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ORIGINAL ARTICLE / ÖZGÜN MAKALE

Aortic valve neocuspidization with the Ozaki procedure in congenital aortic valve disease: Early results

Doğumsal aort kapak hastalığında Ozaki prosedürü ile aort kapak neokuspidizasyonu: Erken sonuçlar

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ABSTRACT

Background: In this study, we present our early results with the Ozaki procedure in the treatment of congenital aortic valve disease.

Methods: Between July 2021 and July 2023, a total of 14 patients (10 males, 4 females; median age: 13.9 years; range, 8.5 to 15 years) who underwent neoaortic valve reconstruction of three leaflets using Ozaki procedure were retrospectively analyzed. Preoperative, postoperative, and follow-up echocardiogram images were evaluated.

Results: Preoperative indications were aortic regurgitation (n=3) or combined aortic stenosis and regurgitation (n=11). The median aortic annular diameter was 23 (range, 19.5 to 25) mm on preoperative echocardiography. The median preoperative peak systolic aortic valve gradient for patients with aortic stenosis was 60 (range, 45 to 93) mmHg. The median preoperative aortic valve regurgitation grade was 4 (range, 3 to 4). Autologous pericardium and bovine pericardium were used in 12 and two patients, respectively. There was no conversion to valve replacement, myocardial infarction, or mortality in the early postoperative period. The median follow-up time was 8.5 (range, 6 to 19) months. One patient who performed the Ozaki procedure with bovine pericardium underwent valve replacement eight months later.

Conclusion: The Ozaki procedure can be performed safely and effectively in congenital aortic valve stenosis and insufficiency with promising early results.

Keywords: Aortic valve neocuspidization, aortic valve reconstruction, Ozaki procedure.

ÖZ

Amaç: Bu çalışmada doğumsal aort kapak hastalığının tedavisinde Ozaki prosedürüne ilişkin erken dönem sonuçlarımız sunuldu.

Çalışma planı: Temmuz 2021-Temmuz 2023 tarihleri arasında Ozaki prosedürü kullanılarak üç kapakçığa neoaortik kapak rekonstrüksiyonu yapılan toplam 14 hasta (10 erkek, 4 kadın; medyan yaş: 13.9 yıl; dağılım, 8.5-15 yıl) retrospektif olarak incelendi. Ameliyat öncesi, ameliyat sonrası ve takip ekokardiyogram görüntüleri değerlendirildi.

Bulgular: Ameliyat öncesi endikasyonlar, aort yetersizliği (n=3) ve aort darlığı ve yetersizliği birlikteliğiydi (n=11). Ameliyat öncesi ekokardiyografide medyan aortik anüler çap 23 (dağılım, 19.5-25) mm idi. Aort darlığı olan hastalar için ameliyat öncesi medyan pik sistolik aort kapak gradyanı 60 (dağılım, 45-93) mmHg idi. Ameliyat öncesi medyan aort kapak yetersizliği derecesi 4 (dağılım, 3-4) idi. On iki hastada otolog perikard ve iki hastada sığır perikardı kullanıldı. Ameliyat sonrası erken dönemde kapak replasmanına geçiş, miyokart infarktüsü veya mortalite görülmedi. Medyan takip süresi 8.5 (dağılım, 6-19) ay idi. Sığır perikardı kullanılarak Ozaki prosedürü yapılan bir hastada sekiz ay sonra kapak replasmanı yapıldı.

Sonuç: Ozaki prosedürü doğumsal aort kapak darlığı ve yetersizliğinde, umut verici erken dönem sonuçlarıyla, güvenli ve etkili bir şekilde uygulanabilir.

Anahtar sözcükler: Aort kapak neoküspidizasyonu, aort kapak rekonstrüksiyonu, Ozaki prosedürü.

Treatment strategies for children and young adults suffering from congenital aortic valve (AV) disease are still controversial.[1,2] The optimal patient-based approach may vary depending on the AV pathology, previous valvular interventions, the patient's body mass index, and the surgeon's experience. The main goal of the treatment strategy is to reduce the need for reintervention and the morbidity related to anticoagulation therapy.[3] Although AV repair is the most viable option in children and young

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adults, AV replacement can be sometimes required.[4,5] Although the Ross operation is considered the main surgical treatment for AV replacement in the pediatric population, long-term complications have led to the investigation of different repair techniques.[6,7]

Ozaki et al.[8,9] reported favorable results of the autologous pericardial AV neocuspidization technique in adult patients. The goal of this technique is to maintain the anatomy of the aortic root and the physiological coordination between the left ventricle, aortic annulus, aortic valve, sinus of Valsalva, and aorta during cardiac systole and diastole.[8,9]

Recent studies have shown promising outcomes for the use of the Ozaki procedure in children.[3,10,11] The Ozaki procedure stands as an encouraging alternative in pediatric patients with aortic stenosis (AS), aortic regurgitation (AR), endocarditis, and annuloaortic ectasia.[11]

In the present study, we report the early results of the AV neocuspidization in children and young adults with congenital aortic valve disease.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, Department of Pediatric Cardiovascular Surgery between July 2021 and July 2023. A total of 14 consecutive patients (10 males, 4 females; median age: 13.9 years; range, 8.5 to 15 years) who underwent neoaortic valve reconstruction of three leaflets as defined by Ozaki et al.[12] were included. The study included only patients treated with the Ozaki procedure by a single surgical team. Patients who underwent any of the AV commissurotomy, single leaflet reconstruction, or AV repair procedures were excluded from the study. The data were retrieved from hospital database.

Echocardiography

Preoperative, postoperative, and follow-up echocardiogram images were taken by a single researcher. All measurements of the left ventricle outflow tract, the aortic valve, the root, and the ascending aorta were indexed to body surface area (BSA). Aortic stenosis was determined by peak gradients categorized as follows: non-trivial <15 mmHg, mild 15 to 25 mmHg, mild-to-moderate 26 to 35 mmHg, moderate 36 to 49 mmHg, moderate-to-severe 50 to 59 mmHg, and severe ≥60 mmHg. Aortic regurgitation was assessed by vena contracta and measured in parasternal long-axis view and was graded from 0 to 4, with Grade 0= absent, Grade 1= insignificant, Grade 2= mild, Grade 3= moderate, and Grade 4= severe. Leaflet mobility was measured in parasternal long- and short-axis views with three-dimensional (3D) imaging, where appropriate. Follow-up echocardiograms were revised to evaluate endurance during the follow-up period.

Surgical technique

All operations were performed via median sternotomy using cardiopulmonary bypass (CPB). A large autologous pericardium was excised and fixated to the plate, adventitial excessive tissues were removed and the pericardium was treated with 0.6% glutaraldehyde solution for 10 min. It was, then, rinsed three times in saline for 6 min. Tissue-made bovine pericardium was used in the absence of native pericardium. After aortic cross-clamping (CC) cardiac arrest was achieved with antegrade del Nido cardioplegia solution. Transverse aortotomy was performed and, in patients with small aorta, aortotomy was extended to the non-coronary sinus to obtain a better exposure. The retraction sutures were placed in each commissure and native leaflets were totally removed from the annulus. The distances between the commissures were measured using the original device (Japanese Organization for Medical Device Development [JOMDD], Tokyo, Japan), and while measuring, care was taken to position the two horns of the sizer correctly over the commissures to ensure measurement accurately. In case of indecision between the two sizes, the preference was made in favor of the larger size. Then, new cusps were created using the pericardium according to the measurement from the template (JOMDD, Tokyo, Japan). Autologous pericardium was used in 12 patients and bovine pericardium was used in two patients due to previous surgery and absence of autologous pericardium. Replacement of new pericardial leaflets was accomplished by a method described by Ozaki et al.[12] using 4-0 ½ circle 13-mm round body polypropylene (Doğsan, Trabzon, Türkiye) sutures. For the first three or four sutures, the distance between the sutures was applied with an annulus-to-cusp ratio of 1:3 as described in the technique. The commissural coaptation was reinforced with additional 4-0 polypropylene sutures. The coaptation of the neoaortic valve was checked by direct visualization before closing the aortotomy. Finally, the ascending aorta was re-approached with a double-layer polypropylene suture. The Ozaki procedure was performed in three patients with other intracardiac procedures and in one patient with ascending aorta replacement concomitantly.

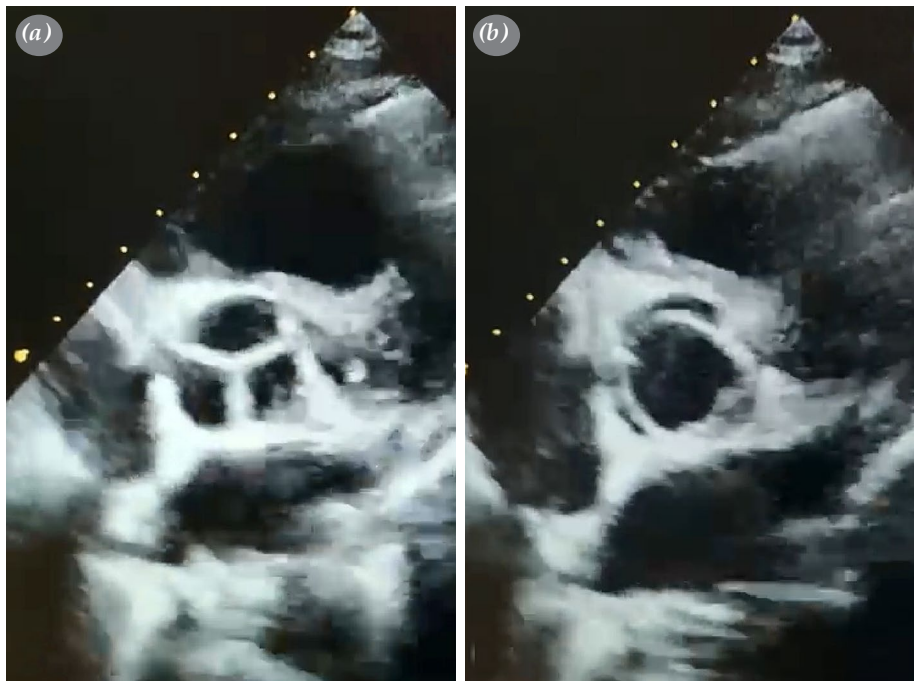

Figure 1. Screenshot from the echocardiography of a patient who underwent Ozaki surgery in our series: 1st-month follow-up after surgery. **(a)** Coaptation of the aortic neocusps. **(b)** Opening of the aortic neocusps.

Antiplatelet/Anticoagulant therapy

All patients received initial anticoagulant therapy with warfarin (target international normalized ratio [INR]: 1.5-2.5) and acetylsalicylic acid (100 mg) for three months, followed by long-term acetylsalicylic acid (100 mg) therapy.

Statistical analysis

Statistical analysis was performed using the SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed in median and interquartile range (IQR), while categorical variables were expressed in number and frequency.

RESULTS

A total of 14 patients underwent the Ozaki procedure. The median body weight of the patients was 47.5 (range, 35 to 62) kg. Twelve patients had bicuspid, and two had tricuspid AVs. Concomitant procedures were performed in four patients including mitral valvuloplasty, ascending aorta and hemiarch replacement, subaortic membrane resection, posterior aortic root enlargement (by using Nicks technique), and ventricular septal defect (VSD) closure. The median time of CPB and aortic CC was 171 (range, 154 to 185) min and 131 (range, 112 to 149) min, respectively.

Eight patients underwent balloon valvuloplasty before surgery and two patients had previous cardiac operations. Previous VSD closure was performed in one patient, and previous atrioventricular septal defect

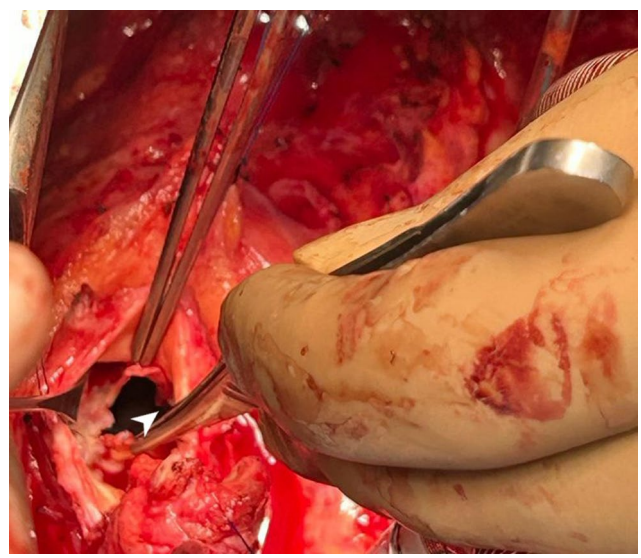

Figure 2. An intraoperative image of the incompetence of the neo-aortic valve which had undergone a successful Ozaki procedure 8 months ago, resulted in severe aortic regurgitation due to detachment of non-coronary and right coronary commissure. The detached commissure is pointed with an arrowhead.

Table 1. Summary of patient characteristics, preoperative findings and operative technique

Patient characteristics and preoperative ECHO findings									Operative technique				
Patient number	Age/sex (year)	Body weight (kg)	Aortic valve pathology	Aortic valve morphology*	Aortic annular diameter (mm)	Peak systolic aortic valve gradient (mmHg)	Aortic valve regurgitation grade	LVEDD (mm)	Leaflet material	AVNeo; Cusp sizes NCC, RCC, LCC	Concomitant procedure	CC time (min)	CPB time (min)
1	17/F	57	AR	Bicuspid type 1 R-N	31	-	4+	59.5	Autologous pericardium	29, 27, 29	Subaortic ridge resection + VSD closure	156	185
2	7.6/F	27	AS/AR	Tricuspid	15	35	2+	44	Bovine pericardium	19, 17, 17	Mitral valvuloplasty + posterior aortic root enlargement	149	176
3	7.6/M	38	AR	Bicuspid type 1 R-N	24	-	4+	58	Autologous pericardium	23, 21, 21	None	101	143
4	19/M	62	AR	Tricuspid	25	-	3+	56	Bovine pericardium	21, 21, 21	None	175	252
5	13.7/M	35	AS/AR	Bicuspid type 0 lateral	22	50	4+	61.4	Autologous pericardium	21, 19, 21	None	110	152
6	14.7/M	40	AS/AR	Bicuspid type 0 lateral	22	60	2+	50	Autologous pericardium	21, 19, 21	None	121	162
7	12.8/M	68	AS/AR	Bicuspid type 1 R-N	23	120	4+	52	Autologous pericardium	25, 27, 25	None	128	171
8	15/M	61	AS/AR	Bicuspid type 1 R-N	19.5	83	2+	44	Autologous pericardium	21, 19, 21	None	140	171
9	14.1/M	72	AS/AR	Bicuspid type 1 R-N	25.5	93	4+	70	Autologous pericardium	29, 27, 25	None	134	180
10	12.7/M	50	AS/AR	Bicuspid type 0 lateral	23	80	4+	66	Autologous pericardium	25, 23, 25	Ascending aorta + hemiarch replacement	148	224
11	8.5/F	16	AS/AR	Bicuspid type 0 AP	15	122	4+	45.4	Autologous pericardium	15, 17, 19	Subaortic ridge resection	120	154
12	24/M	75	AS/AR	Bicuspid type 2 L-R-N	25.8	45	3+	64	Autologous pericardium	23, 19, 21	None	162	204
13	8/F	26	AS/AR	Bicuspid type 1 L-R	17	60	4+	50	Autologous pericardium	19, 17, 19	None	112	156
14	15/M	45	AS/AR	Bicuspid type 1 L-R	25	25	3+	61	Autologous pericardium	27, 27, 25	None	95	125

ECHO: Echocardiography; LVEDD: Left ventricle end-diastolic diameter; AVNeo: Aortic valve neocuspidization; NCC: Non-coronary cusp; RCC: Right coronary cusp; LCC: Left Coronary cusp; CC: Cross clamp, CPB: Cardiopulmonary bypass; AR: Aortic regurgitation; VSD: Ventricular septal defect; AS: Aortic stenosis; L: Left coronary sinus; R: Right coronary sinus; N: Non-coronary sinus; AP: Anteroposterior; * For bicuspid aortic valves, aortic valve morphology was detailed according to the classification of Sievers and Schmidtke[30]

Table 2. Postoperative outcomes and final ECHO findings

Patient number	ICU length of stay (days)	Hospital length of stay (days)	Peak systolic aortic valve gradient (mmHg)	Aortic valve regurgitation grade	LVEDD (mm)
1	6	13	10	2+	45
2	6	12	25	1+	44
3	1	15	30	1+	47
4	2	5	23	1+	55
5	4	7	40	1+	51
6	1	9	15	-	40
7	4	12	12	2+	49
8	4	12	23	2+	55
9	1	7	15	1+	64
10	4	11	0	-	54
11	1	7	40	-	45
12	5	13	0	1+	63
13	4	10	10	1+	46
14	2	7	20	1+	56

ECHO: Echocardiography; ICU: Intensive care unit; LVEDD: Left ventricle end-diastolic diameter.

repair was performed in another patient. The median aortic annular diameter was 23 (range, 19.5 to 25) mm, the left ventricular end-diastolic diameter (LVEDD) was 57 (range, 50 to 61.4) mm, and the left ventricular end-systolic diameter (LVESD) was 36.5 (range, 29.9 to 40.2) mm in the preoperative echocardiography.

As AV pathology, 11 patients had combined AS and regurgitation, and three patients had isolated AR. The median preoperative peak systolic AV gradient for patients with AS was 60 (range, 45 to 93) mmHg. The median preoperative AV regurgitation grade was 4 (range, 3 to 4).

The median duration of intensive care unit stay after operation was four (range, 1 to 4) days, and the median duration of hospital stay after operation was 10.5 (range, 7 to 12) days. The median peak systolic AV gradient was 17.5 (range, 10 to 25) mmHg at the time of discharge. The median postoperative AV regurgitation grade was 1 (range, 1 to 1) (Figure 1). Two patients (14.2%) had postoperative Grade 2 AV regurgitation. Conversion to valve replacement in the early postoperative period and early mortality were not observed in any of the patients. All patients were discharged from the hospital without significant morbidity such as bleeding, cerebrovascular events, and arrhythmia.

The median follow-up was 8.5 (range, 6 to 19) months. Only one patient was reoperated for AV insufficiency at the postoperative eighth month. This patient underwent AV replacement due to severe AR due to detachment of the commissural sutures of the non-coronary and right coronary leaflets from the aortic annulus (Figure 2). Tissue-made bovine pericardium was used in this patient due to a history of previous cardiac surgery for VSD closure. Tube pericardiostomy was performed in one patient due to pericardial effusion in the postoperative second month. At the end of the follow-up period, the median peak systolic AV gradient was 17.5 (range, 10 to 25) mmHg, the median AV regurgitation grade was 1 (range, 1 to 1), the median LVEDD was 50 (range, 45 to 55) mL, and the median LVESD was 30 (range, 28.5 to 35) mm. In our series, there was no late mortality during the follow-up period. Patient characteristics, preoperative findings, and operative technique are summarized in Table 1, and postoperative results and ECHO findings are presented in Table 2.

DISCUSSION

Treatment of congenital AV disease in the pediatric population poses an important challenge as it may require repetitive interventions.[3] Although AV repair is the most reasonable solution for the pediatric

population, AV replacement may sometimes be required.[4,5] The Ross operation is the gold-standard technique for AV replacement in pediatric patients.[10] The Ozaki procedure, an AVNeo technique, has been recently applied as an alternative to the Ross operation, since it has a significant risk of operative mortality[1,2,6] and can develop late complications such as autograft dilatation and pulmonary conduit dysfunction.[7,13] This report presents our experience with 14 patients who underwent the Ozaki procedure for congenital AV disease.

In the treatment of congenital AV pathologies, the Ross procedure has been in use for more than half a century and still remains relevant and up-to-date. However, there are some factors that limit the Ross procedure from being considered as the first choice. Such as, it cannot be applied to patients with truncal valves, patients who have been operated due to transposition of the great arteries, or patients with pulmonary atresia. Some studies have emphasized that pulmonary autograft usage in the aortic position tends to more dilatation in the pediatric patient population with concerns of early or late valve dysfunction.[2-14]

The Ross procedure was performed in 33 patients in our clinic between 2003 and 2023, and the mortality rate was 15%. Mura et al.[10] conducted a study in 38 patients who underwent Ozaki (n=22) and Ross (n=16) procedures. While the early mortality rate was 6.2% in the Ross group, there was no mortality in the Ozaki group. On the other hand, the aortic transvalvular gradient was significantly higher in the Ozaki group than in the Ross group during follow-up. Eventually, they found that there was no significant difference between the two groups in terms of freedom from reoperation or mortality.[10] In our study, consistent with the literature, no mortality was observed in Ozaki patients, whereas in our Ross experience, the early mortality rate was 15%.

Another important issue, particularly for the Ross procedure in developing countries, is the limitation to access the homograft, which is the most optimal option for replacing the pulmonary valve and right ventricular outflow tract reconstruction. In our experience, homograft could be used in only 12 (36.3%) of 33 Ross patients. The inability to obtain homografts (particularly for the recently operated patients in our series) and the documented high reoperation and intervention rates with the available xenografts led us to start using hand-made polytetrafluoroethylene (PTFE) grafts.[15] Secinaro et al.[16] conducted a study with four-dimensional (4D)-flow magnetic resonance imaging in 20 children who underwent Ozaki (n=10) and Ross (n=10) procedures. They compared the two groups in terms of the preservation of the natural motion of the AV valve and the cardiodynamics of the aortic root. No significant difference was reported in the wall shear stress values measured at the proximal ascending aorta level between the two groups. They concluded that the Ozaki procedure provides a physiological laminar flow with the advantage of not causing bivalvular disease. Due to reasons such as the risk of early mortality, the possibility of bivalvular disease, and the difficulty of obtaining a homograft, AVNeo has becoming a more prominent surgical method in the appropriate patient group compared to our current approach.

The AVNeo procedure offers a superior alternative rather than the stented bioprosthesis or mechanical valves in younger patients.[17] The natural growth of the aortic root can continue, as the pericardium is sutured directly to the aortic annulus without a stented frame. Thus, it provides maximum effective orifice area and lower postoperative peak pressure gradients. Moreover, due to the small annulus size, the availability of options to replace the prosthetic valve is limited in smaller annulus size and there is a risk of prosthesis-patient mismatch. Yamamoto et al.[18] reported that the aortic ring after AVNeo was analogous to that of a normal AV by analyzing changes during the cardiac cycle after AVNeo procedures using electrocardiogram-gated computed tomography. Furthermore, Iida et al.[19] conducted a study in 15 patients who underwent AVNeo procedure. No significant difference in aortic annulus dimensions was observed with electrocardiography-gated transthoracic echocardiography between patients who underwent AVNeo and had normal AVs. These studies support the notion that the AVNeo procedure maintains the natural motion of the aortic annulus and has superior hemodynamics.

The predictors of the reoperation after aortic valve replacement (AVR) are valve size and younger age.[2] Several studies have reported a freedom from reoperation rate of only 50 to 55% at 14 years in children with previously inserted mechanical valves.[20,21] Myers et al.[22] conducted a study in 121 patients with a median age of 16 years who underwent prosthetic AVR. They reported a five-year mortality rate of 15% with mechanical AVR. Likewise, low durability of bioprosthetic valves in the younger population causes early reoperation. Saleeb et al.[23] conducted a study in 27 patients who underwent AVR with the pericardial bioprosthetic valve and reported rapid progression to AS. On the other hand,

Marathe et al.[17] carried out a study in 51 patients with a median age of 7.9 years who underwent AVNeo with Ozaki procedure. Although the median aortic annulus was 17 mm, only 6% of patients required reoperation at a mean follow-up of 11.9 months. In our study, there was no mortality, and only one patient required reoperation due to AV insufficiency during the follow-up period.

The ideal tissue material and treatment regimen for leaflet reconstruction remain important for long-term success in AVNeo. Even if the treatment with glutaraldehyde predisposes the autologous pericardium to be more prone to calcification, it theoretically creates a less antigenic environment. It also aims to provide a more durable material for reconstruction, which has greater resistance to retraction and degeneration, and helps to preserve the intrinsic tissue elasticity of autologous pericardium.[24] Duran et al.[25] reported that autologous pericardium treated with 0.5% glutaraldehyde for 10 min followed by rinsing in Ringer's lactate for 10 min resulted in less fibrocalcific degeneration at eight years, although there was no significant difference at 10 years, compared to bovine pericardium.[25,26] Baird et al.[11] reported that after fixation of the pericardium with 0.6% glutaraldehyde, they rinsed three times with normal saline for 6 min. In our series, autologous pericardium that was administered 0.6% glutaraldehyde for 10 min and rinsed three times with normal saline for 6 min was used in 12 patients, and tissue-made bovine pericardium was used in two patients, since there was no native pericardium.

Liu et al.[27] conducted a study in 15 patients with a mean age of 34 years who had pericardial AV replacement using autologous pericardium. They reported a 33% rate of reoperation at 11.4 years of follow-up with the pericardium treated for 10 min using 0.2% glutaraldehyde. Jeong et al.[28] performed a study in 41 patients with a mean age of 32 years who underwent AV repair with the leaflet extension technique. They reported a 15% reoperation rate after seven years with the pericardium treated with 0.625% glutaraldehyde in the same method as Ozaki. Myers et al.[22] reported that fresh autologous and PhotoFix®-treated bovine pericardium tended to have better endurance than glutaraldehyde-treated bovine pericardium in pediatric patients who underwent AV repair. In our study, there was only one patient who underwent reoperation, as the commissural sutures of the non-coronary and right coronary leaflets were detached from the aortic annulus at the postoperative eighth month. In this patient, tissue-made bovine pericardium was used due to the history of a prior open-heart procedure for VSD closure. However, since this detachment of the commissure is in the early stages of our surgical experience, we cannot speculate that it is due to the structure of the bovine pericardium.

The surgical technique of AVNeo in pediatric patients is similar to those essentially defined for adults.[12] New cusps created using the pericardium are stitched to the annulus at a ratio of 3:1. Neocommissures are created with a deep suture and additional supplementary commissural suture. However, there are some key points in creating three symmetrical sinuses, particularly in pediatric patients. Since most pediatric patients have unicuspid or bicuspid valves, the use of raphe as a commissure marker can result in asymmetrical sinuses.[29] Therefore, we attempt to create nearly equal three leaflets/sinuses starting from the intracoronary commissure, as equal or close leaflets/sinuses make coronary occlusion unlikely and allow for more uniform leaflet coaptation.[11]

Antiplatelet or anticoagulation therapy is another important issue after AVNeo procedures. Some studies reported embolic complications with only using acetylsalicylic acid.[5] Baird et al.[11] reported that leaflet motility decreased in 83% of patients with the use of only acetylsalicylic acid and, then, they started using dual therapy with acetylsalicylic acid and warfarin for three months. In our study, consistent with the literature, we preferred to use acetylsalicylic acid and warfarin for the first three months postoperatively and, then, only acetylsalicylic acid. Despite the short follow-up period, we observed no embolic complications or a decrease in leaflet motility in any of the patients. As there are few studies in the literature and pediatric patients would have a much longer potential follow-up than adults, more research is needed to determine an optimal anticoagulation regimen.

The single-center and retrospective design of the study and relatively small sample size are the main limitations to this study. Further multi-center, large-scale, prospective studies are needed to understand the surgical results of the Ozaki procedure in congenital AV disease.

In conclusion, our study shows that the Ozaki procedure can be applied in children and young adults with successful early results. The potential need for reintervention should be kept in mind after the Ozaki procedure, particularly in pediatric patients. A longer follow-up period is required to evaluate the mid- and

long-term valve function and the optimal leaflet material.

Ethics Committee Approval: The study protocol was approved by the Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee (date: 11.07.2023, no: E-28001928-604.01.01-219616289). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from the parents and/or legal guardians of the patients.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: All authors contributed equally to the article.

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