International Journal of Chemical and Biochemical Sciences
(ISSN 2226-9614)

Journal Home page: www.iscientific.org/Journal.html

Outcome of Aortic Valve Neocuspidization in Pediatric Age Group (Early Results)

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Abstract

Aortic valve neocuspidization by autologous pericardium is an attractive choice in the pediatric age group requiring aortic valve intervention, especially in developing countries challenged by the cost and availability of valve prostheses and the need for anticoagulation. The purpose of this study is to describe the immediate intraoperative TEE (trans-esophageal echocardiography) results after aortic valve neocuspidization with glutaraldehyde-treated autologous pericardium using the Ozaki technique and the early outcome at the post-operative-ICU course including morbidities and mortality. Prospective case series analytical descriptive study included 22 pediatric age group patients below 18 years old undergoing aortic valve neocuspidization with glutaraldehyde-treated autologous pericardium using the Ozaki technique for any pathology of aortic valve diseases. The patients were recruited from Cairo University-affiliated hospitals in the period from August 2021 to March 2023. Mean age was 11.9 ± 3.9 years old youngest was 6 years old and oldest was 17 years old. The study included 12 males (54.5%) and 10 females (45.5%). Mean weight was 43.53 ± 22.93. The mean BMI was 20.8 ± 4.16 kg/m2, while the mean BSA was 1.27 ±0.44m2. We had no mortality (0%) and no conversion to other aortic valve surgery replacement option. Aortic valve neocuspidization using glutardehyde treated autologous pericardium in pediatric age group has a good early outcome. However, long term follow up is necessary to assess durability and valve function.

Keywords: Aortic valve replacement, early outcome, congenital aortic valve disease, aortic valve neocuspidization

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1. Introduction

Congenital aortic valve disease is present in up to 2% of the population [1]. Currently available surgical options in children have certain limitations, and several factors determine the choice of valve substitute. In addition to the occurrence of valve-related complications [2]. The influence of patient growth has a major impact on valve performance in children. In current clinical practice, 5 types of aortic valve substitutes can be offered to children who require AVR: the Ross procedure, mechanical prostheses (MPs), homografts (HGs), bioprostheses, and aortic neocuspidization. The Ross procedure (a pulmonary autograft in the aortic valve position and an allograft in the pulmonary position) is considered the preferred surgical option for children who require AVR [3], [4]. Ross procedure is the only living valve substitute and has proven to be hemodynamically superior without the need for long-term anticoagulation, shows diameter increase along with somatic growth, and is associated with a low risk of endocarditis [5], [6]. Nevertheless, the Ross procedure is a complex surgical procedure, and both the pulmonary autograft and the valve substitute in the right ventricular outflow tract (RVOT) may require reintervention [7]. Bioprosthetic valves and aortic valve homografts alleviate the need for lifelong anticoagulation. However, when implanted in young adults, these biological substitutes are associated with predictable higher rates of structural valve deterioration requiring reoperation [8]. The purpose of this study was to describe the immediate intraoperative echocardiography results and the early outcome at the post-operative ICU course including morbidities and mortality after aortic valve neocuspidization.

2. Materials and Methods

This was a prospective case series analytical descriptive study, included 22 pediatrics age group patients age below 18 years old undergoing aortic valve neocuspidization with glutaraldehyde-treated autologous pericardium using Ozaki technique for variable pathologies of aortic valve diseases. The patients were recruited from Cairo University affiliated hospitals in the period from August 2021 to March 2023 after an informed consent has

been taken and after approval of research ethical committee REC, approval number MD-289-2021.

2.1. Ethical approval

An approval of the study was obtained from Cairo University academic and ethical committee. Every patient's guardian signed an informed written consent for acceptance of the operation. This work has been carried out in accordance with the Code of Ethics of the World Medical Association (declaration of Helsinki) for studies involving humans. Patients were selected according to the following criteria:

Inclusion criteria: Patients below 18 years old with Aortic valve disease whether Congenital or rheumatic or other connective tissue disease candidate for Aortic valve surgery according to ESC/AHA guidelines 2018.

Exclusion criteria: above 18 yrs old**,** redo cases, cases candidate for AV Repair and associated congenital heart disease requiring surgical intervention.

2.2. Methods

Data collected included the following:

2.2.1. Preoperative Evaluation

Age and sex, weight, BMI, complaint: Dyspnea, symptoms suggestive of low cardiac output and symptoms suggestive of congestive heart failure, clinical examination: General examination including signs of aortic regurgitation or stenosis, cardiac examination, routine investigations: (CBC, Renal function, Liver function, coagulation profile, CXR) and Echocardiography Data: LVEDV, LVESV, EF, aortic annulus, PG in case of AS, degree of regurge in case of AR, aortic valve morphology. The preoperative parameters: Demograhic data: Age, Sex, weight, BMI, Aetiolgy of aortic valve disease and Echocardiographic Data. ED, ES. EF. aortic Annulus, PG in case of AS, Degree of Regurge in Case of AR. Aortic valve cusps bi or trileaflets.

2.2.2. Operative Parameters

Trans Esophageal Echocardiography: the TEE probe is inserted after induction of anesthesia and placement of lines. It is important to evaluate the adequacy of neocusps and myocardial function. Operative data were collected and steps are photographed in the cardiothoracic operating theater of Kasr El-Aini school of medicine and they are summarized as follows:

Operative procedure: The patients were placed in supine position. All patients are approached via median sternotomy, harvesting large piece of pericardium about 8 by 8 cm, Mark the diaphragmatic end of the pericardium on the rough surface, Fixation of pericardium by putting the plate (which is included in the Ozaki AVNeo™ Sizer System) upside down in the basin with the glutardehyde solution for 10 min, the whole plate should be totally covered by the solution, routine aortic, atrial (single or bicaval) cannulation with left ventricular vent via right superior pulmonary vein, marking the aortotomy 1.5 cm above the RCA, opening the aortotomy in transverse fashion almost 80% of the circumference, suspending the outer wall of the aorta, not the commissures to avoid stretching the annulus, excision the cusps as usual and measuring: first, measuring the annulus with valve sizer or a Hegar**.** Second: add 5 measurements to the size measured and choose the Ozaki sizers in the Ozaki AVNeo™ sizer system**.** Congenital sizes in Ozaki set: from 13 to 21 mm**.** Adult sizes in Ozaki set: from 19 to 35 mm**.** measuring the RCC first then the LCC then the NCC. Measuring from commissure to commissure, If the measurement lies between two sizes, choose the bigger one. In old children/adults: Using 4/0 polypropylene with 17 mm needle and in children: using 5/0 polypropylene with 13 mm needle. Starting to suture the fashioned pericardium from rough side to the smooth side surface and in the annulus from downward to upwards. In template sizes 13 to 17, 5 sutures are used, while in template size 19 to 21, 6 sutures are used and in template sizes 23 to 35 ,7sutures are used. The first 3 stitches on the annulus side, the distance between two stitches must be one third of corresponding cusp distance, which gives the cusp a bird-nest shape. After this point where the remaining cusp and annulus lengths are the same, the distance between two stitches must be the same on both sides. The second last suture is called the precommisure and it is more transvers into the annulus rather than from downwards to upwards like the other sutures. The last suture passes through the Aortic wall from inside to outside, 2.5 mm below the highest point of the commissure. The two sutures are close to each other and at the same level. Starting from the middle of this RCC towards the LCC, Then the RCC towards the NCC. After that, starting at the middle of the LCC towards the RCC with the same technique. The last commissural stitch should pass at the same level and close to the corresponding stitch go the RCC. Take a new stitch to fix the commissure between the RCC & the LCC: First: passing in the RCC between the last stitch and the free edge from the rough to smooth surface then in the LCC from the smooth to rough surface, then pass in the wing of the LCC from rough to smooth surface, then pass outside the Aorta 2.5 mm above the highest point of the commissure lateral to the previous last commissure stitches of the cusps. Second: the other needle towards the RCC passes through the wing from the rough to smooth surface of the wing then outside the Aorta in the same Fashion as its corresponding needle. Third: passing the four needles through a teflon pledgets keeping same relation. Fourth: pulling the sutures to see the alignment of the commissure and look at the height of the two cusp, they should be the same. Starting to close the aorta in double layer fashion, but take care that the new aortic cusps are high so they won't be entangled in the suture line of the aortotomy. So, all sutures should be done under vision.

In the Trans Esophageal echocardiography: short axis to see the degree of regurgitation. Long axis to see the coaptation length. Measure the gradient. After stabilization of hemodynamics, cannulae were removed, and heparinization was reversed using protamine sulfate in a dose of (3-4 mg/Kg IV) aortic decannulation was continued

after reinfusing the remaining amount of patient's blood from the reservoir of the heart-lung machine.

Operative parameters recorded were: Ischemic time, Bypass time, total Operative time, size of neo aortic cusps, autologous pericardium or heterologous pericardium, valve size, TEE: PG, degree of AR and coaptation length, conversion to AV Replacement or Ross, inotropic supports, Rhythm after weaning of Bypass, intraoperative complications and intraoperative mortality.

2.2.3. Postoperative care

Patients were tranferred to cardiac ICU while ventilated and on inotropic support. All patients in ICU were fully monitored: invasive blood pressure monitoring, CVP measuring. continuous ECG monitoring, urine output hourly monitoring, fluid balance every 8 hours. Chest tubes are monitored considering surgical exploration if the tubes draining more than 3-5 ml/kg/hr fresh blood.

2.2.4. Post-operative parameters

These parameters were recorded during the ICU stay and they include all of the following: Duration of Mechanical ventilation, Hemodynamic stability assessment (blood pressure, pulse and central venous pressure), number of Patients who required inotropic support, total blood loss during first 24 hours and amount of blood transfusion, arrhythmia and need for pacemaker, need for Re-exploration for bleeding related reasons ''bleeding or tamponade'', or severe aortic regurge or stenosis, renal complications, neurological complications, total ICU stay, postoperative echo during Hospital stay and 30 days Mortality.

2.3. Statistical analysis

Continuous data were expressed as mean and standard deviation or median with the interquartile range and categorical data as percentage. All reported P values are two-sided, and P values of $\leq$ 0.05 were considered statistically significant. All statistical analyses were performed with SPSS version 22.0 (SPSS, Inc., Chicago, IL, USA). All statistical analyses were done with the help of a departmental statistician.

3. Results and discussion

Our study was carried out on 22 patients in Cairo university affiliated hospital in the period from August 2021 to March 2023. Mean age was 11.9 ± 3.96 years old. Median age was 13 years (6-17 years). The study included 12 males (54.5%) and 10 females (45.5%). Mean weight was 43.53 ± 22.93 kg. Mean BMI was 20.8 ±4.16 kg/m^2 while mean BSA was 1.27 ±0.44 m^2 Table 1. Aetiology of Aortic Valve Disease: In our study, 19 patients were congenital aortic valve disease (86.3%) and 3 patients were Rheumatic Aortic valve disease (13.6%). Table 2. Ejection Fraction (EF) mean was 62.8% ±10.35 minimum 47% and maximum 85%. End diastolic volume (EDV) mean was 42.6 ml ±4.9, minimum 36 ml and maximum 50 ml. End systolic volume (ESV) mean was 17.6 ml ±2.9, minimum 15 ml and maximum 25 ml. Table 3. Mean Peak gradient was 45.9±8.68 mmHg. Ratio of jet width to left ventricular outflow (LVOT) mean was 49.8% ±11.1% and vena contracta mean was 5.83±1.47mm. Mean aortic annulus was 19.4mm ± 3.38. Smallest aortic annulus was 16mm while largest was 29mm. Table 4. 22 patients (100%) required full median sternotomy. All patients underwent on pump aortic valve neo-cuspidization using gluteraldehyde treated autologous pericardium using Ozaki technique in 22 patients (100%), 1.Bypass time, ischemic time and operative time: Mean ischemic time was 93.8 ± 11.20 minutes. Regarding the mean of bypass time it was 136.1 ± 20.01 minutes. Mean Total Operative time was 201.53 ± 25.52 minutes. Table 5. 2. Intra operative annulus size: Mean annulus size was 17.34 ± 2.23mm, 3.Valve size using leaflet sizer in Ozaki Template: Mean size of left coronary cusp was 22.45±3.15, Right Coronary cusp 22.09±3.30 and Non coronary cusp was 23±3.26. Table 6. Intraoperative TEE evaluation: mean EF was 55±5.7 % ranging from (40-70%). Mean Peak gradient was 15±3.7mmHG and Mean Gradient was 9 ±2.6 mmHg. Table 7. 17 cases (68.1%) had no Aortic regurge while 5 cases (22.7%) had trivial Aortic regurge LVOT % ≤20%. Table 8. Post-operative echo results denoted excellent aortic valve reconstruction with a minimum gradient of 5 mm Hg maximum, peak gradient of 18 mmHg maximum. Table 9. In Ozaki procedure, autologous pericardium is harvested, at least 7x3x8 cm. The excised pericardium was then treated with 0.6% glutaraldehyde solution with a buffer for 10 minutes. [9]. This current study aimed to detect the early outcome of aortic valve replacement by pretreated autologous pericardium in cardiothoracic surgery department (Cairo University/Kasr Al Ainy Hospitals). Our study was carried out on 22 patients of pediatric age group with aortic valve disease that required replacement by pretreated autologous pericardium.. The mean age was 11.9 ± 3.9 years. Median age was 13 years (6-17 years). The study included 12 males (54.5%) and 10 females (45.5%). Mean weight was 43.53 ± 22.93. Mean BMI was 20.8 ±4.16kg/m^2 while mean BSA was 1.27 ±0.44m^2. Our results were similar to that of, Baird et al., who studied 57 patients, with median age was 12.4 (0.7-25.4) years, and included 21 males (37%) and 36 females (63%). Median weight was 44 (5.16-121) kg and median BSA was 1.33 (0.86-1.67) m^2. [10] While Polito A. et al., studied 22 patients found that median age 13.4 (8.8–15.8). Median weight was 55 (26.5–66) kg.[11]. Therefore, our study was in the same range of age and weight with other studies in the literature. In This study, 13 patients had severe aortic stenosis (59.1%), 3 patients had severe aortic regurge (13.6%) and 6 patients had mixed pathology (27.2%). 13 cases were bicuspid Aortic valve (59.1%) and 9 cases were trileaflet (40.9%). In our study, mean aortic annulus was 19.4mm ± 3.38 (16-29 mm). In contrast to our study, Baird et al., reported mean aortic annulus 20.9±5.0 mm. [10] Polito A. et al., mean aortic annulus was 20.5mm. [11] Smaller aortic annulus in our study may be related to lower mean age in our study. All our patients required full median sternotomy (22 patients (100%).In a study done by Baird et al., 52 patients (91%) underwent full sternotomy and 5 patients (9%) done partial sternotomy [10].

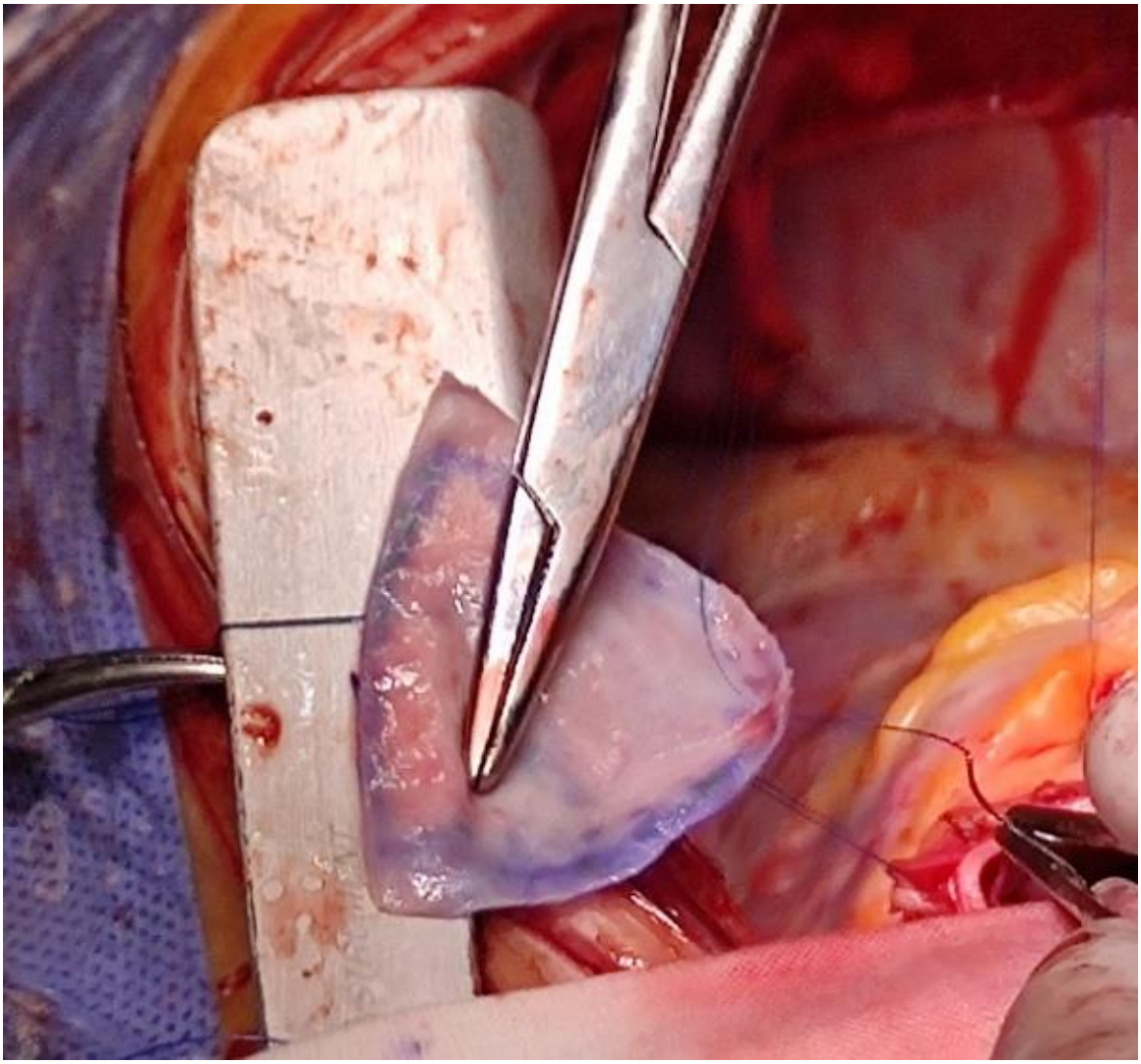

Figure 1. Suturing the cusps

Figure 2. Intra-operative TEE for the neo-AV after weaning from bypass

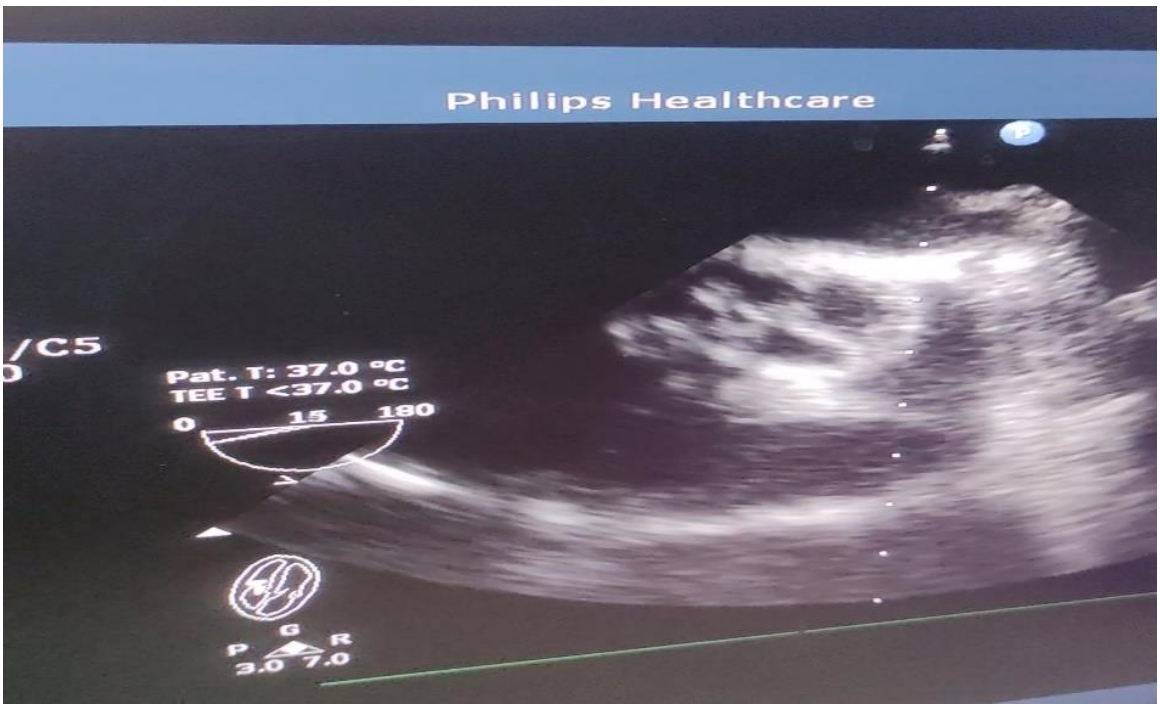

Figure 3. Intra-operative TEE showing coaptation of neocusps

Table 1. Demographic data of the studied group

		N	%
Gender	**Male**	12	54.5%
	Female	10	45.5%
Age		mean	11.9
		SD	3.96
		Median	13
		youngest	6
		oldest	17
		range	11
Weight		mean	43.5
		SD	22.93
BMI		Mean	20.8
		SD	4.16
BSA		Mean	1.27
		SD	0.44

Table 2. Aetiology of Aortic valve disease

		Number	Percentage
Aetiology	**Rheumatic**	3	13.6%
	Congenital	19	86.3%

Table 3. LV function and dimensions

	Minimum	Maximum	Mean	SD (+/-)
EF %	47	85	62.85	10.35
EDV (ml)	36	50	42.6	4.9
ESV (ml)	15	25	17.6	2.9

Table 4. Aortic annulus, gradient of stenosis and degree of regurge

	mean	SD
Aortic Annulus	19.4	3.38
Aortic Stenosis: Peak Gradient (mmHg)	**45.9**	**8.68**
Aortic Regurge: LVOT% Vena contracta (mm)	**49.8 5.83**	**11.1 1.47**

Table 5. Bypass ischemia and total operative times

	Bypass time (min)	Ischemia time (min)	Total Operative Time (min)
Minimum	105	75	150
Maximum	160	115	260
Mean	136.1	93.8	201.53
SD (+/-)	20.01	11.20	25.52

Table 6. Intraoperative annulus size

	mean	SD
Left Coronary Sinus	22.45	3.15
Right Coronary cusp	22.09	3.30
Non coronary cusp	23	3.26

Table 7. Intraoperative TEE

	Mean (SD)	Minimum	Maximum
EF%	55(±5.7)	40	70
Peak gradient	15(±3.7)	10	22
Mean gradient	9(±2.6)	5	15

Table 8. Intraoperative TEE degree of regurge

	No Aortic regurge N (%)	Trivial AR N (%)
patients	**17(68.1%)**	**5(22.7%)**

Table 9. Postoperative Echocardiography

	EF (%)	Mean gradient over AV (mmHg)	Peak gradient over AV (mmHg)
Minimum	45	5	12
Maximum	75	9	18
Mean	52	7.3	14.8
SD (+/-)	5.93	0.98	1.29

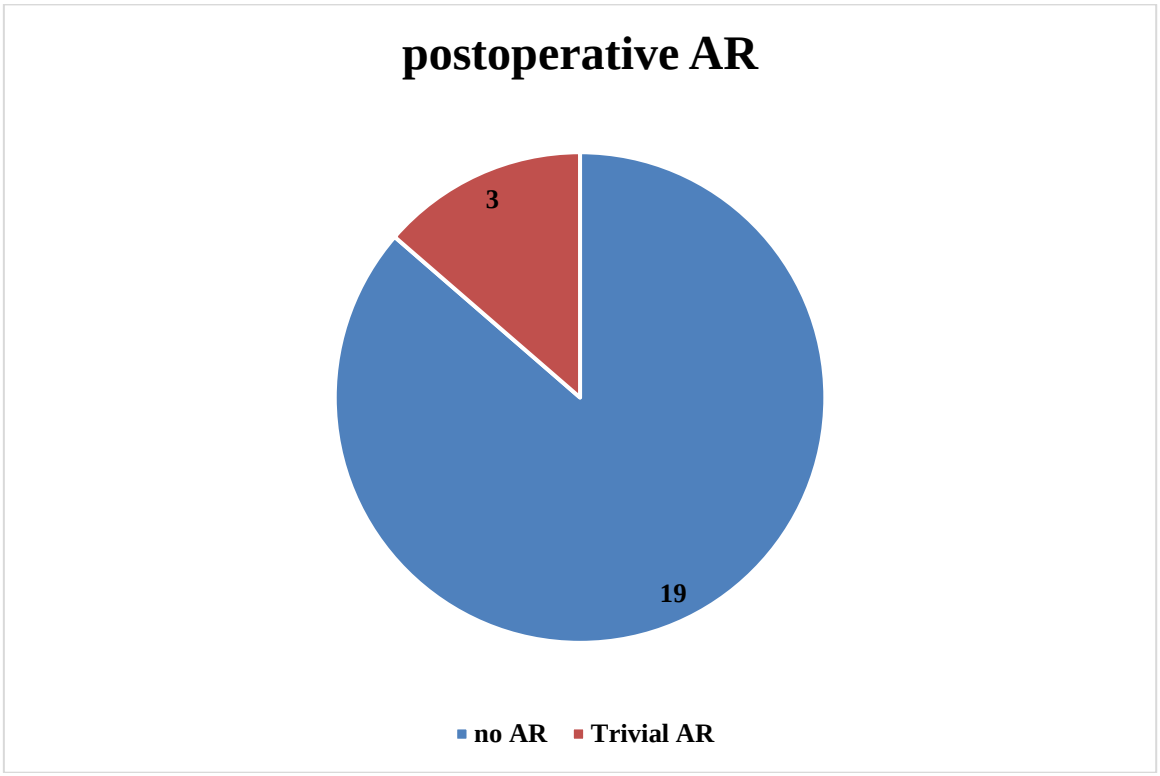

Figure 4. Pie chart of postoperative AR

In our study we did standard full sternotomy as we are in the beginning of our learning curve so we did full sternotomy for better exposure and good harvesting of pericardium as we only used autologous pericardium. In our study, autologous pericardium was used in 22 patients (100%). In contrast to our study , Baird et al., used Autologous pericardium in 20 patients (35%), Photofix bovine pericardium in 35 patients (61%) and CardioCel bovine pericardium in 2 patients (3.5%). [10]. In our study, Mmean ischemic time was 93.8 ± 11.20 minutes. Regarding the mean of bypass time it was 136.1 ± 20.01 minutes. Mean total operative time was 201.53 ± 25.52 minutes. In contrast to our study , Baird et al., mean cardiopulmonary bypass time (min) 156 ±57 and Mean Cross-clamp Time (min) 130 ±45. [10]. Polito A. et al., mean CPB time was 142 minutes and Cross-clamp time was 103 minutes. [11]. Longer ischemic time could be explained by complex pathology in native aortic valve disease in their studies. In current study, Mean annulus size using annulus sizer was 17.34 ± 2.23mm.Mean size of left coronary cusp was 22.45±3.15, Right Coronary cusp 22.09±3.30 and Non coronary cusp was 23±3.26. 16 cases (72.7%) had equal leaflets size and 6 cases (27.3%) had unequal leaflets size.we could not find in the literature other studies about Ozaki procedure in the pediatrics age group who goes into depth by measuring the Aortic annulus as well as the average size of each cusp using the Ozaki sizers. we have no cases who required Aortic root enlargement. In comparison to others, Baird et al., 8 cases (14%) had small aortic annulus and aortic root enlargement has been done with aortic valve neocuspidization. [10]. Polito A., 1 patient (4.5%) required aortic root enlargement. [11] We did not want to do Aortic root enlargement in addition to Ozaki procedure in the beginning of our learning curve. We found mean EF was 55±5.7 ranging from (40-70%). Mean Peak gradient was 15±3.7mmHG and Mean Gradient was 9 ±2.6 mmHg. 17 cases (68.1%) had no Aortic regurge while 5 cases (22.7%) had trivial Aortic regurge LVOT % ≤20%. Similar to our study, Baird et al., found peak gradient was 17.2±9.6 mmHG in AS and AS/AR patients. And all patients had trivial regurge or less. [10] While Polito A. et al., found peak gradient was 12.7 (8.4–16.3) mmHG, Mean gradient was 6.9 (4.4–10.3) mmHg and vena contracta was 0 (0–1.5) mm. [11]. In the Trans Esophageal echo we use short axis to see the Degree of Regurgitation, Long axis to see the coaptation length. All our patients were followed by trans thoracic echocardiography before Hospital discharge, Post-operative echo results showed excellent aortic valve reconstruction with the minimum gradient was 5 mmHg maximum, peak gradient of 18 mmHg maximum. 19 cases had no Aortic regurge while 3 cases had trivial Aortic regurge LVOT % ≤20%. Also Baird et al., At discharge, 98% of patients had mild or less regurgitation, 1 patient (1.8%) had moderate AR didn't require reoperation. peak aortic gradient was 16.9±9.5 mmHg. [10]. And Polito A. et al., peak gradient was 19 (15.3–30) mmHg and mean gradient was 11 (8.5–15) mmHg and vena contracta was 1.8 (0–2.8) mm as 1 patient (4.5%) had moderate AR didn't require reoperation. [11]. There are

several advantages of the Ozaki procedure. First, there is no foreign body including a suture ring. It has been demonstrated that natural movement of the aortic annulus is preserved, and the reconstructed aortic valve has significantly less pressure gradients, compared to conventional aortic valve replacement cases due to maximal effective orifice area, which is particularly important in patients with a small aortic annulus. This technique can be also applied to almost all aortic valve pathologies. There is no need for warfarin postoperatively, and low-dose aspirin is used for three to six months [12].

4. Conclusion

Our study suggested that aortic valve construction using pericardial tissue could be an alternative surgical option in pediatric age group patients presenting with aortic valve disease in which valve repair was not possible. The newly designed templates allow exact sizing of the neo-cusps, optimal commissure implantation even for small aortic annulus and nearly for all valve pathologies, annulus preservation as it allows growth and alleviates the need for anticoagulation; however, long-term follow-up in a larger cohort is warranted to assess the durability of the neo-valves.

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