Short-term outcomes of aortic valve neocuspidization using autologous fixed pericardium versus aortic valve replacement using mechanical prosthesis in patients with aortic valve disease

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Background
Aortic valve replacement by prosthetic valves, either mechanical or biological, is the ultimate known therapy for patients with aortic valve disease whether stenosis or regurgitation. However, these prostheses may have the concern of valve degeneration and the need for reoperation with the biological valves or the need for lifelong anticoagulation with considerable side effects with the mechanical valves. In this study, we compare the application of the new Ozaki technique in Ain Shams University Hospitals Cardiothoracic Academy to the current practice of aortic valve replacement using mechanical valve prosthesis

Aim of the work
To study the hemodynamic performance and major adverse events that are related to the valve of the novel technique in reconstructing the aortic valve using autologous pericardium (AVNeo) versus the conventional aortic valve replacement using a prosthetic mechanical valve.

Patients and methods
This was a nonrandomized clinical trial on 20 patients conducted at Ain Shams University Hospitals Cardiothoracic Academy during the period from November 2021 to December 2022. Inclusion criteria include age from 18 to 65 years, moderate to severe aortic stenosis, and sole aortic valve disease. Exclusion criteria include refusal of the Ozaki technique, concomitant intervention of the aortic arch, emergency surgery, porcelain aorta, and previous cardiac surgery. We divided the patient population into two groups through nonrandom allocation: Group I: aortic valve neocuspidization using autologous fixed pericardium and group II: aortic valve replacement using mechanical prosthesis.

Results
The hemodynamic performance of patients who underwent aortic valve replacement with either the AVNeo or AVR techniques was evaluated at discharge and 3 months postsurgery. No significant differences were observed in mean and median values of MPG, vena contracta, and coaptation length between the groups at discharge and 3 months postsurgery. However, at 3 months, the mean PPG was significantly lower in the AVNeo group compared with the AVR group (14.80±3.01 vs. 24.00±6.80, $P<0.001$). In addition, there was a significant decrease in mean PPG and MPG values within the AVNeo group at 3 months compared with at discharge ($P=0.005$ and $P<0.001$, respectively), whereas no significant change was observed in the AVR group. These findings suggest that the AVNeo technique may offer better hemodynamic outcomes in terms of PPG compared with the AVR technique at 3 months postsurgery.

Conclusion
Results showed that both AVNeo and AVR exhibit comparable outcomes at discharge and at 3 months after the study's conclusion. The postoperative morbidity and mortality are low with the Ozaki procedure, making it dependable and safe.

Keywords:
aortic valve neocuspidization, mechanical aortic valve replacement, Ozaki technique

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Introduction

Aortic valve replacement by prosthetic valves either mechanical or biological is the gold standard therapy for patients with aortic valve disease whether stenosis or regurgitation. However, these prostheses may have

the concern of valve degeneration and the need for reoperation with the biological valves or the need for lifelong anticoagulation with considerable side effects with the mechanical valves. Aortic valve replacement using autologous pericardium was first described by Duran *et al.*, where they performed aortic cusp extension and reconstruction [1]. Halees *et al.* then reported 16 years results of aortic valve reconstruction using a single strip of pericardium [2]. Ozaki *et al.* then highlighted the concept of independent aortic cusp reconstruction, each with its own size determined by the distance between the aortic commissures, which allowed performing this technique on any type of aortic valve disease [3].

Midterm outcomes of AVNeo regarding hemodynamic performance, morbidity, and mortality were satisfactory; in fact, freedom from death, accumulated incidence of reoperation, and recurrent moderate or severe aortic regurgitation were 86%, 4%, and 7%, respectively, Ozaki *et al.* [4]. AVNeo showed also low reoperation rates in the first 2 years, a low postoperative mean pressure gradient across the aortic valve of 8.5±3.7 mm Hg and a high mean effective orifice area of 2.2±0.7 cm^2Krane *et al.* [5]

Aim of the study

To study the hemodynamic performance and major adverse valve-related events of the novel technique in reconstructing the aortic valve cusps using autologous pericardium (AVNeo) versus the conventional aortic valve replacement using a prosthetic mechanical valve

Patients and methods

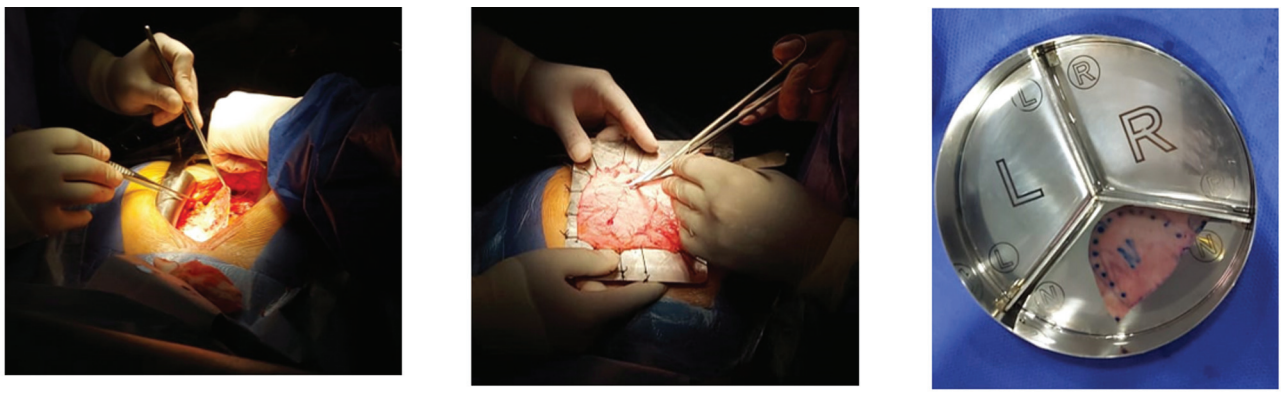
This was a nonrandomized clinical trial on 20 patients conducted at Ain Shams University Hospitals Cardiothoracic Academy from November 2021 to December 2022. Inclusion criteria included age from 18 to 65 years, moderate to severe aortic stenosis, and sole aortic valve disease. Exclusion criteria included refusal of the Ozaki technique, concomitant intervention of the aortic arch, emergency surgery, porcelain aorta, and previous cardiac surgery. We divided the patient population into two groups through the nonrandom allocation: Group I: aortic valve neocuspidization using autologous fixed pericardium and group II: aortic valve replacement using a mechanical prosthesis.

Surgical technique

For AVNeo

According to Ozaki *et al.*, Krane *et al.*, and Amabile *et al.* [3–6], the procedure starts with routine conventional median sternotomy and phrenic to phrenic harvesting of the pericardium (Fig. 1a**)** and mounting the pericardial patch on a metal plate to avoid shrinkage (Fig. 1b). For 10 minutes it is then immersed in a 0.6% glutaraldehyde solution, then rinsed in normal saline solution for 3 times, 6 min each in backward and forward manner. Cardiopulmonary bypass is established and cardioplegia is given routinely. The aortotomy site is marked and done. Diseased cusps are then excised and the annulus is decalcified. Using the AVNeo sizer, the cusp sizes are re-measured between the commissures. New leaflets are then fashioned from the autologous fixed pericardium using the AVNeo template (Fig. 1c), and they are then sutured with running 4-0 Prolene stitches to the native annulus with the smooth surface of the pericardium facing the ventricle. The cooptation of the commissures is then secured with additional 4-0 Prolene sutures together with a Teflon pledget outside the aorta.

Figure 1



(a) Pericardium is harvested, (b) mounted on a metal plate and is being prepared for immersion in glutaraldehyde solution, (c) noncoronary cusp leaflet after being crafted. Suture sites are marked using methylene blue marker.

For valve replacement using a mechanical prosthesis

Median sternotomy, routine cannulation, aortotmy, and excision of the diseased cusps, the annulus is measured using the conventional sizes provided for the St Jude mechanical valve. Valve sutures are taken using a horizontal everted mattress and routinely placed across the prosthesis sewing ring. The prosthetic valve is then parachuted into its place, followed by the tying of the stitches and closure of the aorta.

Results

The study included two groups of participants, the AVNeo group (n=10) and the AVR group (n=10), and their demographics were compared (Table 1). The mean age of the AVNeo group was 43.50±12.65 years, while the mean age of the AVR group was 49.70±13.42 years. The difference is not statistically significant (P=0.302).

Regarding sex, the AVNeo group had 50.0% males and 50.0% females, while the AVR group had 80.0% males and 20.0% females. However, the difference between both sex of the two groups was not statistically significant (P=0.350).

The study groups were compared in terms of their risk factors (Table 2). The AVNeo group (n=10) had no participants with diabetes mellitus (DM) and 20.0% hypertension (HTN), while the AVR group (n=10) had 30.0% with DM and 40.0% with HTN. The difference in DM and HTN prevalence was not statistically significant (P=0.211) and (P=0.628) regarding dyslipidemia, the AVNeo group had 40.0% with this condition, while the AVR group had 20.0% and the difference is not statistically significant (P=0.628).

In terms of chronic obstructive pulmonary disease (COPD), the AVNeo group had 30.0% with this condition, while the AVR group had 40.0%. However, the difference in COPD prevalence was not statistically significant (P=1.000).

The mean NYHA (New York Heart Association) functional class of the AVNeo group was 2.70±0.48,

Table 1 Demographics in the study groups

	Group		
Variables	AVNeo group (n=10)	AVR group (n=10)	P value between groups
Age			
Mean±SD.	43.50±12.65	49.70±13.42	0.302
Median (IQR)	40.00 (36.00–49.00)	52.50 (40.00–57.00)	
	n (%)	n (%)	
Sex			
Male	5 (50.0%)	8 (80.0%)	0.350
Female	5 (50.0%)	2 (20.0%)	
Weight			
Mean±SD	69.90±11.46	87.80±22.62	0.039*
Median (IQR)	68.00 (64.00–75.00)	96.00 (65.00–105.00)	
Height			
Mean±SD	1.68±0.11	1.68±0.11	1.000
Median (IQR)	1.64 (1.62–1.75)	1.67 (1.60–1.76)	
BMI			
Mean±SD.	24.78±2.80	31.07±6.81	0.015*
Median (IQR)	24.80 (23.20–26.40)	33.60 (27.20–35.10)	

Table 2 Risk factors of the study groups

	Group		
Variables	AVNeo group (n=10) n (%)	AVR group (n=10) n (%)	P value between group
DM	0 (0.0%)	3 (30.0%)	0.211
Dyslipidemia	4 (40.0%)	2 (20.0%)	0.628
COPD	3 (30.0%)	4 (40.0%)	1.000
HTN	2 (20.0%)	4 (40.0%)	0.628
NYHA			
Mean±SD.	2.70±0.48	3.44±0.53	
Median (IQR)	3.00 (2.00–3.00)	3.00 (2.00–4.00)	0.015*

while the mean NYHA functional class of the AVR group was 3.44±0.53. The difference in NYHA class between the two groups is statistically significant (*P*=0.015*).

The study groups were compared in terms of their laboratory data, including serum creatinine, hemoglobin (Hb), and hematocrit (Hct) (Table 3). The AVNeo group (*n*=10) had a mean serum creatinine level of 0.93±0.15, while the AVR group (*n*=10) had a mean serum creatinine level of 0.98±0.17 and the difference in serum creatinine levels was not statistically significant (*P*=0.631). Regarding Hb, the AVNeo group had a mean Hb level of 13.260±0.74, while the AVR group had a mean Hb level of 12.93 ±1.01. However, the difference in Hb levels was not statistically significant (*P*=0.415). Similarly, the AVNeo group had a mean Hct level of 39.29±1.91, while the AVR group had a mean Hct level of 38.50 ±0.97. However, the difference in Hct levels was not statistically significant (*P*=0.632).

The pre-echo data of the two study groups are presented in Table 4. The AVNeo group showed a higher mean EF (66.30±6.75) compared with the AVR group (58.90±11.34), although the difference was not significant (*P*=0.093). The mean MPG was higher in the AVR group (39.00±22.18) than in the AVNeo group (31.30±17.91), although the difference did not reach statistical significance (*P*=0.143). There was no significant difference between the groups in terms of PPG, AR, and IVS. In terms of AS and leaflet characteristics, there was no significant difference.

The hemodynamic performance of patients who underwent aortic valve replacement with either the AVNeo or AVR techniques was evaluated at discharge and 3 months postsurgery (Table 5). No significant differences were observed in mean and median values of MPG, vena contracta, and coaptation length between the groups at discharge and 3 months postsurgery. However, at 3 months, the mean PPG was significantly lower in the

Table 3 Laboratory data in the study groups

	Group		
Variables	AVNeo group (*n*=10)	AVR group (*n*=10)	*P* value between groups
Serum creatinine			
Mean±SD.	0.93±0.15	0.98±0.17	0.631
Median (IQR)	1.00 (1.00–1.10)	0.95 (0.90–1.10)	
Hb			
Mean±SD.	13.260±0.74	12.93±1.01	0.415
Median (IQR)	13.45 (12.70–13.90)	13.00 (12.00–14.00)	
Hct			
Mean±SD.	39.29±1.91	38.50±0.97	0.632
Median (IQR)	39.00 (39.00–42.70)	39.00 (39.00–40.00)	

Table 4 Pre-echo data in the study groups

	Group		
Variables	AVNeo group (*n*=10)	AVR group (*n*=10)	*P* value between group
EF			
Mean±SD.	66.30±6.75	58.90±11.34	0.093
Median (IQR)	67.00 (62.00–74.00)	60.50 (48.00–69.00)	
MPG			
Mean±SD.	31.30±17.91	39.00±22.18	0.143
Median (IQR)	38.50 (7.00–41.00)	43.00 (24.00–62.00)	
PPG			
Mean±SD.	62.30±36.52	62.00±33.16	0.853
Median (IQR)	76.00 (12.00–93.00)	66.00 (28.00–94.00)	
AR			
Mean±SD.	2.70±1.25	2.50±1.27	0.796
Median (IQR)	3.00 (3.00–4.00)	2.50 (1.00–4.00)	
IVS			
Mean±SD.	10.50±1.90	11.20±4.42	0.651
Median (IQR)	10.50 (9.00–11.00)	12.00 (10.00–15.00)	

Table 5 Hemodynamic performance at discharge and at 3 months in the study groups

Variables	Group		*P* value between group
	AVNeo group (*n*=10)	AVR group (*n*=10)	
MPG			
Mean±SD.			
At discharge	11.34±3.92	14.93±6.13	0.218
	12.00 (6.00-20.00)	13.00 (7.75-24.00)	
Median (IQR)			
At 3 months	8.70±2.91	13.78±5.26	0.035*
	9.50 (5.00–14.00)	12.00 (8.00-22.00)	
***P* value within the group**	0.005*	0.027*	
PPG			
Mean±SD.			
At discharge	20.07±5.72	25.60±8.81	0.218
	21.00 (12.00-32.00)	25.00 (15.00-39.00)	
Median (IQR)			
At 3 months	14.80±3.01	24.00±6.80	<0.001*
	15.00 (10.00-21.00)	24.00 (17.00-35.00)	
***P* value within the group**	0.005*	0.041*	
Vena contracta			
Mean±SD.			
At discharge	0.12±0.04	0.12±0.04	1.000
	0.10 (0.10-0.20)	0.10 (0.10-0.20)	
Median (IQR)			
At 3 months	0.12±0.04	0.11±0.03	0.780
	0.10 (0.10-0.20)	0.10 (0.10-0.20)	
***P* value within the group**	1.000	1.000	
Coapt. length			
Mean±SD.			
At discharge	1.35±0.05		
	1.35 (1.30-1.40)		
Median (IQR)			
At 3 months	1.35±0.05		
	1.35 (1.30-1.40)		
***P* value within the group**	1.000		

AVNeo group compared with the AVR group (14.80 ±3.01 vs. 24.00±6.80, $P<0.001$). In addition, there was a significant decrease in mean PPG and MPG values within the AVNeo group at 3 months compared with at discharge ($P=0.005$ and $P<0.001$, respectively), whereas no significant change was observed in the AVR group. These findings suggest that the AVNeo technique may offer better hemodynamic outcomes in terms of PPG compared with the AVR technique at 3 months postsurgery.

The secondary outcomes of the study groups are shown in Table 6 The results show that the AVNeo group had significantly higher values for bypass time (BPT) and cross-clamp time (CCT) compared with the AVR group ($P<0.001$); AVNeo group had a mean BPT of 167.20±22.82 min and a mean CCT of 106.90 ±28.77, while the AVR Group had a mean BPT of 102.20±19.04 min and a mean CCT of 68.80±14.48 There were no cases of bleeding, early valve failure, or endocarditis reported in either group. There were no cases of stroke or myocardial infarction reported in the AVNeo group, while one case of myocardial infarction and two cases of permanent pacemaker implantation were reported in the AVR group. The *P* value for the difference in permanent pacemaker implantation incidence between the groups was 0.474.

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 25.0. Qualitative data were described using numbers and percent, using χ^2 test as well as Fisher's exact test for variables with small expected numbers. The Kolmogorov–Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean and standard deviation, median and interquartile range (IQR),

Table 6 Secondary outcomes in the study groups

Variables	Group		*P* value between group
	AVNeo group (*n*=10)	AVR group (*n*=10)	
BPT			
Mean±SD.	167.20±22.82	102.20±19.04	<0.001*
Median (IQR)	167.50 (135.00–212.00)	101.50 (75.00–143.00)	
CCT			
Mean±SD.	106.90±28.77	68.80±14.48	<0.001*
Median (IQR)	92.00 (82.00–173.00)	71.00 (43.00–95.00)	
	n (%)	*n* (%)	
Mortality	0 (0.0%)	1 (10.0%)	1.000
Permanent Pacemaker	0 (0.0%)	2 (20.0%)	0.474
Bleeding	0 (0.0%)	2 (20.0%)	0.474
Early valve failure	0 (0.0%)	0 (0.0%)	
Stroke	0 (0.0%)	0 (0.0%)	
Myocardial infarction	0 (0.0%)	1 (10.0%)	1.000
Endocarditis	0 (0.0%)	0 (0.0%)	

and then compared using independent t-test or Mann–Whitney test. The significance of the obtained results was judged at the 5% level.

Discussion

In this single-center study, we sought to assess the clinical and hemodynamic performance of our initial aortic valve reconstruction patients in comparison to our standard aortic valve replacement using a mechanical prosthesis.

Hemodynamic Performance

In the literature, postoperative gradients are consistently found to be low after the AVNeo procedure, while Mourad et al. reported a mean pressure gradient of 6.8±2.9 mm Hg after a mean of 11.2±4.8 months. Ozaki et al. reported a mean pressure gradient of 15.2±6.3 mm Hg 8 years after the operation [4,7]. Krane *et al.* showed (at 6-12 months) a mean MPG of 8.8±4.4 mm Hg and a mean PPG of 16.1 ±7.9 mm Hg [5]. In our AVNeo group the mean MPG was 8.70±2.91 mm Hg and the mean PPG was 14.80 ±3.01 mm Hg at 3 months. In our study, AVNeo shows results comparable to AVR at discharge and at 3 months follow-up. While in terms of PPG, AVNeo shows lower gradients at 3 months of follow-up, which may indicate better hemodynamic performance.

Operative mortality and morbidity

The complexity of the AVNeo procedure, which results in extended cardiopulmonary bypass and cross-clamp times, is primarily to blame for the numerous worries about patient safety that have been expressed. Krane *et al.* reported a mean BPT of 166±29 min and a mean CCT of 135±20 min [5], while Ozaki *et al.* reported a mean BPT of 149.4±29.9 min and a mean CCT of 110.1±26.8 min [4]. In our study, the AVNeo group had a mean BPT of 167.20 ±22.82 min and a mean CCT of 106.90±28.77 min The Ozaki technique is safe and reliable with minimal postoperative morbidity and mortality. No permanent pacemaker implantations were required.

In our study, there was no need for reoperation for either early valve failure, bleeding, or endocarditis. There is some variance in the stated rates of reoperation and rates of infective endocarditis among patients who underwent aortic valve neocuspidization. During an average follow-up of 53.7 months, Ozaki et al. reported 15 reoperations among 850 patients, which is 0.4 reoperations for every 100 patients, at a 95% CI: 0.2–0.7 [4], And Mourad et al. reported five reoperations among 52 patients, which is equal to 10.3 reoperations for every 100 patients, CI 4.3–24.8 [7]. Endocarditis was the primary factor contributing to the need for reoperation in both studies.

Second, there is variance in the literature on the incidence of aortic valve insufficiency in patients who underwent aortic valve neocuspidization. In a follow-up time of up to 118 months, Ozaki et al. report the incidence of at least moderate aortic regurgitation in 7.3% of patients [4], whereas Mourad et al. report the incidence of trivial aortic regurgitation in 18.6% of patients (*n*=8). Regarding postoperative aortic regurgitation in our study and vena contracta, the AVNeo group showed accepted results compared with AVR.

Conclusion

The 'Ozaki' technique has grown in favor in recent years due to its potential advantages such as not requiring oral anticoagulation, using a foreign material, and being applicable to both aortic stenosis and aortic regurgitation. This study aimed to measure the hemodynamic performance and major adverse valve-related events of the novel technique in reconstructing the aortic valve cusps using autologous pericardium (AVNeo). Results showed that AVNeo and AVR both exhibit comparable outcomes at discharge and 3 months after the study's conclusion. The postoperative morbidity and mortality are low with the Ozaki procedure, making it dependable and safe.

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Nil.

Conflicts of interest

All authors have no conflict of interest to disclose.

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