Nanotechnology Perceptions
ISSN 1660-6795
www.nano-ntp.com

Early Outcome Of Patients Undergoing Neopericardium Aortic Valve Repair (Ozaki) Versus Aortic Valve Replacement By Tissue Bioprosthetic Valve

Mohamed Allam[1], Mohamed Azzam[1], Said Abdelaziz Badr Soliman[1], Fouad Mohamed Rasekh[1], Michael Boulos Saied[1], Mahmoud Gamaleldin Ali [1]

[1]Department of Cardiothoracic Surgery, Faculty of Medicine, Cairo University
Corresponding author: Mohamed Allam
Mobile: 01010007891
Email: cts.m.allam@gmail.com

Background: The Ozaki method, a very recent surgical modality first performed in Japan, involves the creation of new aortic valve leaflets from either autologous pericardium (covering the patient's own heart) or bovine pericardium (covering the cow's heart).

Aim: The objective of this study was to contrast the early results of patients receiving autologous pericardium therapy using glutaraldehyde for an aortic valve neocuspidization (Ozaki method) with those of individuals having bioprosthetic tissue valve replacement for aortic replacement of the valve.

Methods: This randomized study included 40 adult patients aged > 18 years. Twenty patients underwent aortic valve neocuspidization using the Ozaki technique, while the other 20 underwent bioprosthetic tissue valve replacement. Patients were recruited from Cairo University-affiliated hospitals between May 2021 and January 2022.

Results: A statistically significant variation in ejection fraction (EF) was seen between both groups during postoperative echocardiography. The end-diastolic and end-systolic left ventricular diameters (EDD and ESD), ICU stay, and total hospital stay did not differ significantly across the groups. The intraoperative data, which included the overall operation duration, bypass time, and cross-clamp time, showed notable variations.

Conclusion: For some individuals with aortic valve dysfunction, aortic valve neocuspidization with the Ozaki technique could be a good substitute for standard valve replacement surgery.

Keywords: Ozaki, aortic valve replacement, bioprosthetic valve, neocuspidization.

Introduction

The most effective therapy for aortic valve disorders is aortic valve replacement (AVR). Nonetheless, a stent structure is used by both bioprosthetic and mechanical valves to suture and adhere to the aortic valve annulus. This stent can decrease the postoperative aortic valve area (AVA), increase the postoperative pressure gradient, and limit the annulus's natural mobility. After the operation, a patient-prosthesis mismatch (PPM) may also occur in certain individuals.(1). Aortic valve replacement using autologous pericardium, or AVNeo, has been a viable alternative therapy option since 2007. In this surgery, the autologous pericardium that has been treated with glutaraldehyde is sutured directly to the aortic annulus after the aortic cusps are completely removed. In addition to aortic regurgitation (AR), AVNeo may be used to treat various aortic valve diseases such as congenital abnormalities including unicuspid, bicuspid, or quadricuspid valves, as well as aortic stenosis (AS) and infective endocarditis (IE).(2).

Because aortic valve autologous neo-cuspidization (OZAKI) uses the patient's own tissues, it has the major benefit of not requiring lifetime anticoagulant medicine. For patients who intend to become parents or who are contraindicated for anticoagulant medication due to conditions like liver cirrhosis or a history of gastrointestinal bleeding, this makes it an especially advantageous alternative.(3). The potential of autologous aortic valve neocuspidization to treat patients with tiny aortic annuli and aortic stenosis (AS) is a major benefit. In these situations, replacing the prosthetic valve may result in patient-prosthesis mismatch (PPM), a serious issue that might call for further annular expansion techniques like the Nicks or Manouguian operations (4). Bio-prosthetic valves are trileaflet in shape and are frequently stent-mounted for simpler implantation. They are generally manufactured from chemically treated animal tissues, such as pericardium from cows or porcine valve leaflets. The main benefit of bioprosthetic valves is that they eliminate the requirement for continuous anticoagulation, which lowers the risk of bleeding and thrombosis that come with mechanical valves. However, the shortened lifespan of biological tissue cancels out this advantage. Although it is commonly known that bio-prosthetic valves often have a shorter lifespan than mechanical valves, evaluating this issue is made more difficult by the absence of a common criteria for structural valve degeneration (SVD) (5).

The purpose of this study was to evaluate the early results of aortic valve replacement with a bioprosthetic tissue valve prosthesis vs aortic valve neocuspidization using autologous pericardium administered glutaraldehyde.

Patients and methods

This randomized study included 40 adult patients aged > 18 years. Twenty patients underwent aortic valve neocuspidization using the Ozaki technique, while the other 20 underwent bioprosthetic tissue valve replacement. The patients were recruited from Cairo University-affiliated hospitals between May 2021 and January 2022 after an informed consent has been taken

Inclusion criteria:

Patients complaining of severe aortic stenosis or regurgitation and is recommended for surgery

The exclusion criteria were as follows: combined procedure, re-do, and pericardial disease.

Methods:

Operative technique for OZAKI.
The surgical procedure, as described by Ozaki et al. and applied in our institution, begins with a traditional median sternotomy, followed by harvesting and treating the autologous pericardium with 0.6% glutaraldehyde solution. After cardiopulmonary bypass (CPB) is initiated and cardioplegic arrest was achieved, transverse aortotomy was performed, and the native valve was excised with thorough debridement of the annulus. The intercommissural distance was measured, and if the native valve was bicuspid, a tricuspid AVNeo was created using a commercially available sizer and templates. The thickest pericardium is used for larger leaflets, which are then designed and marked with specific "dots" to guide precise suturing. Leaflets were sutured to the native aortic annulus with 4-0 Prolene (or 5-0 for smaller patients) to ensure secure attachment of the wings to the aortic wall. The aortotomy was closed with continuous sutures, the left ventricle was de-aired, and after confirming satisfactory cardiac output, the patient was gradually weaned off the CPB. Heparinization was reversed, aortic de-cannulation was performed, and hemostasis was ensured. The procedure concludes with the placement of ventricular pacing wires and retrosternal chest tubes if necessary, and closure of the sternum, pectoralis fascia, subcutaneous tissue, and skin.

Operative technique of Aortic valve replacement
After the patient was fully heparinized, a median sternotomy was performed, and then the aortic and atrial veins were cannulated. Through the superior pulmonary vein, a vent was inserted into the left ventricle (SPV). Following the initiation of cardiopulmonary bypass (CPB), the valve was exposed by performing a hockey stick aortotomy and applying an aortic cross-clamp. To guarantee improved exposure, traction sutures were positioned at commissures. In order to guarantee safe suture insertion and restore annular pliability, the valve was removed and the surrounding tissue was debrided. Prior to the placement of pledgeted 2-0 braided double-armed horizontal mattress sutures, the annulus was measured using valve sizers. After cleaning and inspecting the bio-prosthesis for flaws, suturing was started at the commissure. Sutures were positioned clockwise for the left coronary cusp and counterclockwise for the non-coronary cusp. To keep the valve from drying out, saline irrigation was used on a regular basis. Once positioned, the sutures were tied, and the surgeon verified proper positioning before closing the aorta, ensuring no risk of coronary ostia obstruction. The aortotomy was closed with continuous sutures, the left ventricle was de-aired, and after confirming satisfactory cardiac output, the patient was gradually weaned off the CPB. Heparinization was reversed, aortic de-cannulation was performed, and hemostasis was ensured. The procedure concludes with the placement of ventricular pacing wires and retrosternal chest tubes if necessary, and closure of the sternum, pectoralis fascia, subcutaneous tissue, and skin.

Results
Table (1): Comparison between the two studied groups according to demographic data

	OZAKI technique (n = 20)		Replacement tissue valve (n = 20)		Test of Sig.	p
	No.	%	No.	%		
Sex						
Male	11	55.0	10	50.0	χ^2= 0.100	0.752
Female	9	45.0	10	50.0		
Age (years)						
Min. – Max.	32.0 – 70.0		60 – 74.0			
Mean ± SD.	56.6 ± 8.6		63.2 ± 3.4		t= 1.384	0.001
Median (IQR)	60 (11.5)		62 (4.6)			

Regarding age, there was a statistically significant difference between both groups. (Table 1).

Table (2): Comparison between the two studied groups according to Hb and HCT

		OZAKI technique	Replacement tissue valve	t	p
Hb	**Pre-operative**	**(n = 20)**	**(n = 20)**		
	Min. – Max.	9.50 – 15.0	9.70 – 13.9		
	Mean ± SD.	12.03 ± 2.1	12 ± 1.69	0.0	1.000
	Median	13.0	12.5		
	Post-operative	**(n = 20)**	**(n = 20)**		
	Min. – Max.	9.0 – 13.0	9.50 – 14.0		
	Mean ± SD.	11.0 ± 1.09	11.41 ± 1.17	1.129	0.266
	Median	11.0	11.25		
	t_0 (p_0)	4.084 (0.001)	3.248(0.004)		
HCT	**Pre-operative**	**(n = 20)**	**(n = 20)**		
	Min. – Max.	26.0 – 46.0	27.0 – 45.0		
	Mean ± SD.	34.8 ± 4.86	35.3 ± 4.78	0.0	1.000
	Median (IQR)	34.0	35.0		
	Post-operative	**(n = 20)**	**(n = 20)**		
	Min. – Max.	27.0 – 43.0	27.0 – 45.0		
	Mean ± SD.	32.63 ± 4.35	34.80 ± 4.85	1.467	0.151
	Median (IQR)	32.0	35.0		
	t_0 (p_0)	2.683 (0.015)	0.395 (0.697)		

Table 2 shows that there was a statistically insignificant difference between the two groups in Hb and HCT levels.

Table (3): Comparison between the two studied groups according to intraoperative data

	OZAKI technique (n = 20)	**Replacement tissue valve (n = 20)**	**t**	**P**
Time of surgery (hours)				
Min. – Max.	4.0 – 6.50	2.5 – 5.0		
Mean ± SD.	5.10 ± 0.74	3.35± 0.73	7.562	<0.001
Median (IQR)	5.0 (4.50 – 5.75)	3.25 (2.75– 4)		
Time of bypass (min.)				
Min. – Max.	74.0 – 156.0	65.0 – 95.0		
Mean ± SD.	114.6 ± 25.28	70.45± 10.64	7.199	<0.001
Median (IQR)	117.5 (95.0 – 130.0)	70.0 (65.0 – 78.0)		
Time of cross clamp time (min.)				
Min. – Max.	50.0 – 118.0	40.0 – 65.0		
Mean ± SD.	85.40 ± 19.33	52.05 ± 7.2	7.232*	<0.001*
Median (IQR)	83.50 (71.50 – 97.50)	50.0 (46.0 – 57.5)		

Table 3 demonstrates a statistically significant difference in intraoperative data (surgical time, bypass time, and cross-clamp duration) between the two groups.

Table (4): Comparison between the two studied groups according to echo in post-operative

Echo (postoperative)	**OZAKI technique (n = 19)#**	**Replacement tissue valve (n=20)**	**t**	**P**
EF				
Min. – Max.	38.0 – 60.0	40.0 – 70.0		
Mean ± SD.	48.58 ± 6.56	56.15 ± 7.65	3.311*	0.002*
Median (IQR)	50.0 (42.50 – 53.0)	57.0 (52.50 – 60.0)		
EDD				
Min. – Max.	4.50 – 6.90	4.20 – 7.0	0.007	0.994
Mean ± SD.	5.37 ± 0.60	5.37 ± 0.71		

Median (IQR)	5.40 (4.95 – 5.70)	5.30 (4.90 – 5.65)		
ESD				
Min. – Max.	2.70 – 5.0	2.60 – 4.90		
Mean ± SD.	3.81 ± 0.64	3.78 ± 0.63	0.175	0.862
Median (IQR)	3.70 (3.30 – 4.30)	3.90 (3.25 – 4.30)		

Table 4 demonstrates that there was a highly significant variation in EF between both groups based on echo (postoperative). Regarding EDD and ESD, there was statistically insignificant difference between both groups.

Table (5): Comparison between the two studied groups according to peak and mean gradient post-operative

	OZAKI technique (n = 19)#	**Replacement tissue valve (n=20)**	**t**	**P**
Peak gradient				
Min. – Max.	12.0 – 17.0	11.0 – 20.0		
Mean ± SD.	14.53 ± 1.12	14.75 ± 2.31	0.387	0.702
Median (IQR)	14.0 (14.0 – 15.0)	15.0 (13.0 – 16.0)		
Mean gradient				
Min. – Max.	5.0 – 9.0	6.0 – 13.0		
Mean ± SD.	7.05 ± 0.97	9.0 ± 1.86	4.122*	<0.001*
Median (IQR)	7.0 (6.50 – 8.0)	8.0 (8.0 – 10.50)		

Regarding the mean gradient, Table 5 demonstrates that there was a very statistically significant difference between the two groups. Regarding the peak gradient, there was a statistically negligible difference between the two groups.

Table (6): Comparison between the two studied groups according to postoperative data

	OZAKI technique (n = 19)[#]	**Replacement tissue valve (n=20)**	**U**	**p**
ICU stay (hours)				
Min. – Max.	36.0 – 108.0	24.0 – 72.0		
Mean ± SD.	55 ± 22	50 ± 15	186.0	0.461
Median (IQR)	50.0 (45.0 – 65.0)	48.0 (48.0 – 55.0)		
Hospital stay (days)				
Min. – Max.	5.0 – 9.0	4.0 – 7.0		
Mean ± SD.	7.0 ± 1.5	5.60 ± 0.88	189.5	0.989
Median (IQR)	7.0 (6.0 – 8.0)	5.5 (5.0 – 6.0)		

Regarding ICU and hospital stays, Table 6 demonstrates that there was a statistically negligible difference between the two groups.

Discussion

We found that in the group studying the OZAKI approach, 55.0% were male and 45.0% were female. Similarly, in the group studying the replacement tissue valve, 50.0% were male and 50.0% were female. The average age of the group being investigated for the OZAKI procedure was 56.6 ± 8.6 SD, ranging from 22.0 to 72.0, whereas the average age of the group being studied for the replacement tissue valve was 63.2 ± 3.4 SD, ranging from 21.0 to 73.0. When comparing the ages of the two groups, a statistically significant difference was found.

In a study comparing the early outcomes of aortic valve neocuspidization and replacement for aortic regurgitation, Amr et al. (6) discovered that patients who underwent aortic valve replacement were considerably older (49.6±7.2 vs. 43.8±8.6 years: P= 0.002), but there were no difference in gender or body mass index between the two groups ($p > 0.05$).

When comparing the two groups' Hb and HCT values, no statistically significant difference was found.

Consistent with our findings, Wong et al. (7) demonstrated that the two groups did not vary significantly with respect to postoperative hemoglobin ($p > 0.05$).

When comparing the two groups' intraoperative data (surgical time, bypass time, and cross-clamp time), a statistically significant difference was found.

The average time for ozaki aortic valve neocuspidization was 143 ± 33 minutes, whereas the average time for cardiopulmonary bypass was 157 ± 37 minutes, according to Khatchatourov et al., (8). The mean cross clamp time for Ozaki was 85.4 ±19.33 and the by pass time was 114.6 ± 25.28, which are lower than the values found in our study.

Patients with an isolated Ozaki had median bypass times of 130.5 (113.5-142.5) minutes and median cross clamp lengths of 103.5 (90.5-111) minutes, according to Wiggins et al. (9).

There was a significantly significant difference in EF between the two groups, according to Echo (postoperative). When comparing the two groups' EDD and ESD scores, no statistically significant difference was found.

In a study conducted by Tanoue et al. (10) on 93 patients with severe AR who had surgical AVR, the left ventricular ejection fraction (LVEF) decreased from 60.2 before surgery to 51.9 immediately after the procedure and to 57.9 after one year of follow-up. At the same time, there were notable drops in LVEDV and LVESV, which persisted even after a year of follow-up.

Since the patients receiving aortic neocuspidization were treated with smaller volumes at baseline compared to the patients having AVR, Regeer et al. (11) discovered that the groups' LVEDV and LVESV changes were considerably different. But LVEF changes were not significantly different among groups.

In terms of the average gradient, the two groups were significantly different from one another. When looking at the peak gradient, the difference between the two groups was not statistically significant.

The use of autologous pericardium in AVNeo tends to mimic the morphology of a normal aortic valve, according to Ozaki et al. (12). This results in a high effective orifice area (EOA) and minimal postoperative gradients, with an average peak gradient of 15.2 ± 6.3 mmHg recorded after surgery.

When looking at intensive care unit and hospital stays, the difference between the two groups was not statistically significant.

Reuthebuch et al. (13) confirmed our findings by showing that patients who received an isolated Ozaki surgery exited the intensive care unit (ICU) after an average of 2.19 ± 2.34 days and were discharged after 8.81 ± 2.04 days. According to our research, patients who underwent an isolated ozaki surgery stayed in the intensive care unit for an average of 55 ± 22 hours and were hospitalized for an average of 7 ± 1.5 days.

While studying patients having AVR, Vukovic et al., (14) discovered that Our study indicated that patients who had AVR stayed in the intensive care unit for 50 ± 15 hours and for 5.6 ± 0.88 days in the hospital, with an average period of 2.3 ± 1.4 days in the ICU and 7.6 ± 2.2 days in the hospital overall.

Conclusion

Some individuals with aortic valve disorders may be candidates for Neopericardium Aortic Valve repair (OZAKI) instead of replacement treatment. Almost all aortic valve diseases may be amenable to this method, which maintains postoperative physiological hemodynamics.

References

1. Mooney J, Sellers SL, Blanke P, Pibarot P, Hahn RT, Dvir D, Douglas PS, Weissman NJ, Kodali SK, Thourani VH, Jilaihawi H. CT-defined prosthesis–patient mismatch downgrades the frequency and severity and demonstrates no association with adverse outcomes after transcatheter aortic valve replacement. JACC: Cardiovascular Interventions. 2017 Aug 14;10(15):1578-87.
2. Ozaki S, Kawase I, Yamashita H, Uchida S, Nozawa Y, Takatoh M, Hagiwara S, Kiyohara N. Reconstruction of the Bicuspid Aortic Valve With Autologous Pericardium–Usefulness of Tricuspidization Circulation Journal. 2014;78(5):1144-51.

3. Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Søndergaard L, Mumtaz M, Adams DH, Deeb GM, Maini B, Gada H, Chetcuti S. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. New England Journal of Medicine. 2017 Apr 6;376(14):1321-31.
4. Chowdhury UK, Sankhyan LK, George N, Singh S, Gayatri S, Avneesh S, Malik V, Chowdhury P. Posterior aortic root enlargement (Nick's procedure), mechanical aortic valve replacement and patch closure of the sacciform proximal aortic arch aneurysm by "open" technique without circulatory arrest: a video presentation. Int Med. 2020;2:92.
5. Hammermeister K, Sethi GK, Henderson WG, Grover FL, Oprian C, Rahimtoola SH. Outcomes 15 years after valve replacement with a mechanical versus a bioprosthetic valve: Final report of a Veterans Affairs randomized trial. Journal of the American College of Cardiology. 2000 Oct;36(4):1152-8.
6. Amr MA, Fayad E. Early outcomes of aortic valve repair versus replacement for aortic regurgitation: a single-center experience. Cardiothoracic Surgeon. 2022 Dec;30:1-6.
7. Wong CH, Chan JS, Sanli D, Rahimli R, Harky A. Aortic valve repair or replacement in patients with aortic regurgitation: a systematic review and meta-analysis. Journal of Cardiac Surgery: Including Mechanical and Biological Support for the Heart and Lungs. 2019 Jun;34(6):377-84.
8. Khatchatourov G, van Steenberghe M, Goy D, Potin M, Orrit J, Perret F, Murith N, Goy JJ. Short-term outcomes of aortic valve neocuspidization for various aortic valve diseases. JTCVS open. 2021 Dec 1;8:193-202.
9. Wiggins LM, Mimic B, Issitt R, Ilic S, Bonello B, Marek J, Kostolny M. The utility of aortic valve leaflet reconstruction techniques in children and young adults. The Journal of Thoracic and Cardiovascular Surgery. 2020 Jun 1;159(6):2369-78.
10. Tanoue Y, Maeda T, Oda S, Baba H, Oishi Y, Tokunaga S, Nakashima A, Tominaga R. Left ventricular performance in aortic valve replacement. Interactive cardiovascular and thoracic surgery. 2009 Aug 1;9(2):255-9.
11. Regeer MV, Versteegh MI, Klautz RJ, Stijnen T, Schalij MJ, Bax JJ, Ajmone Marsan N, Delgado V. Aortic valve repair versus replacement for aortic regurgitation: effects on left ventricular remodeling. Journal of Cardiac Surgery: Including Mechanical and Biological Support for the Heart and Lungs. 2015 Jan;30(1):13-9.
12. Ozaki S, Kawase I, Yamashita H, Uchida S, Takatoh M, Kiyohara N. Midterm outcomes after aortic valve neocuspidization with glutaraldehyde-treated autologous pericardium. The Journal of Thoracic and Cardiovascular Surgery. 2018 Jun 1;155(6):2379-87.
13. Reuthebuch O, Koechlin L, Schurr U, Grapow M, Fassl J, Eckstein FS. Aortic valve replacement using autologous pericardium: single centre experience with the Ozaki technique. Swiss medical weekly. 2018 Feb 9;148(0506):w14591-.
14. Vukovic PM, Milojevic P, Stojanovic I, Micovic S, Zivkovic I, Peric M, Milicic M, Milacic P, Milojevic M, Bojic M. The role of ministernotomy in aortic valve surgery—A prospective randomized study. Journal of Cardiac Surgery: Including Mechanical and Biological Support for the Heart and Lungs. 2019 Jun;34(6):435-9.