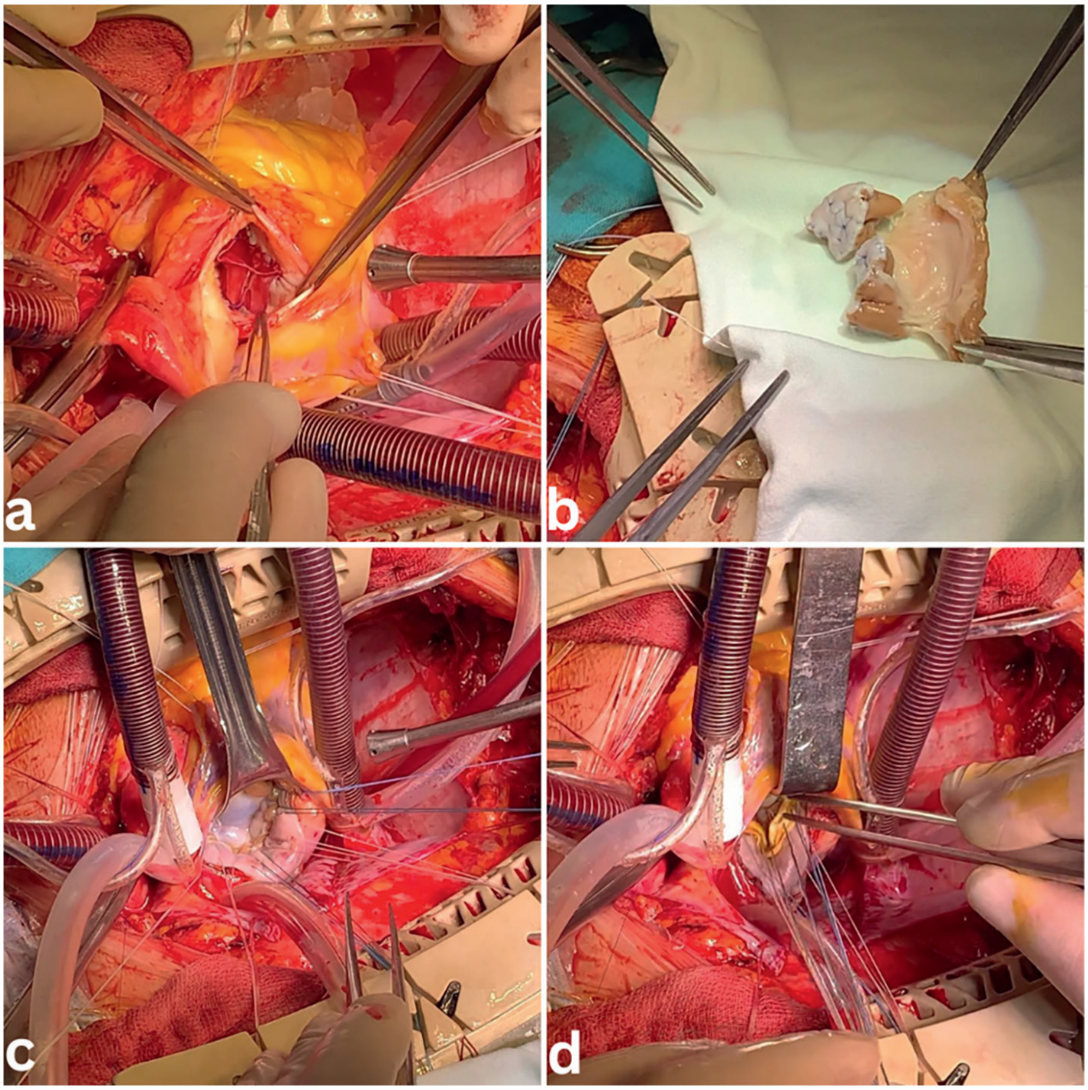

Figure 7.
(a) Aortic valve replacement with autopericardial neo-cuspidalization; (b) mitral allograft; (c) mitral allograft in mitral position; (d) ring implantation.

echocardiography showed improved function of aortic autopericardial neovalve and mitral homograft with only trivial regurgitation. The duration of cardio-pulmonary bypass (CPB) was 182 min, and the aortic cross-clamp duration was 155 min. The patient was discharged on the 14th day after surgery in satisfactory condition, with marked increase in physical tolerance and decreased dyspnea. Transthoracic echocardiography 1 year after the operation shows mild MA regurgitation with peak pressure gradient of 3 mmHg, mean pressure gradient of 2 mmHg, and trivial aortic regurgitation with peak pressure gradient of 8 mmHg, mean pressure gradient of 4 mmHg.

2.5 Homograft tricuspid valve replacement with large atrium septum defect closure and cryoablation procedure in adult

A 40-year-old woman was admitted to the Chelyabinsk Regional Clinical Hospital with severe tricuspid regurgitation, large atrial septal defect (ASD), signs of right sided-heart failure, and persistent atrial fibrillation. The patient reported progressive exercise-induced shortness of breath (New York Heart Association functional class III) during the last 6 months after she had documented the first episode of AF.

2.5.1 Diagnostic assessment

Initial diagnostic workup by echocardiography confirmed large ASD (46 mm), severely dilated right atrium—65 × 81 mm, and right ventricle (RV) – 52 mm, PH of 60 mmHg and severe tricuspid regurgitation (vena contracta—9 mm, regurgitant volume—83 ml). A contrast-enhanced cardiac computed tomography (CCT) revealed a large ostium secundum (53 × 43 mm, 17 cm^2) (**Figure 8**), severely dilated RV (end-diastolic volume of 550 ml, end-systolic volume of 355 ml), and reduced ejection fraction (EF) of 35%, right ventricle fractional area contraction (RV FAC)—25%, tricuspid annulus plane systolic excursion (TAPSE)—10 mm. The patient was scheduled for concomitant surgery. Having discussed all available options for tricuspid surgery, patient's informed concern was obtained with regard to either annuloplasty or homograft replacement. The patient refused either mechanical or stented biological prosthesis because of personal and religious beliefs.

2.5.2 Surgical procedure

Concomitant operation was performed through the medial sternotomy approach with standard cardiopulmonary bypass. The cryoablation procedure was carried before valve repair. TV inspection revealed severely dilated annulus, leaflet shrinkage, and thickening that was assumed to be not appropriate for successful repair. MA was chosen as a valve substitute. ASD was closed by means of a bovine pericardium patch of appropriate size. After several measures had been taken, MA was implanted in the tricuspid orifice. The procedure was accompanied by tricuspid ring implantation. Intraoperative echocardiography (ECHO) demonstrated no residual regurgitation on MA with mean diastolic pressure gradient of 2 mmHg.

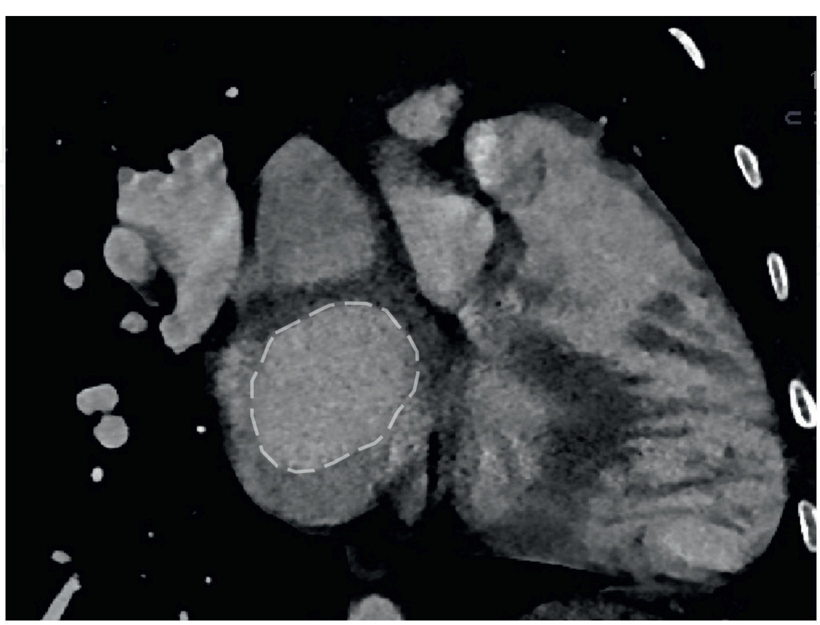

Figure 8.
ECG-gated cardiac CT reformation in interventricular septum plane before operation, mid diastole. Large ASD in the central part of interatrial septum.

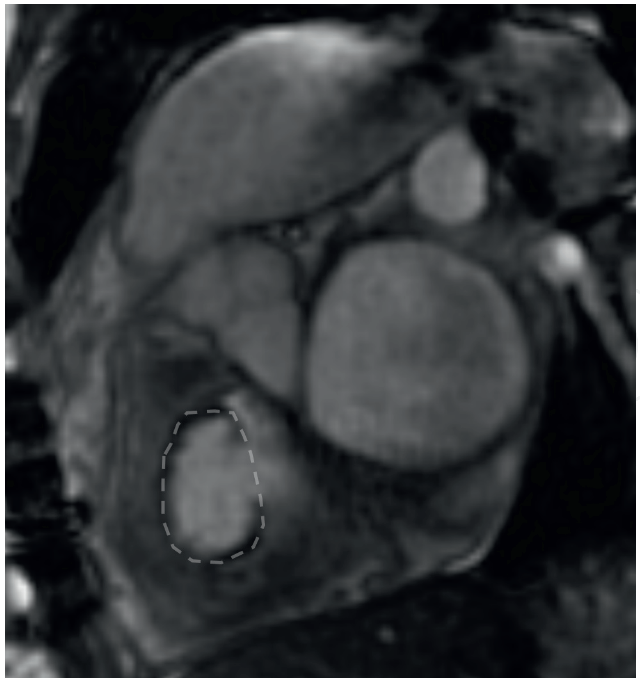

Figure 9.
Short-axis steady-state free precession cardiac MRI in tricuspid plane, diastole. Homograft annulus after surgery. The dashed line indicates valve annulus with annuloplasty ring.

2.5.3 Postoperative follow-up

Postoperative CCT demonstrated reduction in RV volumes with EF of 47%, RV FAC—34% and TAPSE—16 mm. Homograft orifice area was 9 cm^2 and excellent leaflet coaptation was clearly seen (**Figure 9**). TTE demonstrated mean trans-homograft pressure gradient 1.4 mmHg, normal leaflet motion without regurgitation (**Figure 10**). Patient was discharged from the hospital with sinus rhythm and excellent homograft function. Oral anticoagulation therapy was stopped after a 3-month period of intake.

3. Discussion

Cardiac valve allografts have been thought to be plausible valve substitutes in wide spectrum of surgical scenarios. In addition, it is also believed that allograft's availability enables to broad technical opportunities [5, 6]. Regarding radical treatment of hepatocellular carcinoma with tumor thrombi in the inferior vena cava or right atrium, surgical removal of thrombotic masses from the inferior vena cava and the right atrium remains to the most efficient method of treatment that can reduce the risk of systemic metastasis and sudden death due to pulmonary thromboembolism or occlusion of the tricuspid valve by a tumor thrombus [7]. Without surgical repair, the median survival is less than 12 months, and chemotherapy has not demonstrated acceptable survival [8, 9]. Descriptive and comparative analysis of different types of allograft tissue in inferior vena cava replacement has not been provided in available databases. Arterial and venous allografts could also be considered feasible prosthetic material, although pulmonary homograft conduit was optimal for two main reasons. Firstly, pulmonary allograft was available for subsequent use. Secondly, a bigger size

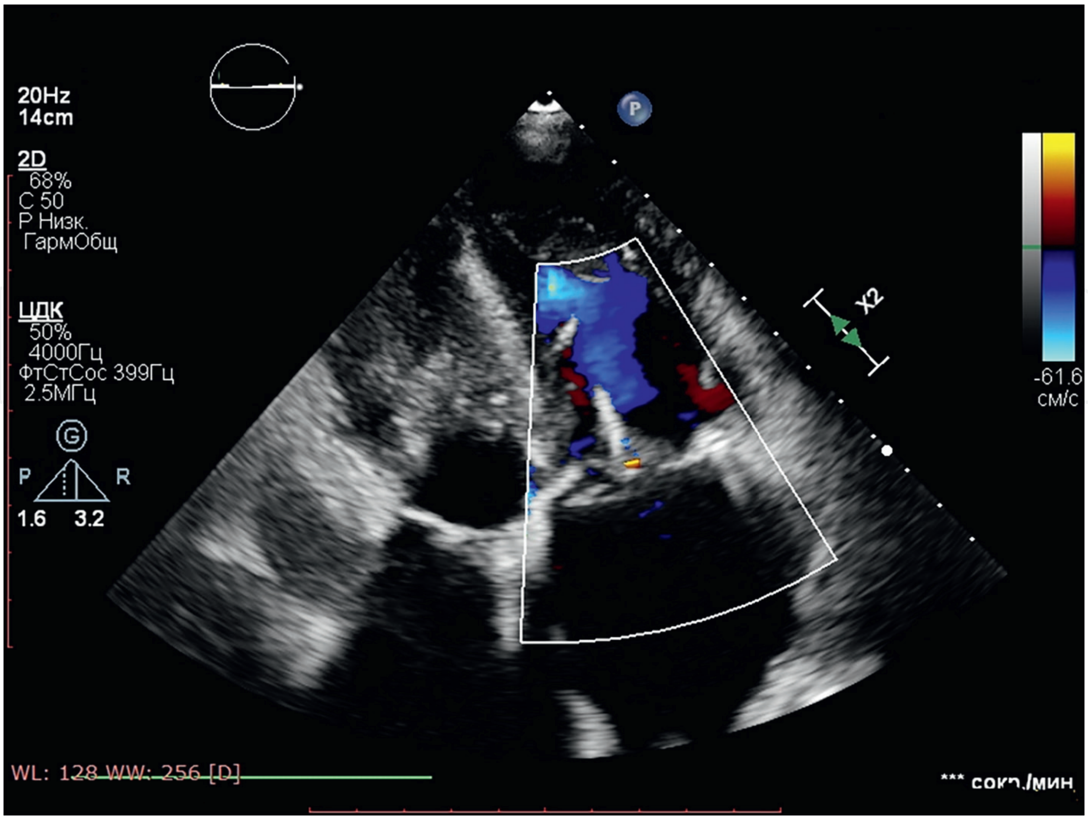

Figure 10.
Postoperative TTE. Apical 4-chamber view. Excellent leaflet coaptation without residual regurgitation on mitral homograft in tricuspid position.

of pulmonary conduit seemed to be more advantageous for dilated patient's inferior vena cava and more suitable for right atrium reconstruction. Nevertheless, diverse spectrum of allograft tissue conduits should be carefully investigated in such procedures. Our experience suggests in favor of radical surgical treatment where allograft tissue demonstrated its relevant implication with excellent results.

Another challenging circumstance is destructive double valve infective endocarditis with central fibrous body involvement. There are no systematic results of aortomitral homograft implantation for such patients, and these operations are rarely performed [10, 11]. Theoretically, the main advantages of the method are the absence of synthetic material and no need for anticoagulation. Another potential benefit of the aortomitral homograft is the preservation of mobility of the supporting apparatus, which may be important for long-term homograft function and cardiac performance. Mechanical valves remain the most commonly used substitute for double valve replacement, still carrying the high risk of bleeding and thromboembolic events in the long run. Potential benefits of allografts in favor of re-infection resistance have not been proved in randomized trials; by the way, such trials are limited. Current clinical guidelines are inconclusive regarding valve choice in different clinical scenarios, which formally enables the heart team to create their own strategy based on the patient's clinical status, urgency, and graft availability. From our point of expertise, allograft double valve replacement might well be taken into account, given full respect to obvious benefits and potential drawbacks in the mid- and long-term.

Concomitant cardiac procedures with cardiac valve allografts are rare and have not been described precisely. Cardiac involvement in Bekhterev's disease usually manifests as aortic insufficiency, aortitis, or cardiac conduction abnormalities. Mitral insufficiency is less commonly defined, predominantly when subaortic fibrosis reaches the anterior mitral valve leaflet [12, 13]. Experience with mitral homograft implantation has shown that valve lesions of rheumatic etiology, which include Bekhterev's disease, may be a major indication for this technique [14]. When it comes to the method of aortic valve repair, there was a choice between a biological valve, the Ross procedure, and neocuspidization, because the patient avoided anticoagulation. Low durability of the Ross procedure in rheumatic disorders may be due to autoimmune response to type IV collagen, which is contained in the valve leaflets [15]. The experience with biological valves in rheumatic diseases is similarly unsatisfactory, with early degeneration and an increased risk of reoperation [16]. We reckon that allografts and reconstructive surgery using autologous materials provide a better hemodynamic profile along with avoidance of lifelong anticoagulation therapy. Autopericardial neocuspidization could be under the scope of surgical interest, regarding their potential "bridging" role in reconstructive surgery, avoiding anticoagulation-related complications and enabling more radical surgery (allograft root replacement) or transcatheter aortic valve replacement in long-term.

Considering MAs application in reconstructive tricuspid surgery, there is a sustained interest in terms of superior initial results, high hemodynamic performance, and potentially lower risk of complication in long-term follow-up [1, 17, 18]. A recent meta-analysis shows neither biological nor mechanical prosthesis provide satisfactory early and long-term results [19, 20]. MA could probably outweigh biological prosthesis in hemodynamic performance and long-term outcomes, but the data is confined to few clinical studies but with promising initial results, which encourage wider acceptance of MA in tricuspid position. Moreover, in cases where tricuspid repair cannot be performed, current guidelines and markets give no particular feedback regarding prosthetic choice, and stented biological valves along with mechanical are still recommended. Our study gives practical insight into feasibility of MA in the treatment of degenerative TV pathology in patients who does not accept traditional prosthetic options. Concomitant cryoablation for atrial fibrillation in combination with homograft implantation has not been described in available databases.

4. Conclusion

Assuming our surgical experience with cardiac valve allografts in unusual clinical cases, we can conclude that allograft valves might take place as a plausible prosthetic tissue in a wide spectrum of diseases. Marked hemodynamic performance and excellent early and mid-term results could be achieved with low risk of complications and zero mortality in selected patients. Technical procedure-related challenges could be confidently resolved by having pliable allograft material available at the time of operation. Patient's desires and preferences still play a crucial role in decision-making. Further investigations are needed to prove potential benefits of allografts in cardiovascular surgery.

Conflict of interest

The authors declare no conflict of interest.

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