Ozaki procedure: A novel technique for aortic valve reconstruction

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Background and aim

Mechanical heart valves require lifelong anticoagulation and therefore predispose to hemorrhagic events. Ozaki developed their aortic valve (AV) reconstruction technique at Toho University Ohashi Medical Center, where they standardized the use of glutaraldehyde-treated autologous pericardium to perform a trileaflet aortic valve. Therefore, it achieves maximum effective orifice area (EOA) and low transvalvular gradients. The current study aimed to assess the short-term Ozaki procedure in our center.

Patients and methods

A total of 86 patients were enrolled in the current study; group A included 43 patients who had undergone AVR using a biological aortic valve prosthesis, and group B included 43 patients who had undergone aortic valve replacement (AVR) using the Ozaki procedure.

Results

Both groups had comparable findings either at baseline, perioperative data, or during the follow-up. During follow-up either in the 3rd or 6th month both groups had insignificant differences. Renal dysfunction was reported in five (11.6%) patients of the biological valve group and two patients of the Ozaki group. Endocarditis was developed in only two patients with biological valves. Mild aortic regurgitation was noticed in one patient in the 3rd month and two patients in the 6th month in the case of the Ozaki procedure, while only one patient in the biological valve group developed mild AR in the 6th month of follow-up. Nearly all patients had improved NYHA classes in both groups. No patient in the Ozaki group was converted to AVR.

Conclusion

We have described our initial experience with the Ozaki procedure in adults. The current study reported promising results for the Ozaki procedure. Yet, multiple future studies in multiple centers are warranted to draw a firm conclusion and support our findings.

Keywords:

aortic valve replacement, biological aortic valve prosthesis, endocarditis, Ozaki procedure

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Introduction

Mechanical heart valves have the advantage of longevity in patients having aortic valve replacement (AVR), but they are associated with the risk of thrombosis, issues with long-term anticoagulation, and the danger of bleeding. Bioprosthetic valves, however, do not require long-term anticoagulation but may pose the risk of structural valve degradation and reoperation [1].

These issues are especially important when considering AVR options in developing countries, where life expectancy, socioeconomic and educational background, availability, cost, anticoagulation monitoring, monitoring of valve function and other valve-related complications, and the possibility of reoperation must all be taken into account [2].

In recent years, much attention has been given to repairing aortic valve disease, and the Ozaki procedure, involving the use of autologous pericardium for the aortic valve neocuspidization, is emerging as a very promising technique with the potential benefits of avoiding oral anticoagulation, foreign material, and is suitable for patients with small aortic annuli and infectious endocarditis [3,4]. This study aimed to assess the short-term outcome of the Ozaki procedure and its effect on morbidity and mortality.

Patients and methods

Study setting and design

A comparative, retrospective, prospective study was conducted at the Cardiothoracic Surgery Department of Assiut University Hospital, Assiut, Egypt, and

the Cardiothoracic Surgery Department, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol Heart Institute, United Kingdom. Patients signed an informed consent. Assiut Faculty of Medicine approved the study with IRB was 19/29000.

Participants

Inclusion criteria

Any patient was suitable for scanning under our protocol if all the following criteria applied:

(1) Patients with AVR either as an Ozaki leaflet reconstruction with autologous pericardium or biological aortic valve prosthesis.
(2) Patients over 18 years old who have given informed consent.

Exclusion criteria

Any patient presented with at least one of the following criteria was excluded from the study:

(1) Patients who were under 18 years of age
(2) Double-valve lesion or who had a history of CABG
(3) Patients with contraindications for CMR (MRI-incompatible CRT-D, metallic implants, claustrophobia)
(4) Patients with stage 4-5 chronic kidney disease (eGFR <30 ml/min/1.73 m^2).
(5) Pregnant patients
(6) Previous known allergy/reaction to gadolinium chelates
(7) The patient was unable to provide informed consent.

Participants(not calculated before enrolment)

A total of 86 patients were enrolled in the current study;

(1) Group A included 43 patients who had undergone AVR using a biological aortic valve prosthesis.
(2) Group B included 43 patients who had undergone AVR using the Ozaki procedure.

Methods

All patients were subjected to thorough history taking and clinical evaluation. The gathered data included age, sex, body mass index, and smoking status. Comorbidities included diabetes mellitus, hypertension, chronic kidney disease, and others. Details of intraoperative data were recorded. The Ozaki procedure was done based on its standard. Follow-up of those patients with CMR was done after 3 and 6 months [4].

Statistical analysis

Statistical analysis was performed with the use of SPSS statistical package version 18.0 for Windows. The Kolmogorov–Smirnov test was used to determine the normality of data distribution. Data are presented as mean (SD) or median (interquartile range) depending on the distribution of the variable.

Means between groups were compared with the use of the nonpaired Student's *t*-test or Wilcoxon–Mann–Whitney test. Chi-square was used to compare percentages. A P value of <0.05 was considered to be statistically significant.

Results

The study enrolled 100 patients with aortic valve disease, but 14 patients were excluded secondary to double-valve lesion (6 patients) and history of CABG (8 patients). So, a total of 86 patients were enrolled in the analysis; group A included 43 patients who had undergone AVR using a biological aortic valve prosthesis and group B included 43 patients who had undergone AVR using the Ozaki procedure. The majority (69.8%) of the biological valve group was females and the majority (62.8%) of those who underwent the Ozaki procedure were males with significant differences between both groups (P = 0.02) (Table 1). A higher frequency of aortic stenosis among the biological valve group (58.2%) and the majority of the Ozaki group had a significantly higher frequency of aortic regurgitation (62.8%) (Table 2).

Table 3 shows that both groups had insignificant differences as regards preoperative data. Five patients of the Ozaki procedure and two patients of the biological valve group had preoperative arrhythmia that was controlled preoperatively. Also, both groups had insignificant differences as regards intraoperative data. The majority of patients had full sternotomy incision (Table 4).

A lower length of stay was noticed with the Ozaki procedure (7.68 ± 1.57 vs. 14.76 ± 1.77 (days); P = 0.04) (Table 5). Renal dysfunction was reported in five (11.6%) patients of the biological valve group and two patients of the Ozaki group. Endocarditis was developed in only two patients with biological valves.

Mild aortic regurge was noticed in one patient in the 3rd month and two patients in the 6th month in the case of the Ozaki procedure, while only one patient in the biological valve group developed mild AR in the 6th month of follow-up. Nearly all patients had

Table 1 Baseline data of the studied groups

	Biological valve group (*n*=43)	Ozaki group (*n*=43)	*P*
Age (years)	44.56±8.99	55.44±12.45	<0.001
Sex			0.02
Male	13 (30.2%)	27 (62.8%)	
Female	30 (69.8%)	16 (27.2%)	
Body mass index (kg/m^2)	23.33±2.09	24.01±4.44	0.36
Comorbidities			
Diabetes mellitus	7 (16.3%)	4 (9.3%)	0.33
Hypertension	3 (6.9%)	2 (4.6%)	0.64
Pulmonary disease	2 (4.6%)	1 (2.3%)	0.55
Chronic kidney disease	1 (2.3%)	2 (4.6%)	0.55
Others	2 (4.6%)	1 (2.3%)	0.55

Data expressed as mean (SD) and frequency (percentage). *P* value was significant if <0.05.

Table 2 Disease characteristics among the studied groups

	Biological valve group (*n*=43)	Ozaki group (*n*=43)	*P*
Canadian Cardiovascular Society grade			0.34
0	1 (2.3%)	2 (4.6%)	
I	10 (23.2%)	9 (21%)	
II	25 (58.2%)	27 (62.8%)	
III	7 (16.3%)	5 (11.6%)	
New York Heart Association class			0.11
I	11 (25.5%)	10 (23.2%)	
II	25 (58.2%)	27 (62.8%)	
III	5 (11.6%)	5 (11.6%)	
IV	2 (4.6%)	1 (2.3%)	
Valve morphology			0.23
Trileaflet	25 (58.2%)	26 (60.5%)	
Bileaflet	18 (31.8%)	17 (29.5%)	
Aortic valve disease			<0.001
Aortic stenosis	25 (58.2%)	12 (28%)	
Aortic regurgitation	10 (23.2%)	27 (62.8%)	
Combined	8 (18.6%)	4 (9.2%)	

Data expressed as frequency (percentage). *P* value was significant if <05.

improved NYHA classes in both groups. None of the patients in the Ozaki group was converted to AVR.

Discussion

Renal dysfunction was reported in five (11.6%) patients of the biological valve group and two patients of the Ozaki group. Endocarditis was developed in only two patients with biological valves. Mild aortic regurgitation was noticed in one patient in the third month and two patients in the 6th month in the case of the Ozaki procedure, while only one patient in the biological valve group developed mild AR in the 6th month of follow-up. No patient in the Ozaki group was converted to AVR. Ngo *et al.* reported that two patients (3.3%) were required to be converted to aortic

Table 3 Preoperative data among the studied groups

	Biological valve group (*n*=43)	Ozaki group (*n*=43)	*P*
Hemoglobin (mg/dl)	11.45±2.22	12.01±2.11	0.11
Platelets (10^3/ul)	234.56±55.56	256.09±65.09	0.10
Leukocytes (10^3/ul)	5.66±1.11	5.90±2.01	0.33
Creatinine (mg/dl)	1.02±0.22	0.99±0.25	0.07
Aortic diameter (cm)	2.11±0.44	2.22±0.11	0.09
LVEDD (mm)	61.33±12.56	60.11±18.98	0.22
LVESD (mm)	59.44±13.11	57.88±10.10	0.90
Maximum gradient (mmHg)	89.44±22.19	90.11±23.34	0.20
Mean gradient (mmHg)	55.30±12.09	53.33±11.11	0.11
Preoperative LVEF (%)	54.74±4.15	55.44±4.40	0.42
Arrhythmia	2 (4.6%)	5 (11.6%)	0.19

Data expressed as frequency (percentage) and mean (SD). *P* value was significant if <05. LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter.

Table 4 Operative data among the studied groups

	Biological valve group (*n*=43)	Ozaki group (*n*=43)	*P*
Incision			0.44
Full sternotomy	38 (88.4%)	35 (81.4%)	
Mini-sternotomy	5 (11.6%)	8 (18.6%)	
Operation time (minute)	212.09±34.45	210.45±55.65	0.06
Cross-clamp time (minute)	115.70±3.64	114.67±4.84	0.11
Total bypass time (minute)	145.56±4.11	146.50±4.79	0.29
Intraoperative LVEF (%)	44.60±4.26	43.04±3.37	022
Number of DC shock	1 (0-2)	2 (0-3)	0.20
Joules of DC shock	17.11±10.73	18.60±9.69	0.08
Cardioplegia dose	2 (2-3)	2 (1-2)	0.07

Data expressed as median (range) and mean (SD). *P* value was significant if <05. LVEF, left ventricular ejection fraction.

valve replacement surgery [5]. In previous studies, no conversion was reported [4,6].

Although it was reported that the Ozaki technique lowered aortic valve size, this observation had no real impact. The inflexible frame restricts the functional orifice area of the stented bioprostheses and hinders the normal mobility of the aortic annulus. The Ozaki approach reconstructs the cusps while maintaining normal annulus size and motility and increasing the systolic-phase effective orifice area by utilizing three discretely sized and shaped pieces of the pericardium [7,8].

In our study, endocarditis was reported in only two patients of the biological valve group and was absent in all patients of the Ozaki procedure. Similar results were obtained [9]. These were consistent with previous studies [7,8]. Lower or no risk of endocarditis with the Ozaki procedure may be attributed to the use of the biological tissue from the same patient or prothesis.

Although the 5-year risk of severe AR significantly lowered after the first 300 cases,

Table 5 Postoperative data among the studied groups

	Biological valve group (*n*=43)	Ozaki group (*n*=43)	*P*
Hematocrit value (%)	28.64±2.01	28.26±1.80	0.32
Creatinine (mg/dl)	1.02±0.17	1.04±0.18	0.11
Creatine kinase (u/l)	478.40±134.26	429.22±159.76	0.45
Troponin (ng/ml)	0.53±0.22	0.59±0.17	0.56
Blood loss (ml)	517±183.11	509±235.97	0.33
Transfused blood unit	1.04±0.96	1.06±1.11	0.09
Hospital stay (days)	14.76±1.77	7.68±1.57	0.04
Time for extubation (days)	6.26±1.91	6.72±2.68	0.85
Dose of inotropes (mic/kg/min)	0.05±0.02	0.06±0.03	0.33
Duration of inotropes (hour)	9.32±4.97	10.24±3.81	0.30
Postoperative LVEF (%)	48±5.24	46.90±4.61	0.26
Temporal pacemaker	2 (4.6%)	1 (2.3%)	0.13
Reexploration	2 (4.6%)	3 (6.5%)	0.33

Data expressed as frequency (percentage) and mean (SD). *P* value was significant if <05. LVEF, left ventricular ejection fraction.

the Ozaki method was modified twice to address potential causes of AR. A 5-mm 'wing' extension was added to aid in commissure fixation. To diminish AR, equal tricuspidization was also implemented; however, a longer-term follow-up is required to validate the efficacy and durability of these alterations [10].

We discovered that patients who received the Ozaki treatment stayed in the hospital for a longer period. According toNgo *et al.*, patients who received the Ozaki operation spent 4.7 days in the intensive care unit. Because this is a novel procedure, the patients were detained in the intensive care unit for longer than normal. Despite this, the average mechanical ventilation time in their trial was 12.6 h, which is equal to standard aortic valve replacement operation [5]. These variations in our results may be secondary to different experiences with such procedures.

The Ozaki method also has the advantage of preserving the radial expansion of the crown-shaped aortic annulus and completely avoiding the use of a sewing ring. The Ozaki method has been demonstrated to yield outstanding hemodynamic results with EOA comparable to native, disease-free AV [11].

Only two patients died in our research, and both had AVR. The higher risk of death in the Ozaki group early on reflects the operation's complexity, which originally required a cross-clamp time of more than 2 h. A 30-day mortality rate of 1% is comparable to recently published aortic valve replacement outcomes [12].

Using autologous pericardium for aortic valve surgery has shown erratic results in terms of long-term consequences. With a mean age of 34 years and a follow-up of 11.43 years, Liu *et al.* reported their long-term results of aortic valve replacement using autologous pericardium in 0.2% glutaraldehyde for 10 min in 15 young patients with a 33% reoperation rate [13].

The current study's key limitations were that it was a single-center study with a limited sample size. The short follow-up period makes comparisons with aortic valve replacement surgery outcomes difficult. We will continue to monitor our patients to assess long-term outcomes.

However, based on the short-term outcomes reported in this study and the midterm results reported by Ozaki's group, aortic valve reconstruction surgery utilizing the Ozaki approach is safe, effective, and linked with favorable short-term outcomes. This could be a viable therapeutic alternative for people who cannot have close monitoring or who prefer not to use anticoag ulants.

Aortic valve disease as part of rheumatic heart disease is a common health problem in Egypt. The Ozaki technique could be the solution not only clinically but also economically.

Ozaki surgery contributes actively to reducing the financial burden that aortic valve replacement by a bioprosthetic valve constitutes on the national economy and reduces the future need for risky and expensive redo surgeries in the life of those patients.

In our center, a combined mitral repair and Ozaki procedure was safely performed in a child with RVD with promising short-term outcomes (Table 6).

Declarations: Ethics approval and consent to participate: The current study was approved by the Ethics Committee of the Faculty of Medicine, Assiut University (IRB no: 17200395). All the regulations of the Ethics Committee of the Faculty of Medicine were followed. The study was registered on *clinicaltrials.com* with Identification: NCT04277572.

Consent for publication: Consent was taken from participants for publication.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on request.

Competing interest: Not applicable.

Table 6 Three months follow-up among the studied groups

	Biological valve group (*n*=43)	Ozaki group (*n*=43)	*P*
LVEF (%)	52.64±2.01	52.26±1.80	0.55
Renal dysfunction	5 (11.6%)	2 (4.6%)	0.19
Endocarditis	2 (4.6%)	0	0.31
New York Heart Association class			0.09
I	39 (90.7%)	40 (93.1%)	
II	3 (6.9%)	3 (6.9%)	
III	1 (2.3%)	0	
Cardiac magnetic resonance in the 3rd month			
Aortic valve area (cm^2)	2.90±0.22	2.88±0.32	0.11
Aortic regurgitation			0.33
None	43 (100%)	42 (97.7%)	
Mild	0	1 (2.3%)	
Maximum gradient (mmHg)	19.40±4.44	20.11±5.11	0.9
Mean gradient (mmHg)	5.39±1.09	6.01±0.87	0.10
Cardiac magnetic resonance in the 6th month			
Aortic valve area (cm^2)	2.88±0.20	2.87±0.12	0.91
Aortic regurgitation			0.56
None	43 (97.7%)	41 (95.4%)	
Mild	1 (2.3%)	2 (4.6%)	
Maximum gradient (mmHg)	17.40±4.22	18.01±4.40	0.22
Mean gradient (mmHg)	5.11±1.03	5.02±0.89	0.98

Data expressed as frequency (percentage) and mean (SD). *P* value was significant if <05. LVEF, left ventricular ejection fraction.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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