

Outcomes of Ozaki Procedure/Aortic Valve Neocuspidization for Aortic Valve Diseases: A Systematic Review

ABSTRACT

Background: Perfect heart valve prostheses have optimized hemodynamics, reduced surgical morbidity, long-lasting durability, and extended patient survival with greater quality of life. Mechanical valves are recommended; however, young children may need anticoagulant medication for life. In this study, we looked at the success rate and viability of aortic valve neocuspidization (AVNeo) surgery for a variety of aortic disorders.

Methods: A methodical search strategy was used to fully evaluate the AVNeo results. Boolean operators were used to combine important words like "Ozaki Procedure," "Aortic Valve Neocuspidization," "AVNeo," and associated terms. Reputable databases such as PubMed, MEDLINE, Embase, Web of Science, and Scopus were the focus of our search. Study quality was assessed using a critical evaluation created with the Critical Appraisal Skills Programme tool.

Results: The findings are summarized in the "Results" section that contains descriptive and critical analysis, ramifications, and explanations. According to research, AVNeo improved valve function and had few side effects. Aortic valve neocuspidization has a lower mean pressure gradient and a larger mean efficient orifice area than Trifecta. Aortic valve neocuspidization surgery reduces aortic valve regurgitation and pressure gradients. Postoperative echocardiograms indicated a decrease in peak and a rise in mean pressure gradient.

Conclusion: The Ozaki method restores a healthy laminar flow pattern while preventing bivalvular disease. Ozaki procedure should be explored for valve repair in infants with truncal valve and congenital aortic disease. Aortic valve tricuspidization with glutaraldehyde-treated autologous pericardium results in considerable effective orifice area, modest pressure gradients, and little regurgitation.

Keywords: Aortic valve, aortic valve tricuspidization, aortic valve diseases, aortic valve neocuspidization, AVNeo, Ozaki procedure, heart diseases

INTRODUCTION

Optimized hemodynamics, low surgical morbidity, long-lasting durability, and eventually longer patient survival with a higher quality of life are the cornerstones of the notion of the perfect heart valve prosthesis.¹ Mechanical valves are prone to hemorrhagic episodes because they require lifelong anticoagulation. Contrarily, biological prostheses mount a persistent inflammatory response, are vulnerable to structural degradation, and often need to be replaced after 10–15 years.² Since the 1960s, attempts have been made to substitute aortic valve (AV) tissue with biological components, including the fascia lata and pericardium.³ Adults with aortic stenosis (AS) or aortic replacement still receive the best care with aortic valve replacement (AVR) by biological or mechanical prosthesis (AR).⁴ Heterologous tissue bioprostheses often deteriorate within 10–15 years in adults and much sooner in younger patients.⁵ For neocuspidization, the majority of facilities stick to the established Ozaki technique and use autologous pericardium. Despite this, xenologous pericardium in aortic valve neocuspidization (AVNeo) has also been reported.⁶ The anti-calcification tissue engineering procedure involves the removal of lipids, cellular remains, nucleic acids, and α -Gal epitopes from the

REVIEW

Samson S. Badalyan¹ 

Syune V. Markosyan² 

Alisher M. Ismailbaev³ 

Andleeb Asghar⁴ 

Aniq Ur Rehman⁵ 

¹Department of Cardiology, I.M. Sechenov University Hospital First Moscow State Medical University, Moscow, Russia

²Department of Cardiology, Yerevan State Medical University after Mkhitar Heratsi, Yerevan, Armenia

³Department of Cardiovascular Surgery, I.M. Sechenov University Hospital First Moscow State Medical University, Moscow, Russia

⁴Institute of Pharmaceutical Sciences, University of Veterinary and Animal Sciences, Lahore, Pakistan

⁵Department of Food Science and Human Nutrition, University of Veterinary and Animal Sciences, Lahore, Pakistan

Corresponding author:

Samson S. Badalyan
✉ sambadalyan06@gmail.com

Received: May 19, 2023

Accepted: August 31, 2023

Available Online Date: October 25, 2023

Cite this article as: Badalyan SS, Markosyan SV, Ismailbaev AM, Asghar A, Ur Rehman A. Outcomes of Ozaki procedure/aortic valve neocuspidization for aortic valve diseases: A systematic review. *Anatol J Cardiol.* 2023;27(11):619–627.



Copyright@Author(s) - Available online at anatoljcardiol.com.
Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

DOI:10.14744/AnatolJCardiol.2023.3477

typically used bovine pericardium, followed by low-concentration glutaraldehyde crosslinking to reduce cytotoxicity.⁷ Subsequent detoxification eliminates any remaining glutaraldehyde in the final product. Ozaki reconstruction may be a feasible alternative to the Ross technique, or at least a bridge solution, until further research can be conducted on the topic.

The primary aims of this study were to investigate the success rate and viability of AVNeo surgery across a range of aortic disorders. Aortic valve neocuspidization serves as a potential alternative to traditional aortic valve replacement techniques and holds the promise of improved hemodynamics, reduced surgical morbidity, and enhanced valve durability. The study aimed to assess the procedure's outcomes, encompassing parameters such as valve function, pressure gradients, and the occurrence of adverse effects. By examining various research papers and employing systematic search strategies, the study sought to provide a comprehensive, evidence-based analysis of AVNeo's effectiveness and its potential role in addressing aortic valve diseases.

METHODS

To comprehensively explore the outcomes of the AVNeo for aortic valve diseases, we employed a systematic search strategy. The primary keywords and phrases forming the foundation of our search included "Ozaki procedure," "aortic valve neocuspidization," "AVNeo," "aortic valve diseases," and "aortic valve tricuspidization." To ensure the inclusiveness of our search results, we combined these keywords using Boolean operators. Specifically, we created combinations such as (Ozaki Procedure or Aortic Valve Neocuspidization or AVNeo) and (Aortic valve diseases or Aortic valve tricuspidization). We also incorporated synonyms and related terms, such as "heart diseases," to account for potential variations. In order to focus our search on recent developments, we limited the scope of our search to scholarly papers published between the years 2018 and 2022. This time frame aimed to encompass the most up-to-date research findings relevant to the topic. To ensure a comprehensive search across various reputable sources, we conducted our search in several prominent databases. These databases included PubMed, MEDLINE, Embase, Web of Science, and Scopus. The search strategy was tailored to the specific requirements and search syntax of each database. Following the completion of our initial search, we meticulously screened the search results for relevance. The studies that met our

inclusion criteria underwent a rigorous critical appraisal process. This appraisal was carried out using the established Critical Appraisal Skills Programme (CASP) tool, allowing us to assess the quality and validity of the selected studies. By adhering to this systematic search strategy and employing the CASP tool for critical appraisal, we aimed to provide a well-rounded and evidence-based analysis of the outcomes of AVNeo surgery for aortic valve diseases, as evidenced by the scholarly literature published during the specified time frame.

Data Extraction and Synthesis of Results

During data extraction, researchers glean useful details from included studies, such as demographics and outcomes.⁸ Each review has a different set of questions that must be answered through data extraction. Hence, the forms used to do so must be tailored to each review individually.⁹ Both the abstracts and the entire papers were evaluated for their applicability to the review's aims, and those that did not make the cut were not included. The references used are all up-to-date and thoroughly researched to help you pick apart conflicting arguments. A number of previously published papers were evaluated by researchers using a rigorous data collection procedure. The features of a medical study include its authors, the date of publication, the stage of research, the types of patients examined, and the total number of cases. The sources are provided, and any possible biases are noted. The findings are summarized in a report that includes a descriptive and critical analysis, a description of the consequences, and an explanation of those consequences.

RESULTS

The research articles were assessed to determine if they met the specific criteria set by the current study. The selection of articles was based on the potential of their abstracts to provide distinct research findings. Initially, 365 documents were gathered from online sources. However, after removing duplicate articles, 141 studies were excluded. It was crucial to ensure that no duplicate research was included in the review, so we checked for reports of the same study published in multiple locations. In certain cases, multiple publications might be necessary, such as when a study is translated into different languages, when there are multiple follow-up time points, or when different outcomes are reported.¹⁰ By applying search restrictions to the title, abstract, keywords, and occasionally the full text, we narrowed down the initial results to 130 publications, excluding 94 investigations. After thorough evaluation, 77 studies were deemed inadequate and disregarded. Consequently, only 8 publications remained, as 45 studies were excluded due to flawed study designs, such as conference presentations, comments, and articles lacking sufficient data. Figure 1 shows the entire procedure as described by PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analysis).

Characteristics of Studies

The results and implications of the AVNeo procedure for patients with aortic valve diseases are clarified by the combined findings from the reviewed studies. Despite the fact

HIGHLIGHTS

- Aortic valve neocuspidization provides a substitute for traditional aortic valve replacement.
- The technique shows favorable results with improved valve performance and minimal adverse effects.
- The Ozaki operation is recommended for pediatric patients with congenital aortic and truncal valve disease, offering significant benefits such as improved valve function and reduced regurgitation.

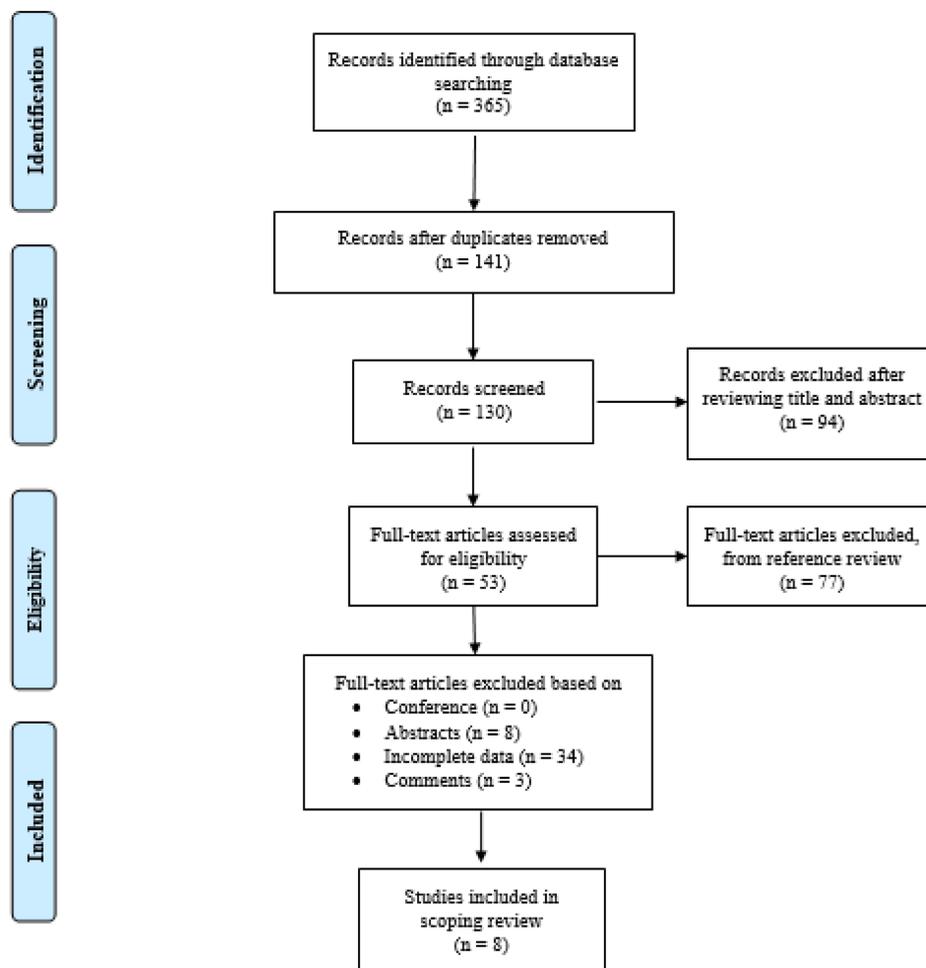


Figure 1. PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analysis) flowchart of study selection process.

that the studies' patient populations, sample sizes, and follow-up times varied, they all added to our knowledge of the advantages and disadvantages of this novel approach. The pericardium is removed using a median sternotomy, fixed to a metal plate to prevent shrinkage, and treated with glutaraldehyde before being washed with saline as part of the meticulous AVNeo procedure. In order to recreate a trileaflet aortic valve, the reconfigured pericardium is next sutured to the aortic annulus in a specific pattern. Despite its complexity, this procedure demonstrates the potential to return the aortic valve to its more natural state of function. Age, aortic valve type, and underlying conditions varied among patient populations across the studies. The 2 pathologies that the AVNeo procedure was primarily used to treat were aortic stenosis (AS) and aortic regurgitation (AR). These studies included patients with aortic valves that had different anatomies, such as tricuspid, bicuspid, unicuspid, and quadricuspid valves. Additionally, people with infective endocarditis or those who had previously had an aortic valve replacement found representation. It is clear from looking at the descriptive results that the AVNeo procedure produced excellent outcomes. Regardless of the initial valve morphology, the reconstruction of a trileaflet aortic valve was generally successful. Given the variety of aortic valve pathologies, this shows the potential of AVNeo to be efficient across various

valve types. But there were difficulties along the way. The technical complexity of the procedure was highlighted by some cases that required on-the-spot conversions to prosthetic valve replacement because of complications like aortic insufficiency or coronary occlusion. The studies showed comparatively low 30-day mortality rates, with one study reporting a 0.97% mortality rate. This information represents the short-term safety profile of the procedure.

Aortic stenosis patients in particular seemed to benefit from AVNeo's improved pressure gradients in terms of hemodynamic outcomes. Additionally, there was generally little need for secondary interventions, indicating favorable mid- to long-term durability. Positive indicators of the procedure's efficacy and stability over time included freedom from mortality rates and the cumulative incidence of reoperation or recurrent conditions. The findings from the studies taken together imply that AVNeo may be beneficial for patients with particular conditions. For instance, AVNeo may be advantageous for people with aortic stenosis and small annuli, who are frequently regarded as difficult cases for conventional valve replacement techniques. It might be used as an alternative method to enhance aortic valve performance without prosthetic valve replacements. Although the reviewed studies significantly advance our knowledge of

AVNeo, it is critical to recognize their limitations. Regarding patient characteristics, follow-up times, and evaluation methodologies, the studies varied. It is difficult to reach firm conclusions about the procedure's broad applicability and long-term durability because of this heterogeneity.

In cases of aortic stenosis and regurgitation, the AVNeo procedure shows promise as a treatment for aortic valve diseases. Despite some obstacles and restrictions, the studies show that it has the potential to successfully reconstruct the aortic valve and deliver positive results. To fully evaluate the procedure's applicability across various patient profiles and its sustainability over extended periods, more research is necessary (Table 1).

Table 1 explains the summary of outcomes from included studies.

Critical Appraisal Skills Programme Tool Appraisal

Table 2 presents a summary of the evaluation of research papers based on various criteria. Each paper is represented by the name of the author, followed by a series of plus (+) or minus (-) signs indicating the assessment of specific aspects related to the research. Additionally, a numerical score out of 10 is provided to indicate the overall evaluation of the research paper's quality.

Starting with the evaluation of the aims of research, all papers received a clear statement (+) except for Akiyama et al¹¹ (-), which suggests that their research objectives may not have been explicitly stated. The appropriateness of a qualitative methodology was considered appropriate (+) for all papers, indicating that this approach was suitable for the research conducted. The research design's appropriateness to address the aims of research was rated positively (+) for all papers, indicating that the chosen designs aligned with their research goals.

Regarding the recruitment strategy, most papers received a positive rating (+), implying that their recruitment strategies were appropriate for their research aims. However, Akiyama et al¹¹ received a negative rating (-), suggesting that their recruitment strategy may not have been aligned with their research objectives.

The data collection methods were considered appropriate (+) for all papers, indicating that the data collected were suitable for addressing the research issues. The relationship between researchers and participants was adequately considered (+) for all papers, highlighting that ethical considerations were taken into account in establishing a proper interaction between the researchers and participants.

The ethical issues were taken into consideration (+) for all papers, indicating that the researchers addressed the ethical concerns associated with their research. Data analysis was deemed sufficiently rigorous (+) for most papers, except for Akiyama et al¹¹ (-), suggesting that their data analysis may have been lacking in rigor.

A clear statement of findings was present (+) for all papers, indicating that they effectively communicated their research

outcomes. The research was generally considered valuable (+), as indicated by the high scores given to most papers.

Table 2 provides an overview of the evaluation of multiple research papers based on various criteria. The majority of papers received positive ratings in most categories, demonstrating that they exhibited strong scientific rigor and valuable contributions to their respective fields of study.

Resolution of Bias in Studies and Conflict Resolution

This study explores the effects of AVNeo, a different treatment option for aortic valve disorders. However, it's crucial to address potential sources of bias and conflicts that can have an impact on the findings and conclusions of any research in order to assure its credibility and objectivity. Publication bias is a typical bias that causes an imperfect representation of the entire data since studies with noteworthy results are more likely to be published. This may be avoided by researchers preregistering their investigations in clinical trial registries, which would guarantee that all findings—positive or negative—would eventually be published. This would lessen the propensity to publish only positive results. Financial considerations may introduce funding bias when studies supported by organizations with vested interests slant their conclusions in a particular manner. Full disclosure of funding sources and possible conflicts of interest would be part of a proactive strategy. To lessen the impact of commercial biases, researchers can actively seek for independent funding sources.

If the study population isn't representative of the larger group it's intended to study, selection bias may become evident. In addition to using randomization or matching approaches, it is imperative to pay close attention to the inclusion and exclusion criteria in order to handle this. Researchers can lessen selection bias by making sure that the study cohort appropriately matches the intended population. A thorough representation of the results can help to mitigate publication selectivity bias. In order to prevent an imbalance in the literature, journals should implement inclusive practices that encourage the publication of unfavorable or inconclusive results. Researchers should be open and honest about all findings, regardless of their statistical significance.

DISCUSSION

A variety of adult individuals with aortic valve dysfunction have benefited from the use of AVNeo.¹² It permits free aortic root growth during systole while maintaining the largest possible effective orifice size. In contrast to previous methods of repair, this 1 totally replaces the 3 damaged leaflets with 3 cusps taken from the patient's own or a bovine pericardium.¹³ At 4.5 years, 93% of people were free of recurrent moderate or higher AR, and 96% were free of aortic valve reoperation, indicating encouraging results.¹⁴ When compared to published mortality rates after surgical aortic valve replacement, the results of Krane et al¹⁵ are consistent with a 30-day death rate of 0.97% in the study population. In a long-term observational investigation, Kim and Lee¹⁶ observed that the rate of permanent pacemaker implantation (PPI) was 3.9% in the first 30 days following conventional aortic replacement, and

Table 1. Summary of Outcomes from Included Studies

Author (s) Names and Year	Aim	Research Design	Sample Population	Results	Conclusion
(Krane et al 2021) ¹⁵	To analyze the hemodynamic and clinical outcomes in patients who underwent AVNeo	Prospective retrospective study	103 patients	All patients had a successful restoration of a trileaflet aortic valve. Aortic valve neocuspidization was shown to have a much lower mean pressure gradient and a greater mean efficient orifice area than the virtually implanted Trifecta Bioprosthesis.	Reoperation rates were minimal with AVNeo within the first 2 years following surgery. Within the first year, the effective orifice area and mean pressure gradient were steady, indicating excellent hemodynamic performance.
(Iida et al 2018) ³⁶	To elucidate the surgical outcome of AVNeo in patients with AS	Prospective study	144 patients	Two people deceased from causes other than heart disease; liver failure and sepsis were to blame. One week after the surgery, echocardiography indicated a peak pressure gradient of 22-10.7 mm Hg, and 20 months later, it was 19.2-9.7 mm Hg.	Regarding short- and long-term benefits of AVNeo, it is clear that it is a good option for AS patients.
(Arutyunyan et al 2020) ²²	To determine the feasibility of AVNeo with glutaraldehyde-treated autologous pericardium.	Prospective multicenter study	170 patients	There was no change to aortic valve replacement using a prosthesis. Although 8 patients required further surgery owing to bleeding, no patients required additional surgery because to early infective endocarditis. There were 5 non-cardiac fatalities that occurred in hospitalization. Postoperative echocardiographic tests showed a considerable reduction in peak pressure gradient (from 58.7 ± 1.7 mm Hg to 11.2 ± 5.6 mm Hg) and a significant increase in mean pressure gradient (from 3.02.5 mm Hg to 6.03.5 mm Hg).	Good clinical outcomes are achievable and repeatable with AVNeo. The aortic valve regurgitation is reduced, and the pressure gradients are low right after surgery using the AVNeo procedure.
(Ozaki et al 2018) ³⁵	To evaluate mid-term results of AVNeo with the longest follow-up of 118 months	Prospective study	850 patients	Aortic stenosis, as detected by preoperative echocardiography, was associated with a peak pressure gradient of 68.9 mm Hg. The diameter of the surgical annulus was 20.9 mm. There was no change to a valve replacement with a prosthesis. At least 16 people died while being treated in hospitals. One week after surgery, the average peak pressure gradient was 19.5 mm Hg, and 8 years later, it was 15.2 mm Hg, as measured by echocardiography.	In patients with a range of aortic valve disorders, AVNeo performed using autologous pericardium produced encouraging mid-term results.
(Akiyama et al 2020) ¹¹	To evaluate the midterm outcome of AVNeo for AS with a small annulus	Prospective study	34 patients	No annulus expansion or conversion to aortic valve replacement occurred. Two people died within the hospital from non-cardiac causes. Because for aortic regurgitation and infectious endocarditis, 3 patients had to have surgery again.	For AS with a tiny annulus, the midterm results of AVNeo were outstanding.

(Continued)

Table 1. Summary of outcomes from included studies (Continued)

(Secinaro et al 2022) ¹⁹	To evaluate the aortic blood flow characteristics after AV neocuspidization in pediatric patients	Prospective study	20 patients	The Ozaki group showed increased transvalvular maximum velocity	In the short-term follow-up, the Ozaki approach restores a healthy laminar flow pattern while avoiding the development of bivalvular illness.
(Baird et al 2021) ³³	To report early outcomes of the Ozaki procedure for congenital aortic and truncal valve disease.	Retrospective study	57 patients	About 51 patients had simultaneous operations. The median length of time spent in the intensive care unit was 1.87 days, while the median length of time spent in the hospital was 6.38 days. No patients died in the hospital, and no one had to have their valves replaced prematurely. Peak aortic gradient was 16.99.5 mm Hg, and 98% of 9 patients with regurgitation at discharge had it be moderate or less.	In children with truncal valve and congenital aortic disease, the Ozaki operation provides satisfactory short-term outcomes and should be considered for valve reconstruction.
(Marathe et al 2020) ³⁷	To report early outcomes in young patients with small native aortic valve annuli	Retrospective study	51 patients	The average duration of stay in the intensive care unit was 2 days, whereas the average length of stay in the hospital was seven and a half days. No more procedures were necessary, and there was just 1 hospital-related death that was unrelated to the aortic valve. The median peak gradient was 18 mm Hg at discharge, and 94% of patients were classified as having mild AR. Moderate AR and AS were present in 80% and 82% of patients, respectively, after a mean follow-up of 11.9 months. Reoperation was necessary for 3 patients.	Young patients with tiny aortic annuli had good short-term outcomes following the Ozaki surgery. With annular expansion surgery, the aortic annulus can be made bigger.

AS, aortic stenosis; AVNeo, aortic valve neocuspidization.

it continued to rise over the course of the long-term follow-up. Further up to 9% PPI rates have been documented following the implantation of quick deployment valves. Similarly, Krane et al¹⁷ found that a mean pulmonary gradient (MPG) of 3.55 mm Hg at discharge was safe for patients.

A total of 3 patients with preoperative paroxysmal atrial fibrillation were prescribed oral anticoagulants, and 1 patient with chronic atrial fibrillation was prescribed warfarin, according to the research published by Iida et al¹⁸ in 2020. Another individual post-operatively received antiplatelet medication. Patients with anticoagulant treatment contraindications, such as liver cirrhosis or gastrointestinal bleeding, may potentially benefit from these procedures.¹⁹ The pressure gradient is reduced after surgery, which is another benefit of AVNeo. Caused by a near-equivalence between the effective orifice area (EOA) and the aortic annulus area.²⁰ As shown by Iida et al¹⁸, it is possible to reduce the pressure gradient after surgery to a level below that which existed before. Midway through the term, this continued to be the case. Patients with AS with a narrow aortic annulus had no evidence of an elevated pressure gradient. Since

the aortic annulus enlarges and makes adjustments before the stenosis worsens, this is the case. In this case, the pressure gradient will shift after the implantation of an artificial valve. Because the natural expansion and contraction of the aortic annulus cannot occur once an artificial cuff has been sutured and fixed to the annulus. When everything is working as it should, the annulus of the aortic valve expands during the systolic phase and contracts during the diastolic phase.²¹

In addition to a reduced surgical mortality rate, the most notable findings by Arutyunyan et al²², were the statistically significant reductions in pressure gradients and rise following AVNeo. The aortic annulus after AVNeo surgeries is identical to that of a normal aortic valve, as shown by an examination of alterations to the annulus during the cardiac cycle.²³ When compared to patients who had AVR, both groups exhibited smaller peak pressure gradients and retained systolic annular motion.²⁴ In 147 patients, Iida et al¹⁸ used AVNeo to treat a wide range of aortic valve diseases. Following AVNeo for aortic valve disease, the aortic annulus diameters of 25 patients were measured and compared to those of 15 patients with normal aortic valves. The transthoracic echocardiographic

Table 2. Critical Appraisal Skills Programme Tool Appraisal Score

Authors	Was There a Clear Statement of Aims of Research?	Is a Qualitative Methodology Appropriate?	Was the Research Design Appropriate to Address the Aims of Research?	Was the Recruitment Strategy Appropriate to the Aims of Research?	Was the Data Collected in a Way that Addressed the Research Issue?	Has the Relationship Between Researcher and Participants Adequately Considered?	Have the Ethical Issues Been Taken into Consideration?	Was the Data Analysis Sufficiently Rigorous?	Is there a Clear Statement of Finding?	How Valuable is the Research?	Score
(Krane et al 2021) ¹⁵	+	+	+	+	+	+	+	+	+	+	10/10
(Iida et al 2018) ³⁶	+	+	+	-	+	+	+	+	+	+	9/10
(Arutyunyan et al 2020) ²²	+	+	+	+	+	+	+	+	+	+	10/10
(Ozaki et al 2018) ³⁵	+	+	+	+	+	+	+	+	+	+	10/10
(Akiyama et al 2020) ¹¹	-	+	+	+	-	+	+	+	-	+	7/10
(Secinaro et al 2022) ¹⁹	+	+	+	-	+	+	+	+	+	+	9/10
(Baird et al 2021) ³³	+	+	+	+	+	+	+	+	+	-	10/10
(Marathe et al 2020) ³⁷	+	+	+	+	+	+	-	+	+	+	9/10

measurements of the aortic annulus in patients receiving AVNeo were shown to be statistically indistinguishable from those of patients with normal aortic valves by the group of researchers.²⁵ Unlike a rigid prosthetic valve, the annulus area in the systolic phase of the cardiac cycle was always bigger than that in the diastolic phase.²⁶ These findings provided substantial support for the hypothesis that the AVNeo operation keeps the aortic annulus mobile, leading to a larger effective orifice area and improved hemodynamics.

Electrocardiography-gated multidetector computed tomography was used to determine aortic annular diameters in 23 individuals.²³ They included 5 patients who had AVR, 10 patients with normal aortic valves, and 8 patients who had AVNeo. Comparisons were made between the AVNeo and AVR groups in terms of peak pressure gradients after surgery. Patients who had AVNeo did not have statistically different annulus variations from those with normal aortic valves. Both groups showed a greater annular area during systole compared to diastole. The peak pressure gradients in the AVNeo group after surgery were substantially lower than in the AVR group. Multiple clinical studies from additional facilities are available. Post-operative echocardiography has shown that patients with AVNeo had a greater effective orifice area of the aortic valve and lower values of the aortic valve pressure gradient than patients with traditional bioprosthetic valves.²⁷ People with AVNeo had aortic annular alterations that were comparable to patients with normal aortic valves. Electrocardiography-gated multidetector computed tomography provided evidence of this by measuring annulus motion throughout the cardiac cycle. Patients with AVNeo were also shown to have a lower pressure gradient compared to those with AVR.²⁸ The diameter of the aortic annulus may be measured by trans-esophageal echocardiography utilizing speckle tracking.²⁹

According to Akiyama et al¹¹, even in AS with a tiny annulus, the natural annulus is successfully utilized, suggesting that AVNeo can collect enough EOAI. Additionally, the rebuilt leaflets are less stressed by the annulus's unconstrained motions than they are by the prosthetic valves where the annulus is locked, which is helpful in preventing structural valve degeneration. The aortic annulus has the same diameter following AVNeo as it does with a normal aortic valve, and its movement during the cardiac cycle is unrestricted.¹⁸ Given that the aortic valve's properties are preserved during AVNeo, it may be said that this procedure is more physiological than surgical AVR. For dialysis patients, AVNeo was beneficial.³⁰ However, dialysis patients are susceptible to hypercalcemia brought on by secondary hyperparathyroidism, which is accompanied by an increase in cardiovascular events.³¹ According to Saisho, the management of hyperphosphatemia is crucial for the therapy of vascular calcification. Therefore, it could be crucial to control the serum calcium and phosphate concentrations following AVNeo in dialysis patients.³²

There have been conflicting outcomes in Baird et al³³ when employing autologous pericardium for aortic valve surgery. Albertini et al³⁴ presented their long-term outcomes of aortic valve replacement utilizing autologous pericardium treated

in 0.2% glutaraldehyde for 10 minutes with a 33% reoperation rate. In a similar treatment plan to that described by Ozaki, Carotti³⁸ reported the long-term outcomes of the leaflet extension approach employing autologous pericardium. In that series, a 15% reoperation rate after 7 years was seen in 41 patients with a mean age of 32 years, indicating that autologous pericardial patches may outlast bioprosthetic aortic valves in younger individuals. Autologous and Photofix-treated bovine pericardium tended to be more durable than glutaraldehyde-fixed bovine pericardium in juvenile patients having aortic valve replacement.

CONCLUSION

Aortic valve neocuspidization provided a substitute for established traditional AV. The technique has shown favorable results, showing a significant hemodynamic improvement in valve performance and minimal incidence of adverse effects. For valve repair in pediatric patients with congenital aortic and truncal valve disease, the Ozaki operation should be taken into account. The results demonstrate that aortic valve tricuspidization with glutaraldehyde-treated autologous pericardium results in significant EOA, immediate postoperative low-pressure gradients, and little aortic regurgitation. Although the procedure's success in treating AS and AR is well documented, its applicability to all aortic valve diseases is still under debate. Patients with AS and AR who have aortic valves with different morphologies, such as tricuspid, bicuspid, unicuspid, and quadricuspid configurations, may be especially well-suited for AVNeo. In cases where the aortic annulus is small or when patients have had prior aortic valve replacements, this procedure provides an alternative to traditional valve replacement techniques.

Ethics Committee Approval: Not Applicable.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.A., A.R.; Design – A.A., A.R.; Supervision – S.B., S.M.; Resources – S.B., A.I.; Materials – A.A., S.B.; Data Collection and/or Processing – A.A., S.M.; Analysis and/or Interpretation – A.R., A.I.; Literature Search – S.B., S.M.; Writing – S.B., A.I.; Critical Review – S.B., A.I.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

REFERENCES

- Chahine J, Kadri AN, Gajulapalli RD, et al. Outcomes of transcatheter aortic valve replacement in mixed aortic valve disease. *JACC Cardiovasc Interv.* 2019;12(22):2299-2306. [CrossRef]
- Kostyunin AE, Yuzhalin AE, Ovcharenko EA, Kutikhin AG. Development of calcific aortic valve disease: do we know enough for new clinical trials? *J Mol Cell Cardiol.* 2019;132:189-209. [CrossRef]
- Yadgir S, Johnson CO, Aboyans V, et al. Global, regional, and national burden of calcific aortic valve and degenerative mitral valve diseases, 1990-2017. *Circulation.* 2020;141(21):1670-1680. [CrossRef]

4. Cho KI, Sakuma I, Sohn IS, Jo SH, Koh KK. Inflammatory and metabolic mechanisms underlying the calcific aortic valve disease. *Atherosclerosis*. 2018;277:60–65. [\[CrossRef\]](#)
5. De Paulis R, Salica A. Surgical anatomy of the aortic valve and root—implications for valve repair. *Ann Cardiothorac Surg*. 2019;8(3):313–321. [\[CrossRef\]](#)
6. Karabacak K, Kubat E, Erol G, et al. Aortic neocuspidization with autologous pericardium: initial experience of single center. *World J Cardiovasc Surg*. 2021;11(6):51–60. [\[CrossRef\]](#)
7. Sivalingam S, Haranal M, Pathan IH. Aortic valve neocuspidization for aortic regurgitation associated with ventricular septal defect. *Interact Cardiovasc Thorac Surg*. 2022;34(2):315–321. [\[CrossRef\]](#)
8. Busetto L, Wick W, Gumbinger C. How to use and assess qualitative research methods. *Neurol Res Pract*. 2020;2(1):14. [\[CrossRef\]](#)
9. Bougie R, Sekaran U. *Research Methods for Business: A Skill Building Approach*. Chichester: John Wiley & Sons; 2019.
10. Dekker R, Franco Contreras J, Meijer A. The living lab as a methodology for public administration research: A systematic literature review of its applications in the social sciences. *Int J Public Admin*. 2020;43(14):1207–1217. [\[CrossRef\]](#)
11. Akiyama S, Iida Y, Shimura K, Fujii S, Shimizu H, Sawa S. Midterm outcome of aortic valve neocuspidization for aortic valve stenosis with small annulus. *Gen Thorac Cardiovasc Surg*. 2020;68(8):762–767. [\[CrossRef\]](#)
12. Blitzer D, Nguyen S, Bacha E, LaPar DJ. Aortic valve neocuspidization in a pulmonary autograft. *Ann Thorac Surg*. 2022;113(2):e123–e124. [\[CrossRef\]](#)
13. Benedetto U, Gergely S, Dimagli A, Sinha S. AVNeo (Ozaki) and transaortic mitral valve repair using autologous pericardium only for aortomitral endocarditis. *JTCVS Tech*. 2020;3:101–103. [\[CrossRef\]](#)
14. Kawashima T, Umeno T, Terazawa T, et al. Aortic valve neocuspidization with in-body tissue-engineered autologous membranes: preliminary results in a long-term goat model. *Interact Cardiovasc Thorac Surg*. 2021;32(6):969–977. [\[CrossRef\]](#)
15. Krane M, Boehm J, Prinzing A, Ziegelmüller J, Holfeld J, Lange R. Excellent Hemodynamic Performance After Aortic Valve Neocuspidization Using Autologous Pericardium. *Ann Thorac Surg*. 2021;111(1):126–133. [\[CrossRef\]](#)
16. Kim J, Lee JW. Aortic valve neocuspidization: oversized shoes for children? *J Thorac Cardiovasc Surg*. 2019;157(2):729. [\[CrossRef\]](#)
17. Krane M, Wirth F, Boehm J, Lange R. Do we need to rethink treatment of aortic valve pathologies in younger patients? *Eur J Cardiothorac Surg*. 2021;60(1):46–47. [\[CrossRef\]](#)
18. Iida Y, Sawa S, Fujii S, Shimizu H. Aortic valve neocuspidization in patients under 65 years old. *Gen Thorac Cardiovasc Surg*. 2020;68(8):780–784. [\[CrossRef\]](#)
19. Secinaro A, Milano EG, Ciancarella P, et al. Blood flow characteristics after aortic valve neocuspidization in paediatric patients: a comparison with the Ross procedure. *Eur Heart J Cardiovasc Imaging*. 2022;23(2):275–282. [\[CrossRef\]](#)
20. Blitzer D, Lapar D, Montana D, et al. Aortic Valve Neocuspidization (Ozaki technique) for Pediatric Patients: an Early Single Center Experience. *Struct Heart*. 2020;4:47. [\[CrossRef\]](#)
21. Ricciardi G, Biondi R, Tamagnini G, Giglio MD Del. Aortic valve reconstruction with Ozaki technique. *Braz J Cardiovasc Surg*. 2022;37(1):118–122. [\[CrossRef\]](#)
22. Arutyunyan V, Chernov I, Komarov R, et al. Immediate outcomes of aortic valve neocuspidization with glutaraldehyde-treated autologous pericardium: A multicenter study. *Braz J Cardiovasc Surg*. 2020;35(3):241–248. [\[CrossRef\]](#)
23. Yamamoto N, Ito H, Inoue K, et al. Impact of valvuloarterial impedance on left ventricular reverse remodeling after aortic valve neocuspidization. *J Cardiothorac Surg*. 2022;17(1):13. [\[CrossRef\]](#)
24. Seese L, Yoon P, Morell VO, Chu D. Aortic root replacement with autologous pericardium valved conduit. *Ann Thorac Surg*. 2022;113(3):e227–e229. [\[CrossRef\]](#)
25. Liogky A, Karavaikin P, Salamatova V. Impact of material stiffness and anisotropy on coaptation characteristics for aortic valve cusps reconstructed from pericardium. *Mathematics*. 2021;9(18):2193. [\[CrossRef\]](#)
26. Prinzing A, Böhm J, Sideris K, Vitanova K, Lange R, Krane M. AVNeo improves early hemodynamics in regurgitant bicuspid aortic valves compared to aortic valve repair. *Interact Cardiovasc Thorac Surg*. 2022;35(5). [\[CrossRef\]](#)
27. Baird CW, Marathe SP, Del Nido PJ. Aortic valve neo-cuspidation using the Ozaki technique for acquired and congenital disease: where does this procedure currently stand? *Indian J Thorac Cardiovasc Surg*. 2020;36(1)(suppl 1):113–122. [\[CrossRef\]](#)
28. Lansac E, de Kerchove L. Aortic valve repair techniques: state of the art. *Eur J Cardiothorac Surg*. 2018;53(6):1101–1107. [\[CrossRef\]](#)
29. Terazawa T, Kawashima T, Umeno T, et al. Mechanical characterization of an in-body tissue-engineered autologous collagenous sheet for application as an aortic valve reconstruction material. *J Biomech*. 2020;99:109528. [\[CrossRef\]](#)
30. DeRoo SC, Aldea GS. Commentary: AVneo—impressive early results; however, long-term durability remains unknown. *JTCVS Open*. 2021;8:205–206. [\[CrossRef\]](#)
31. Liakopoulos OJ. Commentary: AVNeo (Ozaki) and transaortic mitral valve repair using autologous pericardium only for aortomitral endocarditis: the perfect solution in double-valve invasive aortomitral endocarditis? *JTCVS Tech*. 2020;3:108–109. [\[CrossRef\]](#)
32. Saisho H, Scharfschwerdt M, Schaller T, et al. Ex vivo evaluation of the Ozaki procedure in comparison with the native aortic valve and prosthetic valves. *Interact Cardiovasc Thorac Surg*. 2022;35(3):ivac199. [\[CrossRef\]](#)
33. Baird CW, Cooney B, Chávez M, Sleeper LA, Marx GR, Del Nido PJ. Congenital aortic and truncal valve reconstruction using the Ozaki technique: Short-term clinical results. *J Thorac Cardiovasc Surg*. 2021;161(5):1567–1577. [\[CrossRef\]](#)
34. Albertini A, Raviola E, Zucchetta F, Brega C, Mikus E, Tripodi A. Aortic valve neocuspidization with glutaraldehyde-treated autologous pericardium to avoid the prosthesis-patient mismatch of a severely obese 57-year-old patient—a case report. *J Vis Surg*. 2021;8:24. [\[CrossRef\]](#)
35. Ozaki S, Kawase I, Yamashita H, Uchida S, Takatoh M, Kiyohara N. Midterm outcomes after aortic valve neocuspidization with glutaraldehyde-treated autologous pericardium. *J Thorac Cardiovasc Surg*. 2018;155(6):2379–2387. [\[CrossRef\]](#)
36. Iida Y, Fujii S, Akiyama S, Sawa S. Early and mid-term results of isolated aortic valve neocuspidization in patients with aortic stenosis. *Gen Thorac Cardiovasc Surg*. 2018;66(11):648–652. [\[CrossRef\]](#)
37. Marathe SP, Chávez M, Sleeper LA, Marx G, Del Nido PJ, Baird CW. Modified Ozaki Procedure Including Annular Enlargement for Small Aortic Annuli in Young Patients. *Ann Thorac Surg*. 2020;110(4):1364–1371. [\[CrossRef\]](#)
38. Carotti A. *Pediatric Aortic Valve Neocuspidization. Multimedia Manual of Cardiothoracic Surgery: MMCTS*; 2022.