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CT-Derived Leaflet Sizing Discrepancy Is Associated With Valve-Related Events After Aortic Valve Neocuspidization

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Research Article

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Posted Date: November 16th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10887219/v1

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Additional Declarations: No competing interests reported.

Title:

CT-Derived Leaflet Sizing Discrepancy Is Associated With Valve-Related Events After Aortic Valve Neocuspidization

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Abstract

Background

Accurate leaflet sizing is essential for aortic valve neocuspidization (AVNeo), yet objective anatomical references for selecting leaflet size remain limited. We investigated whether the discrepancy between a patient-specific computed tomography (CT)-derived anatomical reference and intraoperatively selected leaflet size was associated with valve-related events after AVNeo and assessed the reproducibility of the CT-derived measurements.

Methods

We retrospectively investigated 32 consecutive patients who underwent AVNeo with preoperative ECG-gated CT. A CT-derived reference leaflet size was geometrically estimated from the intercommissural distance. Sizing discrepancy was defined as the difference between the CT-derived reference and intraoperatively selected leaflet size, with maximum Δ representing the largest discrepancy among the three cusps. Interobserver reproducibility was assessed using independent measurements by a radiologic technologist, an experienced cardiovascular surgeon, and a cardiovascular surgery trainee. Associations with valve-related events were assessed using Cox proportional hazards and receiver operating characteristic analyses, and interobserver reliability was evaluated using intraclass correlation coefficients.

Results

During a median follow-up of 23 months, valve-related events occurred in eight patients. Greater maximum Δ was associated with valve-related events (hazard ratio, 1.39 per 1-mm increase; 95% confidence interval [CI], 1.09–1.78; $P = 0.004$). Exploratory receiver operating characteristic analysis identified 4.9 mm as the optimal cutoff (area

under the curve [AUC], 0.818; 95% CI, 0.647–0.989), and patients with maximum Δ ≥4.9 mm had lower valve-related event-free survival (log-rank P = 0.020). Interobserver reliability was moderate to good, with intraclass correlation coefficients of 0.726 (95% CI, 0.339–0.881), 0.703 (95% CI, 0.231–0.879), and 0.832 (95% CI, 0.516–0.932) for the right coronary, left coronary, and noncoronary cusps, respectively. Observer-specific AUCs for maximum Δ were 0.776 for the radiologic technologist, 0.818 for the experienced cardiovascular surgeon, and 0.667 for the cardiovascular surgery trainee.

Conclusions

Greater discrepancy between the CT-derived anatomical reference and intraoperatively selected leaflet size was associated with subsequent valve-related events after AVNeo. CT-derived measurements showed moderate-to-good interobserver reliability, although discriminatory performance varied among observers. These findings support further investigation of CT-derived anatomical sizing as a patient-specific reference for AVNeo, while highlighting the need for standardized measurement methods and external validation in larger cohorts.

Keywords: Aortic valve neocuspidization; Aortic valve reconstruction; Computed tomography; Leaflet sizing; Aortic regurgitation; Interobserver reproducibility

Introduction

Aortic valve neocuspidization (AVNeo), originally described by Ozaki et al., has emerged as an alternative to prosthetic aortic valve replacement by reconstructing the native aortic valve using glutaraldehyde-treated autologous pericardium [1,2]. Several studies have demonstrated favorable early and mid-term clinical outcomes, including low transvalvular pressure gradients and freedom from prosthesis-related complications [3–5]. Despite these encouraging results, long-term valve durability remains an important concern. Although several mechanisms of valve failure have been proposed, the potential influence of leaflet sizing on subsequent valve-related outcomes has not been fully elucidated.

Accurate leaflet sizing is a critical step in AVNeo because the geometry of the reconstructed valve is determined by the dimensions of the implanted pericardial leaflets. Currently, leaflet size is selected intraoperatively using the dedicated Ozaki sizing system after complete excision of the native cusps [1]. Although this technique is simple and clinically established, sizing is performed under nonphysiological conditions during cardiac arrest and may be influenced by surgical exposure, traction on the aortic root, and operator judgment. Therefore, an established objective anatomical reference against which intraoperatively selected leaflet size can be evaluated remains lacking.

Computed tomography (CT)-guided leaflet preparation has recently been proposed to facilitate preoperative planning for AVNeo [6]. However, this approach was primarily developed to enable patient-specific leaflet preparation before surgery rather than to quantify the discrepancy between preoperative anatomy and intraoperative sizing. Furthermore, for a CT-derived sizing method to serve as an objective anatomical reference, its reproducibility across observers with different levels of clinical experience

is also important. Thus, whether CT-derived anatomical sizing can be measured reproducibly and whether discrepancies between CT-derived and intraoperative leaflet sizes are associated with subsequent valve-related outcomes remain unclear.

To address these questions, we developed a geometrically derived method for estimating leaflet size from the intercommissural distance measured on preoperative electrocardiography-gated CT. The linear intercommissural distance was converted into the corresponding commissural arc length using a geometric model, providing a patient-specific anatomical reference that could be directly compared with the intraoperatively selected leaflet size.

We hypothesized that greater discrepancy between the CT-derived reference leaflet size and the intraoperatively selected leaflet size would be associated with subsequent valve-related events after AVNeo. Accordingly, this study aimed to evaluate the association between CT-derived leaflet sizing discrepancy and valve-related events and to assess the interobserver reproducibility of the CT-derived sizing method.

Methods

Study design and patient population

This retrospective observational study was conducted at Kakogawa Central City Hospital and was approved by the Institutional Review Board (Approval No. 2020-58) on June 11, 2020. The requirement for written informed consent was waived because of the retrospective nature of the study.

Between July 2020 and February 2026, 40 consecutive patients underwent aortic valve neocuspidization (AVNeo) using glutaraldehyde-treated autologous pericardium according to the original Ozaki technique. Patients with tricuspid aortic valves and those

with bicuspid aortic valves with a raphe who had undergone preoperative electrocardiography (ECG)-gated contrast-enhanced computed tomography (CT) were eligible for inclusion.

Patients with bicuspid aortic valves without a raphe (Sievers type 0) were excluded because the geometric calculation used in this study requires three identifiable commissural landmarks and has not been established for valves without a raphe. Patients undergoing emergency surgery for active infective endocarditis, those with quadricuspid aortic valves, and those with inadequate CT image quality were also excluded. Finally, 32 patients were included in the analysis.

Surgical procedure and intraoperative leaflet sizing

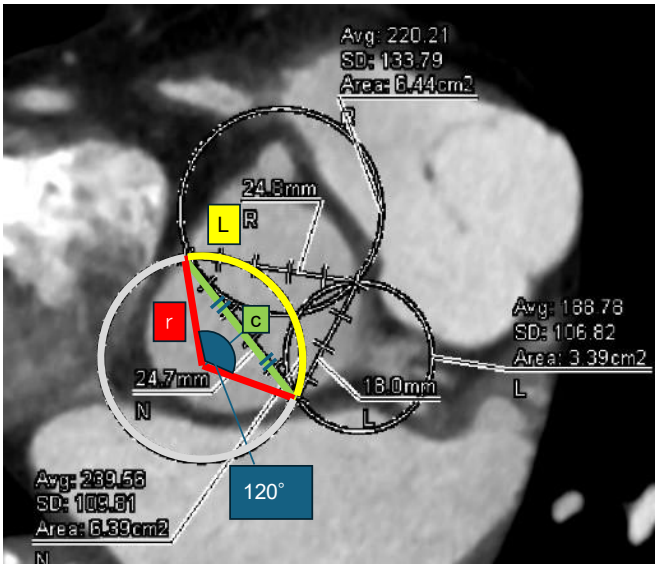
AVNeo was performed according to the original technique described by Ozaki et al. [1]. After complete excision of the native aortic cusps, the leaflet size for each cusp was determined intraoperatively using the dedicated Ozaki sizing system. Glutaraldehyde-treated autologous pericardium was trimmed using the corresponding template and sutured to reconstruct the three cusps. The intraoperatively selected leaflet size for each cusp was recorded for subsequent comparison with the CT-derived reference leaflet size.

CT-derived reference leaflet size

All patients underwent preoperative ECG-gated contrast-enhanced CT using a multidetector CT scanner. Multiplanar reconstruction was performed to obtain the aortic annular plane, and the intercommissural chord length of each cusp was measured at end-diastole.

Because AVNeo sizing is based on the commissural free-edge length rather than the linear intercommissural chord length, we developed a geometric conversion model to

estimate the corresponding leaflet free-edge length from the measured chord length (Figure 1).



Chord length (c) : $2r*\sin 60^\circ$

Arc length (L) : $2r*\pi/3$

$$\frac{\text{Arc length (L)}}{\text{Chord length (c)}} = \frac{2r\pi/3}{2r*\sin 60^\circ}$$

$$\frac{\text{Arc length (L)}}{\text{Chord length (c)}} = \frac{2\pi}{3*\sqrt{3}} = 1.209\ldots\ldots$$

$$\frac{\text{Arc length (L)}}{\text{Chord length (c)}} \approx 1.2$$

$$\text{Arc length (L)} = 1.2 \times \text{Chord length (c)}$$

Assuming that each reconstructed cusp occupies approximately one-third of a circular annulus, corresponding to a central angle of 120°, the measured intercommissural distance (c) was considered the chord of a 120° circular segment. The corresponding arc length (L) was calculated geometrically as follows:

$$c = 2r * sin(60°)$$

where represents the radius of the reconstructed circle. Substitution of the geometric relationships yields:

$$L = \frac{2\pi r}{3}$$

where L is the estimated leaflet free-edge length.

Thus, the estimated leaflet free-edge length was calculated by multiplying the measured intercommissural distance by a constant coefficient of 1.209. This value was defined as the CT-derived reference leaflet size for each cusp.

$$L = \left(\frac{2\pi}{3\sqrt{3}}\right)c$$

Definition of sizing discrepancy

Sizing discrepancy (Δ) was defined as:

Δ = CT-derived reference leaflet size − intraoperatively selected leaflet size

A positive Δ indicated that the intraoperatively selected leaflet was smaller than the CT-derived reference size, whereas a negative Δ indicated that the intraoperatively selected leaflet was larger than the CT-derived reference size.

Sizing discrepancies were calculated separately for the right coronary cusp (ΔR), left coronary cusp (ΔL), and noncoronary cusp (ΔN). Maximum Δ was defined as the largest of the three cusp-specific discrepancies for each patient. Relative sizing discrepancy was also calculated as:

$$\text{Relative sizing discrepancy (\%)} = \frac{\Delta}{\text{CT-derived reference leaflet size}} \times 100$$

Interobserver reproducibility analysis

To assess the reproducibility of the CT-derived measurements, all 32 preoperative CT datasets were independently reassessed by three additional observers with different professional backgrounds and levels of clinical experience: an experienced radiologic technologist, an experienced cardiovascular surgeon, and a cardiovascular surgery trainee. The observers were blinded to the original CT measurements, intraoperative leaflet sizes, and postoperative outcomes. Each observer independently measured the intercommissural distances of the right coronary, left coronary, and noncoronary cusps using the same measurement protocol described above.

CT-derived reference leaflet sizes and maximum Δ values were subsequently recalculated separately using the measurements obtained by each observer. Interobserver

reliability and agreement were evaluated to assess the reproducibility of the CT-derived measurements. In addition, observer-specific receiver operating characteristic (ROC) analyses were performed to examine whether the discriminatory performance of maximum Δ for valve-related events was preserved across independent measurements.

Study endpoint

The primary endpoint was valve-related events during follow-up, which were defined as any of the following:

- moderate or greater aortic regurgitation,
- infective endocarditis,
- hospitalization for heart failure,
- aortic valve reoperation.

Statistical analysis

Continuous variables are presented as mean ± standard deviation or median with interquartile range, as appropriate, and categorical variables as frequencies and percentages. Continuous variables were compared using Student's *t*-test or the Mann–Whitney *U* test, as appropriate, and categorical variables using Fisher's exact test.

Cox proportional hazards regression analysis was used to evaluate the association between sizing discrepancy and valve-related events. Because of the limited number of events, analyses were restricted to univariable models, and no multivariable model was constructed. Hazard ratios (HRs) are reported with 95% confidence intervals (CIs). Maximum Δ was evaluated primarily as a continuous variable. Additional analyses of cusp-specific discrepancies and relative sizing discrepancy were considered exploratory.

ROC curve analysis was performed to assess the discriminatory ability of maximum Δ

for valve-related events. The cutoff derived from the original measurements using the Youden index was regarded as exploratory because of the limited sample size and absence of external validation. Valve-related event-free survival according to this exploratory threshold was estimated using the Kaplan–Meier method and compared using the log-rank test.

Interobserver reliability of the CT-derived measurements was assessed separately for each cusp using intraclass correlation coefficients based on a two-way random-effects model for single measurements and absolute agreement [ICC(2,1)], with 95% CIs. Pairwise agreement between observers was further evaluated using Bland–Altman analysis, with the mean difference (bias) and 95% limits of agreement calculated for each cusp. Proportional bias was assessed by linear regression of the differences between paired measurements against their corresponding mean values. Observer-specific ROC analyses were performed using the recalculated maximum Δ values to evaluate whether the discriminatory performance of maximum Δ was preserved across independent measurements.

Statistical analyses were performed using BellCurve for Excel version 4.10 (Social Survey Research Information Co., Ltd., Tokyo, Japan) and Python version 3.13 (Python Software Foundation, Wilmington, DE, USA). Bland–Altman analyses were conducted using Python. All tests were two-sided, and $P < 0.05$ was considered statistically significant.

Results

Patient characteristics

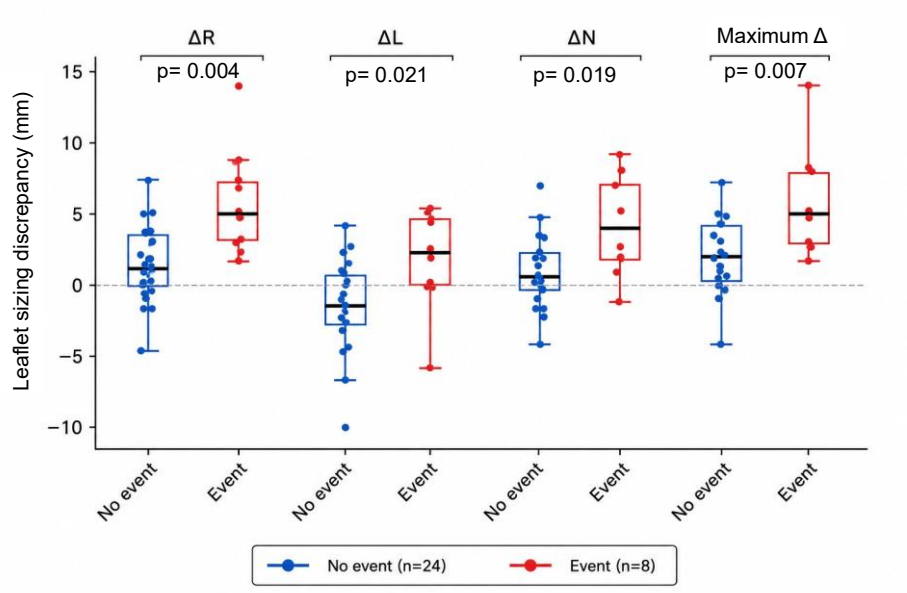
Of the 32 patients included in this analysis, valve-related events occurred in 8 patients (25.0%), whereas 24 patients remained free from valve-related events during a

median follow-up of 23 months (interquartile range, 6.5–32 months).

Table 1 summarizes the baseline clinical characteristics of the study population. Baseline characteristics, including age, sex, body surface area, clinical presentation, and etiology, were comparable between patients with and without valve-related events (Table 2).

CT-derived reference leaflet size and sizing discrepancy

The comparison between the CT-derived reference leaflet size and the intraoperatively selected leaflet size is summarized in Table 2 and illustrated in Figure 2.

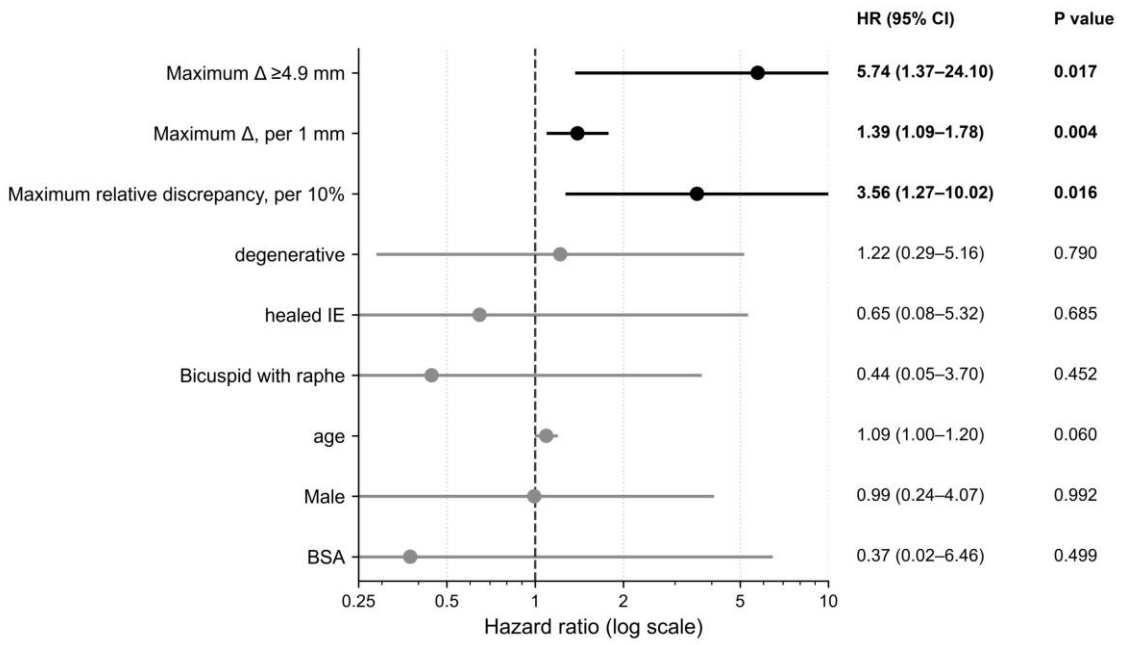


Patients who experienced valve-related events had significantly greater positive sizing discrepancies for all three cusps than patients without events. Maximum Δ, defined as the largest discrepancy among the three cusps, was also significantly greater in patients with valve-related events. Similarly, the maximum relative sizing discrepancy was significantly greater in patients with valve-related events.

Association between sizing discrepancy and valve-related events

In univariable Cox proportional hazards analysis, maximum Δ, analyzed as a continuous variable, was significantly associated with valve-related events. Each 1-mm increase in

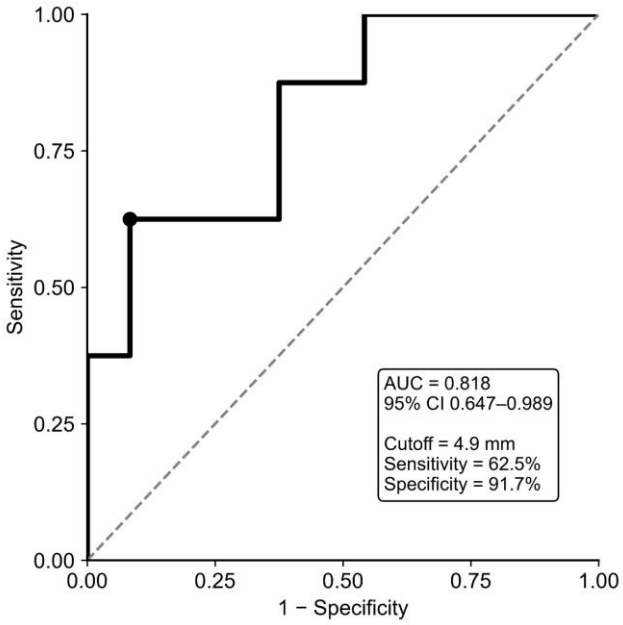
maximum Δ was associated with a 39% increase in the hazard of valve-related events (HR, 1.39; 95% CI, 1.09–1.78; $P = 0.004$) (Figure 3).



Maximum relative sizing discrepancy was also significantly associated with valve-related events, with each 10% increase associated with a higher hazard of valve-related events (HR, 3.56; 95% CI, 1.27–10.02; $P = 0.016$).

Exploratory ROC analysis

In an exploratory ROC analysis, maximum Δ showed an area under the curve (AUC) of 0.818 (95% CI, 0.647–0.989) for discrimination of valve-related events. The Youden index identified 4.9 mm as the optimal cutoff, with a sensitivity of 62.5% and a specificity of 91.7% (Figure 4).



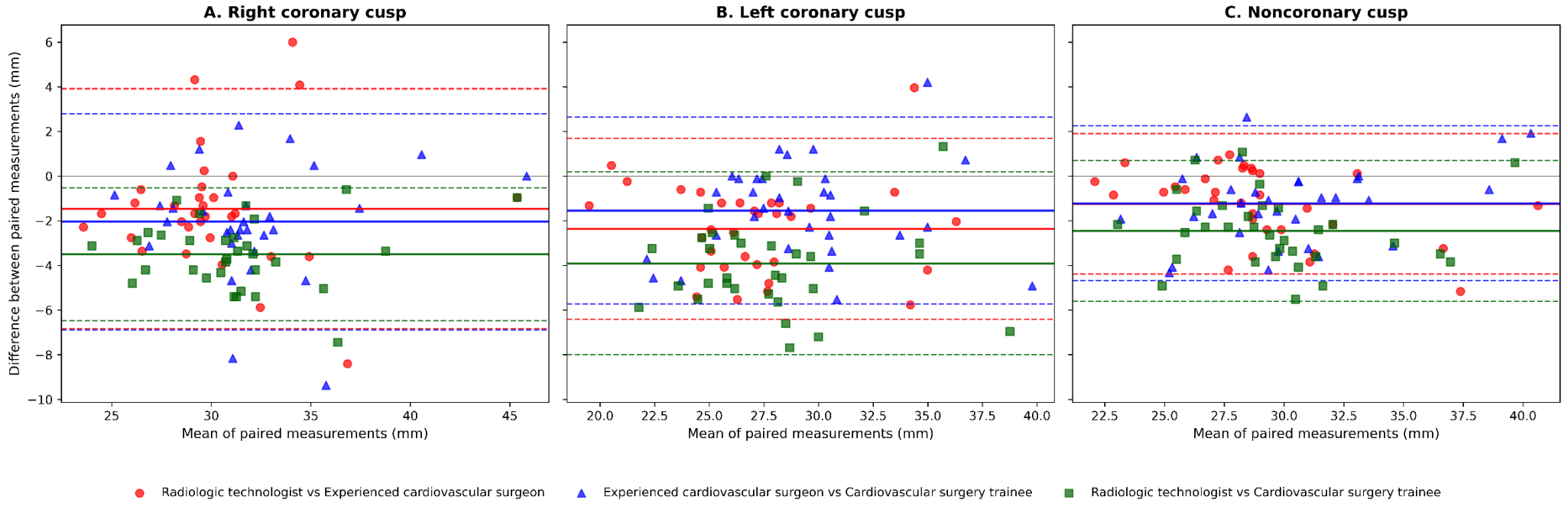
Interobserver reproducibility and observer-specific analyses

Interobserver reproducibility of the CT-derived measurements was assessed using independent measurements obtained by a radiologic technologist, an experienced cardiovascular surgeon, and a cardiovascular surgery trainee. The single-measure intraclass correlation coefficients [ICC(2,1)] were 0.726 (95% CI, 0.339–0.881) for the right coronary cusp, 0.703 (95% CI, 0.231–0.879) for the left coronary cusp, and 0.832 (95% CI, 0.516–0.932) for the noncoronary cusp, indicating moderate-to-good interobserver reliability (Table 3).

Pairwise agreement between observers was further evaluated using Bland–Altman analysis. Systematic differences in absolute measurements were observed between some observer pairs, with the magnitude and direction of these differences varying according to the observer pair and cusp (Table 4 and Figure 5).

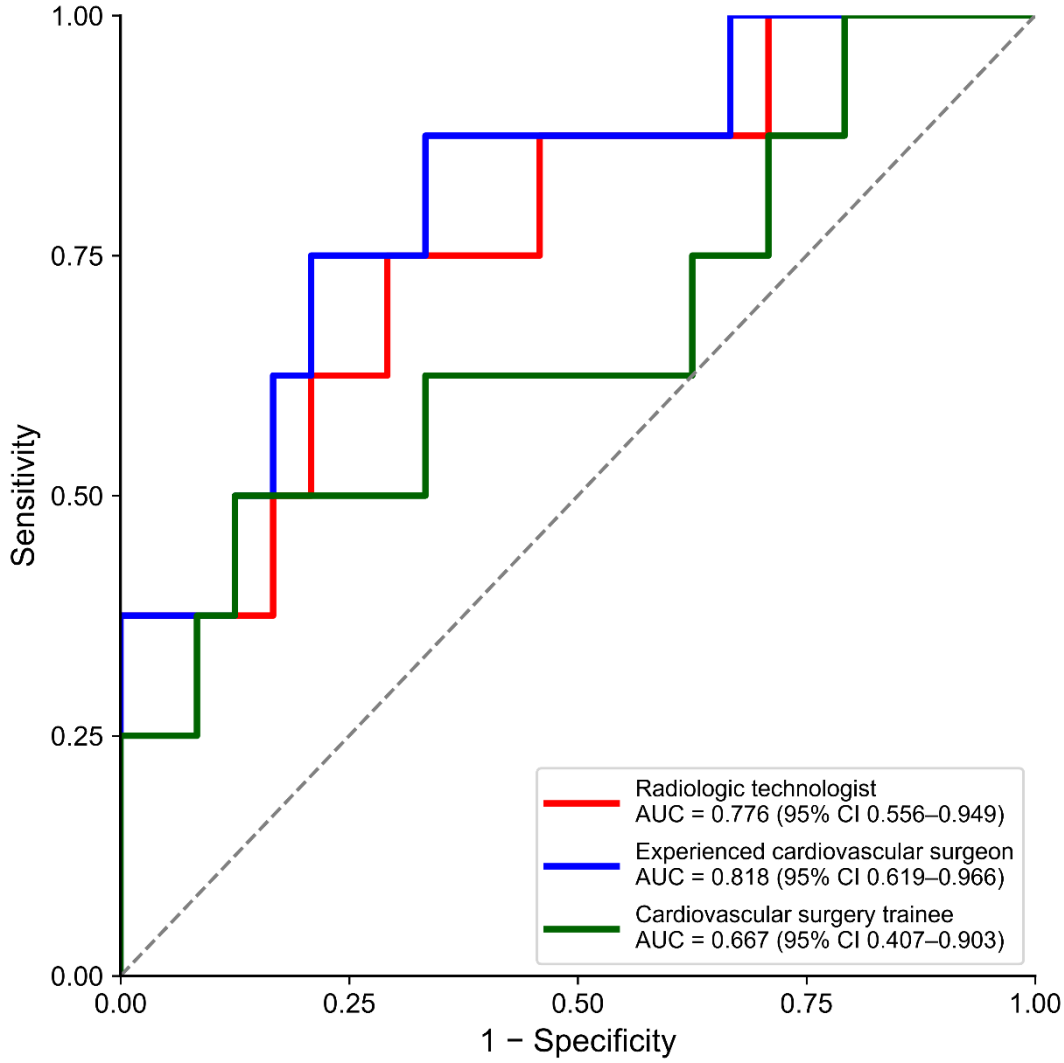
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258


A. Right coronary cusp
B. Left coronary cusp
C. Noncoronary cusp
Difference between paired measurements (mm)
Mean of paired measurements (mm)
Mean of paired measurements (mm)
Mean of paired measurements (mm)
Radiologic technologist vs Experienced cardiovascular surgeon
Experienced cardiovascular surgeon vs Cardiovascular surgery trainee
Radiologic technologist vs Cardiovascular surgery trainee

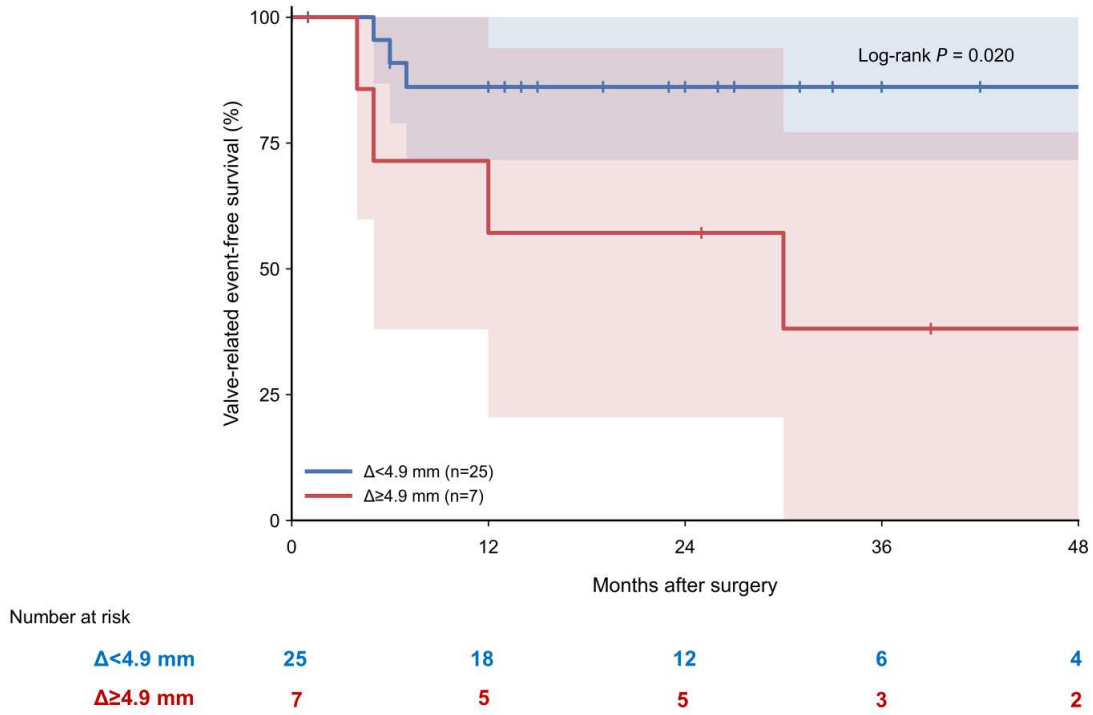
Significant proportional bias was observed for the noncoronary cusp in comparisons between the radiologic technologist and experienced cardiovascular surgeon (P = 0.006) and between the experienced cardiovascular surgeon and cardiovascular surgery trainee (P = 0.047), whereas no significant proportional bias was detected in the remaining comparisons (Table 4 and Figure 5).

To examine whether the discriminatory performance of maximum Δ was dependent on the observer performing the CT measurements, maximum Δ was independently calculated from the measurements obtained by each observer. The AUCs for discrimination of valve-related events were 0.776 (95% CI, 0.556–0.949) for the radiologic technologist, 0.818 (95% CI, 0.619–0.966) for the experienced cardiovascular surgeon, and 0.667 (95% CI, 0.407–0.903) for the cardiovascular surgery trainee (Figure 6). Discriminatory performance was higher for measurements obtained by the radiologic technologist and experienced cardiovascular surgeon than for those obtained by the cardiovascular surgery trainee.



Exploratory time-to-event analysis

When patients were stratified according to the exploratory 4.9-mm threshold derived from the original measurements, a maximum Δ of ≥4.9 mm was associated with a higher hazard of valve-related events (HR, 5.74; 95% CI, 1.37–24.10; P = 0.017). Kaplan–Meier analysis demonstrated significantly lower valve-related event-free survival in patients with a maximum Δ of ≥4.9 mm than in those with a maximum Δ of <4.9 mm (log-rank P = 0.020) (Figure 7).



Echocardiographic findings

Table 2 summarizes the early postoperative and latest follow-up echocardiographic findings. Postoperative valve hemodynamics were preserved in both groups. Early postoperative effective orifice area was 1.56 ± 0.36 cm² in the valve-related event group and 1.76 ± 0.34 cm² in the event-free group (P = 0.155). The corresponding mean transvalvular pressure gradients were 9.8 ± 4.6 and 7.6 ± 2.1 mmHg, respectively (P = 0.129).

At the latest available follow-up, the effective orifice area remained comparable between the valve-related event and event-free groups (1.86 ± 0.47 vs. 1.87 ± 0.49 cm², P = 0.942). Similarly, the mean transvalvular pressure gradient showed no significant difference (9.1 ± 2.4 vs. 8.0 ± 3.8 mmHg, P = 0.430).

No patient developed moderate or greater aortic stenosis during follow-up.

Discussion

This study demonstrated that discrepancies between the CT-derived reference

leaflet size and the intraoperatively selected leaflet size were associated with postoperative valve-related events after AVNeo. The principal finding of this study was not the identification of a definitive cutoff value, but rather the observation that greater discrepancies from the CT-derived anatomical reference were associated with subsequent valve-related events. To our knowledge, this is the first study to use a geometrically derived CT-based anatomical reference to quantify the discrepancy between reference leaflet sizing and the leaflet size actually selected intraoperatively and to explore its association with clinical outcomes after AVNeo. Exploratory analyses further suggested that a maximum discrepancy of approximately 5 mm may identify patients at increased risk of valve-related events, although this threshold requires validation in larger cohorts.

Leaflet geometry is an important determinant of valve durability. In aortic valve repair and valve-sparing procedures, restoration of physiological leaflet geometry and adequate coaptation are considered fundamental principles for durable valve function. Schäfers et al. introduced effective height as an objective parameter for the assessment of aortic cusp geometry [7]. Subsequent studies demonstrated that valve configuration and restoration of appropriate cusp geometry are important determinants of long-term outcomes after aortic valve repair and valve-preserving root surgery [8,10]. Lansac et al. further emphasized the importance of restoring appropriate cusp geometry and coaptation in contemporary aortic valve repair [9]. Although AVNeo reconstructs the valve using autologous pericardium rather than preserving the native cusps, similar biomechanical principles may apply. Appropriate leaflet sizing determines the geometry of the reconstructed valve and may therefore influence leaflet coaptation and subsequent valve durability. The association between valve configuration, effective height, and long-term outcomes after aortic valve repair is supported by previous clinical studies.

Our findings support this concept. Greater discrepancies between the CT-derived reference leaflet size and the intraoperatively selected leaflet size were observed in patients who subsequently developed valve-related events. Rather than indicating that a specific leaflet size is universally optimal, these findings suggest that the relationship between patient-specific anatomy and the selected leaflet size may be important. Restoration of patient-specific leaflet geometry has become a major principle of contemporary aortic valve repair, and our results suggest that this concept may also be relevant to AVNeo [7–10].

Interestingly, the right coronary cusp exhibited the greatest sizing discrepancy among the three cusps. The reason for this finding remains speculative; however, technical factors during intraoperative sizing may contribute. Placement of the Ozaki sizer in the right coronary cusp often requires a backhand approach, while simultaneous retraction of the aortic root may be necessary to obtain adequate visualization. These technical constraints could increase variability in leaflet sizing. Whether this observation represents a reproducible anatomical or technical feature should be examined in larger cohorts.

An important methodological aspect of this study is that the CT-derived reference leaflet size was not empirically determined but mathematically derived from the geometric relationship between the intercommissural chord length and the corresponding circular arc length. The resulting conversion coefficient was also consistent with the structural concept of the original Ozaki sizing system. Direct measurement of the commercial Ozaki sizer showed that the indicated leaflet size was approximately 1.2 times the distance between the measuring pins, suggesting that the sizing device itself incorporates a similar geometric relationship. Thus, our CT-derived

reference does not represent an arbitrary sizing model but was designed to reproduce the geometric concept underlying the original intraoperative sizing system [1].

The use of preoperative CT for AVNeo sizing itself is not novel. Todurov et al. described a CT-guided approach to AVNeo in which patient-specific leaflet templates were developed from preoperative CT measurements, allowing leaflet preparation before cardiopulmonary bypass [6]. More recently, Mokryk et al. reported mid-term outcomes of personalized CT-guided AVNeo compared with the standard Ozaki technique [11]. These studies demonstrated the feasibility of incorporating preoperative CT into patient-specific AVNeo planning. The present study addressed a different question. Rather than using CT primarily to prepare the leaflets before surgery, we used a CT-derived anatomical reference to quantify the discrepancy between the reference size and the leaflet size actually selected intraoperatively and explored whether this discrepancy was associated with postoperative valve-related events. Thus, the present approach may provide a means of objectively evaluating intraoperative leaflet sizing relative to patient-specific anatomy. Todurov et al. specifically described preoperative CT-based personalized templates, while the subsequent clinical series compared seven CT-guided cases with 15 standard AVNeo cases.

In exploratory ROC analysis, a maximum Δ of approximately 5 mm provided the greatest discrimination of valve-related events. This finding may have practical relevance because leaflet templates are selected according to absolute dimensions during AVNeo, making an absolute discrepancy potentially more intuitive for surgeons than a relative percentage. However, this threshold should be interpreted cautiously. The number of patients and events was limited, the cutoff was derived and evaluated within the same cohort, and no independent validation was performed. Therefore, the approximately 5-

mm value should be regarded as a hypothesis-generating threshold rather than an established criterion for intraoperative decision-making. Larger studies are required to determine whether a clinically useful and reproducible threshold can be defined.

An additional finding of this study was the observer dependency of the CT-derived measurements. Interobserver reliability was moderate to good across the three cusps; however, Bland–Altman analysis demonstrated systematic differences in absolute measurements between some observer pairs. Significant proportional bias was also observed for the noncoronary cusp in two observer comparisons, indicating that measurement differences may vary according to the magnitude of the underlying measurement. Furthermore, the discriminatory performance of maximum Δ varied according to observer experience. Measurements obtained by the radiologic technologist and experienced cardiovascular surgeon retained relatively good discrimination of valve-related events, whereas discrimination was attenuated when measurements were performed by the cardiovascular surgery trainee. These findings indicate that although conversion from intercommissural distance to the CT-derived reference leaflet size is mathematically deterministic, the reliability and agreement of the resulting reference size remain dependent on identification of the anatomical landmarks and the underlying CT measurement.

This distinction is important for the potential clinical application of CT-derived sizing. A mathematically reproducible conversion formula does not necessarily guarantee reproducibility of the measurement from which it is derived. Standardization of the reconstruction plane, definition of the commissural landmarks, and measurement technique, together with appropriate observer training, will therefore be necessary before this approach can be broadly applied. At the same time, the preservation of discriminatory

performance in measurements obtained independently by two experienced observers suggests that the underlying relationship between sizing discrepancy and valve-related events may not be restricted to a single observer. Future studies should determine whether a standardized measurement protocol and dedicated training can reduce interobserver variability and improve the reproducibility of CT-derived sizing across institutions.

Another notable finding was that postoperative effective orifice area and transvalvular pressure gradients remained comparable between patients with and without valve-related events, and no patient developed clinically relevant aortic stenosis during follow-up. These observations suggest that valve opening was generally preserved irrespective of subsequent events. In contrast, moderate or greater aortic regurgitation contributed to the valve-related endpoint, raising the possibility that leaflet sizing discrepancy may affect leaflet coaptation rather than leaflet opening. This interpretation is consistent with principles established in aortic valve repair, in which appropriate cusp configuration and coaptation are important determinants of long-term valve competence [7–10]. Nevertheless, postoperative coaptation geometry was not directly quantified in the present study. Therefore, this proposed mechanism remains hypothetical and should be evaluated using dedicated echocardiographic or CT-based geometric assessment in future studies.

Limitations

This study has several limitations. First, it was a retrospective, single-center study with only 32 patients and eight valve-related events. The limited number of events precluded robust multivariable adjustment and resulted in relatively wide confidence intervals for some effect estimates. Accordingly, the present findings should primarily be interpreted as hypothesis-generating.

Second, the ROC-derived cutoff of approximately 5 mm was identified and evaluated within the same small cohort and was not independently validated. Although the observed threshold may be clinically intuitive, it should not be regarded as an established criterion for intraoperative leaflet selection.

Third, although the CT-derived reference leaflet size was based on a mathematically defined geometric model, interobserver analyses demonstrated variability in the underlying CT measurements. Bland–Altman analysis also identified proportional bias in some observer comparisons, indicating that agreement was not uniform across the measurement range. In particular, observer-specific analyses suggested that measurement experience may influence the discriminatory performance of the derived sizing discrepancy. Standardization of image reconstruction, anatomical landmark identification, and measurement technique will therefore be necessary before broader clinical application.

Fourth, the geometric model assumes that each reconstructed cusp corresponds approximately to a 120° circular arc. Although this assumption reflects the conceptual geometry of tricuspid AVNeo and the original sizing system, individual variations in aortic root and commissural geometry are not fully captured by this simplified model.

Fifth, negative sizing discrepancies, indicating selection of a larger leaflet than the CT-derived reference, were uncommon. The present study therefore cannot determine whether leaflet oversizing is clinically benign or whether adverse effects might become apparent with a larger sample size or longer follow-up.

Finally, the follow-up duration was relatively short. Larger patient populations with longer follow-up are required to determine whether the association between sizing discrepancy and valve-related events persists over time and whether more accurate and

reproducible leaflet sizing can ultimately improve long-term valve durability.

Conclusion

An objective CT-derived reference leaflet size based on a geometrically derived model enabled quantitative assessment of the discrepancy between anatomical reference sizing and the intraoperatively selected leaflet size in AVNeo. Greater sizing discrepancy was associated with postoperative valve-related events, whereas exploratory analyses suggested that a maximum discrepancy of approximately 5 mm may warrant particular attention. However, interobserver variability in CT measurements and the limited sample size highlight the need for standardized measurement protocols and validation in larger cohorts. These findings provide an initial step toward more objective and reproducible leaflet sizing in AVNeo. Further studies with larger patient populations and longer follow-up are required to validate the association between sizing discrepancy and valve-related events and to determine whether standardized, patient-specific leaflet sizing can improve long-term valve durability.

Declarations

Ethics approval and consent to participate

This retrospective observational study was approved by the Institutional Review Board of Kakogawa Central City Hospital (Approval No. 2020-58; June 11, 2020). The requirement for written informed consent was waived by the Institutional Review Board of Kakogawa Central City Hospital because of the retrospective nature of the study. The study was conducted in accordance with relevant guidelines and regulations and the

Declaration of Helsinki and its later amendments.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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Acknowledgements

The authors sincerely thank Takashi Igaki, radiologic technologist, for performing independent CT measurements for the assessment of interobserver reproducibility. The authors also thank Enago for English language editing.

Clinical trial registration

Not applicable. This study was a retrospective observational study and was not a clinical trial.

Figure legends

Figure 1. Geometric derivation of the CT-derived reference leaflet size.

The intercommissural distance (chord length, c) was measured on ECG-gated CT. Assuming an ideal tricuspid valve with a central angle of 120°, the corresponding commissural arc length (L) was calculated geometrically. The resulting relationship ($L/c = 1.209$) was simplified to $L = 1.2 \times c$, which was used to estimate the CT-derived reference leaflet size.

Figure 2. Comparison of leaflet sizing discrepancies between patients with and without postoperative valve-related events.

Box-and-whisker plots depict the distribution of leaflet sizing discrepancies for the right coronary cusp (ΔR), left coronary cusp (ΔL), noncoronary cusp (ΔN), and the maximum discrepancy among the three cusps (maximum Δ). Individual data points are superimposed. Leaflet sizing discrepancy (Δ) was defined as the CT-derived reference leaflet size minus the intraoperatively selected leaflet size. Positive values indicate the selection of a smaller leaflet intraoperatively than the CT-derived reference.

Figure 3. Univariable Cox proportional hazards analysis for postoperative valve-

related events.

Hazard ratios (HRs) with 95% confidence intervals (CIs) are shown for clinical characteristics and leaflet sizing discrepancy variables. Sizing discrepancy was analyzed as a continuous variable (per 1-mm increase), a categorical variable using the ROC-derived cutoff (maximum Δ ≥4.9 mm), and a relative discrepancy (per 10% increase).

Figure 4. Receiver operating characteristic (ROC) curve of maximum Δ for predicting postoperative valve-related events after aortic valve neocuspidization (AVNeo).

The optimal cutoff identified using the Youden index was 4.9 mm (AUC, 0.818; 95% confidence interval, 0.647–0.989). The black dot indicates the optimal cutoff point. Maximum Δ represents the largest sizing discrepancy among the three cusps.

Figure 5. Bland–Altman analysis of interobserver agreement in CT-derived measurements.

Bland–Altman plots demonstrate pairwise agreement in CT-derived measurements among the radiologic technologist, experienced cardiovascular surgeon, and cardiovascular surgery trainee for the (A) right coronary cusp, (B) left coronary cusp, and (C) noncoronary cusp. Solid lines indicate the mean differences (bias), and dashed lines indicate the 95% limits of agreement.

Figure 6. Observer-specific receiver operating characteristic curves for maximum sizing discrepancy.

Receiver operating characteristic curves demonstrate the discriminatory performance of maximum sizing discrepancy (maximum Δ) for postoperative valve-related events based on independent CT measurements obtained by the radiologic technologist, experienced cardiovascular surgeon, and cardiovascular surgery trainee. The corresponding areas

under the curve were 0.776 (95% CI, 0.556–0.949), 0.818 (95% CI, 0.619–0.966), and 0.667 (95% CI, 0.407–0.903), respectively.

Figure 7. Kaplan–Meier curves for freedom from valve-related events according to the maximum sizing discrepancy (maximum Δ).

Patients with a maximum Δ of ≥4.9 mm demonstrated significantly lower freedom from valve-related events than those with a maximum Δ of <4.9 mm (log-rank $P = 0.020$). Shaded areas indicate 95% confidence intervals, and tick marks represent censored observations. Numbers at risk are depicted below the plot.

Table 1. Baseline patient characteristics

Variable	Overall (n = 32)
Age, years	63.7 ± 9.6
Male sex	15 (46.9%)
Body surface area, m^2	1.64 ± 0.22
Clinical presentation	
Aortic stenosis	12 (37.5%)
Aortic regurgitation	18 (56.2%)
Mixed AS/AR	2 (6.2%)
Etiology	
Degenerative	19 (59.4%)
Healed infectious endocarditis	4 (12.5%)
Bicuspid valve with raphe	8 (25.0%)

Others*	1 (3.1%)

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550 **Table 2. Comparison between patients with and without valve-related events**

Variable	**Event (n = 8)**	**No event (n = 24)**	***P* value**
Age, years	68.4 ± 7.7	62.1 ± 9.7	0.122
Male sex	4 (50.0%)	11 (45.8%)	1.000
Body surface area, m^2	1.60 ± 0.22	1.66 ± 0.23	0.622
Clinical presentation			
Aortic stenosis	2 (25.0%)	10 (41.7%)	0.676
Aortic regurgitation	5 (62.5%)	13 (54.2%)	1.000
Mixed AS/AR	1 (12.5%)	1 (4.2%)	0.444
Etiology			
Degenerative	5 (62.5%)	14 (58.3%)	1.000
Healed infective endocarditis	1 (12.5%)	3 (12.5%)	1.000
Bicuspid valve with raphe	1 (12.5%)	7 (29.2%)	0.642
Others	1 (12.5%)	0 (0.0%)	0.250
Sizing discrepancy			
ΔR, mm	5.8 ± 3.9	1.5 ± 2.9	0.004
ΔL, mm	1.9 ± 3.5	−1.2 ± 3.1	0.022
ΔN, mm	4.3 ± 3.6	1.1 ± 2.4	0.021
Maximum Δ, mm	6.0 ± 4.0	2.2 ± 2.5	0.008

Maximum relative discrepancy, %	17.6 ± 8.2	7.2 ± 8.3	0.006
Echocardiographic findings			
Postoperative EOA, cm^2	1.56 ± 0.36	1.76 ± 0.34	0.155
Postoperative mean PG, mmHg	9.8 ± 4.6	7.6 ± 2.1	0.129
The latest EOA, cm^2	1.86 ± 0.47	1.87 ± 0.49	0.942
The latest mean PG, mmHg	9.1 ± 2.4	8.0 ± 3.8	0.430

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Supplementary Table 3. Interobserver reproducibility of CT-derived measurements

Cusp	n	ICC(2,1)	95% CI	P value
Right coronary cusp (RCC)	32	0.726	0.339–0.881	<0.001
Left coronary cusp (LCC)	32	0.703	0.231–0.879	<0.001
Noncoronary cusp (NCC)	32	0.832	0.516–0.932	<0.001

ICC, intraclass correlation coefficient; CI, confidence interval. ICC values represent single-measure reliability using a two-way random-effects model [ICC(2,1)].

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Supplementary Table 4. Pairwise Bland–Altman analysis of CT-derived measurements

Cusp	Observer 1	Observer 2	n	Mean bias (mm)	Bias 95% CI lower	Bias 95% CI upper	SD of differences (mm)	Lower LoA (mm)	Upper LoA (mm)	Proportional bias slope	P value
RCC	Radiologic technologist	Experienced cardiovascular surgeon	32	-1.459	-2.447	-0.470	2.742	-6.832	3.915	-0.004	0.977
RCC	Radiologic technologist	Cardiovascular surgery trainee	32	-3.503	-4.051	-2.954	1.521	-6.484	-0.521	0.026	0.706
RCC	Experienced cardiovascular surgeon	Cardiovascular surgery trainee	32	-2.044	-2.934	-1.153	2.469	-6.884	2.796	0.031	0.787
LCC	Radiologic technologist	Experienced cardiovascular surgeon	32	-2.362	-3.105	-1.620	2.061	-6.401	1.676	-0.016	0.865
LCC	Radiologic technologist	Cardiovascular surgery trainee	32	-3.904	-4.657	-3.150	2.090	-8.001	0.193	0.048	0.628
LCC	Experienced cardiovascular surgeon	Cardiovascular surgery trainee	32	-1.541	-2.311	-0.772	2.134	-5.723	2.641	0.065	0.522
NCC	Radiologic technologist	Experienced cardiovascular surgeon	32	-1.241	-1.820	-0.663	1.605	-4.388	1.905	-0.195	**0.006**
NCC	Radiologic technologist	Cardiovascular surgery trainee	32	-2.460	-3.040	-1.880	1.607	-5.610	0.690	-0.040	0.622
NCC	Experienced cardiovascular surgeon	Cardiovascular surgery trainee	32	-1.219	-1.856	-0.582	1.767	-4.683	2.245	0.157	**0.047**

Bias was calculated as Observer 1 minus Observer 2. LoA, limits of agreement; CI, confidence interval; RCC, right coronary cusp; LCC, left coronary cusp; NCC, noncoronary cusp. The P value refers to the test for proportional bias.

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