Combined simulation and ex vivo assessment of free-edge length in bicuspidization repair for congenital aortic valve disease

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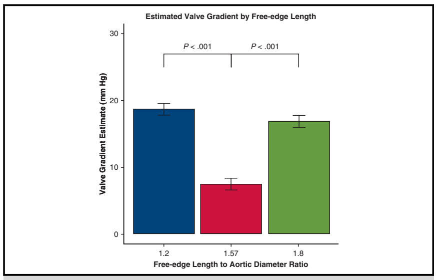
ABSTRACT

Objective: The study objective was to investigate the effect of free-edge length on valve performance in bicuspidization repair of congenitally diseased aortic valves.

Methods: In addition to a constructed unicuspid aortic valve disease model, 3 representative groups—free-edge length to aortic diameter ratio 1.2, 1.57, and 1.8—were replicated in explanted porcine aortic roots (n = 3) by adjusting native free-edge length with bovine pericardium. Each group was run on a validated ex vivo univentricular system under physiological parameters for 20 cycles. All groups were tested within the same aortic root to minimize inter-root differences. Outcomes included transvalvular gradient, regurgitation fraction, and orifice area. Linear mixed effects model and pairwise comparisons were used to compare outcomes across groups.

Results: The diseased control group had a mean transvalvular gradient of 28.3 ± 5.5 mm Hg, regurgitation fraction of 29.6% ± 8.0%, and orifice area of 1.03 ± 0.15 cm^2. In ex vivo analysis, all repair groups had improved regurgitation and transvalvular gradient compared with the diseased control group ($P < .001$). Free-edge length to aortic diameter of 1.8 had the highest amount of regurgitation among the repair groups ($P < .001$) and 1.57 the least ($P < .001$). Free-edge length to aortic diameter of 1.57 also exhibited the lowest mean gradient ($P < .001$) and the largest orifice area ($P < .001$).

Conclusions: Free-edge length to aortic diameter ratio significantly impacts valve function in bicuspidization repair of congenitally diseased aortic valves. As the ratio departs from 1.57 in either direction, effective orifice area decreases and both transvalvular gradient and regurgitation fraction increase. (JTCVS Open 2024;22:395-404)



FELAD ratio of 1.57 results in the lowest transvalvular gradient.

CENTRAL MESSAGE

FELAD ratio of 1.57 optimizes the hemodynamic profile of bicuspidization repair of aortic valves.

PERSPECTIVE

The technical parameters of bicuspidization repair for congenital aortic valve pathology have yet to be fully delineated. Building on prior simulation work, this ex vivo study shows that the leaflet FELAD affects valve function in bicuspidization repair. Sizing to a ratio of 1.57 is associated with improved valve performance compared with both lower and higher values.

See Discussion on page 405.

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Abbreviation and Acronym
FELAD = free-edge length to aortic diameter

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Popularized by Schäfers and colleagues[1] approximately 2 decades ago, bicuspidization repair remains an important tool in the cardiac surgeon's armamentarium for congenital aortic valve disease. Originally reserved for the unicuspid aortic valve—a defect characterized by 2 rudimentary commissures of abnormally low height—the technique has been successfully adapted to bicuspid, tricuspid, and even quadricuspid aortic valve pathology.[2-6] Despite its utility, there remains much unknown about how best to optimize gross morphology.

Our group previously published a simulation-based assessment on the relationship between leaflet free-edge length and valve performance, showing a clear trend toward stenosis with shorter free-edge length and toward subannular billowing with longer free-edge length.[7] Moreover, ideal flow patterns were observed at a free-edge length to aortic diameter (FELAD) ratio of approximately 1.57, which one can predict from calculating half the aortic circumference (ie, free-edge length when the valve is maximally open):

$$FELAD = \frac{free - edge\ length}{aortic\ diameter} = \frac{\frac{\pi}{2}\times D}{D} \sim 1.57$$

Alternatively, in reference to the free-edge length alone:

$$free - edge\ length\ (FEL) = \frac{aortic\ circumference}{2} = \frac{\pi}{2}\times D \sim 1.57D$$

Following these previous results, an ex vivo experiment was designed to test the validity of simulation results in a biologic framework.

MATERIAL AND METHODS

Study Design

Based on results from previous work, 3 representative groups (FELAD 1.2, 1.57, 1.8) in addition to a diseased unicuspid control model were replicated in explanted juvenile porcine aortic roots (n = 3) (Figure 1).[7] Porcine specimens were processed according to standard agricultural practices by and obtained from Animal Technologies Inc (ISO 9001 and US Department of Agriculture approved and certified). Aortic diameter was determined at the level of the sinotubular junction as done in previous simulation design and measured using standard aortic valve sizers. Free-edge lengths were modified within the same root using a bovine pericardial patch (St Jude Medical Pericardial Patch with EnCap Technology) and run on a validated univentricular simulator.[8] At each stage (control, FELAD 1.2, 1.57, 1.8), these valves were run under physiological parameters (mean arterial pressure 65 mm Hg, stroke volume 80 mL, cardiac output 4 L/min, heart rate 75 bpm) for 20 runs (each run corresponds to one cardiac cycle) for each condition. To avoid ordering bias, the repair groups were completed in randomized fashion. All groups were tested within the same root to minimize inter-root differences. There were 3 operators involved in the experiment, and all repairs sewn for a given root were done by the same operator. All models are run within 24 hours of defrosting to minimize tissue degradation. Measured outcomes included mean transvalvular gradient, regurgitation fraction, and orifice area. Transvalvular gradient and regurgitation were automated outputs from the univentricular simulator, and mean orifice area was calculated manually via ImageJ software and high-speed videography by averaging 20 measurements of the largest valve orifice for each condition. Because no human or animal subjects were involved in the study, Institutional Review Board approval was not deemed necessary.

Surgical Technique

After harvesting the aortic root, the 3 aortic valve leaflets were examined and the largest set was the reference leaflet (Figure 2, *A*). To mimic the rudimentary commissures characteristic to a unicuspid valve, the opposing and immediately rightward commissures were inferiorly displaced approximately 5 mm and the adjoining leaflets sutured partially to create pseudoraphe (Figure 2, *B*). To facilitate subsequent symmetric bicuspidization repairs, the immediately rightward commissure was also moved centrally to create a 180/180 configuration (Figure E1). To support the validity of the diseased control model, moderate stenosis and regurgitation were confirmed via univentricular pump before commencing with bicuspidization repair.

For the repair groups, each of the predetermined FELAD groups (1.2, 1.57, and 1.8) were created based on the premeasured free-edge length of the reference leaflet. Because the native FELAD was typically between 1.2 and 1.57, for groups 1.57 and 1.8 the FELAD was achieved by sewing augmentation patches at the rightward and opposing commissures, whereas group 1.2 was achieved by decreasing the free-edge length via commissuroplasty (Figure 2, *C* and *D*). The geometric height of the augmentation patches was set to that of the native reference leaflet, and the new rightward commissure was resuspended to be at the same height as the untouched leftward commissure. Furthermore, to ensure a symmetric bicuspid repair, the opposing commissure was excised inferiorly such that the nadir of both leaflets was at equal heights. This symmetric annular attachment in addition to the constant geometric height minimized the number of structural variables and kept free-edge length as the main structural variable of interest.

Statistical Analysis

To account for repeated measures within roots (each hosting multiple repair groups) and across multiple runs, linear mixed effects model was used. The repair group (control, FELAD 1.2, FELAD 1.57, FELAD 1.8) was considered a fixed effect, and aortic roots and individual runs on the simulator were treated as random effects. The nested structure of the data, with runs being nested within roots, was explicitly accounted for in the model. To decipher differences in outcomes among the groups, post hoc pairwise comparisons were made using Tukey's honestly significant difference test. Significance of valve characteristics was calculated using the Kruskal–Wallis rank-sum test. R version 4.3.1 was used for analysis.

RESULTS

For the 3 porcine aortic roots, the mean aortic diameter (measured at the sinotubular junction) was 20.3 ± 1.0 mm (Table 1). The mean leaflet free-edge length

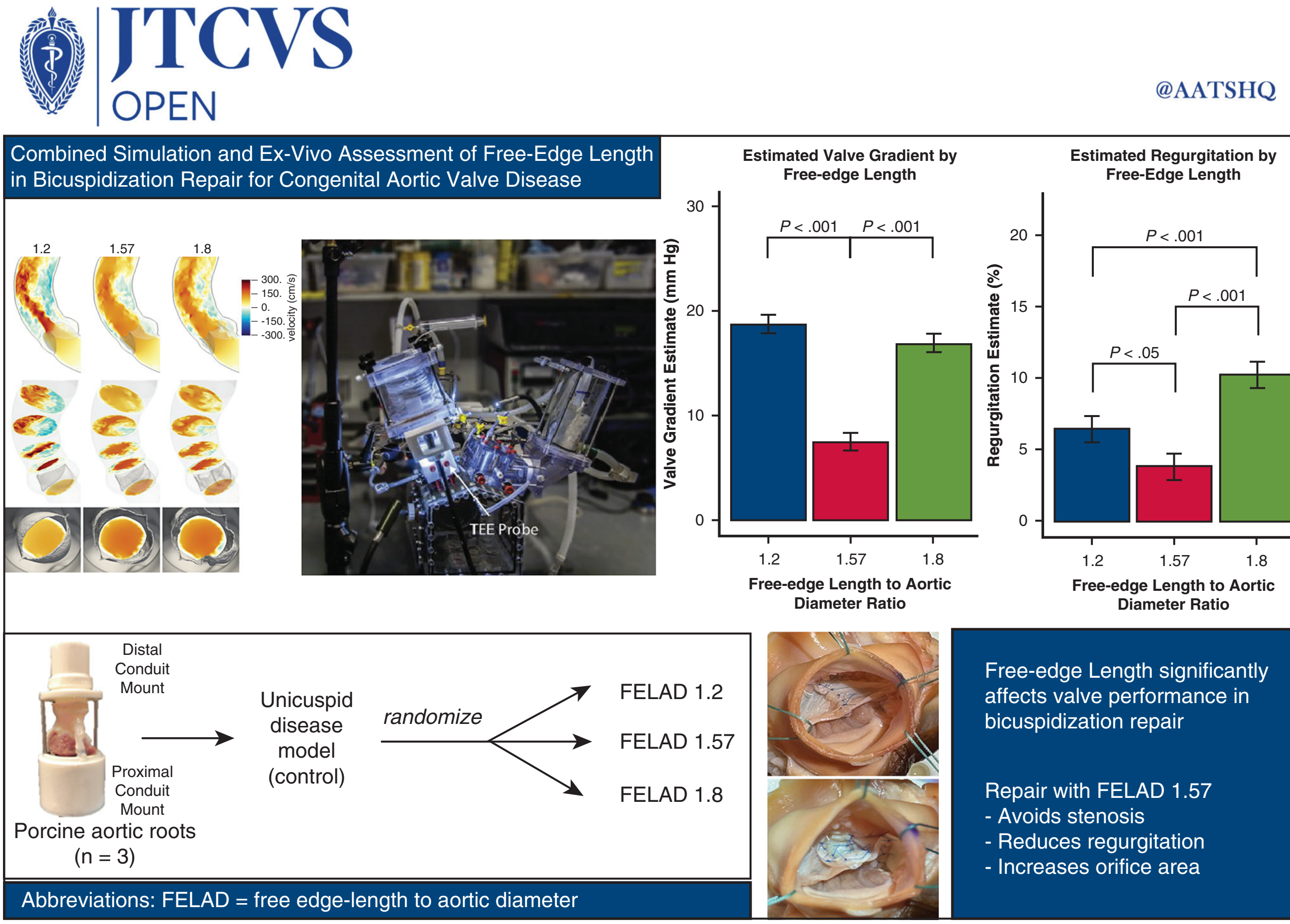

FIGURE 1. Graphical Abstract. Based on prior simulation work (*upper left*),[7] 3 porcine aortic roots underwent bicuspidization repair and were tested in a validated univentricular simulator for 20 runs across varying FELAD ratios: 1.2, 1.57, and 1.8. The control model was based on a diseased unicuspid aortic valve with moderate stenosis and regurgitation. All repair conditions were tested in the same root by the same operator to minimize inter-root differences. Free-edge length significantly affected valve function after repair, with FELAD of 1.57 exhibiting improved stenosis and regurgitation in ex vivo assessment.

was 28.3 ± 1.7 mm, and the mean FELAD was 1.39 ± 0.03. These roots were tested on the univentricular simulator at a mean aortic pressure of 64.0 ± 5.8 mm Hg. The diseased control model had a mean transvalvular gradient of 28.3 ± 5.5 mm Hg, mean regurgitation fraction of 29.6% ± 8.0%, and mean orifice area of 1.03 ± 0.15 cm^2.

Given a mean aortic diameter of 20.3 ± 1.0 mm, the mean free-edge length was 24.3 ± 1.0 mm for the FELAD 1.2 group, 32.0 ± 1.4 mm for the FELAD 1.57 group, and 36.7 ± 1.9 mm for the FELAD 1.8 group (Table 2). The mean gradient was 18.7 ± 2.7 mm Hg for FELAD 1.2, 7.5 ± 2.7 mm Hg for FELAD 1.57, and 16.9 ± 7.3 mm Hg for FELAD 1.8. Mean regurgitation fraction was 6.4% ± 3.5% for FELAD 1.2, 3.8% ± 1.6% for FELAD 1.57, and 10.2% ± 5.9% for FELAD 1.8. The mean valve orifice area was 1.08 ± 0.26 cm^2 for FELAD 1.2, 1.49 ± 0.11 cm^2 for FELAD 1.57, and 1.06 ± 0.22 for FELAD 1.8. Valve orifice area and transvalvular gradient were inversely correlated across repair groups (Figure E2, $R^2 = 0.53$).

Linear mixed effects modeling revealed all repair groups had significantly improved stenosis compared with the diseased control group (estimate −9.6 mm Hg for FELAD 1.2, −20.8 mm Hg for FELAD 1.57, −11.4 mm Hg for FELAD 1.8, $P < .001$) (Figure 3). Pairwise comparison showed that FELAD 1.57 had a significantly lower gradient than both the 1.2 and 1.8 groups (estimate +11.2 mm Hg for FELAD 1.2, +9.4 mm Hg for FELAD 1.8, $P < .001$). Stenosis was similar between the FELAD 1.2 and 1.8 groups ($P = .16$).

Similar to transvalvular gradient, all repair groups had significantly improved regurgitation compared with the diseased control group (estimate −23.2% for FELAD 1.2, −25.9% for FELAD 1.57, −19.5% for FELAD 1.8, $P < .001$) (Figure 4). Pairwise comparison showed that FELAD 1.8 had significantly higher regurgitation than both the 1.2 (estimate 3.8%, $P < .001$) and 1.57 groups (estimate 6.4%, $P < .001$). Moreover, FELAD 1.57 had significantly lower regurgitation than the 1.2 group (estimate −2.6%, $P = .02$).

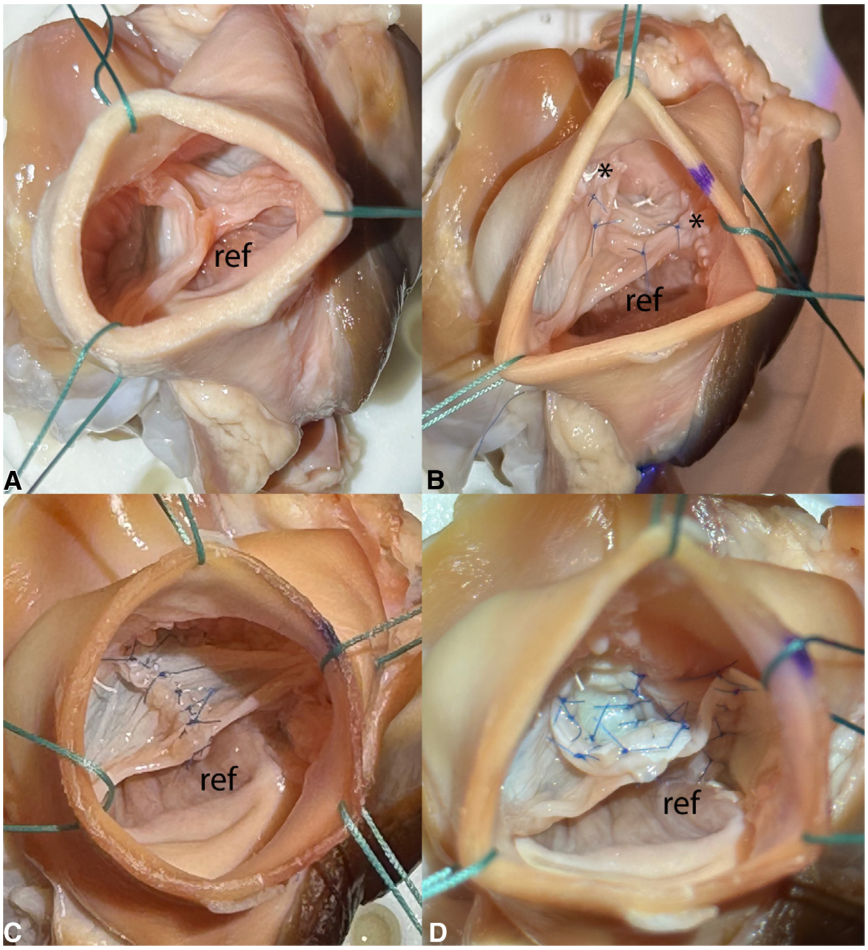

FIGURE 2. Creation of unicuspid disease and bicuspidization repair models. A, Top view of tricuspid aortic valve in a harvested juvenile porcine aortic root. The largest leaflet is set as the reference leaflet (*ref*). B, Unicuspid aortic valve disease model constructed by dropping the opposing and immediately rightward commissures approximately 5 mm (*) and partially suturing closed the adjoining leaflets to create rudimentary pseudoraphe. To facilitate subsequent symmetric bicuspidization repairs, the immediately rightward commissure is also moved centrally to create a 180/180 configuration. C, Because the native FELAD ratio was typically between 1.3 and 1.4, the 1.2 group was achieved by decreasing the free-edge length via commissuroplasty. D, To construct FELAD of 1.57 and 1.8, bovine pericardium was sewn at the rightward and opposing commissures, with geometric height set to that of the native leaflet.

Although the FELAD 1.2 and 1.8 groups had a similar orifice area as the diseased control ($P > .05$), the 1.57 group had a significantly larger orifice area than all other groups ($P < .001$) (Figure 5). Specifically, pairwise comparison showed that FELAD 1.57 had a significantly larger orifice area than the diseased control model (estimate 0.46 cm^2, $P < .001$), FELAD 1.2 (estimate 0.42 cm^2, $P < .001$), and FELAD 1.8 (estimate 0.43 cm^2, $P < .001$).

DISCUSSION

The present ex vivo study provides critical biologic context to our previously published simulated results. As expected, there was a clear relationship between FELAD ratio and valve performance, with the FELAD 1.57 group demonstrating significantly lower transvalvular gradient than the 1.2 group. This difference in transvalvular gradient was further supported by a significantly higher orifice area for the FELAD 1.57 group. Clinically, these results are intuitive. The less free-edge length for a given aortic diameter (ie, decreasing the FELAD), the more the leaflets are stretched and the less surface area available for coaptation. In a bileaflet semilunar valve, this stretching results in progressive stenosis as the free-edge leaflet becomes too short relative to the annular circumference to fully open. This explains the observed increase in mean gradient and decrease in orifice area going from FELAD 1.57 to 1.2; however, the FELAD 1.8 group also exhibited significantly higher transvalvular gradient and lower orifice area compared with the FELAD 1.57 group. These unexpected results are most likely due to the presence of excess leaflet tissue, because significant crowding of material inside the annulus (as opposed to crowding in the sinuses as was observed in simulation) was observed during model construction by operators and via high-speed videography during the

TABLE 1. Valve characteristics for native aortic root and unicuspid disease controls across aortic roots

Characteristic	Overall	Root 1*	Root 2*	Root 3*	*P*†
Native aortic root					
Aortic diameter (mm)	20.3 ± 1.0	19	21	21	<.001
Geometric height (mm)	16.3 ± 3.3	12	20	17	<.001
Free-edge length (mm)	28.3 ± 1.7	26	30	29	<.001
FELAD ratio	1.39 ± 0.03	1.37	1.43	1.38	<.001
Unicuspid control					
Valve gradient (mm Hg)	28.3 ± 5.5	35.4 ± 1.2	26.8 ± 2.1	22.7 ± 1.0	<.001
Valve regurgitation fraction (%)	29.6 ± 8.0	36.2 ± 8.0	28.5 ± 7.2	24.2 ± 2.7	<.001
Valve orifice area (cm^2)	1.03 ± 0.15	0.84 ± 0.05	1.12 ± 0.11	1.13 ± 0.02	<.001
Repair groups					
Free-edge length (mm)					
FELAD 1.2	24.3 ± 1.0	23	25	25	<.001
FELAD 1.57	32.0 ± 1.4	30	33	33	<.001
FELAD 1.8	36.7 ± 1.9	34	38	38	<.001

FELAD, Free-edge length to aortic diameter. *Mean ± SD. †Kruskal–Wallis rank-sum test.

univentricular simulator runs. This is consistent with the observation that the FELAD 1.8 group also had a significantly smaller orifice area. These findings suggest a bimodal distribution with both oversizing and undersizing the free-edge length leading to significant stenosis.

As expected, all repair groups had significantly lower regurgitation compared with the diseased control model. Among the repair groups, the FELAD 1.8 group had the most regurgitation compared with the 1.2 and 1.57 groups. This aligns well with the increased billowing previously observed at higher FELAD in simulated results, but this is difficult to reconcile with actual transvalvular regurgitation in the current ex vivo setup. Moreover, the FELAD 1.2 group exhibited increased valve regurgitation compared with the 1.57 group, although with a clinically irrelevant effect size.

It is important to mention that although the best performing condition was described primarily as FELAD 1.57 in the current study to maintain consistency with prior simulation results, in practical terms, it may be equivalently thought of as simply half the aortic circumference or 1.57 times the aortic diameter. The method of calculation may depend on the measuring norms (ie, diameter vs circumference) or simply preference of the operating team.

Study Limitations

The use of a diseased control model was deliberately chosen a priori to best mimic the conditions an operator would face when conducting a bicuspidization repair, thereby improving relevance of the experiment's results, as well as establishing an internal positive control to improve the validity of comparison across groups. An important study limitation is the use of intrinsically nondiseased porcine tissue, which was done to match prior simulation conditions and because of the unavailability of diseased models. Although the general trends observed in the study likely remain true, the differences between normal versus diseased and porcine versus human tissue properties may affect the actual inflection point of optimal performance. Moreover, these results are limited to the acute biomechanical

TABLE 2. Valve characteristics across the 3 aortic roots

Characteristic	Control	FELAD 1.2*	FELAD 1.57*	FELAD 1.8*	*P*†
Aortic diameter (mm)	20.3 ± 1.0	20.3 ± 1.0	20.3 ± 1.0	20.3 ± 1.0	>.9
Free-edge length (mm)	28.3 ± 1.7	24.3 ± 1.0	32.0 ± 1.4	36.7 ± 1.9	<.001
Geometric height (mm)	16.3 ± 3.3	16.3 ± 3.3	16.3 ± 3.3	16.3 ± 3.3	>.9
FELAD ratio	1.39 ± 0.03	1.20 ± 0.01	1.57 ± 0.01	1.80 ± 0.01	<.001
Valve gradient (mm Hg)	28.3 ± 5.5	18.7 ± 2.7	7.5 ± 2.7	16.9 ± 7.3	<.001
Valve regurgitation fraction (%)	29.6 ± 8.0	6.4 ± 3.5	3.8 ± 1.6	10.2 ± 5.9	<.001
Valve orifice area (cm^2)	1.03 ± 0.15	1.08 ± 0.26	1.49 ± 0.11	1.06 ± 0.22	<.001

FELAD, Free-edge length to aortic diameter. *Mean ± SD. †Kruskal–Wallis rank-sum test.

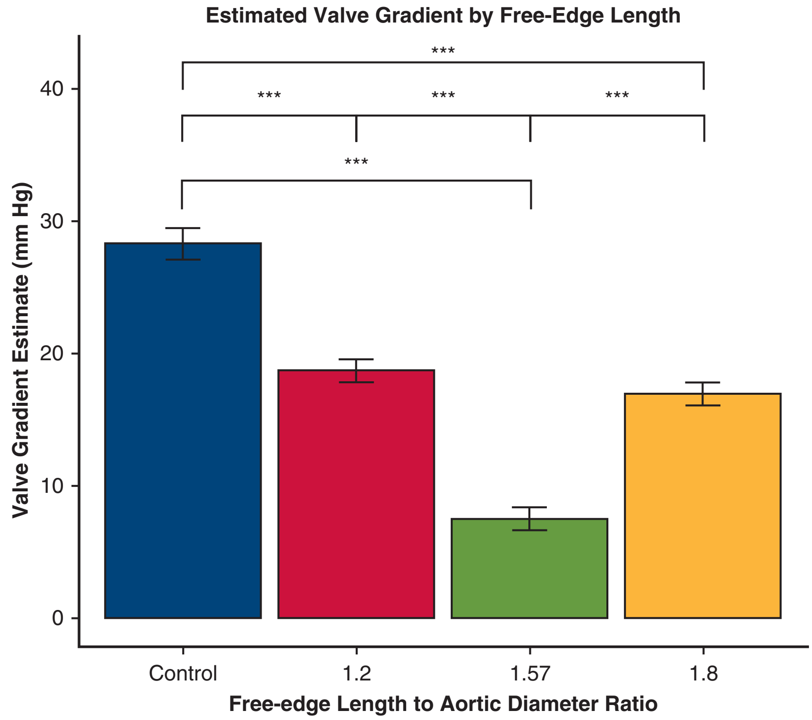

FIGURE 3. Transvalvular gradient based on FELAD ratio. ***$P < .001$. Linear mixed effects modeling across repair groups showed significantly lower mean transvalvular gradient for all repair groups compared with control. Pairwise comparisons confirmed these results and showed that among the repair groups the 1.57 group had the lowest mean gradient ($P < .001$). Error bars denote standard error from linear mixed effects model.

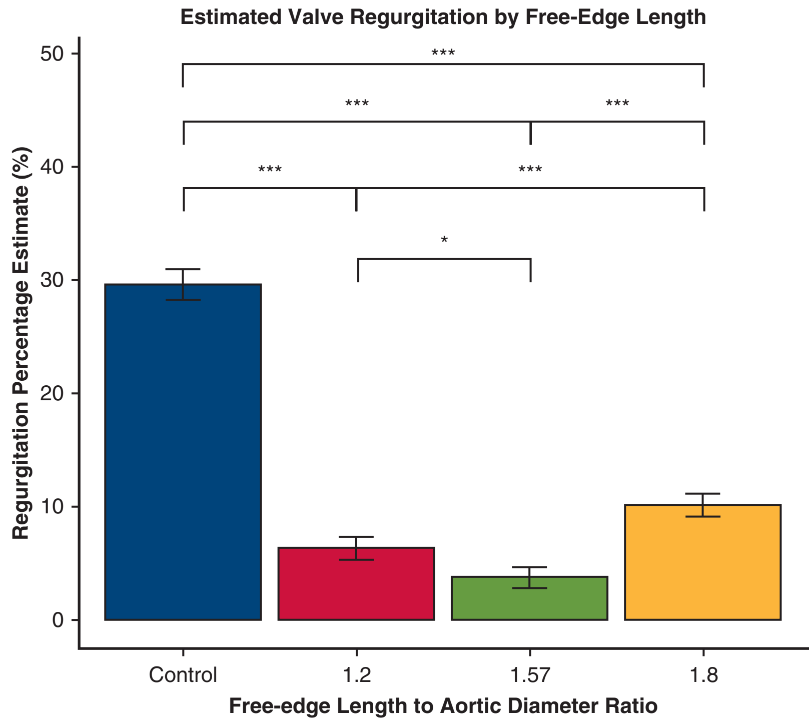

FIGURE 4. Valve regurgitation based on FELAD ratio. *$P < .05$, ***$P < .001$. All repair groups had significantly improved regurgitation compared with control. Pairwise comparison showed that the 1.8 group had significantly higher regurgitation than both the 1.2 and 1.57 groups. The 1.57 group had significantly lower regurgitation than the 1.2 group. Error bars denote standard error from linear mixed effects model.

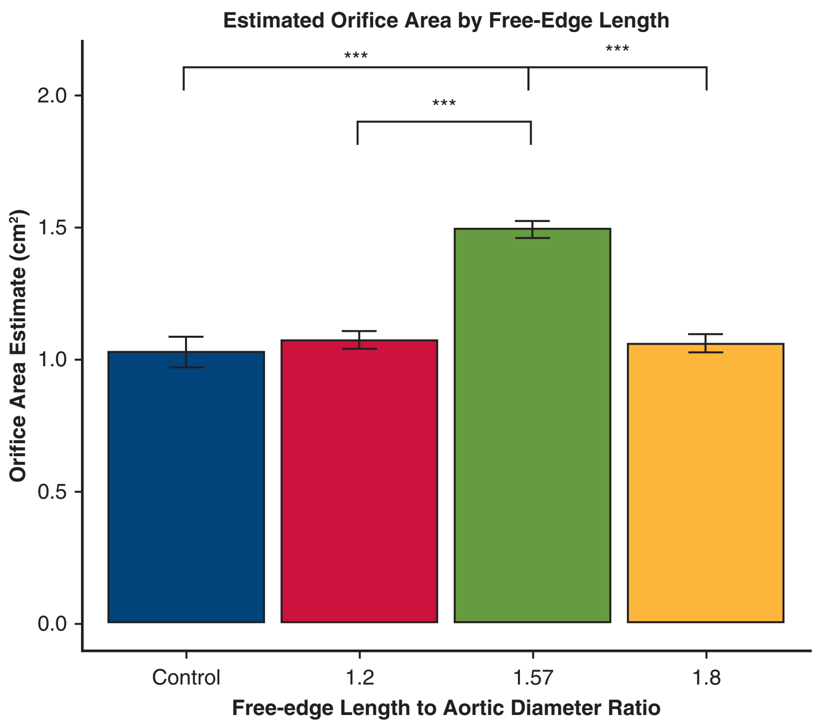

FIGURE 5. Valve orifice area based on FELAD ratio. ***$P < .001$. Pairwise comparison showed that although the 1.2 and 1.8 groups had similar orifice area to the diseased control, the 1.57 group had significantly larger orifice area than all other groups. Error bars denote standard error from linear mixed effects model.

performance of these repairs and should not be extrapolated to longer-term performance, which must include the impact of biologic processes such as calcification and growth. Furthermore, the spectrum of FELAD was only partially sampled. Although prior work suggests division into 3 subgroups would be sufficient because of a predicted bimodal distribution, the precision of results would be enhanced with additional subgroups. Namely, a bimodal distribution for stenosis was not expected, so future studies to assess valve performance in the gaps of FELAD values on either side of the 1.57 group are planned. This will help further delineate the inflection points across these outcomes to better inform surgeons.

CONCLUSIONS

Free-edge length significantly impacts valve performance after bicuspidization repair for congenital aortic valve disease. Compared with FELAD of 1.2 and 1.8, sizing to a ratio of 1.57 can significantly improve stenosis by optimizing orifice area. Although the impact of free-edge length on regurgitation fraction is less striking, sizing to FELAD 1.57 is still associated with superior performance.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://www.aats.org/resources/a-novel-approach-for-aortic-va-7040.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: aortic valve repair, bicuspid, free-edge length, unicuspid

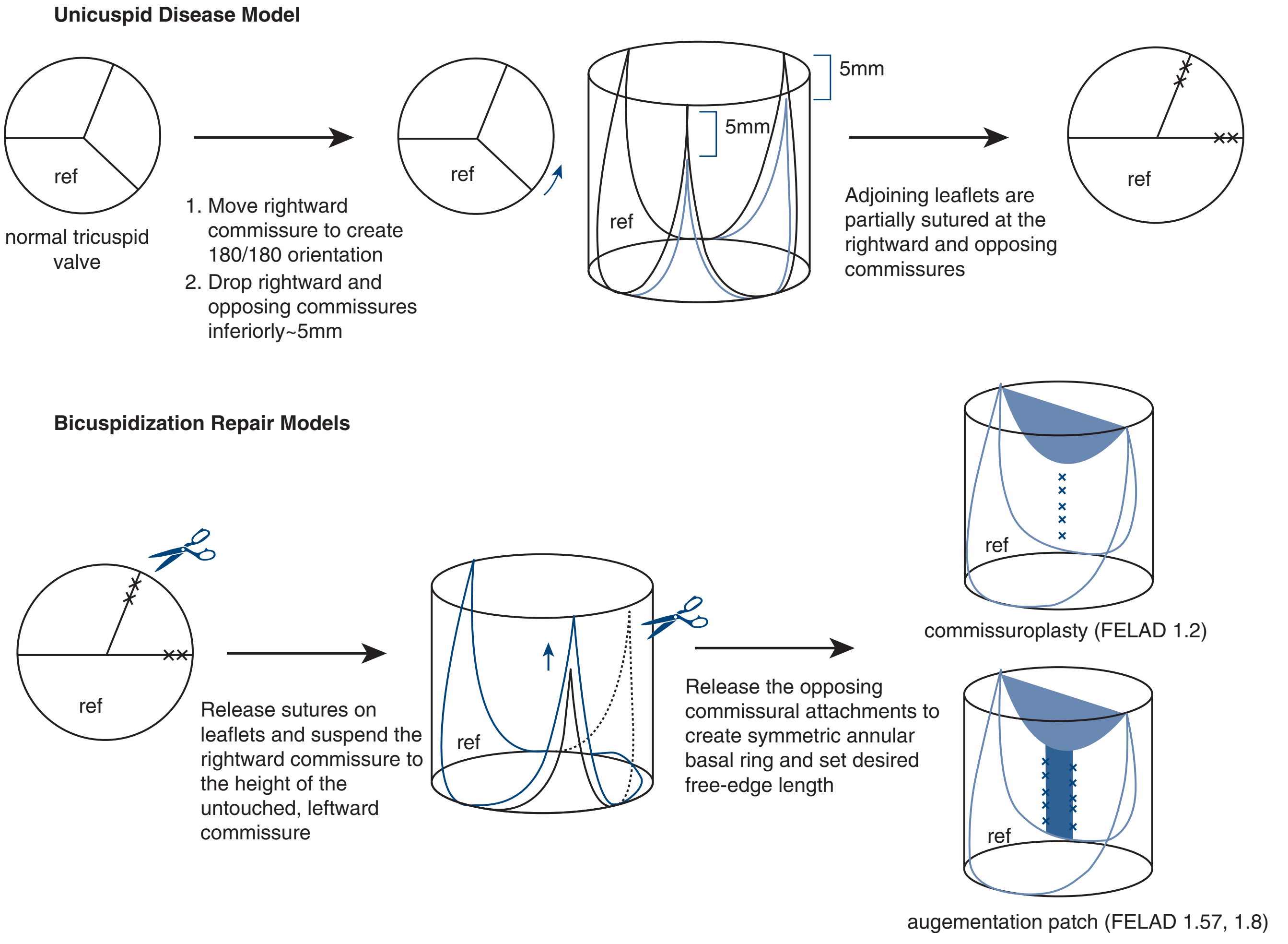

FIGURE E1. Surgical techniques. Detailed description of surgical techniques implemented in the experiment, outlining creation of unicuspid disease model from normal porcine aortic valve (positive control) and modified bicuspidization repair approaches used to repair the unicuspid disease model. *FELAD*, Free-edge length to aortic diameter.

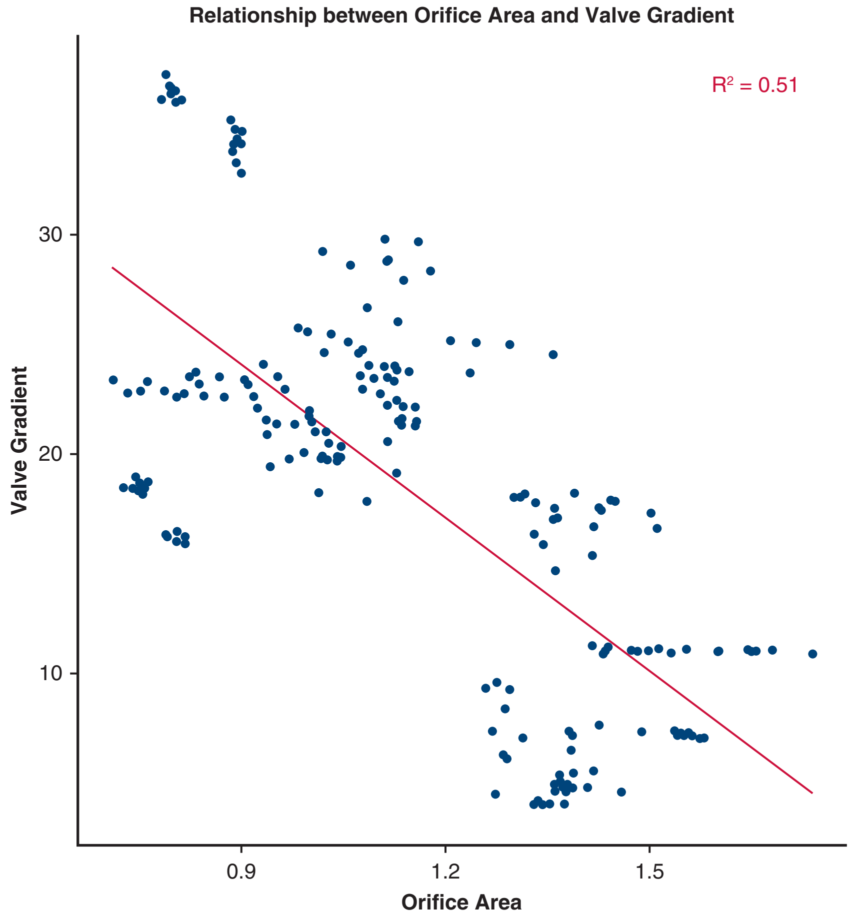

FIGURE E2. Relationship between valve orifice area and transvalvular gradient in repair models. Scatter plot illustrating the relationship between valve orifice area and valve gradient for the repair models. Each point represents an individual measurement. The *red trend line* indicates the linear fit, with an R^2 value of 0.53, demonstrating that 53% of the variability in valve gradient is explained by orifice area. The moderate correlation suggests a meaningful relationship between these variables within the context of the repair models.